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Chemical Consequences of the Polar Axis in Organic Solid-State Chemistry[1]

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Introduction

The formation of crystals possessing a polar axis, a property shown by many common organic and inorganic materials, is one of the most remarkable aspects of the chemistry of the solid state. The special properties of polar materials have led to their enormous importance in industry. Applications ranging from the microphone and ultrasonic cleaner to frequency-doubling crystals in laser technology depend on the properties of the polar crystalline state. It has been pointed out[2a] that polar materials are very promising candidates as a basis of major components of the programmable digital computer such as output and memory. The polar axis in crystals has also played an important historical role in chemistry. It underlay the recognition of the relationship between optical activity and molecular structure and was fundamental to the first resolution of an organic compound by Pasteur. In view of the past, present, and future importance of the polar axis, perhaps the most remarkable thing about it is how little it is understood or its very existence even recognized by solution chemists. This is particularly unfortunate because the synthetic chemist is likely to have many opportunities to encounter unusual phenomena by accident during everyday chemical work with crystalline solids and without the proper background will not be prepared to recognize and take advantage of such chance discoveries. There is the further misfortune that those workers in areas where the most dramatic applications of polar materials have occurred are, in general, uncomfortable when dealing with structures of complex organic molecules; the result is a serious lack of communication between groups whose interaction should be mutually beneficial.

Some implications of the presence of polar axes to chemical and physical properties of crystals are listed below.

1. **Crystal growth**: understanding and control of development of crystal faces.
2. **Optical activity of crystals**: distinguishing between enantiomeric crystals and assignment of absolute configuration.
3. **Pyroelectric effect**: change in the separation of centers of positive and negative charge by temperature change and the reverse—used as thermal detectors.
4. **Piezoelectric effect**: relationship between a change in the separation of the centers of positive and negative charge and expansion or contraction of the crystal; uses include microphones, headphones, pho-

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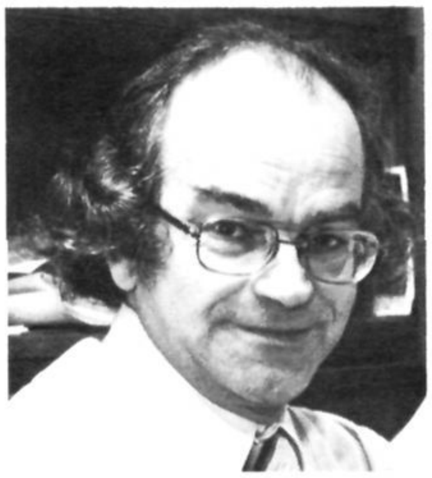

Iain C. Paul is a native of Scotland. He received his B.Sc. and Ph.D. degrees from the University of Glasgow, Scotland, working for the latter under Professor J. Monteath Robertson. After 2 years of postdoctoral research at Harvard University, he joined the University of Illinois Chemistry Department in 1964, becoming a full Professor in 1974. In 1968–1970, he was an Alfred P. Sloan Research Fellow. His research interests are in the areas of X-ray crystallography, solid-state chemistry, and structural organic chemistry.

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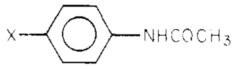
nograph cartridges, and ultrasonic cleaners.

5. **Ferroelectric effect**: change of the direction of spontaneous polarization of a crystal by application of an electric field; applications include information storage, displays, and capacitors.
6. **Second harmonic generation (SHG)**: nonlinear optical effect; applications include frequency-doubling crystals use in laser technology.
7. **Triboluminescence**: emission of light on grinding of a crystal.[2c]
8. **Chemical reactivity in the solid state**: dependence of chemical reactivity on the direction of a polar axis.

Many of these effects are already of enormous technological significance.[2] For example, the importance of the ferroelectric effect is attested to by the observation that more than 1000 papers per year are published on this subject[2b] and that there exists a journal, *Ferroelectrics*, devoted entirely to it.

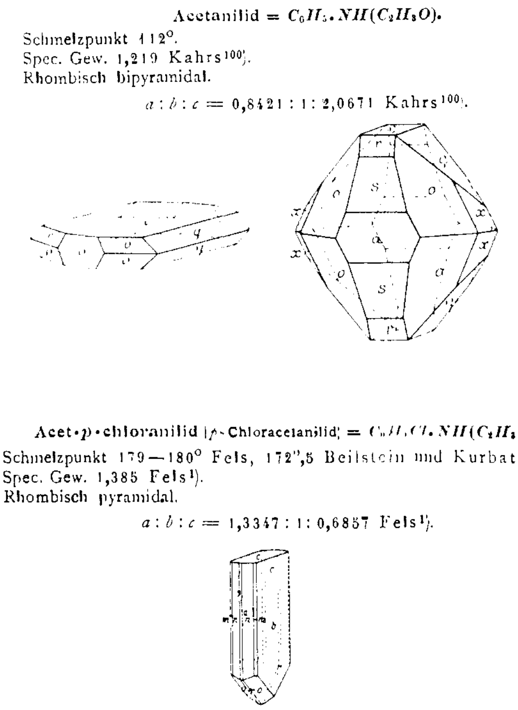
The Polar Axis and Crystal Morphology

The polar axis is a uniquely solid-state phenomenon; it has no counterpart in the liquid or gas phase where molecules can undergo relatively ready reorientation. One of the earliest opportunities to recognize the presence of polar axes in crystals was provided by studies well before 1900 of the shapes of crystals. P. Groth, in the period from 1906 to 1919, published a series of volumes entitled *Chemische Kristallographie* in which data were presented on the shapes of crystals of over 7000 substances.[3] In Figure 1 are shown two examples taken from this collection. At the top of the figure are drawings of crystals of acetanilide (1), a



1, X = H
2, X = Cl

compound crystallizing in a centrosymmetric structure[4] with no polar axes. It will be seen that the faces of each of the two habits occur in parallel pairs at opposite sides of the crystal. This symmetrical and orderly behavior would perhaps seem to be the natural growth pattern of all crystals. At the bottom of Figure 1, however, is shown a crystal of *p*-chloroacetanilide (2),[5] a substance almost as commonplace as acetanilide (1). In the case of 2 the centrosymmetry of 1 is absent—faces labeled o, *r*, and c occur without corresponding parallel faces at the opposite sides of the crystal. Such a crystal shape implies that the crystal is noncentrosymmetric and has a polar axis (in this case parallel to the long direction of the crystal). Thus the morphology reveals a characteristic of the internal structure with implications important for the physical and chemical properties of the compound in its crystalline state.



Acetanilid = $C_6H_5.NH(C_2H_3O)$.
Schmelzpunkt 112°.
Spec. Gew. 1,219 Kahrs[100]).
Rhombisch bipyramidal.
$a:b:c$ = 0,8421 : 1 : 2,0671 Kahrs[100]).

Acet-*p*-chloranilid [*p*-Chloracetanilid] = $C_6H_4Cl.NH(C_2H_3O)$.
Schmelzpunkt 179—180° Fels, 172°,5 Beilstein und Kurbatow.
Spec. Gew. 1,385 Fels[1]).
Rhombisch pyramidal.
$a:b:c$ = 1,3347 : 1 : 0,6857 Fels[1]).

Figure 1. Pictures from P. Groth's *Chemische Kristallographie*. Upper drawing: centrosymmetric crystals of acetanilide (1), space group *Pbca* (class *mmm*). Lower drawing, a polar crystal of *p*-chloroacetanilide (2), space group *Pna*2_1 (class *mm*2).

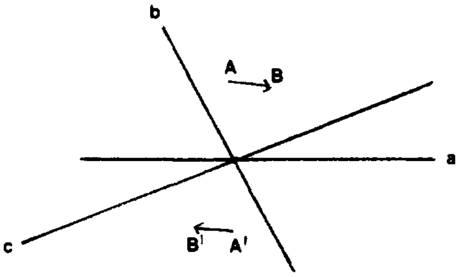


Figure 2. Effect of a center of symmetry on a vector from atom A to atom B. The crystallographic axes are at oblique angles from each other and different units of measurement are employed in the three axial directions. Vector A′–B′ is produced by the operation of a center of symmetry on A–B.

A Brief Mathematical Introduction to the Polar Axis

First, consider a centrosymmetric crystal (which can have no polar directions). Any pair of atoms, for example, atoms A and B (whose relative positions may be described by the vector from A to B), must have a corresponding pair of like atoms A′ and B′ whose interatomic vector is parallel to that between A and B but opposite in direction (see Figure 2). In mathematical terms any interatomic vector with a direction given by $[x, y, z]$ must be accompanied by a corresponding interatomic vector with the direction $[-x, -y, -z]$. Similarly, it can be shown that any plane with Miller indices (hkl) (that is, which intersects the a, b, and c axes at $1/h$, $1/k$, and $1/l$) must be accompanied by a symmetry-related parallel plane $(-h, -k, -l)$. A noncentrosymmetric crystal, on the other hand, must have at least some interatomic vectors not accompanied by parallel counterparts reversed in sign (that is, some vectors $[x, y, z]$ not accompanied by $[-x, -y, -z]$) and at least some possible crystal faces (hkl) not required by symmetry to be accompanied by parallel faces $(-h, -k, -l)$ at the opposite side of the crystal. (It should be noted, however, that a parallel face $(-h, -k, -l)$ may occur even though not required by symmetry.)

These ideas can be illustrated by a continuation of the discussion of the acetanilides 1 and 2 whose crystal morphologies were shown in Figure 1. Stereopair drawings of the crystal structures of 1 and 2 are shown in Figure 3.[6,7] It is seen that each molecule of acetanilide is accompanied by a counterpart whose orien-

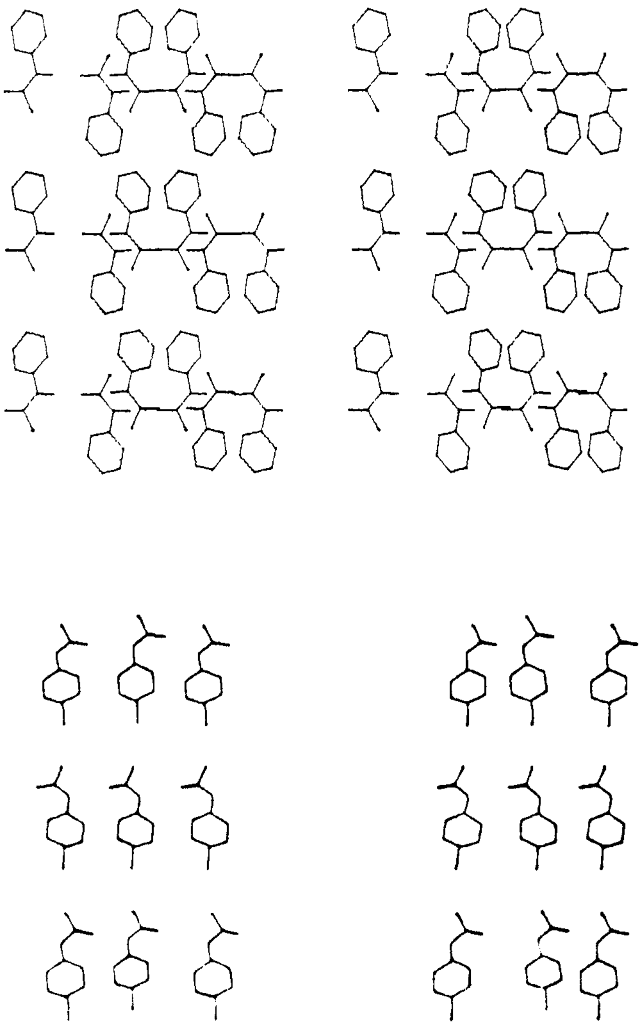


Figure 3. (a, upper drawing) Stereopair drawing of the centrosymmetric (nonpolar) structure of acetanilide (1). The view is down the *c* axis with the *a* direction from the bottom to the top of the page. Although individual molecules are not precisely planer and are therefore chiral, there are equal numbers of the two enantiomers in a single crystal. The structure is held together along the *b* direction (from right to left in the plane of the page) by hydrogen bonds between the NH of one molecule and the O=C of the next. (b, lower drawing) Stereopair drawing of acet-4-chloroanilide (2) in approximately the orientation of the crystal drawing of the same substance in Figure 1. (The *b* axis is out of the page with *a* to the right and *c* down in the plane of the page.)

tation is exactly reversed and which is related to the first molecule by inversion through a point of symmetry. The structure of 2, however, is another matter. Although some carbon–chlorine vectors point slightly into the page and some slightly out, each has a substantial component parallel to the *c* axis and directed toward the bottom of the page—there are no corresponding carbon–chlorine vectors pointing toward the top of the page. The crystal morphology shown in Figure 1 then fits onto the crystal structure in Figure 3b either with the morphological "arrow heads" pointing toward the bottom of the page or with the "arrow heads" pointing to the top. In the first case the sloping faces forming the pointed end of the crystal contain the chlorine atoms. If the absolute direction of the polar axis is such that the "arrow heads" point toward the top of the page, then the sloping faces are composed of methyl groups and carbonyl oxygen atoms. The absolute direction of the polar axis is not known in this case. It could, in principle, be determined by X-ray crystallography by using the anomalous dispersion technique, and if enough were known about crystal growth, the absolute direction of the axis could be assigned from crystal morphology. This point will be discussed later in connection with the determination of the absolute direction of the polar axes and absolute configurations of *p*-bromobenzoic anhydride and tartaric acid.

TABLE I: Crystal Symmetry and Space Group Frequency for Organic Crystals[10]

space group	frequency of occurrence	symmetry of crystal class: chiral	symmetry of crystal class: centrosym.	major axes polar?
$P2_1/c$	1783	(−)	(+)	(−)
$P2_12_12_1$	722	(+)	(−)	(−)
$P2_1$	458	(+)	(−)	(+)
$P\bar{1}$, $C2/c$, $Pbca$, $Pnma$	1026	(−)	(+)	(−)
$P2_12_12$	104	(+)	(−)	(−)
$Pna2_1$	100	(−)	(−)	(+)
$C2$	80	(+)	(−)	(+)
$P4_12_12$	37	(+)	(−)	(−)
Pc	31	(+)	(−)	(+)
total compounds				5926

How complex must a molecular structure be to form a polar crystal? This question is simply answered; even a diatomic structure A–B is sufficient provided the A–B axis is oriented with a significant component parallel to some polar direction of the crystal (that is, the A–B axis is not at right angles to a sole polar direction of the crystal). A classic example is cubic zinc sulfide or zinc blende, ZnS. Crystals of this substance, although not strictly speaking molecular crystals, are remarkable because the end faces of the polar axis are bright at one end and dull at the other and so can be distinguished by visual observation. Coster, Knol, and Prins,[8] in 1930, used anomalous dispersion to determine the absolute direction of the polar axis; the bright faces are the ones terminated by sulfur atoms and the dull faces by zinc. It will be noted that there is no requirement of covalent bonding in order for a polar axis to be present, only that the spacings between a sulfur atom and the two adjacent zinc atoms be unequal, i.e.

$$\text{Zn S} \qquad \text{Zn S} \qquad \text{Zn S}$$

Thus, a submicroscopic traveler proceeding along such a path of zinc and sulfur atoms could tell which direction he was going because from left to right after passing a sulfur atom there is a long distance to the next zinc atom whereas from right to left the reverse is true.

In this review the relationship between space group and point group symbols and the physical properties of crystals will be referred to from time to time, but no detailed discussion will be given. A summary of these relationships is given in Volume 1 of the "International Tables for X-Ray Crystallography."[9]

Frequency of Occurrence of the Polar Axis in Organic Crystals[10]

Data for the most common space groups among organic compounds are given in Table I.

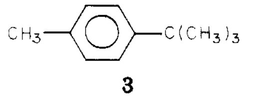
Several points need to be stressed. The presence or absence of polar directions in an ideal crystal of theoretical perfection can be deduced from the presence or absence of a center of symmetry; if there is a center, there can be no polar directions, but if there is no center, there must be at least some polar directions (although they do not need to be parallel to the crystal axes). The presence or absence of a center of symmetry can be inferred by inspection of the space group symbol.[9] Thus in Table I, the most frequent space group among organic crystals, $P2_1/c$, has a center of symmetry and is therefore not of interest in the present discussion. The two following space groups, $P2_12_12_1$ and $P2_1$, are both noncentrosymmetric and therefore have polar directions. There is a more subtle distinction between these two space groups: $P2_1$ has a polar crystal axis (the *b* axis) whereas none of the three crystal axes (the three 2_1 axes) of space group $P2_12_12_1$ are polar—the polar directions are in fact any directions not parallel to *a*, *b*, or *c*.

These two space groups are followed in the table by several centrosymmetric space groups, but the last four are polar space groups. In summary, of the 5926 organic compounds in the survey, more than 1500 or 25% of them are in noncentrosymmetric (i.e., polar) space groups and can therefore be regarded as candidates for the interesting behavior possible when a polar axis is present. Of particular interest is the point made in the table of space group frequencies that, while chiral crystals must have polar directions, polar crystals need not be chiral. The space group $Pna2_1$, for example, has a polar *c* axis but is not chiral; for chirality to be present, centers of inversion, mirror planes, glide planes, and rotation–reflection axes must be absent. *p*-Chloroacetanilide (**2**), discussed at the beginning of this paper, belongs to this space group; in it are molecules of both possible chiralities, and any (ideal) single crystal is identical with its mirror image.

A further point is that crystallization in a chiral space group can always be assured by choice of a compound which even in solution is locked by the nature of its structure into a single chirality. On the other hand, racemic mixtures or even compounds considered by the solution chemist to be achiral [such as acetanilide (**1**) or *p*-chloroacetanilide (**2**)] may exist in the crystalline state frozen into a chiral conformation. As a result, such crystals will be chiral or achiral depending on whether the crystal contains pairs of enantiomeric molecules in the proper steric relationship (as in these examples) or only a single enantiomer. In the latter case crystallization is sometimes said to have been accomplished by "spontaneous resolution", although there has been no practical resolution until enantiomeric crystals have been identified and separated from each other. An analysis of space group data has suggested that 28% of the racemates surveyed crystallize in chiral space groups.[11] The implications of these points will be discussed further below.

Molecular Structure and Crystal Polarity

On introducing this subject we need to clarify our use of "polar". Although the word has been widely adopted by chemists to refer to the presence of a substantial dipole moment as in "polar substance" or "polar solvent", there is an equally venerable alternative usage in crystallography. Thus the substance 1-*tert*-butyl-4-methylbenzene (**3**), generally agreed to be a "nonpolar" compound, crystallizes in a "polar" space group with all of the molecules parallel and with all of the methyl groups pointed in the same direction (Figure 4).[12] Such a crystal is "polar" in the sense we will employ here because one end of the crystal is formed by the methyl groups and the other by the *tert*-butyl. Even though the molecule in this case has no large permanent dipole moment, the "polarity" (in the crystallographic sense) of such a crystal could still be chemically of interest; for example, it is not unlikely that crystal faces bounded by *tert*-butyl groups would behave differently from those bounded by methyl groups at the opposite end of the crystal.



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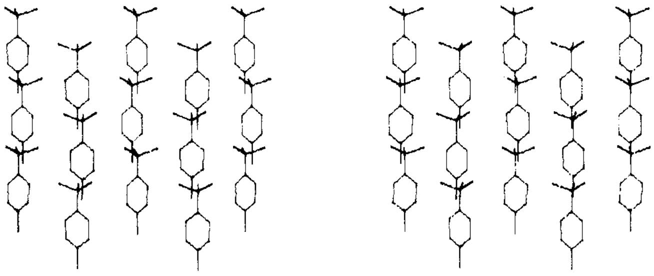


Figure 4. Stereopair drawing of the polar structure of *p-tert*-butylbenzene (**3**), space group *Fdd*2, class *mm*2. The view is along *b* with *a* to the right and *c* toward the bottom in the plane of the page. Individual molecules lie on a crystallographic 2-fold axis and therefore must have 2-fold disorder (not shown) of the *tert*-butyl groups.

TABLE II. Space Groups of Some Disubstituted Benzenes[a]

	relative positions		
benzene substituents	ortho	meta	para
amino hydroxy[b]	*Pbca*	$Pca2_1$ (p)	$Pna2_1$ (p)
amino nitro[c]	$P2_1/a$	$Pbc2_1$ (p)	$P2_1/n$
bromo nitro[d]		$Pbn2_1$ (p)	$P\bar{1}$
chloro nitro[e]	$P2_1/n$	$Pbn2_1$ (p)	$P2_1/c$
dihydroxy form I[f]	$P2_1/a$	$Pna2_1$ (p)	$P2_1/c$
form II[g]		$Pna2_1$ (p)	
dinitro[h]	$P2_1/c$	$Pbn2_1$ (p)	$P2_1/n$

[a] p indicates that the space group is polar. MSD = Molecular Structure and Dimensions". CD = Crystal Data", 3rd ed., Vol. 1. [b] See Table 3 in M. Haisa, S. Kashino, and T. Kawashima, *Acta Crystallogr., Sect. B*, B36, 1598 (1980). [c] MSD 10 16.1; MSD 5 16.2; MSD 1 16.10. [d] MSD 1 15.9; CD A 0.9730. [e] CD M 1.2831; MSD 1 15.11. [f] MSD 4 17.2; MSD 1 17.14; MSD 1 17.13. [g] MSD 1 17.16. [h] CD M 0.6115; MSD 9 15.1; MSD 9 15.2.

The problem of predicting or controlling crystallization of organic molecules to obtain crystals of a desired symmetry is still largely unsolved. Certain crystal symmetries tend to be favored by certain types of molecular structures; for example, it has long been recognized that meta-disubstituted benzenes are more likely to crystallize in polar space groups than are the ortho or para derivatives.[13] In Table II are presented data for a few such compounds most of whose crystal structures have been determined.

These compounds were chosen because their meta isomers crystallize in polar space groups; note, however, that none of the known space groups of the ortho isomers and only one of the para are polar. A perusal of the literature gives the further impression that aromatic compounds with certain functional groups such as, for example, the amino group are rather more prone to crystallize in polar space groups than with others, as,

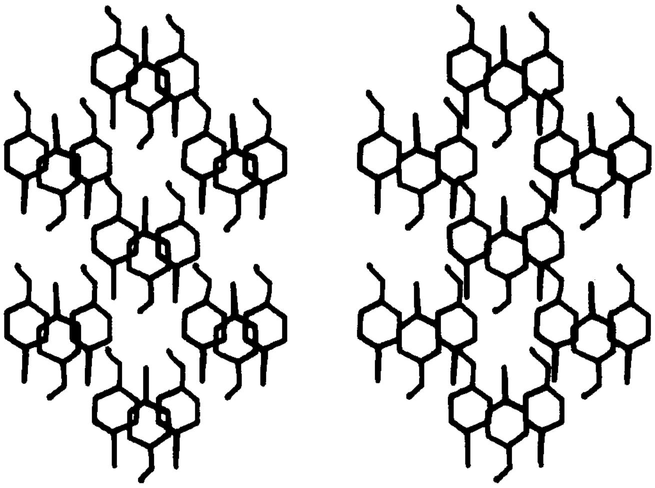
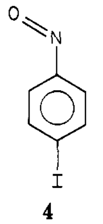


Figure 5. Stereopair drawing of the crystal structure of *p*-iodonitrosobenzene (4) (space group *Cc*). The *a* axis is to the right in the page with *c* out of the page. The *b* axis, vertical in the plane of the page, is nonpolar in this space group. Note that much of the potential polarity of the crystal is lost because of this (half of the molecules have the C–I vector pointing nearly along +*b* and half nearly along −*b*. However, the polarity is not completely lost because all of the N–O vectors have a component to the left in the drawing with no compensating molecules oriented toward the right.

for example, the carboxyl group. In spite of the discernible tendency for certain types of compounds to prefer particular symmetries, we seem to be some time away from being able to control or even to predict with real assurance the packing a compound will adopt when it crystallizes or the relationship of the crystal symmetry to molecular structure.

A further point to be considered is the important distinction to be made between a crystal which is polar in a strictly mathematical sense and one whose polarity is of chemical interest. There are ways whereby the polarity implied by the space group symbol can be largely nullified by some feature of the crystal structure.

For example, a molecule with a well-defined polar direction can be so oriented in the crystal that the molecular polar axis is almost perpendicular to the polar axis of the crystal. An example of this kind of packing is provided by the structure of *p*-iodonitrosobenzene (4) shown in Figure 5.[14] Here only a small component of the molecule's polar vector is contributing to polarity of the crystal.



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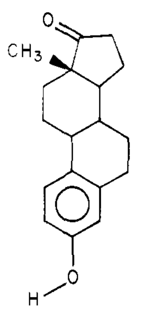

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Furthermore, crystallization can occur with a pair of molecules in the asymmetric unit, mutually oriented so as nearly to cancel each other's effect on crystal polarity. An example is estrone-III (5) whose structure[15] is shown in Figure 6.

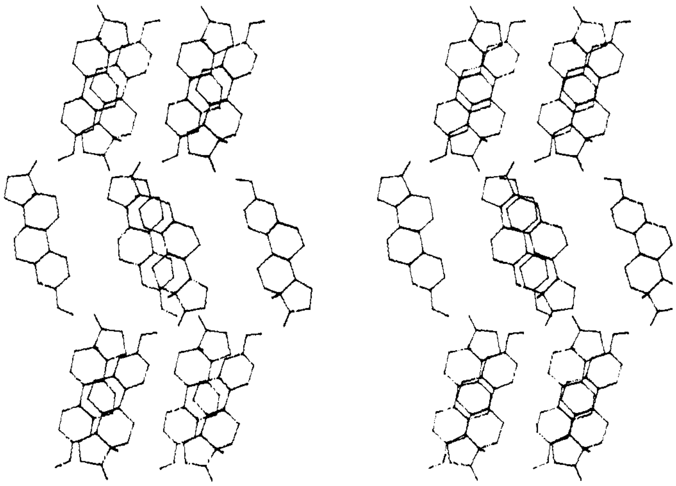


Figure 6. Stereopair drawing of estrone-III (5) (space group $P2_1$) looking along *a** with the polar *b* axis vertical in the plane of the page and with *c* to the right. This structure has two independent estrone molecules turned approximately head to tail so that the intrinsic molecular polarity is cancelled out to a large extent.

Finally, it is important to bear in mind that the results from ordinary X-ray structure determination give the average structure of a particular crystal. There can in real crystals be disorder or twinning or other structural aberrations which result in a crystal whose structure differs drastically from that represented by the idealized stereopair drawing obtained from the X-ray results. It is apparent, then, that inspection of the space group symbol is not sufficient to show that a particular substance crystallizes in a structure whose polarity is of interest.

Growth and Dissolution of Polar Crystals

Certainly one of the most fascinating aspects of polar crystals is their not infrequent assumption of shapes which reveal the presence (and orientation) of a polar axis. It is simple to predict from the space group of the crystal which crystal planes might lead to hemihedral faces (faces (*hkl*) present on one side of the crystal without corresponding parallel faces $(\overline{hkl})$ on the other). However, whether crystal growth under certain specified conditions will produce hemihedral faces is at best difficult to predict, explain, or control. The absence of a center of symmetry permitting such facial development by no means requires that faces grow in pairs, and, in fact, it has been suggested[16] that, as a general rule, polar development of molecular crystals is likely to be hard to detect on morphological grounds. There are, of course, numerous examples in which the morphology of polar crystals has failed to reveal their polar nature. Our experience has suggested, however, that even molecular crystals can often be induced to adopt a polar morphology if a sufficient attempt is made.

The special effect of solvent on polar development has been studied by Wells.[17a] Growth of the low-temperature-stable form of resorcinol in benzene takes place on both sides of the polar axis, but in water growth has been observed to take place selectively at one end of the crystal. This behavior has been correlated with the internal structure since the hydroxyl groups are accessible at one end, assumed to be that at which growth occurs, but not at the other. Further, from ethyl acetate a remarkable conical shape results, and no deposition of crystallizing solid occurs on the conical end of the crystal.

A more thorough investigation[18] has been made of crystals of lithium iodate (space group $P6_3$). Although this is not an organic crystal, it deserves mention because it has been investigated to a degree which is lacking in most studies of polar organic crystals. The crystal structure and absolute direction of the polar axis of this crystal have been correlated with the selective etching by water at that end of the crystal whose faces contain the iodate oxygen atoms. Unfortunately there are few data on crystal growth where the absolute direction of the polar axis of an organic crystal is known and even fewer where such phenomena as crystal growth have been studied in any detail.

The recently reported[17b] use of selective poisoning of crystal growth by adsorption of tailored "impurities" to achieve optical resolution points out the possible utility of a better understanding of crystal growth and should arouse renewed interest in the relationship between the polar axis and crystal morphology.

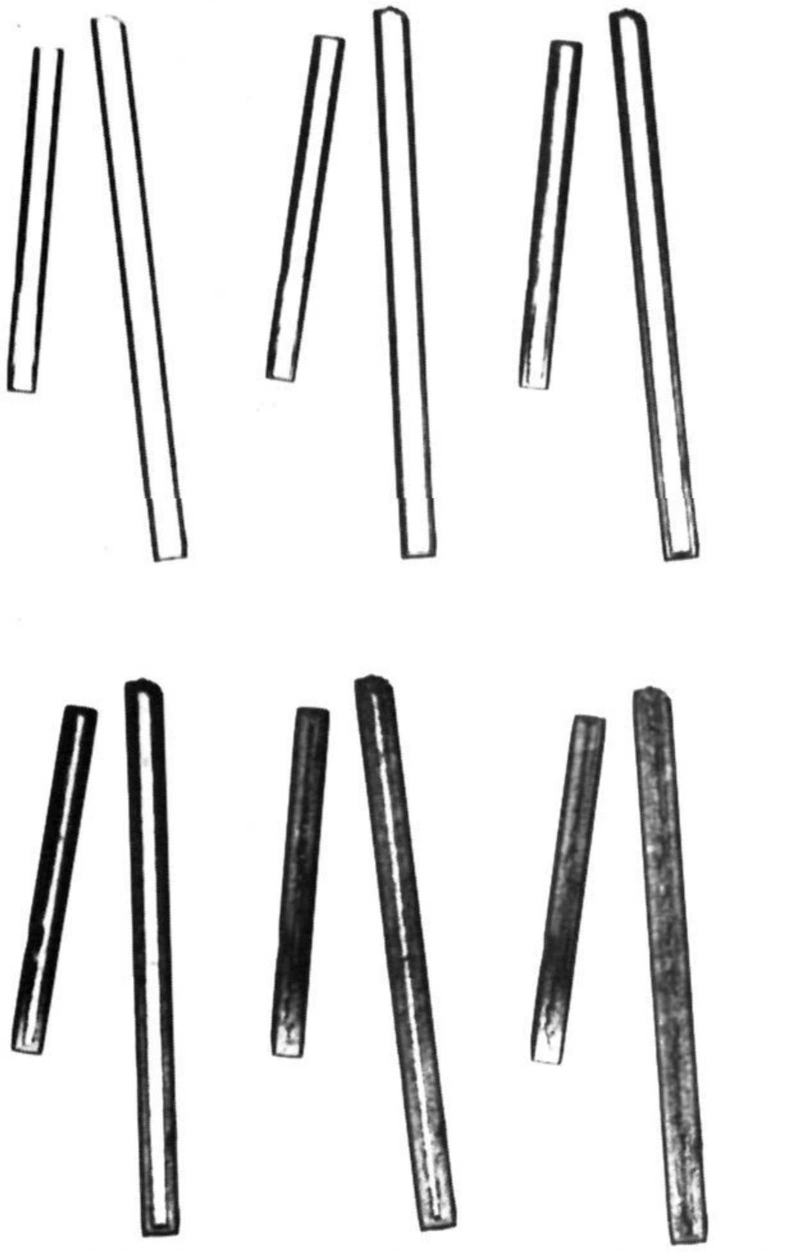


Figure 7. Pair of centrosymmetric crystals of *p*-chlorobenzoic anhydride (**7b**) undergoing reaction with ammonia gas. Regions where reaction has occurred appear dark because the microcrystalline products scatter the transmitted light. (Reprinted with permission from R. S. Miller, D. Y. Curtin, and I. C. Paul, *J. Am. Chem. Soc.*, **94**, 5778 (1972). Copyright 1972, American Chemical Society.)

Chemical Consequences of Polar Axes

Polar Reactions of Crystals with Gases. Crystalline benzoic acid (**6**) or benzoic anhydride (**7a**) and

$$\underset{\mathbf{6}}{C_6H_5COOH} + NH_3 \rightarrow C_6H_5COO^-NH_4^+$$

$$p\text{-}\underset{\mathbf{7}}{XC_6H_4COOCOC_6H_4X}\text{-}p + NH_3 \rightarrow$$

$$\underset{\mathbf{8}}{XC_6H_4CONH_2} + \underset{\mathbf{9}}{XC_6H_4COO^-NH_4^+}$$

a, X = H; **b**, X = Cl; **c**, X = Br

related compounds have been found[19] to react with ammonia gas. Reaction leads to disruption of the crystal with formation of microcrystalline product so that the progress of a reaction front (or fronts) can be readily observed and photographed with the aid of a polarizing microscope. These reactions are highly anisotropic; attack of the gas occurs from the sides of the crystal whereas the top (best developed) face is relatively inert. The ammonia is better able to attack the side faces at which the functional group containing acid or anhydride groups are exposed than the top face which is dominated by the aromatic rings. An example is the reaction with ammonia of *p*-chlorobenzoic anhydride (**7b**), which crystallizes in the centrosymmetric space group $P2/c$, to give a microcrystalline conglomerate of *p*-chlorobenzamide (**8b**) and ammonium *p*-chlorobenzoate (**9b**).[19,20] Figure 7 shows a pair of crystals undergoing this reaction. It will be noted that the reaction front (as revealed by the scattering of light by microcrystallites of product) proceeds rather uniformly from each of the four sides of the crystal. The crystal structure is shown in Figure 8a.[21] Reaction occurs by attack of the ammonia molecules along the various directions parallel to the top surface of the crystal and thus along layers containing the anhydride carbonyl groups. The related bromo anhydride **7c** has a structure[22] (Figure 8b) which is very similar to that of the chloro compound **7b**. However, in this case the space group is $C2$; the center of symmetry which had been present in the chloro compound is absent, and the C–O vectors of the carbonyl groups have substantial components along a polar (*b*) axis. In certain crystals of *p*-bromobenzoic anhydride oblique faces occurring on one side of the crystal (unaccompanied by corresponding parallel faces on the other) reveal the presence of the polar axis. Again the major face of the crystal is formed by the *p*-bromophenyl groups so that access of the ammonia molecules to the carbonyl groups appears to be from the sides and not the top face of the crystal. In Figure 9 is shown a crystal photographed at various stages of reaction.[23] In this case initiation of the reaction is favored at a single side of the crystal and occurs preferentially in a direction parallel to the *b* axis; in other words, the polar axis of the crystal directs the reaction. The selectivity can best be seen in small crystals relatively free from defects.[19] These observations fail to show, however, whether the reaction proceeds along the polar axis by approaching the anhydride groups from the side of the carbonyl oxygen atoms or from the opposite side of the carbonyl carbon atoms. To settle this question we must know the absolute direction of the polar axis of the actual crystal undergoing reaction. This is exactly the problem which had been solved in the case of polar zinc sulfide crystals by the use of X-ray diffraction, taking advantage of anomalous dispersion. The same method applied here[23] reveals that the ammonia gas attacked the crystal preferentially from the side composed of the carbonyl

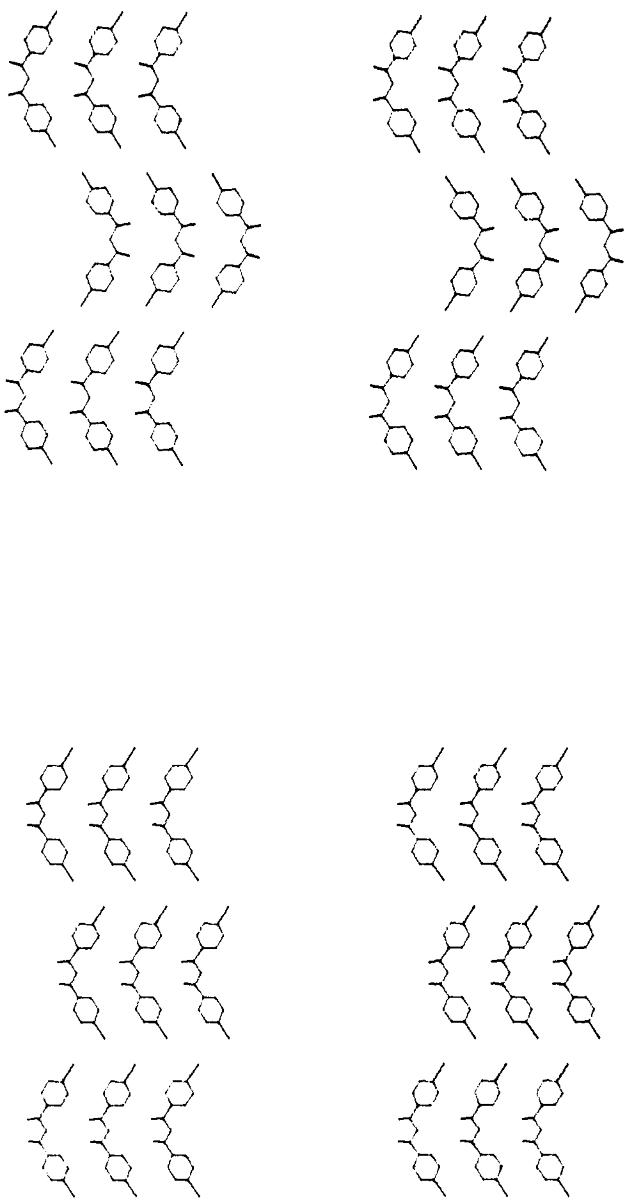


Figure 8. (a, upper) Stereopair drawing of the crystal structure of *p*-chlorobenzoic anhydride (**7b**). The (102) plane is in the plane of the page with the *b* axis to the left in the page. Chains of molecules from the top to the bottom of the page are along the [$\bar{2}$01] direction. Along this axis are layers related by crystallographic centers of symmetry with carbonyl groups pointed alternately to the left and to the right. (b, lower) Stereopair drawing of the polar crystal structure of *p*-bromobenzoic anhydride (**7c**). The plane (201) is in the plane of the page. Although the structure is superficially like that of the chloro anhydride above, alternate layers are related by translation rather than by the center in (a). As a result, the carbonyl groups in a single crystal all point to the left in the example shown here.

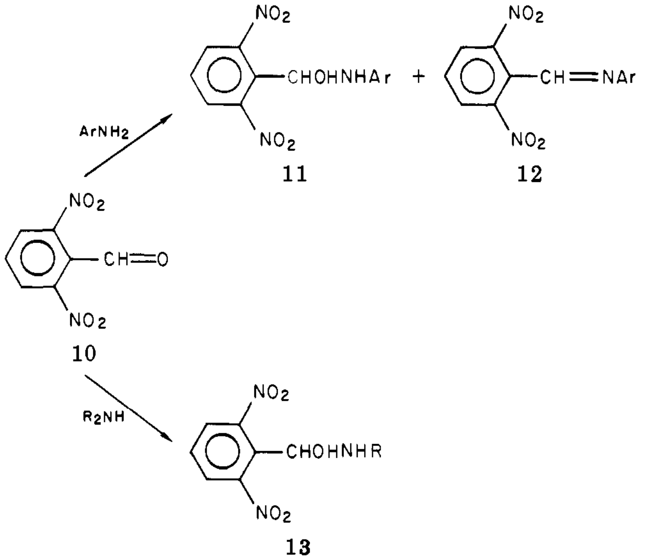
oxygen atoms. Although such a result might seem surprising at first sight, a careful analysis of the geometry of a molecule of the anhydride in the conformation found in the crystal shows that, if an ammonia molecule becomes hydrogen bonded to an oxygen atom of one of the carbonyl groups, the nitrogen atom is in a favorable position for attack at the sp^2 face of the other carbonyl group (Figure 10). It is quite reasonable, therefore, that the reaction direction should be the one observed.

A puzzling difference in the anisotropy of the reactions of the bromo and chloro anhydrides is that, while the chloro anhydride **7b** undergoes reaction at approximately the same rate in any direction parallel to the major face of the crystal, the bromo anhydride **7c** reacts much faster along one axis, the polar axis, than along those directions normal to it. One possible factor contributing to this difference is that the carbonyl–carbonyl dihedral angle of the bromo anhydride is larger (49°) than that of the chloro anhydride (41°). The overall rate is undoubtedly affected by many factors, however, including how rapidly molecules "peel away" from the interface between parent crystal and product microcrystallites to permit entry of ammonia to the next layer of reactant molecules.

The similarity in packing of the centrosymmetric *p*-chlorobenzoic anhydride (**7b**) to the noncentrosymmetric *p*-bromo compound **7c** suggests that it might be possible to induce the *p*-chloro anhydride to crystallize with a polar structure by application of an electric field during the crystallization process.[24] Several examples of the influence of an electric field on crystallization have been reported previously. For example, an electric field has been used to promote nucleation of the crystallization process.[24b] The solidification of carnauba wax and more recently of certain polymers such as poly(vinylidene fluoride) in an electric field has been used to produce permanently polarized structures. These have been referred to as "electrets" and have been used commercially as a source of an emf in applications where no current is drawn.[25] Such inorganic salts as lithium niobate are polarized by crystallization in an electric field; crystals more than 1 cm in length can be drawn from the melt under such conditions.[26] In spite of these encouraging examples in the literature, our preliminary attempts to induce *p*-chlorobenzoic anhydride to adopt a polar space group analogous to that of *p*-bromobenzoic anhydride have been unsuccessful.[27]

Single crystals of *p*-bromobenzoic anhydride have the further interesting property that they are chiral as well as polar. This will be discussed further in a later section on the relationship between the polar axis and crystal chirality.

Attempts to extend the control of reaction rate by the asymmetry implied by the polar axis have been at least partially successful. A promising substance has been 2,6-dinitrobenzaldehyde (**10**).[28] This aldehyde crystallizes in space group *Pca*2$_1$ and has a crystal mor-



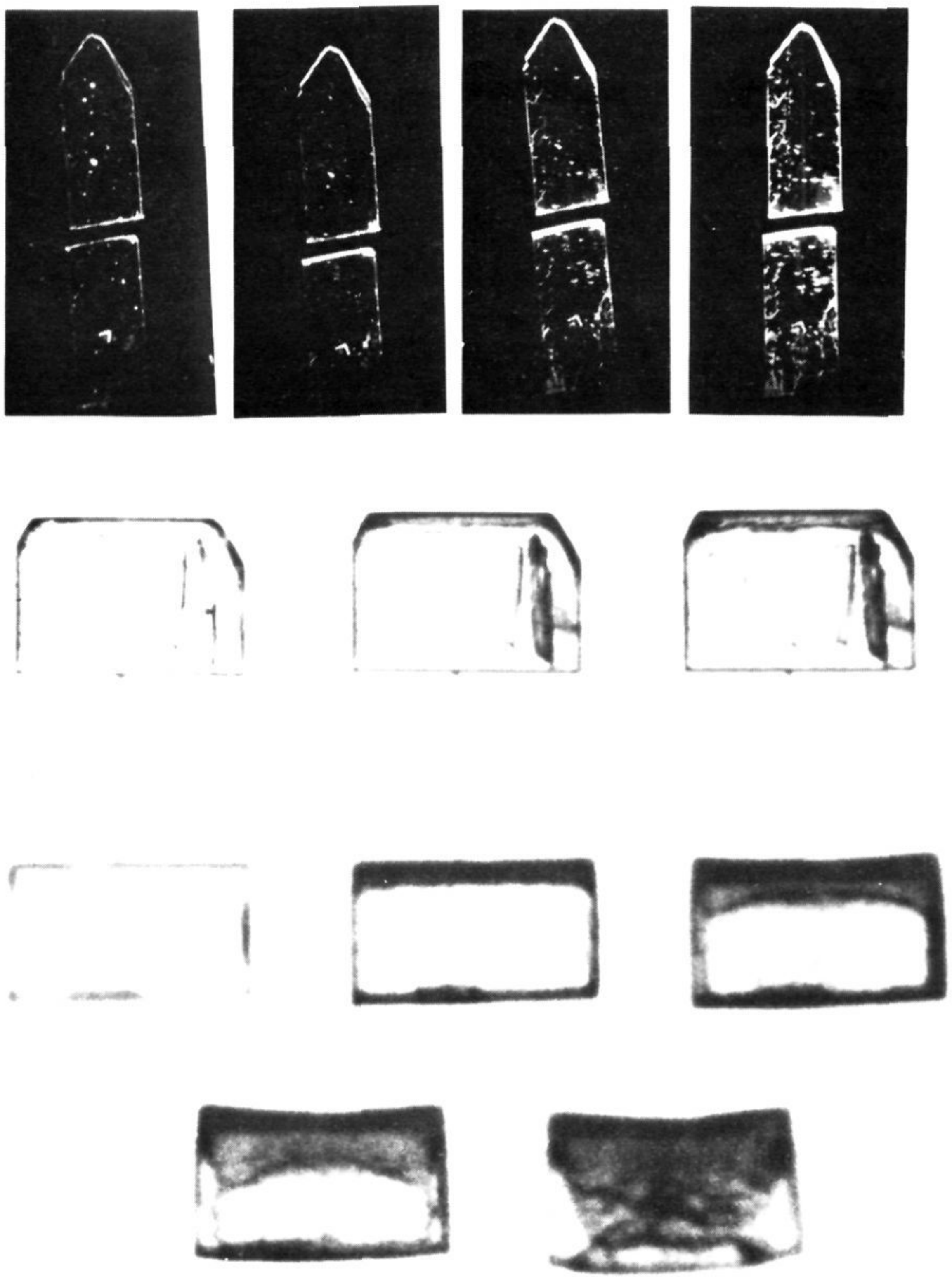


Figure 9. Reaction of polar crystals of *p*-bromobenzoic anhydride (**7c**) with ammonia gas. Crystals in all of these photographs have the same internal structure. (Upper series) Plates of **7c** with the polar axis along the long direction of the crystals. In this series there is a marked preference for reaction from the pointed end of the crystal, although surface defects permit reaction from the top surface which tend with these larger crystals to obscure the directional specificity. (Middle series) Crystals with oblique faces again showing the presence of a polar axis. In this case, unlike the first series, the polar *b* axis is parallel to the medium length morphological axis. (The first two series of photographs are reproduced from ref 23.) (Bottom series) Small well-formed crystal with the polar (*b*) axis vertical in the plane of the paper. Although the crystals are polar, no faces have developed which show this. (Reproduced from ref 19 with permission. Copyright 1975, American Association for the Advancement of Science.)

phology which clearly shows the orientation of the polar axis. The crystal structure (Figure 11) shows that the polar *c* axis runs vertically in the plane of the page and the carbon–oxygen vector of the carbonyl group has a substantial component parallel to the polar axis. Reaction with primary amines gives, first, a carbinolamine (**11**) formed by addition of the amine to the aldehyde carbonyl group. This reaction is followed by a slower dehydration reaction, leading to the imine **12**. Reaction can be observed under the microscope to occur initially at the pointed ends of the crystals but unfortunately is often accompanied by melting in later stages. Secondary amines such as piperidine, which undergo the initial carbonyl addition to give carbinolamine (**13**, R = $-(CH_2)_5-$), a product prohibited by the nature of its structure from undergoing a subsequent dehydration, also show preferential attack at the pointed end of the crystal and are less prone to melting in later stages of reaction. In this case the absolute direction of the polar axis—that is, alignment of the carbonyl's carbon–oxygen vector—has not been determined. It is hoped that methods more convenient than that employing anomalous dispersion of X-rays will become available for such determinations.

The Polar Axis and the Mobile Proton. A group of reactions which could have practical as well as theoretical interest can be described as those whose molecules can undergo chemical reaction in the crystalline state by rearrangement of one or more hydroxylic or amine protons with only minor perturbations in the positions of the heavier atoms. Such reactions are of possible technological interest because they might be designed so that proton switching leads to a change in the absorption of electromagnetic radiation or to a change in crystal symmetry—that is, a change in the direction of one (or more) polar axes. Such processes

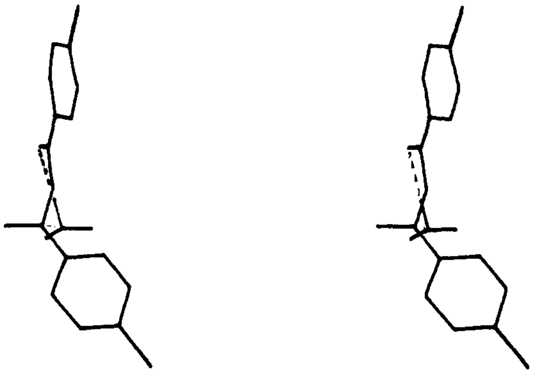


Figure 10. Stereopair drawing of a molecule of *p*-bromobenzoic anhydride (**7c**) in the conformation found in the crystal. An ammonia molecule has been drawn in as it might appear if it were hydrogen bonded to the upper carbonyl oxygen atom. The nitrogen atom is then above the face of the lower carbonyl group. (Reproduced from ref 23.)

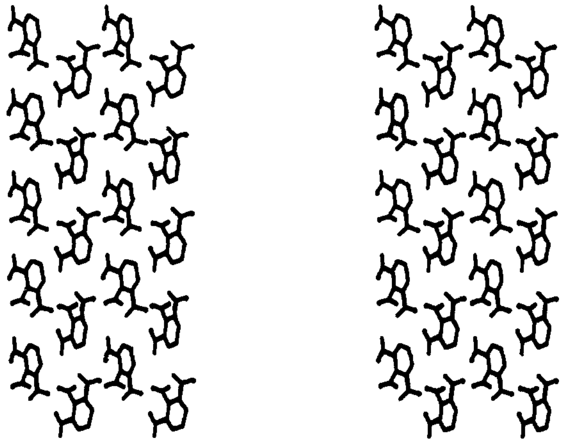


Figure 11. Stereopair drawing of the structure of the polar 2,6-dinitrobenzaldehyde (**10**) (space group $Pca2_1$). The view is along *b* with the *a* axis toward the top of the page and *c* to the right. All of the carbonyl groups are oriented with the O-atom toward the right in this drawing.

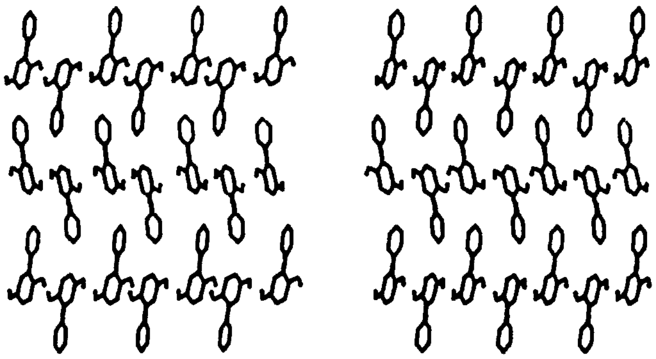


Figure 12. Stereopair drawing of the structure of phenylquinhydrone (**14a**) with the hydroxylic protons shown in each of the two positions which are one-half occupied. The view is along *a* with *b* to the left and *c** toward the bottom of the page. (Reproduced from ref 29 with permission. Copyright 1979, Gordon & Breach.)

might be used as the basis for information storage: a device with two states corresponding to the two limiting sets of proton positions could, in principle, be switched by an external electrical or electromagnetic stimulus and read by a spectroscopic or other method. As was mentioned in the introduction, switching of the direction of polarization of a polar material (the ferroelectric effect) is a well-known and important property of a number of inorganic salts.[2]

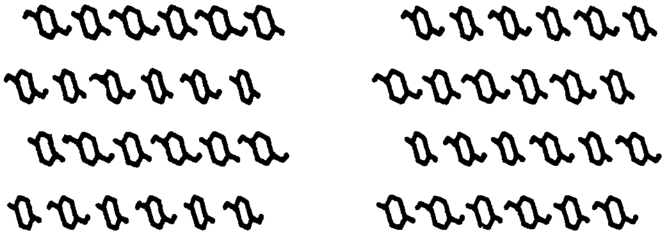
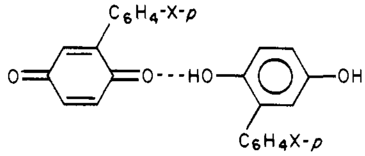
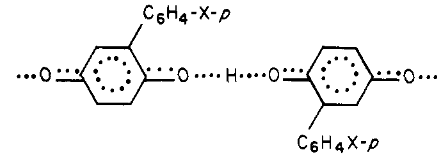


Figure 13. Stereopair drawing of the structure of quinhydrone (**16**). The view is down *b* with *a* to the right and *c* down and to the left in the page. The similarity to the phenyl compound in Figure 12 is apparent.

The quinhydrone **14a** (a 1:1 complex derived from phenylbenzoquinone and phenylhydroquinone) and its relatives are substances whose crystal structures[29] (Figure 12) and solution chemistry[30] have unusual features.



14a, X = Y = H
b, X = Y = Cl
c, X = H; Y = Cl
d, X = Cl; Y = H



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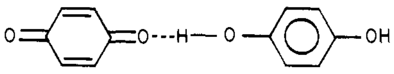

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Both the phenyl complex (**14a**) and its di-*p*-chloro derivative (**14b**) apparently crystallize in space group $P2_1/c$, and determination of their structures by X-ray diffraction has indicated[29] that a crystallographic center of symmetry lies midway between an oxygen atom of a hydroquinone molecule and that oxygen atom of the adjacent quinone molecule to which it is hydrogen bonded. This might at first sight seem to suggest a structure (**15**) with the hydroxylic protons at points midway between the oxygen atoms of the two molecules to which they are bonded. However, chemical evidence suggests strongly that this conclusion is incorrect. The isomeric mixed quinhydrones (**14c** and **14d**) formed from phenylbenzoquinone and *p*-chlorophenylhydroquinone on the one hand and from *p*-chlorophenylbenzoquinone and phenylhydroquinone on the other have been prepared and shown by NMR studies of the freshly dissolved crystals to be nonidentical and, although the H-transfer interconverting them occurs rapidly in solution, it proceeds slowly, if at all, in the solid state;[30] even when the crystals were heated for a number of hours at 142 °C they showed no signs of undergoing interconversion. Furthermore, the crystal structures of the phenylbenzoquinone–phenylhydroquinone complexes **14a** and **14b** have intermolecular interactions very similar to those of the structures[31] of the two crystalline forms of the parent compound,

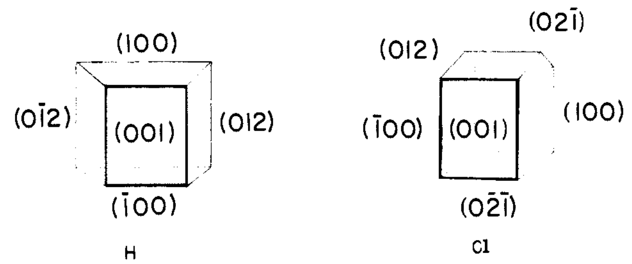


Figure 14. Drawings of single crystals of (left) phenylquinhydrone (**14a**) and (right) its *p*-chloro derivative (**14b**) showing the polar development of crystal faces. The faces (012) and (012) but not (012) or (012) are developed in the crystal of (12a) and (012) and (021) but not (012) and (021) in the crystal of **14b**. (Reproduced from ref 29 with permission. Copyright 1979, Gordon & Breach.)

quinhydrone (**16**) (without the aryl substituents), both of which show normal unsymmetrical hydroquinone–quinone hydrogen bonds (Figure 13); thus, the geometry of the C—O—H- - -O=C part of the two arylquinhydrones (**14a** and **14b**) as revealed by X-ray diffraction is very much like that of the quinhydrone (**16**) except for the hydroxylic proton position. The presence of a center of symmetry in the arylquinhydrone structures **14a** and **14b** as suggested by the X-ray results was further rendered questionable by the crystal morphology; a number of crystals of both the unsubstituted and *p*-chloro-substituted quinhydrones showed development of crystal faces characteristic of a polar crystal (Figure 14). The most powerful direct evidence against a crystallographic center of symmetry in these structures has been the observation of strong second harmonic generation when a 1.32-μm wavelength beam of a Nd-YAG laser is passed through such crystals. If this combined evidence is accepted, then instead of centrosymmetric structures these crystals must have ordered polar regions which, when averaged over a large volume of the crystal, give the appearance to the X-ray diffractometer of being centrosymmetric. These ordered regions must be greater in extent than the wavelength of the radiation used to detect them, 1.32 μm or 13 200 Å. Furthermore, since the proton-exchange reaction of the unsymmetrically substituted quinhydrones was negligible in the solid state at room temperature, the structures, including the positions of the hydroxylic protons, of these quinhydrones must be fixed at the time crystallization occurs.

The nature of such disorder, which can give rise to second harmonic generation on the one hand and yet permits a "normal" crystal structure determination on the other, deserves further investigation. A most interesting study by Green and Knossow[32] of lamellar twinning in the crystallization of chiral hexahelicene might be relevant and will be discussed in the following section of this review.

A particularly interesting aspect of the structures of the arylquinhydrones is that with the heavy atoms in their positions as determined by X-ray scattering assuming the centrosymmetric space group $P2_1/c$ the hydroxylic protons can be arranged in a hypothetical crystal so as to reduce the crystal symmetry either to $P2_1$ or to Pc (see Figure 15). Needless to say, real crystals would undoubtedly make at the very least minor adjustments in the positions of the heavy atoms as well. Nevertheless, the possible existence of crystals with polar structures closely related to the "centrosymmetric" structures which have been determined and with the polar axis of one structure at right angles to a polar axis of the other suggests an interesting and possibly useful area of investigation. It might be added that, although the proton switching in the solid state of the unsymmetrically substituted quinhydrones has not yet been accomplished, possible methods of achieving it have by no means been exhausted.

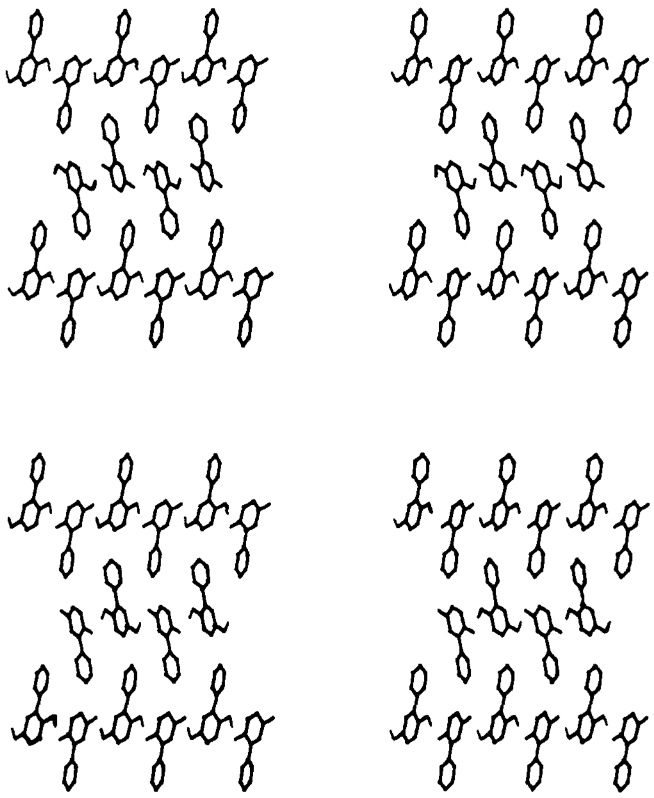
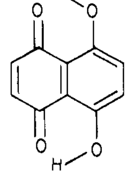


Figure 15. Stereopair drawing showing how hypothetical crystals of **12a** could be imagined to exist in the polar space groups $P2_1$ (upper drawing) of Pc (lower drawing). The orientation is that of Figure 12. The heavy atoms have been placed in their positions as determined in the "centrosymmetric" X-ray structure and the hydroxylic hydrogen atoms relocated in plotting to give the desired crystal symmetry. In the upper drawing the polar axis is b (to the left in the plane of the page). All the phenyl groups attached to quinone molecules are inclined toward the right and phenyl groups attached to hydroquinone molecules toward the left. In the lower drawing b is the only nonpolar direction in the crystal. All of the phenyl groups attached to hydroquinone molecules are inclined out of the plane of the page while those attached to quinone molecules are inclined slightly into the plane of the page. (Reproduced from ref 29 with permission. Copyright 1979, Gordon & Breach.)

Naphthazarin (**17**), although it might seem structurally unrelated to the quinhydrones above, presents a similar structural situation in some important respects. It would be more appropriate to say "naphthazarins" because naphthazarin crystallizes in three forms which have been designated A, B, and C. A number of crystal structure investigations have been made of each of the three forms (each of them is in



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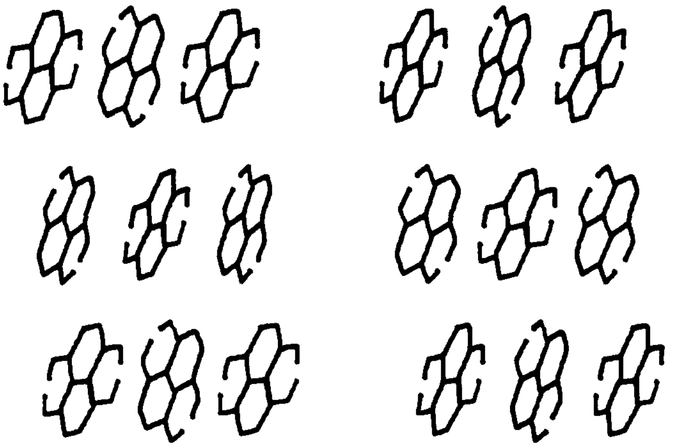


Figure 16. Naphthazarin C (17C). The view is along *b* with the *a* axis to the right in the page and *c* down and left. Protons are located in each of their positions of twofold disorder.

space group $P2_1/c$ as were the quinhydrones), and in each case the naphthazarin molecule has been found to lie on a crystallographic center of symmetry.[33]

The structure of naphthazarin has been carefully studied in solution,[34] and it clearly is not a centrosymmetric molecule but rather has the 1,4-dihydroxy-5,8-naphthoquinone structure 17 with the hydroxylic protons rapidly rearranging from one pair of oxygen atoms to the other. Proton NMR studies showed that this proton exchange is rapid on the NMR time scale even at −60 °C in solution. More recently, analysis of the infrared spectra of solutions of naphthazarin and the oxygen-deuterated compounds in carbon tetrachloride have been interpreted as showing that the interconversion of the two equilibrating species is by rapid synchronous tunnelling of the hydroxylic protons which is eliminated by substitution of deuterons for the hydroxylic protons.[36]

In the solid state at room temperature proton exchange in the A, B, and C crystalline forms is rapid on the NMR time scale, as was shown by ^{13}C NMR (measured with magic angle spinning with cross-polarization). At low temperatures naphthazarin B is transformed to a new crystalline form in which exchange is frozen out at −160 °C.[37] The similarity of the infrared and NMR spectra in the solid to those in solution provides strong evidence against a solid-state structure with the protons centered between the two oxygen atoms (a single potential minimum).[38] Clearly the crystal structure determinations at room temperature must have given an averaged structure (Figure 16). As with the quinhydrones discussed above, the possibility exists that under suitable external influence such crystals could be induced to adopt polar structures with space groups such as *Pc* and $P2_1$, having the heavy atoms in approximately the positions found by X-ray diffraction in the $P2_1/c$ structures (Figure 17). As with quinhydrones, such structures are of interest because proton flipping might be expected to rotate the direction of the polar axis by 90°. In such cases it is not too far-fetched to imagine that the direction of the polar axis could be detected by some physical method such as second harmonic generation or even (if appropriately substituted naphthazarins were available) by more traditional UV or visible spectroscopy.

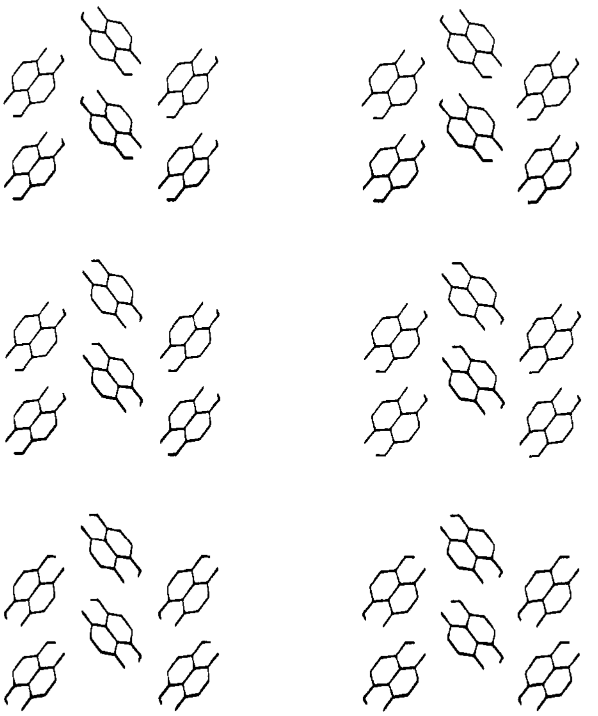


Figure 17. Naphthazarin B (17B) showing the proposed effect on crystal symmetry of proton flipping. The view is down *a** with *b* up in the page and *c* to the right. (Top drawing) One of the two enantiomeric structures in space group $P2_1$. (Middle drawing) Achiral structure (space group *Pc*). (Lower drawing) Mirror image of the top structure.

It is very much to be hoped that the combination of organic synthesis and X-ray structure determination with studies of the electrical and other physical properties of crystals may lead to discovery of interesting behavior of such compounds and, ultimately, to substances whose properties might be of practical value.

The Polar Axis and Crystal Chirality. As was pointed out earlier a crystal, if it has no center of symmetry, must have at least some directions which are polar. A further consequence, possible but not required by the absence of a center of symmetry, is that the crystal may be chiral (that is, nonsuperimposable on its mirror image).

The importance of crystal morphology to the first laboratory resolution of a chiral chemical compound has been so great that Pasteur's resolution of sodium ammonium tartrate tetrahydrate (18) is mentioned in

$Na^{+-}OOCCHOHCHOHCOO^{-+}NH_4{}^{+}\cdot 4H_2O$
18

$HOOCCHOHCHOHCOOH$
19

every beginning course in organic chemistry.[39] It is generally not mentioned, however, that the requirements for development of faces which reveal crystal chirality include the necessity both that the substance crystallize in a chiral space group (so that a single crystal contains only a single enantiomer) and also that there be appropriately located polar axes. Only if a crystal face cuts a polar axis can that face be hemihedral (that is, not required by crystal symmetry to be accompanied by a parallel counterpart at the opposite side of the crystal).[40] In Figure 18 are shown drawings of the crystals of sodium ammonium tartrate tetrahydrate similar to those obtained by Pasteur by recrystallization of the racemic salt.[41] This compound crystallizes in class 222 (space group $P2_12_12_1$) so that its crystallographic axes *a*, *b*, and *c* are nonpolar.[42] Application of

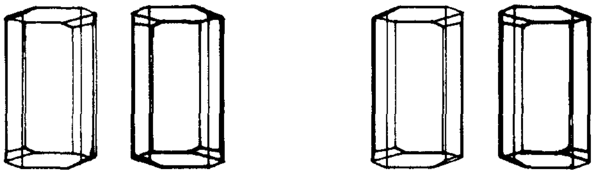
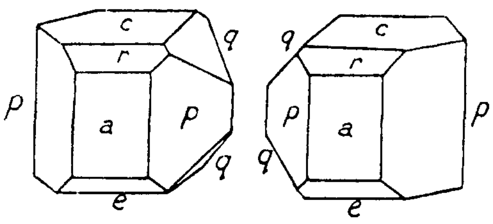


Figure 18. Drawings of the enantiomeric crystals of sodium ammonium tartrate tetrahydrate (**18**), space group $P2_12_12$. The chirality is revealed by the various members of the {111} set of faces.



(*a*) Dextrorotatory. (*b*) Lævorotatory.

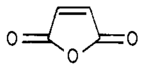
Figure 19. Drawings of enantiomeric crystals of tartaric acid (**19**). These crystals must be formed from the previously resolved acid since racemic tartaric acid crystallizes only in the form of achiral crystals.

the symmetry operations of point group 222 to the Miller indices of the general face (*hkl*) produces a corresponding parallel face if any of the indices *h*, *k*, or *l* is 0; that is, only faces with Miller indices (111) or higher could be expected to reveal the chirality of a single crystal. This is another way of saying that a crystal face cannot be parallel to a 2-fold axis (or 2-fold screw axis) or else it will be accompanied by a parallel face at the opposite side of the crystal. Crystals of sodium ammonium tartrate (**18**) of one chirality have the face (111) together with the faces $(\bar{1}1\bar{1})$, $(\bar{1}\bar{1}1)$, and $(1\bar{1}\bar{1})$ produced by the 2-fold axis of rotation while crystals of the opposite chirality have faces $(\bar{1}\bar{1}\bar{1})$, $(1\bar{1}1)$, $(11\bar{1})$, and $(\bar{1}11)$. In neither case are any members of one set of four the parallel counterparts of any other members of the same set (Figure 18).

It has been pointed out[41] that Pasteur's success in achieving the first resolution of a chiral compound depended not only on his keen powers of observation but also on an enormous amount of luck. In addition to the fact just discussed that, if no face with Miller indices of order (111) or higher had been formed, he would have been unable to distinguish enantiomeric crystals, most tartaric acid salts do not crystallize as conglomerates of enantiomeric crystals but rather as racemic crystals containing equal numbers of molecules of each configuration. Furthermore, even sodium ammonium tartrate tetrahydrate, the salt studied by Pasteur, fails to crystallize as a conglomerate at temperatures above 26 °C.

An important point not generally appreciated is that if we knew enough about crystal growth and rates of development of crystal faces it would have been possible to assign the absolute configuration of Pasteur's tartaric acid salt (**18**) by crystal morphology alone. What is required is the same kind of knowledge that was needed to assign by inspection of the crystal faces the absolute direction of the polar axis of the pointed crystals of *p*-chloroacetanilide (**1**) discussed at the beginning of this review; in that case the question was "does the pointed end of the crystal contain faces terminated by *p*-chlorophenyl rings or does it have faces made up of acetyl groups", as would be the case if the absolute direction of the polar axis were reversed. In the present case the problem is somewhat more complicated, but its solution requires the same degree of understanding of crystal growth. This potential use of crystal morphology was pointed out by Waser,[43a] who analyzed the problem in the context of the crystal structure[43b] of optically active neutral tartaric acid (**19**) (Figure 19). Unfortunately, we are not yet close to solving the problem of predicting the relative rates of development of crystal faces—particularly since crystal growth (and, hence, crystal morphology) can be altered drastically by "minor" changes in crystallization conditions and especially by changes in solvent or even traces of "impurities".[17]

Of course a crystal composed of molecules of a single enantiomer of an "optically active" compound (chiral in solution) must itself be chiral. However, it is less generally known that many "optically inactive" substances form chiral crystals by crystallizing in chiral space groups. For example, maleic anhydride (**20**) crystallizes in space group $P2_12_12_1$ (Figure 20).[44] This is so in spite of the fact that the molecules are achiral in solution and even in the crystal have a plane of symmetry to within the limits of error of the crystal structure determination (Figure 20b). Furthermore, a crystal can be chiral and yet contain both members of an enantiomeric pair of molecules in equal numbers.[45] In such cases the chirality of the crystal results from the relative orientations of the molecules in the crystal.



20

$C_6H_5COCOC_6H_5$

21

A chemically interesting situation can also occur on crystallization of a substance whose molecules in solution are rapidly interconverting mixtures of enantiomeric conformers (conformational isomers which are nonidentical mirror images). Crystallization may lead to a structure composed of molecules frozen by the crystal environment into a chiral conformation. Whether the crystals form a conglomerate or a racemate is then determined by whether a single crystal contains both enantiomers or only one.

An example of particular interest is the substance benzil (**21**). It was suggested by Morawetz[46] in 1966 that, since an ideal single crystal of benzil (Figure 21) contains molecules of only one chirality,[47] such a crystal might react to form a product with a stable chiral center, the chirality of the product being governed by the chiral environment of the benzil crystal. Although benzil crystals are prime candidates for such an experiment in every other respect, it has not been possible thus far to induce them to undergo a reaction under such conditions that the crystal structure directs the steric course of the reaction. However, workers in Israel beginning with Penzien and Schmidt[48] have designed other reactions showing that crystal chirality can indeed be employed in this way to obtain optical yields of chiral product of as high as 100%. This work has been well reviewed by Green, Lahav, and Rabinovitch.[49]

The crystals of *p*-bromobenzoic anhydride (**7c**) discussed earlier are chiral as well as polar (Figure 8b); that is, in the crystalline state molecules are constrained by the crystal packing to adopt a nonplanar chiral con-

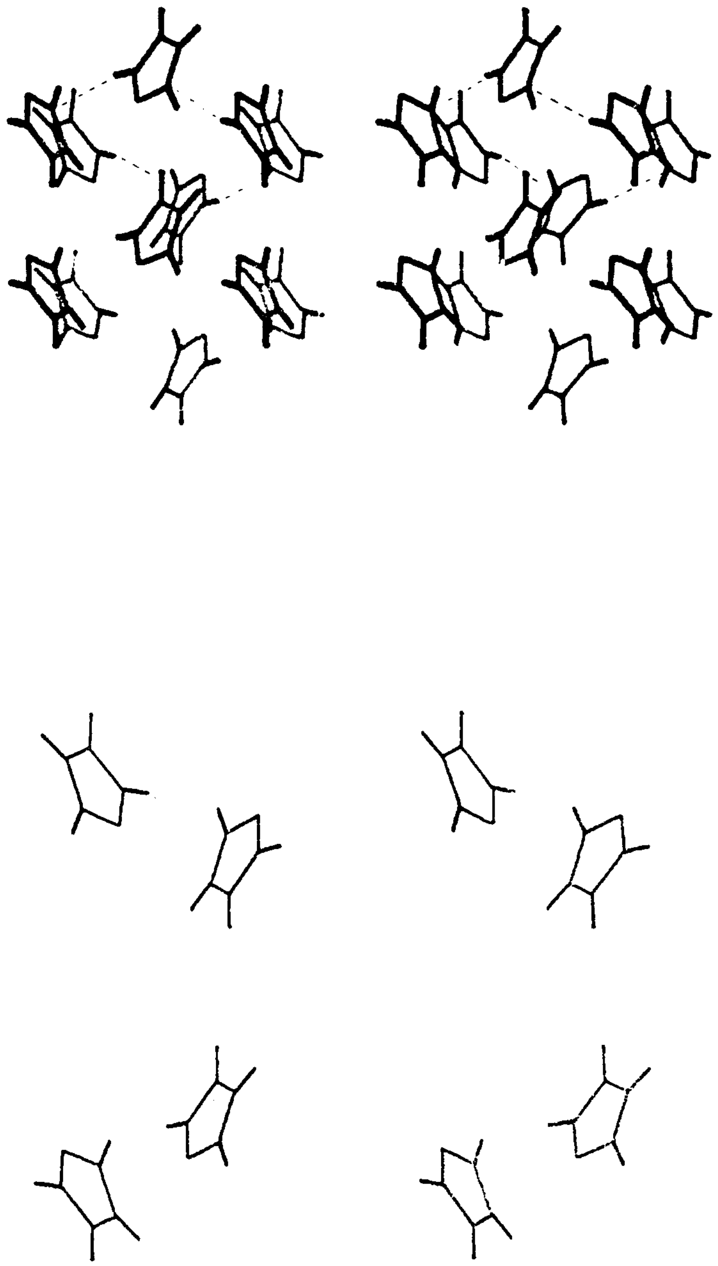


Figure 20. Stereopair drawing of (top) the structure of maleic anhydride (**20**) (space group $P2_12_12_1$) and (bottom) the two-molecule unit which defines the crystal chirality.

formation. As is indicated by the space group $C2$, an ideal single crystal contains anhydride molecules of only one chirality. It follows that the determination of the absolute direction of the polar axis also determines the absolute configuration of the *p*-bromobenzoic anhydride molecules and of the crystal. In fact, the crystal morphology has been correlated with the absolute configuration so that the configuration can be assigned by visual inspection of the crystal.[23]

Although in solution the enantiomeric anhydride molecules are in rapid equilibrium with each other, it should be possible to utilize the molecular chirality of *p*-bromobenzoic anhydride in the crystal by carrying out reaction in such a way that the conformation is frozen until the instant when reaction occurs—as in, for example, the reaction of crystalline anhydrides with gaseous reagents. Thus, the chirality of crystalline *p*-bromobenzoic anhydride might be used to resolve a racemic gaseous amine by virtue of the preference of the chiral anhydride for reaction with one of the amine enantiomers rather than the other. Preliminary work[50] in collaboration with Dr. William Pirkle of this department has shown that when a single crystal of *p*-bromobenzoic anhydride (**7c**) is ground and exposed to vapor of racemic phenylethylamine (**22**), the resulting

$$\underset{\mathbf{7c}}{p\text{-BrC}_6\text{H}_4\text{COOC}_6\text{H}_4\text{Br-}p} \qquad \underset{\mathbf{22}}{\text{C}_6\text{H}_5\text{CHNH}_2\text{CH}_3}$$

$$\underset{\mathbf{23}}{\text{C}_6\text{H}_5\text{CH(CH}_3\text{)NHCOC}_6\text{H}_4\text{Br-}p}$$

amide (**23**) contains one of the two enantiomers in at least a 20% enantiomeric excess.

Recent work has emphasized the need for a better understanding of the nature of "chiral" crystals like those of the bromo anhydride **7c**. Racemic hexahelicene crystallizes in space group $P2_12_12_1$, and perfect single crystals should therefore contain molecules of only one chirality and be optically pure. However, crystals indistinguishable by X-ray analysis from optically pure crystals have been shown by measurements of optical

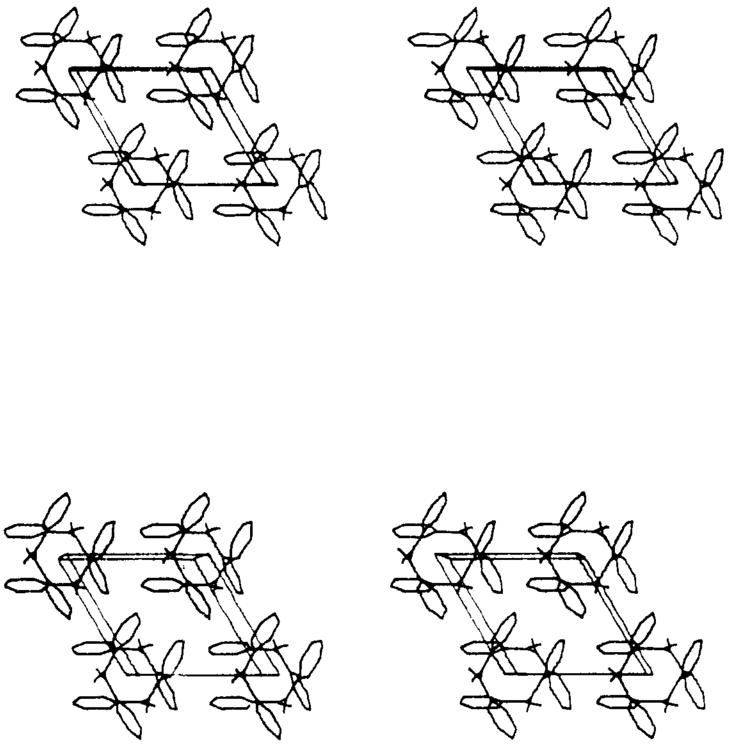
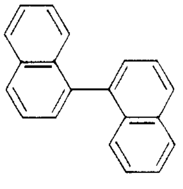


Figure 21. Crystal packing of benzil (21) showing the right- and left-handed spirals of the two kinds of chiral crystals. In each case the view is down the *c* axis. In the upper drawing the space group is $P3_121$ and in the lower drawing the enantiomeric crystal is in $P3_221$.

rotations to contain as little as 5% excess of one enantiomer over the other. Green and Knossow[32] showed by using etching techniques and cleavage/enantiomer analysis that the explanation is that the crystals are twinned—that is, adjacent layers of the crystal in certain directions are composed of molecules of opposite configuration ("lamellar twinning"). These layers when cut apart with a razor blade were shown to be nearly optically pure, but the aggregate, although having the appearance and X-ray reflections of a single crystal, was a composite of oriented layers of alternating chiralities. This phenomenon may be far more general than has been appreciated, and the possibility of such behavior obviously must be explored before experiments such as reaction of chiral crystals of the anhydride **7c** with racemic phenylethylamine can be fully interpreted.

An illustration of the unique aspects of crystal chirality and also the problem of assignment of configuration to crystals by studying their morphology is provided by the chemistry of 1,1′-binaphthyl (**24**). This



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substance crystallizes in two forms. In one, the low-temperature-stable form, crystals are racemic, composed of left- and right-handed binaphthyl molecules in equal numbers. The other, the high-temperature stable form, is chiral; an idealized single crystal of that form contains only right-handed or left-handed 1,1′-binaphthyl molecules.

The crystal structure of the low-temperature form (Figure 22) was first determined by Kerr and Robertson.[53] The structure of the high-temperature form (Figure 22) was recently determined independently in at least three laboratories.[54,55] This compound has been shown to undergo spontaneous resolution when its crystals are heated. Examination of the phase diagram of the 1,1′-binaphthyl system guided Pincock and Wilson to the conditions needed to convert the crystalline racemic low-temperature form seeded with a small excess of one of the enantiomers to the chiral high-temperature form with a high enantiomeric excess of that same enantiomer.[56] Recent further examination of this rearrangement[54] (in collaboration with Dr. M. C. Etter of 3M Co.) has shown that, at least under our conditions, a major part of the reaction occurs not as a solid-solid transformation but through the vapor phase. Crystals of the low- and high-temperature forms are shown in Figure 23, a and b. The result of heating such crystals is shown in Figure 23c. The characteristic tetragonal bipyramids of the high-temperature form are growing in the vicinity of the starting crystal of the low-temperature form. After being heated for a length of time sufficient for production of large numbers of microcrystallites of the high-temperature form, the initial crystal showed that it still had the unchanged structure of the low-temperature form.

A drawing of an idealized crystal is shown in Figure 24 with the faces indexed. Although this crystal is chiral, its morphology gives no hint as to whether it has a right-handed or a left-handed internal structure. The problem here is that the crystal class is 422, and in this class none of the major crystal axes is polar. It may be asked, then, what faces would have to be developed to reveal the chiral nature of the internal structure? Simple application of the crystal symmetry operations to a general face (hkl) shows that if a face $(\overline{hkl})$ is not to be produced by crystal symmetry from (hkl), then $h \neq 0$, $k \neq 0$, $l \neq 0$, and $h \neq k$. Thus the simplest

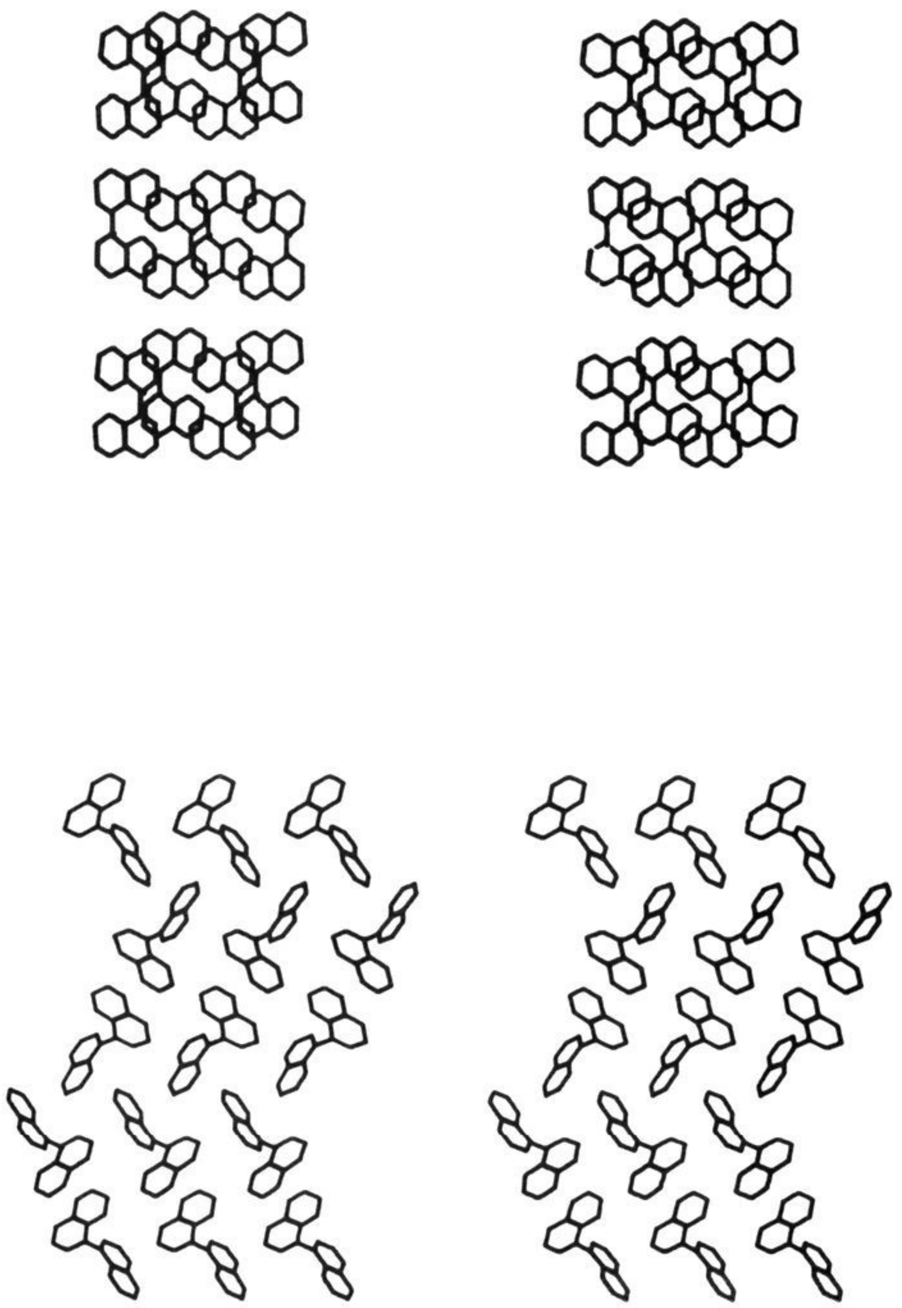


Figure 22. Stereopair drawings of (top) the racemic low-temperature-stable form and (bottom) the chiral high-temperature-stable form of binaphthyl (**2**). In the upper drawing *a* is up and *b* to the left in the plane of the page. In the bottom drawing *a* is to the right and *c* down in the plane of the page. Molecules were selected to show the composition of the (012) face, one of the major faces as shown in Figure 23.

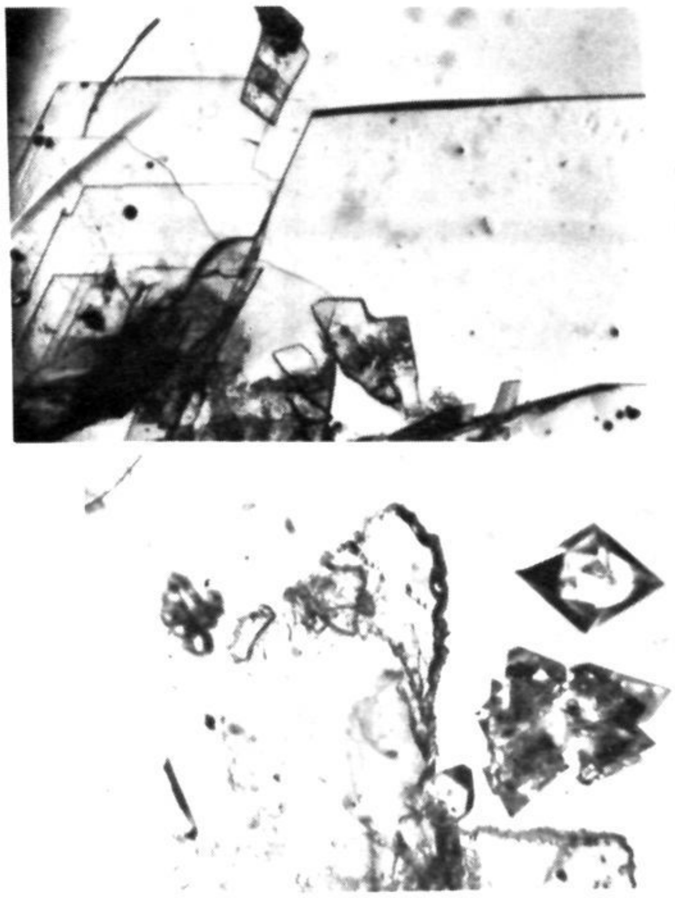
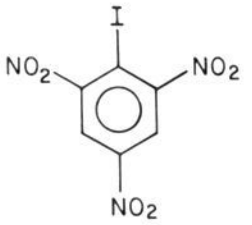


Figure 23. (Upper left) A thin plate of the low-temperature achiral form of binaphthyl (**24**). (Upper right) A tetragonal bipyramid of the high-temperature form. (Below) A plate of the low-temperature form which has been heated. The product crystals can be seen growing at the right side of the photograph. (Reproduced with permission from ref 54. Copyright 1980, American Chemical Society.)

hemihedral face (one without a symmetry-required parallel counterpart) would be (121) or (211). We have made an unsuccessful search for such higher order faces; it seems likely that they occur rarely if at all.

At this point we return to a crystal drawing published[57] in 1900 of picryl iodide (**25**) (Figure 25), a



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substance shown much later to crystallize in the same space group as chiral binaphthyl, $P4_12_12$, and whose structure was determined by Huse and Powell.[58] Although facial development of this crystal is somewhat different from that of 1,1′-binaphthyl, there is still no higher order face which would reveal the chirality of the crystal. A point of interest is that the crystal is unaxial with the optic axis perpendicular to the *c* face (and vertically in the page in Figure 25). Under such circumstances it may be possible to measure the optical rotation of the crystal with an ordinary polarizing microscope converted to a polarimeter by equipping it with a monochromatic source of illumination. The rotation (D line of sodium) of crystalline picryl iodide measured in this way was 10°/mm (D line of sodium).[57] Benzil mentioned earlier, crystallizing as hexagonal plates normal to the optic axis, has been found to have a rotation of 25°/mm (D line of sodium).[59] Although there has apparently been no attempt to measure the rotation of chiral binaphthyl crystals, it might be possible to sort them into (+) and (−) crystals by this method; in this way making the measurement does not require that they be destroyed by being dissolved. Rotations of substances such as benzil and picryl iodide which, unlike 1,1′-binaphthyl, undergo racemization in solution too rapidly for measurement by ordinary polarimetry can, of course, be measured only in the crystalline state.

Conclusion

Although the crystallographic polar axis has played an extremely important role at certain crucial points in the development of chemistry, as, for example, in the first resolution of a racemic compound by Pasteur, and in inorganic crystals plays a major role in modern technology, its importance and potential utility have generally been overlooked by organic chemists. It is hoped that this will change as knowledge of the stereochemistry of organic crystals becomes more widespread and there is increased awareness of the common occurrence of polar organic crystals and the potential utility of their unique properties. The very large numbers of organic compounds and their great structural diversity suggest that many interesting phenomena

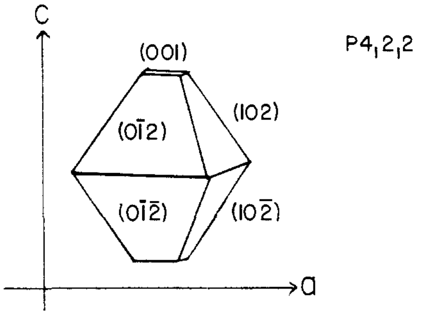
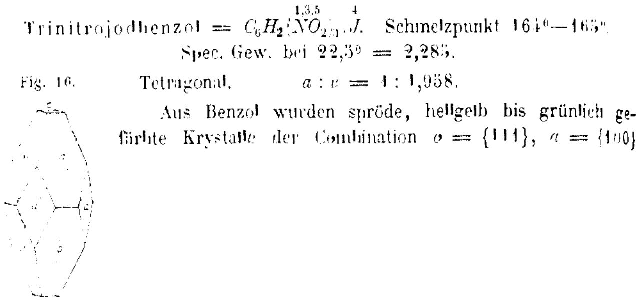


Figure 24. Drawing of a crystal of 1,1-binaphthyl (**24**). Note that all observed faces have at least one Miller index which is equal to 0. Faces which might have revealed the chirality of the crystal would have had to have indices (211) or the equivalent.



Trinitrojodbenzol = $C_6H_2\overset{1,3,5}{\{NO_2\}_3}.\overset{4}{J}$. Schmelzpunkt 164°—165°.
Spec. Gew. bei 22,5° = 2,285.

Fig. 16. Tetragonal. $a : c = 1 : 1{,}958$.

Aus Benzol wurden spröde, hellgelb bis grünlich gefärbte Krystalle der Combination $o = \{111\}$, $a = \{100\}$

Figure 25. Drawing of a crystal of trinitroiodobenzene (**25**) which like binaphthyl **22**, is in space group $P4_12_12$. Although the facial development in this case is somewhat different from that of binaphthyl in Figure 24, again faces which would have revealed the crystal chirality are missing.

await discovery in this area.

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