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CRYSTAL ENGINEERING AND CHEMICAL REACTIVITY OF ORGANIC MOLECULAR SOLIDS*

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Organic solid state chemistry is a field which lies at the crossroads of solid state science, organic chemistry, structural chemistry and X-ray crystallography. In general, it is concerned with the ways in which organic molecules pack in crystals. Reactions which are controlled by the manner of packing are termed topochemical and some recent extensions to the topochemical principles are discussed. In order to systematise the subject, however, a predictive control over structure is required and this leads to the concept of crystal engineering which has been illustrated by the importance of secondary molecular motifs. A better ability in manipulating crystal structures implies that more reliable values for non-bonded atom potentials are becoming available. This information can in turn be employed to carry out crystallography with packing or real-space considerations. It is clear that there are several applications of crystal dissymmetry to academic and practical questions. The chirality of a crystal structure may be exploited in asymmetric synthesis, determination of absolute configuration and in the choice of materials for non-linear optics. Organic solid state chemistry is also related to the design of organic metals and a clear understanding of packing can only result in more deliberate searches for new molecular conductors and superconductors.

Key Words : Organic Solid State; Topochemistry; Crystal Engineering; Real-Space Crystallography; Organic Metals

INTRODUCTION

THE twentyfirst and final chapter of a recent monograph[1] on solid state chemistry begins thus: "This book could not be concluded without at least some mention of organic materials. Usually the fact that many organic substances are solids at room temperature has little bearing on their chemistry." Notwithstanding the apologetic tone of this quotation and the empirical origins of organic solid state chemistry (OSSC), the present article will attempt to show that progress in the last few years has hinted at exciting possibilities for this latest addition to the discipline of solid state chemistry.

Research in OSSC today has important implications in diverse areas of chemical research. Using the principles of OSSC, one may for instance monitor organic reactivity at the molecular level, answer stereochemical questions of a fundamental nature, carry out novel organic transformations and study various ways in which

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organic molecules organise themselves, be they in a crystalline solid, a nematic mesophase, a polymer, a film or a micelle. Impetus to research in OSSC also stems from the fact that such work may lead to the development of molecular materials which are important for electronics and communications applications. Chemical memory devices, organic conductors and frequency doublers are not yet commercial products while a high temperature organic superconductor may remain a dream for some time to come. But all these represent worthwhile goals to strive towards since a substantial amount of new chemistry and an improved understanding of structural principles is bound to emerge in such a quest.

At the very outset one must be aware that there are notable differences in the methods employed in the practice of OSSC when compared to the solid state chemistry of non-molecular materials. The physical and chemical properties of organic substances are such that the standard techniques of preparation and characterisation of inorganic materials may be of only marginal utility. Spectroscopy, in the bulk and on surfaces, and microscopy, both optical and electron, are vital tools of modern solid state chemistry. These techniques have, however, not been generally adapted to OSSC. In many cases, even suitable methods of purification have not been standardised. The traditional token of purity for solution organic chemists, that is $\pm$ 0.3 per cent variation from the calculated C, H and N elemental analyses, is clearly inappropriate in many solid state studies!

Since OSSC is still in the descriptive phase with occasional forays into the realms of correlation and prediction, X-ray crystallography occupies a central position in this subject. It is the most common way of determining molecular and, more importantly, crystal structures of organic molecular solids. Many categories of organic solid state reactions are governed by the crystal structure of the reactant and determining the structure of this reactant assembly of molecules is a *sine qua non* to rationalising solid state reaction mechanisms or to acquiring a body of information that is representative enough to make considered structural predictions. X-ray crystallography will therefore continue to remain very important to OSSC and this situation is unlikely to change in the near future as there is yet no definitive answer to the question: "Can one reliably predict the crystal structure of an organic solid?"

The issue of structure is a principal one in OSSC, as indeed it is in all branches of solid state chemistry.[2] Generally, an understanding of structural concepts may be utilised in two distinct ways : to carry out novel chemical reactions and to devise new materials with specific physical properties, be they optical, electronic or mechanical. In this article, some significant recent developments in OSSC and some potentially important prospects for the future are highlighted. Almost all these areas are concerned with obtaining, understanding or exploiting the crystal structure of an organic compound.

Topochemistry and the Prediction of Solid State Reactivity

The work of Gerhardt Schmidt and his co-workers is of such seminal importance to OSSC that, more than twenty years after its publication[3,4,5] it still remains the

inevitable starting point for reviews in the field.[6–15] Though early work on the photodimerisation of crystalline olefins to give cyclobutanes had been reported,[16–18] Schmidt was the first to be able to correlate a large number of seemingly unrelated chemical and crystallographic facts and in doing so to lay the foundations of OSSC.

Schmidt found that for many photodimerisable olefins, the molecular packing plays a crucial role in determining the course and outcome of the solid state reaction. These reactions are termed topochemical[19] since they are considered to occur with a minimum of atomic or molecular movement. Since any molecular diffusion of the conventional type is precluded in the solid state, such topochemical reactions have also been termed 'diffusionless'.[20] In a topochemical situation, reaction only takes place if the geometry of the molecules in the reactant crystal permits it. Conversely, no reaction occurs if the geometry of the adjacent molecules in the crystal is inappropriate. As a corollary, the topochemical principle, as stated above, also implies that the structure of a product of such a reaction bears a close relationship to the crystal structure of the reactant. Because of this fact, there are a very small number of products in the typical topochemical reaction.

These features were illustrated by Schmidt with reference to the *trans*-cinnamic acids. These compounds crystallise in one or more of three structural types α, β and γ. While the α-acids have short crystallographic axes greater than 5.2Å, the β-acids are characterised by short axes of ca. 4.0Å. Fig. 1 shows that in both these cases, 'potentially reactive' double bonds are parallel and approximately 4.0Å apart when measured from bond centre-to-centre. In the case of the γ-acids, however, the short axes are around 4.7 Å with the result that nearest parallel double bonds are at this increased separation. These crystallographic observations when coupled

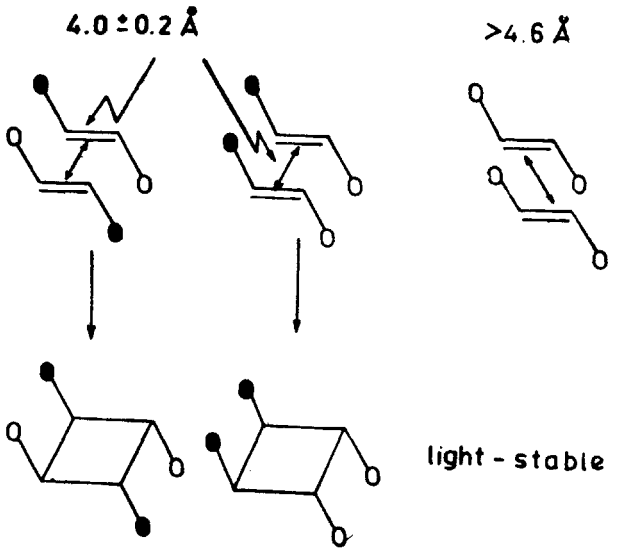

FIG 1 Photoactive (α, β) photostable (γ) forms of *trans*-cinnamic acid.

with the photoreactivity of the α-and β-forms and with the photostability of the γ-form lead to a formulation of the topochemical rules for the 2 + 2 photodimerisation of olefins:—

(1) The solid state reaction only occurs if the double bonds are closer than some 'threshold' separation which lies between 4.0 and 4.7Å (Schmidt used a value of 4.2Å for this cut-off).

(2) The crystal symmetry of the reactant transforms as the molecular symmetry of the product.

Several examples of solid state photodimerisation reactions which obey these rules have been described.[21] While Schmidt extended the topochemical argument to aliphatic unsaturated acid derivatives,[22] and to quinones,[23] Thomas and co-workers have found that in the 2-benzyl-5-benzylidenecyclopentanone (BBCP) class of compounds, solid state dimerisation is not only topochemical but also topotactic with 'potentially reactive' double bonds being related by a centre of inversion in the reactant crystal.[20,24-26] The solid state photodimerisation of 3-methyl-4 nitro-5-styrylisoxazole,[27] thymine[28] and α-benzylidene-γ-butyrolactone[29,30] have all been found to be topochemical as defined above (Fig. 2).

However, other solid state photodimerisations have been described where the reacting double bonds are non-parallel. A notable case is 2,5-dibenzylidenecyclopentanone where the angle between the two reacting bonds is nearly 56°.[31] Another definitive example is 1, 4-dicinnamoylbenzene which photodimerises to give an unusual δ-truxinic product.[32,33] Again there are cases such as 2-benzylidene-cyclopentanone where even though parallel double bonds are aligned at less than 4.2Å

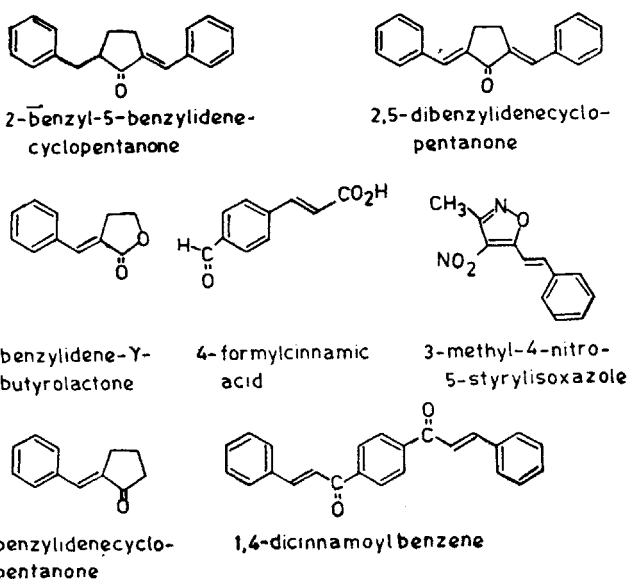

FIG 2

separation, no solid state photoreaction occurs on irradiation[30] while in the photoreactive 4-formylcinnamic acid, a 100 per cent yield of topochemical dimer is obtained even though the reacting double bonds have their centres greater than 4.8Å apart in the crystal.[34]

In general, it is chemically unreasonable to expect a 100 per cent correlation between the disposition of point atoms in the solid state and the reactivity which is predominantly an electronic phenomenon. Indeed, it is probably the almost hypnotic fascination for the topochemical rules as formulated by Schmidt (parallel double bonds, distance less than 4.2Å) which, if anything, has led to many of these reactions being considered 'unusual' or 'anomalous'. As early as 1978, it was pointed out that arbitrary geometric criteria could not be used to predict solid state photoreactivity.[35] More recently, it has been shown that many of these supposedly anomalous situations may be better understood if orbital overlap rather than double bond centre-to-centre separation is considered.[36,30] Such an analysis explains the preference for the intermolecular over the intramolecular reaction in 1,1′-trimethylene*bis*thymine[37] and for the formation of the 7-methoxycoumarin dimer in the solid state.[2] A simple geometrical argument will show that consideration of both centre-to-centre and plane-to-plane separation of the potentially reactive double bonds is necessary to determine the extent of orbital overlap. Cases like 2-benzylidenecyclopentanone and 4-formylcinnamic acid illustrate the pitfalls of using the centre-to-centre separation alone.

There are yet other situations where a topochemically expected photoproduct is not obtained even though the orbital overlap is favourable. One such case is the 1 : 1 Donor-Acceptor complex between 3,4-dimethoxy- and 2,4-dinitrocinnamic acids. Here, energy transfer from the $\pi\pi^*$ excited state to an $n\pi^*$ state is facile with efficient intramolecular quenching preventing chemical reaction.[38,39]

In summary, a classification of these various categories of topochemical processes is attempted in Table I. In *A* and *B*, topochemical and orbital overlap predictions are borne out while in *C*, non-parallel double bonds are considered. In *D*, however, the reaction is formally non-topochemical. Early work[40] seemed to suggest that such a reaction takes place through defect-controlled energy transfer, but the discovery of metastable phases in anthracene[41] has cast new light on this problem and the possibility of a topochemical reaction proceeding through polymorphs cannot be ruled out. A type *E* process is a seeming violation of the topochemical rules but the anomalies are because of intramolecular energy transfer. These five situations describe all possible combinations of topochemical allowedness or non-allowedness and the presence or lack of solid state reactivity.

Although much work has been carried out on the prediction of topochemical reactivity from geometrical criteria, not much progress has been made in attempting to chart the course of an organic solid state reaction once it has been initiated. The concept of local packing densities has been used to estimate most probable directions for molecular movement during a solid state nucleophilic substitution.[43] Crystallographic studies have been carried out on partially reacted photodimerisable

TABLE I

Classification of solid state 2 + 2 cycloaddition reactions

Category	Double bonds parallel	Distance between double bond centres (Å)	Overlap i.e. Topochemically allowed	Reaction	Topochemical product	Examples	Reference
A	Yes	< 4.2	Yes	Yes	Yes	Cinnamic acid BBCP Diacetylenes Benzylidene-butyrolactone	Cohen and Schmidt[3] Thomas[20] Wegner[56] Kearsley and Desiraju[30]
B	Yes	*ca.* 4.2	No	No	—	2-Benzylidenecyclopentanone	Kearsley and Desiraju[30]
C	No	< 4.2	Yes	Yes	Yes	2,5-Dibenzylidenecyclopentanone	Theocharis *et al.*[31]
						1,4-Dicinnamoylbenzen	Hasegawa *et al.*[32]
D	Yes	> 4.2	No	Yes	No	9-Cyanoanthracene	Cohen *et al.*[40]
E	Yes	> 4.2	Yes	No	—	2,4-dinitro cinnamic acid 3,4-Dimethoxycinnamic acid 1 : 1 complex	Desiraju and Sarma[35]

crystals in the benzylbenzylidenecyclopentanone family of compounds.[41,45] Such studies were possible since the crystallographic unit cells of the reactant and product are virtually identical (Fig. 3). These X-ray measurements reveal the positions of unreacted and reacted molecules and, by implication, the direction of movement of molecules towards the transition state for this 'diffusionless' reaction. Theoretical modelling of such transformations should become feasible with the appearance of better and faster computers, and such reactions are possibly easier to handle computationally than their solution counterparts. The next several years will probably see an increased emphasis on the 'dynamics' rather than the 'statics' of an organic solid state reaction.

Novel Reactions—Organic Synthesis

Although the major application of OSSC is not in the area of organic synthesis, the topochemical principle may be exploited in sequences towards compounds with unusual structures and/or high molecular symmetry. There are several examples where a novel product is obtained in a high yield in a solid state process even though it occurs in reduced yield or not at all in the corresponding solution transformation.[46–48] An ingenious example is the eight-centre dimerisation of tetrachlorodibenzylidene acetone to yield a novel tricyclic cyclohexanedione framework.[49] A

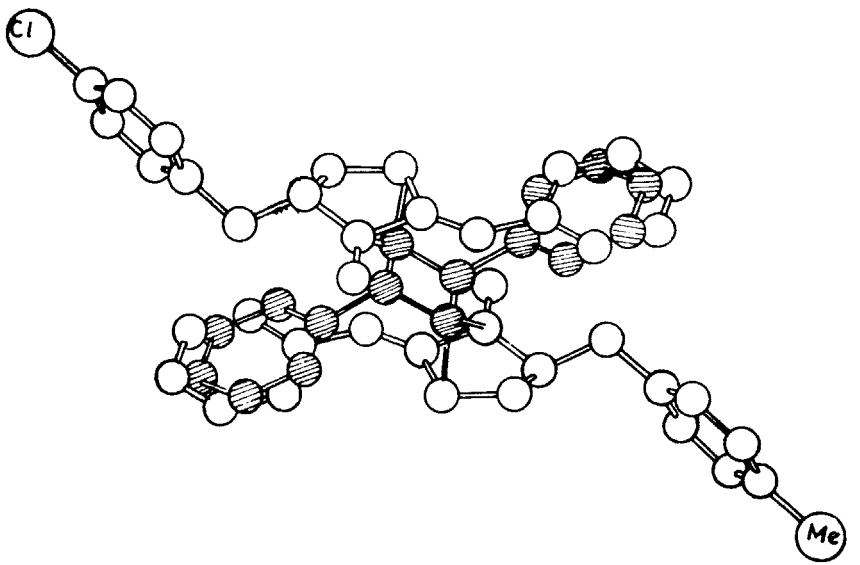

FIG 3 Positions of the monomer (○) and dimer (●) molecules during photoirradiation of mixed crystals of the BBCP's **1** and **2** as determined by *in-situ* X-ray diffractometry on partially reacted single crystals. Notice the formation of the cyclobutane ring and the puckering of the two cyclopentanone residues as the reaction progresses. The atomic positions of the Cl-benzyl and Me-benzyl rings do not change appreciably during the reaction. This 'anchoring' effect is, in large measure, responsible for the single crystal single-crystal nature of the reaction (From Theocharis *et al.* 1984).

very real problem with using topochemical reactions in organic synthesis is however, the lack of generality. Much attention in OSSC has been paid to a single reaction, the 2 + 2 photodimerisation of olefins and not much is known about reactions between two different substances in the solid state, be they photochemical or thermal.[50,51] An unusual case of a solid state intermolecular Diels-Alder reaction has been reported.[52] Many solid state intramolecular processes have been described. These include photochemical isomerisation[53] and H-atom abstraction.[54,55] In the latter category, the solid state and solution products are generally different in spite of the reaction being intramolecular and several mechanistic insights have been obtained.

The polymerisation of diacetylene derivatives[56,57] is an unprecedented solid state transformation where single crystals of monomer are converted to *single crystals* of polymer in quantitative yields. Since there are not many methods of making such perfectly oriented macromolecules, polydiacetylene chemistry has been the subject of extensive investigation. The commercial importance of these materials is obvious. With their highly extended conjugated framework, ease of oxidation, molecular linearity and considerably dichroic character, these substances are potentially very significant for optical and electronic applications. The study of polydiacetylenes doped or otherwise, continues to be one of the more attractive areas of OSSC where collaborative studies between chemists and physicists hold out opportunities for significant breakthroughs.

Another elegant synthetic strategy in OSSC is to use the dissymmetry inherent in a non-centrosymmetric crystal structure to generate molecular optical activity through topochemical reactions. Such reactions were first demonstrated for diarylbutadiene derivatives[58] and are illustrated in Fig. 4. A compelling reason for interest in such reactions stems from the fact that crystal lattice controlled asymmetric syntheses might well have been involved in the generation of or, at least, in the amplification of optical activity in prebiotic conditions on the earth.[59] Using these principles, it has been possible to devise a route for an absolute asymmetric synthesis with close to quantitative enantiomeric yield,[60] while a conceptual route towards pseudo mirror-symmetrical chiral cyclobutanes has been outlined through the device of optimising donor-acceptor interactions in a molecular complex.[38]

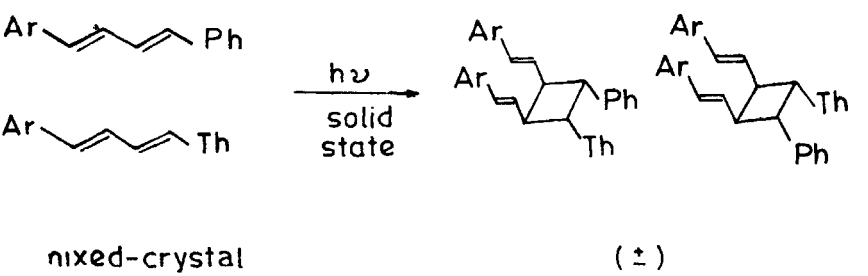

FIG 4 Asymmetric synthesis employing crystal chirality. The mixed crystals of the phenyl (Ph) and thienyl (Th) compounds belong to the non-centrosymmetric space group $P2_12_12_1$ (after Elgavi *et al.* 1971).

While it has been recognised that novel organic transformations may be carried out in the interlamellar regions of inorganic layered structures such a montmorillonite clay,[68] the principles underlying such reactions may be transplanted into the realm of asymmetric synthesis by clathration or enclosure of a potential substrate as a guest material in a chiral host. In this context, a well-studied host material is tri-*ortho*-thymotide, TOT, space group $P3_1$, which shows effective enantiomeric discrimination.[61] A recent report[62] deals with the oxidation of a prochiral olefin (guest) in the TOT cavity, to yield chiral peroxides in good enantiomeric excesses. Another very effective class of chiral encapsulating materials are the cyclodextrins. For example, α-cyclodextrin and crotonic acid, CH_3-CH = CH-CO_2H, from a complex which can be chlorinated in the solid state to yield dichlorobutyric acid, CH_3-CHCl-CHCl-CO_2H in quantitative enantiomeric yield.[63]

Crystal Engineering and Intermolecular Interactions

Although much structural and chemical data have been correlated on the basis of topochemistry, it was realised[21,8] that sustained development of OSSC could not be expected unless it was somehow possible to predict crystal structures. The emphasis has been shifting inevitably from the reactions and crystallographic details to predictive exercises. These have proved to be more difficult because an organic crystal structure is the consequence of a balance of many minor and subtle intermolecular forces. In broad terms, a crystal structure of a molecular solid results from a play of dispersive and repulsive interactions[64,65] and most structures can be somehow painted on this conceptual canvas. However, many alternative structures are seemingly possible within this framework and actually realised in practice as polymorphic modifications. The ultimate choice of a stable molecular packing seems to depend on the relative importance of secondary effects such as coulombic and dipole interactions or weak bonding. These effects all but render transferability of atomic non-bonded potentials impossible in any predictive effort and further they may vary drastically with molecular modifications that are apparently trivial from the solution viewpoint. Realising such facts, it has been the usual practice to study (crystallographically) a series of closely-related compounds so that a common structural principle may be made to emerge. Such activity has been termed crystal engineering.[21,8]

Crystal engineering is concerned with obtaining topochemical control in systematic ways and with predicting and exploiting crystallisation patterns in organic solids.[10,66,67,15] By suitable engineering of a family of structures, very specific reaction pathways and products may be obtained repeatedly and reproducibly. The strategy, therefore, involves the choice of molecules according to their shape, size and stereochemistry and then inducing them to crystallise into certain pre-designated crystallographic arrangements. The key to crystal engineering lies in being able to understand the nature of delicate yet non-trivial intermolecular forces.

One of the consequences of Kitaigorodskii's model for the crystal structures of organic compounds is that close-packing is of paramount importance and that

molecules pack in ways such that the 'voids' of one are locked into the 'protrusions' of the other. Volume and shape considerations hold sway rather than electronic factors. Each non-polar substituent of a certain volume can be exchanged for another non-polar group of a similar shape and volume without a change in the crystal structure. Chloro-methyl interchange (volumes Cl, 19Å^3, CH_3, 24Å^3) is, in fact, well known and a pair of compounds like **1** and **2** is isostructural. As it turns out, each of the individual compounds is photoactive in the solid state and the mixed crystals also react to form pseudoinversion-symmetry cyclobutanes (Fig. 5).

However, volume effects may be used to force the conformations and crystal structures of such compounds into variations. The main difference between the photoactive **3** and the photostable **4** lies in the molecular conformations (Fig. 5). Yet these two compounds will form mixed crystals, isostructural to **3**, primarily as a result of forced changes imposed upon the molecular geometry of the minor component **4** by the major component **3**. In the mixed crystals, the photostable chloro derivative **4** is forced to adopt the molecular conformation, crystal structure and solid state reactivity of the photoactive methyl derivative **3**.[44,45]

When the crystal structure is defined as a result of optimisation of dispersive and repulsive forces only, such volume effects are likely to be important. The appearance of secondary interactions, however, leads to violations of one type or another from the close-packing principle. It is hardly surprising that the crystal structures of strongly hydrogen bonded compounds depends mostly on the H-bonding requirements. The simplest compounds may adopt the most complex of crystal structures, as for example, hydroquinone (1,4-dihydroxybenzene) or trimesic acid (benzene-1,3,5-tricarboxylic acid). What is noteworthy, however, is the fact that even

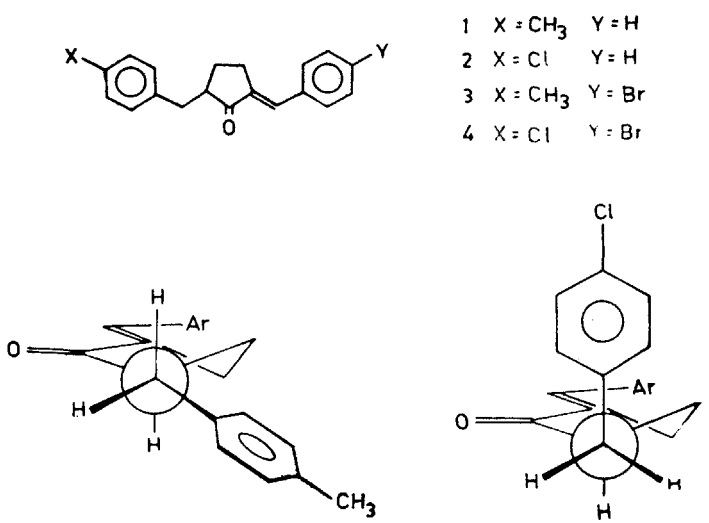

FIG 5 The molecular conformations of the methyl and chloro derivatives **3** and **4** respectively are different as are the crystal structures and solid state reactivity (Ar = *p*—Br—C_6H_4—) (adapted from Jones *et al.* 1983).

relatively weak intermolecular forces such as C-H...O, Cl...Cl, C...Cl, C-H...N or S...S may cause deviations from 3-dimensional closepacking. Still, these forces are quite weak and there is a substantial dependence on van der Waals interactions which means that such structures may be understood as gradual perturbations from the Kitaigorodskii model. Substitution of two or more chloro groups on aromatic rings, for instance, leads to preferential adoption of unit cells having a short axis of *ca.* 4Å which is characteristic of a structure made up of highly overlapped molecules stacked with a plane-to-plane separation of around 3.4Å (van der Waals separation). At least a hundred such chloro compounds are known.[21,69]

A common feature in the crystal structures of these planar chloro aromatics is the occurrence of a large number of Cl...Cl non-bonded contacts is the 3.2 to 3.6Å region. These contacts are generally along directions which are parallel to or close to the planes of the aromatic rings, so that molecules which are related by them can be arranged in planar sheet or ribbons. In order then that C...C contacts can be optimised, these sheets can be stacked with an inter-sheet perpendicular distance of 3.4Å as mentioned above. This kind of structure is illustrated by a compound such as hexachlorobenzene (Fig. 6).[70] Such secondary interactions may also be possible within the framework of stronger forces such as O-H...O H-bonding and a recent analysis of the crystal structures of the dichlorophenols is a representative example.[71]

These directional preferences for Cl...Cl interactions have been confirmed in the co-crystallisation of compounds such as 6-chloro-3,4-methylenedioxy cinnamic acid and 2,4-dichlorocinnamic acid as a stoichiometric molecular complex.[66,69] While specific in-plane Cl...Cl interactions lead to sheet-ordering, the lack of such intermolecular specificity between parallel adjacent molecular sheets leads to a structure which is disorded in the stack direction. It may be shown that such concepts may also be extended to C-H ..O interactions and that there is a significant tendency to adopt sheet-based 4Å structures among compounds which can optimise a large number of such bonds.[67,72]

A substantial amount of crystallographic information is necessary before reliable structural predictions may be made and it may not always be possible to carry out such a large number of structure determinations for practical reasons. A very

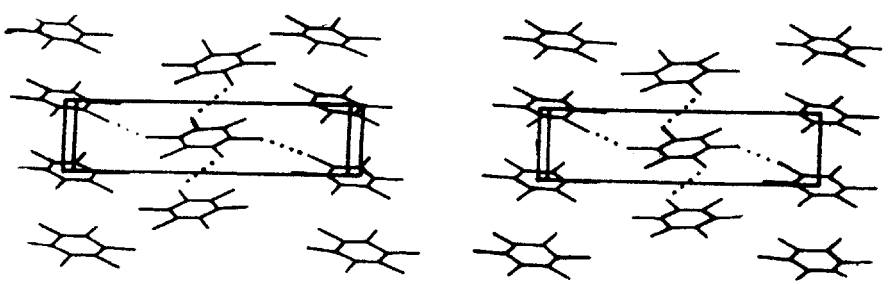

FIG 6 Stereodrawing of the crystal structure of hexachloro-benzene to show molecular ribbons linked by Cl...Cl interactions (after Sarma and Desiraju, 1985).

recent alternative strategy has been to retrieve the desired structural information from the Cambridge crystallographic database.[73,74] Since organic structures hinge on the manifestation of relatively weak interactions, a valuable insight into the consequences of these interactions, if not their nature, may be obtained by examining an entire family of structures with the database. Several such pioneering studies have appeared in recent years.[75-77] Such studies indicate that certain types of intermolecular interactions are associated with only certain geometrical arrangements of patterns or motifs. Hence, approaches through the database may be more fruitful, in this context, than attempting to grapple computationally with weak intermolecular forces.

This section would be incomplete without reference to studies concerning crystal engineering into non-centrosymmetric (NC) space groups. Notwithstanding possible applications in synthesis as outlined earlier, there is considerable interest in obtaining single crystals of organic compounds, which lack a symmetry centre since such crystals would show a non-linear second harmonic generation (SHG) effect upon suitable irradiation. Such molecular materials may be used in the up-conversion in the visible or near UV of powerful IR laser radiation, frequency modulation of a laser beam and for oscillation and amplification in solid state IR-tunable coherent devices. Although early applications have used inorganic materials like quartz, it has been realised that organic compounds have SHG efficiencies that are greater by several orders of magnitude.[78-80] A trivial means of ensuring crystallisation in a NC space group is to use a resolved material but such substances are, in general, neither very common nor need they always exhibit good SHG effects

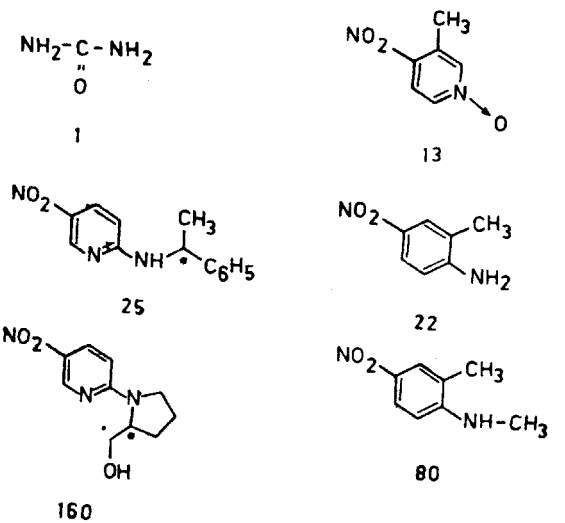

FIG 7 Some organic compounds which show sizable Second Harmonic Generation on laser irradiation. SHG efficiencies are given relative to urea. Asymmetric carbon atoms are marked with an asterisk. Note that only some of these compounds exhibit solution optical activity.

since non-centrosymmetry is a necessary but not a sufficient condition for appreciable SHG. On the other hand, organic compounds which may be electronically suitable for this purpose such as dyes and conjugated polymers rarely adopt NC space groups. Therefore, finding a material for SHG application has been largely a 'hit-and-miss' affair. It is still unknown why some optically inactive molecules resolve spontaneously and pack in enantiomorphous (and therefore, by necessity, NC) space groups. Correlations between molecular structure and the tendency to adopt NC packing are sparse and empirical. For instance, it is reported that, for disubstituted benzenes, the *meta* isomers may have a statistically greater tendency for NC space group adoption than the *ortho* and *para* derivatives.[81] The structures of some organic compounds which show large SHG effects are given in Fig. 7. It may be noted that many of them cannot show solution optical activity.

The Absolute Configuration of Chiral Molecules

As described above, non-centrosymmetric crystal structures are often packed with enantiomeric molecules. While chemists have recognised the existence of such molecules ever since Pasteur's experiments on hemihedrism in sodium ammonium tartrate in 1848, the philosophical question of how to determine absolute configuration remained unanswered for more than a century till, in 1951, J.M. Bijvoet showed that for a noncentrosymmetric crystal, an X-ray diffraction pattern could be obtained where violations of Friedel's Law ($I_{hkl} \neq I_{\bar{h}\bar{k}\bar{l}}$) could be observed. Using this anomalous dispersion of X-rays, the assignment of absolute configuration was possible.

In recent years, there have been two sets of experiments by organic solid state chemists to determine absolute configuration without using the Bijvoet method. The fundamental concept recognised in both experiments[82,83] is that any method which fixes the orientation of any functional group of the chiral molecule with respect to the crystallographic axes establishes the absolute configuration of the molecule. These arguments rest on the existence of the polar axis in crystals of chiral molecules. All such molecules must crystallise in enantiomorphous space groups and these have associated with them one or more polar directions. The polar axis is, therefore, a uniquely solid state phenomenon and at a molecular level, its structural implications are that when one views a crystal from the opposite ends of such an axis, chemically distinct parts of the molecules are revealed.[81] In the method of Curtin and Paul, a crystal is chosen which exhibits different solid state reactivity at different ends of the polar direction.[82] Gas-solid reactions are convenient for this purpose.[84] These reactivity differences may be monitored through some physical or spectroscopic technique and the direction of a particular functional group is therefore known. From the necessarily chiral morphology of the polar crystal, the sense of the polar axis is also known. A combination of these two facts leads directly to the absolute configuration of the crystalline chiral molecule.

The alternative approach is to monitor changes in the morphology of crystals of pure enantiomer upon the addition of carefully selected impurities. Since crystal morphology depends on the directions of weak intermolecular forces, the presence

of a small amount of an impurity may result in selective absorption on certain faces only, thereby inhibiting further growth on these faces and so effecting gross morphology changes. Since different functional groups emerge at opposite ends of the polar direction, it is possible to design impurities that will be adsorbed selectively at one end only. Observation of the resulting morphology changes establishes a method of fixing the orientation of a certain functional group with respect to the polar axis and therefore of fixing the absolute configuration.[83]

Packing Calculations and Real Space Crystallography

There are several situations in OSSC where X-ray crystallography is neither possible nor completely reliable. For compounds that are insoluble, unstable, non-volatile or of high molecular weight, obtaining single crystals may in itself be a formidable problem while any attempt at crystal engineering leaves the rhetorical question as to whether polymorphism is important or not in the system under consideration. Finally there are those cases, albeit small in number, where the solution of the phase problem is either ambiguous or intractable with conventional vector space of reciprocal space methods.

In the Kitaigorodskii model, the molecular arrangement in the crystal is based on the intermolecular potential being expressed as a sum of non-bonded atom-atom interactions.[65] These component interactions are a function of non-bonded distance and a set of, ideally, universal constants which are referred to as the atom-atom potentials for a given atom type pair. Therefore, by applying the argument in reverse, crystal packings may be derived with the use of such potentials.[85] The results of such calculations are usually quite reliable if only dispersive and repulsive interactions are important in crystal stabilisation. For hydrocarbons this is indeed the case and much work has therefore dealt with this category of compounds. The classical case of biphenyl has been studied[86] and it was found that the planar conformation and the stretching of the central bond characteristic of the solid state structure could be modelled accurately. Calculations on the crystal packing of *p*, *p'*-bitolyl also give values of the torsion angle within 1° of the experimental value of *ca.* 35°.[87] Such packing calculations have also been used to describe the orientation of guest impurities in a host matrix[88] and to explain the phenomenon of chiral turnover in hexahelicene crystals through a mechanism of cellular twinning.[89]

A natural extension of such techniques of minimisation of non-bonded intermolecular interactions is in the solution of the phase problem, that is in the determination of unknown crystal structures. For reasons indicated above, the crystal structures of hydrocarbons may be solved with the greatest ease. A typical example is the case of the bridged annulene in Fig. 8. It was found that while the crystal symmetry permitted only six molecular orientations, five of these were prohibited on the grounds of packing energy. The final orientation gave the correct structure.[90] Another well-known example concerns the combined use of packing calculations and electron microscopy to determine the structure of a metastable phase of anthracene.[41] This polymorph could not be studied by X-ray crystallography. The

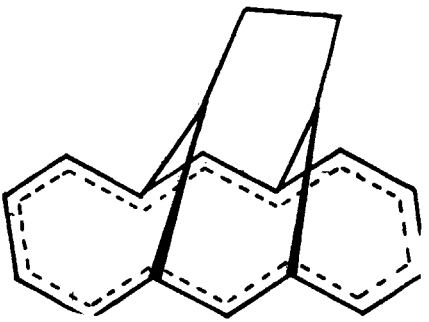

FIG 8

importance of this structure in the reconsideration of a defect-controlled mechanism for the 'non-topochemical' photodimerisation of anthracene derivatives has been alluded to earlier in this article.

It has been shown that compounds containing polar functional groups are more complicated to analyse because of the more dominant Coulombic terms in the potential and poorer heteroatom non-bonding potential parameters.[91] Topochemical arguments have been used as an alternative to an accurate knowledge of potentials for the oxgyen atom in the C-H...O bond in the crystal structure determination of the photoactive α-benzylidene-γ-butyrolactone shown in Fig. 2.[30] This is a rare case of a fairly small molecule whose crystal structure solution proved to be unusually resistant to Direct Methods. Since the material undergoes, what was assumed to be topochemical, photodimerisation in the solid state, the starting point in the structure analysis was not the monomer lactone but an incipient dimer pair, the centroid of which was constrained to lie at the origin of the centrosymmetric space group (Fig. 9). This topochemically derived starting point greatly simplified the packing analysis. The optimisation of two features : (*a*) the plane-to-plane interactions within the incipient dimer and (*b*) the orientation of the incipient dimer with respect to the cell axes allowed the structure to lock into the global minimum, in other words into the correct structure.

The appearance now of faster and more powerful computers will mean that non-hydrocarbon crystal structures can probably be handled with increasing confidence. The use of even minimal auxiliary chemical or crystallographic information (unit cell parameters, topochemistry) greatly enhances the power and extends the scope of these energy minimising search programs with the result that crystal structures or, in the most general sense, structures of any molecular assembly may be reliably and accurately predicted in increasing numbers.

ORGANIC METALS

The discovery of metallic conduction in the molecular solid tetrathiafulvalene-tetracyanoquinodimethane, TTF-TCNQ (Fig. 10) more than a decade ago[92] launched one of the most highly publicised areas of collaborative research between physicists

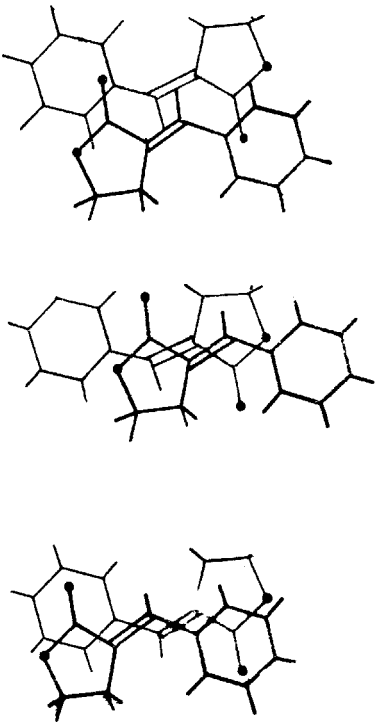

FIG 9 Some starting positions for the incipient dimer configuration in the crystal structure determination of α-benzylidene-γ-butyrolactone. The configuration in the centre led to the correct structure ultimately.

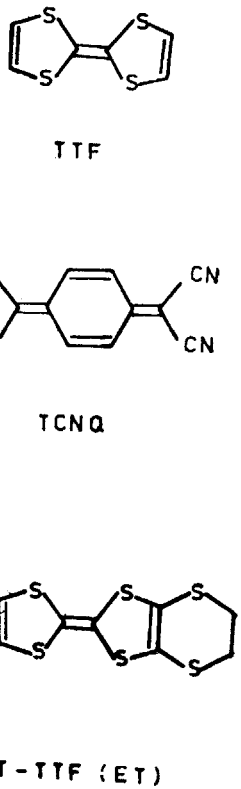

FIG 10

and chemists. It was realised that the molecular framework of organic compounds offerred considerable scope for subtle and effective variation of structural and electronic properties. Therefore, there has been much activity geared towards the discovery of new conducting molecular solids. Such activities have involved, for the most part, novel chalcogen heterocycles and have resulted incidentally in a large body of interesting synthetic, electrochemical and crystallographic data. This field has been extensively reviewed[93–98] and the accent here will be to show that the gaps in the area are such that they may be bridged with methods that have been developed in OSSC. Although the synthetic and theoretical efforts have been novel and varied, the structural uncertainties in persuading organic molecules to crystallise in preordained ways seems to have rendered the search for new organic metals a frustrating task.[99]

TTF-TCNQ is a donor-acceptor (DA) complex and there are generally two ways of stacking D and A molecules in crystals : (a) mixed stacks in which D and

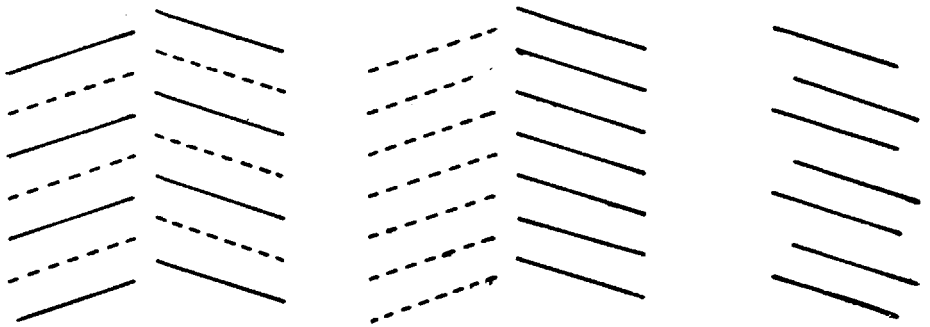

FIG 11 Mixed and segregated stacks for Donor-Acceptor complexes. Peierls distortion of a segregated stack.

A molecules alternate and (b) segregated stacks in which the molecules from separated D stacks and A stacks (Fig. 11). The potential ability of these two types of stacks to conduct electricity is quite different. The outstanding characteristic of the highly conducting TTF-TCNQ and related materials is the formation of segregated stacks of donor and acceptor molecules. This seemingly unlikely organisation of all the negatively changed ions into one set of stacks and the positively charged ions into another set is generally agreed to be an essential prerequisite for high conductivity in DA complexes. It is therefore extremely critical to know why compounds like TCNQ and TTF form segregated stacks while TCNQ, and other donors like, say anthracene form mixed stack complexes. Yet, the application of clearly appropriate techniques such as crystal engineering and packing calculations to predicting structural trends for DA complexes is a science still in its infancy. This gap in our present understanding of organic metals could well be because most of the work being done in this area has been conceived by solid physicists and not many structural chemists seem to be actively involved.

It has been theoretically predicted that in favourable cases, a segregated stack organic metal may exhibit superconductivity at lower temperatures and the quest for an organic 77 K superconducting substance continues fiercely. However, it is known that in a segregated stack compound there is a very high probability of a metal-to-insulator transition at low temperature (Peierls transition). The structural characteristic of such a transition is the appearance of unequal molecular separations along the stack direction (Fig. 11). The Peierls transition is the most serious obstacle to be overcome in developing a molecular superconductor and in order to obtain such a substance, the transition must be suppressed. There have been three approaches to the problem.[100] The first is the introduction of non-periodicity and many unsymmetrical donors and acceptors were synthesised to modify the Fermi surface of the low dimensional organic metal. The structural results of such synthetic manipulation are, however, very difficult to predict. The second approach is to increase the dimensionality by the physical device of high pressure.[101] In the third approach, chemical modification has been attempted to increase the dimensionality of the system. When the TTF skeleton is extended by chalcogen atoms, the

material BEDT-TTF is obtained (Fig. 10). The cation radical salt of this material, $(BEDT\text{-}TTF)_2I_3$ is the first ambient pressure organic superconductor. The most striking characteristic of this salt is that the S...S non-bonded contacts perpendicular to the stack direction (parallel to the molecular planes) are actually shorter than those along the stack direction with the result that the dimensionality is greatly enhanced. An understanding of molecular packing and structure are of central importance to all aspects of OSSC and the application of these ideas to the study of one-dimensional materials has all possibilities for synergistic growth.

Conclusions

Organic solid state chemistry far from being an esoteric sub-discipline has been borrowing concepts and ideas from chemistry, crystallography and physics and in turn seems poised at a stage when it can have considerable impact on apparently quite unrelated areas of research in the physical sciences. The development of this subject might have been delayed somewhat because of unwise attempts to classify it as 'organic chemistry', 'physical chemistry', 'chemical physics', 'crystallography', 'materials research', or 'solid state chemistry'. Happily the artificiality of such attempts is acknowledged today since there are so many areas of scientific endeavour which similarly attempt to stride across the gaps between major disciplines. There is thus in organic solid state chemistry every indication for sustained and healthy progress.

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