

Designer crystals: intermolecular interactions, network structures and supramolecular synthons

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Questions relating to the prediction of the crystal structure or structures of a given organic molecule may be more gainfully reversed so that retrosynthetic analysis of a target crystal network leads to the identification of molecular precursors. Crystal engineering is solid state supramolecular synthesis and supramolecular synthons, units formed by synthetic operations involving intermolecular interactions, may be used to focus efforts in such logic-driven retrosynthesis.

Introduction

Crystal engineering has been defined as the understanding of intermolecular interactions in the context of crystal packing and in the utilisation of such understanding in the design of new solids with desired physical and chemical properties.¹ The origins of this subject lie in the work of Gerhard Schmidt who realised, more than 25 years ago, that the systematic development of organic solid state chemistry required a proper theory of crystal packing.² The term 'crystal engineering' was also introduced by Schmidt in the context of solid state reactions and early papers in the subject,³ including the first *Chemical Communications* from my research group in 1983,⁴ were concerned almost exclusively with crystal engineering as a means of developing better organic reactions.

Crystal structures are mediated by intermolecular interactions and the easiest way of obtaining reliable information on these interactions is through crystallography. With the ever-increasing number of accurate X-ray and neutron diffraction analyses, a distinct change in perception occurred with regard to crystal engineering during the late eighties.¹ Instead of concentrating exclusively on topochemical reactions, structural chemists also began to conceive of organic crystals that could act as catalysts, microporous materials, frequency doublers, ferromagnets and superconductors. A particular crystal packing may also be attractive for aesthetic reasons, just as targets like cubane or dodecahedrane have been attractive molecular targets in the past. A crystal is as respectable a synthetic target as a molecule and form and function motivate current efforts in crystal design.

The awareness that a crystal is the supermolecule *par excellence* further heightened interest in crystal engineering and brought the subject into the mainstream of supramolecular chemistry.⁵ Crystal engineering is recognised today as an important form of supramolecular synthesis and the full rigour of synthetic methodology and strategy may now be brought to bear in the quest for complex and general supramolecular synthetic targets in the solid state. An important consequence of these developments is the identification of a crystal as a retrosynthetic target.⁶

This article is a personal view of the development and growth of crystal engineering, seen mainly through the 25 or so *Chemical Communications* from my research group.

From molecular to crystal structure

Crystals are built from molecules and the natural question that has been posed with respect to crystal engineering is, 'given the

molecular structure of an organic substance, what is its crystal structure?' The molecular basis of organic chemistry makes such a question seem almost intuitive and much progress was made and is continuing to be made in seeking answers here. The first well-documented attempt in this direction is the correlation, established in 1951 by the great chemical crystallographer J. Monteath Robertson, between the molecular structures of planar fused-ring aromatic hydrocarbons and their packing type as revealed by the crystallographic short axis.⁷ Robertson divided such hydrocarbons into two rather broad but fairly distinct types. He observed that disk-like molecules with an area large compared with their thickness (coronene, ovalene) tend to stack in columns and that the periodicity along this short axis, which is usually the monoclinic *b* axis, is about 4.7 Å. In the second class he included molecules which are still flat and disk-like, but of smaller area (naphthalene, anthracene) and noted that there is a tendency for such molecules to be steeply inclined to the symmetry plane and for the periodicity to be about 6.0 Å. It is remarkable that a statement of such prescience was made more than 45 years ago.

In 1988, Angelo Gavezzotti of the University of Milan and I re-examined Robertson's correlation and further amplified it.^{8–10} With hindsight of knowledge on intermolecular forces, notably the ubiquitous herringbone and stacking forces, that are prevalent in all types of crystals of aromatic compounds, it was possible to divide fused aromatic hydrocarbons into four categories that are illustrated in Fig. 1: (a) the pure herringbone structure (naphthalene, anthracene) contains nearest-neighbour molecules which are related *only* by the inclined T-geometry and have short axes in the 5.4–8.0 Å region; (b) the coronene group of Robertson was designated as γ -packing and was shown to contain *both* herringbone and stacking geometries. The short axis range for this group is between 4.6–5.4 Å; (c) another group of structures with a monoclinic axis greater than 8.0 Å was also found to exhibit both herringbone and stacking geometries but here, molecular dimers were observed. This group is exemplified by pyrene and perylene and was designated the 'sandwich-herringbone' structure; (d) planar hydrocarbons do not crystallise so that *only* stacking interactions are found between nearest-neighbours, but such a possibility exists for cup-shaped molecules like tribenzopyrene. This category was designated as β -packing and it has short axes less than 4.2 Å.

With such an analysis it became possible to predict the packing pattern of any given aromatic hydrocarbon. It was recognised that the herringbone interaction (glide or screw-forming tendency) was promoted by the presence of hydrogen atoms and rim-carbon atoms, while the stacking interactions would be favoured by the presence of many internal carbon atoms in the molecular structure. Glide-stack ratios were therefore derived on the basis of empirically designated glide and stack-forming propensities for each atom in the molecular structure. Plotting these ratios against molecular surface area introduces the idea of molecular shape and with it a mapping from molecular to crystal structure. Our predictions of crystal structure from molecular structure were satisfying but even at the time we were well aware that they are accurate only because the forces in hydrocarbon crystals are isotropic.

Hydrocarbon crystals are exceptional in this regard. Most organic compounds contain heteroatoms and the intermolecular interactions in their crystals are a complex mosaic of forces of varying strengths, directionalities and distance dependence characteristics.¹ Anisotropic, long-range forces tend to dominate crystallisation preferences even as the isotropic forces contribute to the bulk of the crystal sublimation energy. These anisotropic forces are not minor irritants but conspire to render almost impossible direct and simple extrapolations from molecular to crystal structure. A functional group approach is unsuitable because the molecular recognition events during crystallisation depend on the complementarity of molecular structural features rather than on their identity. This is a fundamental problem. Suppose a general molecule to have recognition sites A, B, C, ... and so on. Then, possible recognition patterns could be found from among combinations such as A...B, B...C, A...C or from more complex patterns such as (A,C)...(B,D) or (A,B,C)...(D,E). Each favourable pattern would limit the possibilities for subsequent, subsidiary patterns, but in general the presence of even a moderate number of competitive recognition sites in a molecule, say three or four functional groups capable of hydrogen bonding, could result in a large number of crystal structures $C_1, C_2, C_3 \dots C_n$ from a single molecular structure M_1 . Most of these structures C_1-C_n

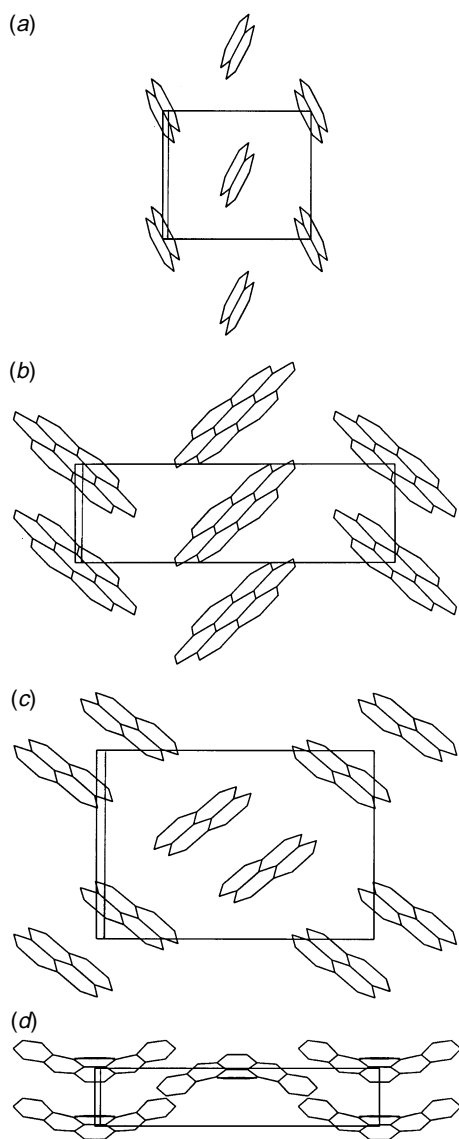
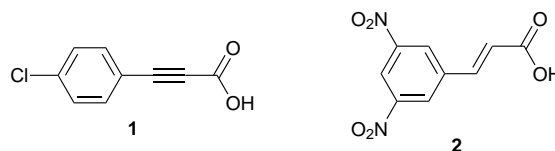


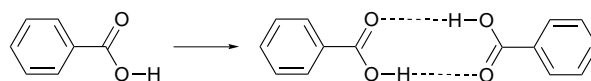
Fig. 1 The four basic aromatic crystal packings: (a) naphthalene, (b) coronene, (c) pyrene, and (d) tribenzopyrene. The short axes are vertical in each case.

are not routinely realisable in the solid state because polymorphism is not a universal phenomenon. However, even in this mitigating circumstance, the prediction of the experimentally observed structure C_m is not trivial.¹¹ Computer simulations show that structures C_1-C_n are often closely related enthalpically and the global minimum structure is not always the one that is obtained experimentally, either because the computations are approximate or because the crystallisation process is subject to both kinetic and thermodynamic factors.

A typical manifestation of these problems is illustrated by the anomalous crystal structures of 4-chlorophenylprop-2-ynoic acid **1** and 3,5-dinitrocinnamic acid **2**. Usually it is expected that



carboxylic acids, especially those containing aromatic groups, crystallise with the dimer structure. A few acids adopt the catemer structure but such occurrences have been well-rationalised.¹² This molecular monomer \rightarrow crystalline dimer transform is the basis of several recent experiments in crystal engineering and many would accept this transform as an article of faith.



However, acid **1** adopts a rare crystal structure with two symmetry independent molecules (Fig. 2).¹³ In one, the carboxy group has a *syn* conformation while in the other, it is *anti*. The hydrogen bonding pattern is not quite a catemer but contains alternating molecules with the *syn* and *anti*-conformations. To compound the confusion, each hydrogen bond lies on a centre of inversion and the resulting hydrogen atom disorder does not disappear even at low temperature. In contrast, the almost identical (in molecular terms) 4-chlorocinnamic acid, adopts the 'normal' dimer structure. Again, while acid **2** (space group $C2/c$) forms an O-H...O dimer ring, this ring lies on the 2-fold axis rather than on the inversion centre.¹⁴ These anomalous occurrences have been rationalised on the basis of C-H...O hydrogen bonding. In acid **2**, C-H...O hydrogen bonds are dominant and numerous and seem to be so significant that they are able to change the site symmetry of the carboxylic acid O-H...O dimer ring. In **1**, however, their absence (because of the lack of a critically large number of acidic C-H groups in the molecular structure) seems to lead to the unusual *quasi*-catemer structure. C-H...O hydrogen bonds are just one of the several secondary features that can influence, often unpredictably, crystal packing and they have been discussed extensively elsewhere.¹⁵⁻¹⁷

To summarise, a molecular functional group approach is often difficult in attempting to answer the question, 'given the

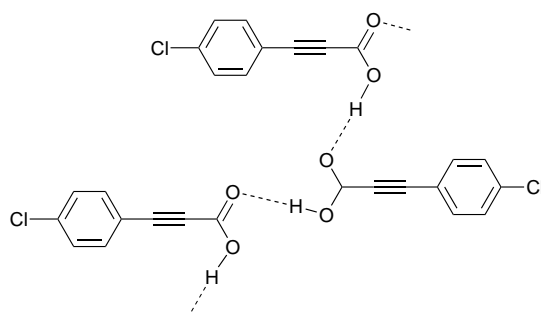


Fig. 2

molecular structure of an organic substance, what is its crystal structure?' Of course, this question betrays the molecular basis of classical organic chemistry. Crystals are supermolecules and their structural features are best described in terms of supramolecular descriptors, that is patterns of interactions rather than in terms of molecular descriptors, that is functional groups. A one-to-one correspondence does not exist between functional groups and patterns of interactions and so questions relating to the prediction of supramolecular (crystal) structure from molecular structure (i) are difficult to answer, (ii) may have multiple answers, and (iii) may not even be the most relevant questions one might want to ask.

The crystal as a supramolecular entity

The term 'supramolecular' signifies that which is beyond the molecule and supramolecular concepts have had the greatest influence in organic chemistry where the molecule is paramount. Supermolecules are not merely collections of molecules but they have structural features and properties that are characteristic not of the molecules themselves but of larger, more extended assemblies.¹⁸ In keeping with this, structural chemists and crystallographers have had little difficulty in recognising an organic crystal as the ultimate example of a supermolecule.^{5,19} Indeed, crystals constitute one end of the supramolecular continuum and may be viewed as 'hard' supermolecules in contrast to the 'softer' supramolecular aggregates which exist in solution. Atoms, covalent bonds and molecules have their counterparts in molecules, intermolecular interactions and supermolecules. Accordingly, it is not hard to visualise polymorphism as superisomerism and to identify structural homologous series such as benzene, naphthalene and anthracene.

If a crystal is a supermolecule, then crystal engineering is the solid state supramolecular equivalent of organic synthesis.⁶ Synthesis is the distinctive feature that demarcates chemistry from the other physical sciences—*la chimie crée son objet*;²⁰ yet it is only in recent times that synthetic supramolecular chemistry has assumed definite contours. If studies of supramolecular systems should even be a part of chemistry, then the time-tested principles of synthesis should be found to be applicable to them. In this regard, the role of the solid state is especially relevant. Unlike solution supermolecules whose formation could often be influenced by solvent effects, the formation of stable crystal forms permits the establishment of even weak interactions which, when numerous, may affect supramolecular structure decisively. So, crystal structure as defined as a networking of intermolecular interactions is the supramolecular equivalent of molecular structure as defined as a networking of covalent bonds.

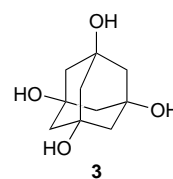
Crystal engineering and organic synthesis

In general, any synthetic activity, in chemistry or elsewhere, may be said to possess three attributes: target identification, strategy and methodology. In loose terms, these attributes amount to knowing the job at hand, what to do, and how to do it. It is pertinent to examine the subject of crystal engineering from this standpoint.

Target identification in traditional organic synthesis consists in knowing the molecular formula of the goal molecule with all the attendant stereochemistry. Crystal engineering is supramolecular synthesis and so targets here must be defined supramolecularly, that is as networks. This is not a familiar exercise. Traditionally, structural chemists have viewed a molecular crystal as an assembly of atoms in which the distances between atoms in certain groups (molecules) are much smaller than the distances between atoms in different groups.²¹ This depiction owes to Kitaigorodskii but again betrays the molecular view of organic chemistry. Even the title of Kitaigorodskii's classic *Molecular Crystals and Molecules* reflects this bias. Yet, any organic crystal may be depicted as a

network with the molecules as nodes. Such a depiction, although unusual, is not completely new. In Powell's 1948 illustrations of the β hydroquinone clathrates, for example, only the network structures are shown.²² The molecules have been reduced to points. If such an operation is carried out on the orthorhombic polymorph of benzene, the result is not far from a face-centred cubic lattice. Of course, hydrogen bonded structures lend themselves easily to a network depiction but in the end, any organic structure may be thus viewed.

The development of network theory to organic crystal chemistry is novel but this is hardly the case for inorganic crystal structures. Thus the logical step after depicting an organic crystal structure as a network is to search for its inorganic counterpart. Such comparisons are not just chemical curiosities but play a very important part in the development of a proper theory of crystal engineering, because one is able to draw from the very considerable literature which exists in the inorganic structural domain to choose new target networks. In this context, the structure of 1,3,5,7-tetrahydroxyadamantane **3**



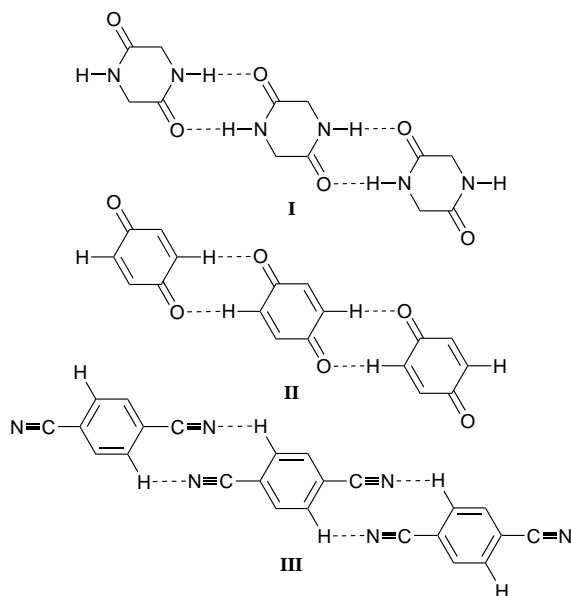
is especially interesting.²³ The crystal packing of this compound may be clearly understood only when it is simplified and reduced in terms of its hydrogen bond network. The structure is intricate and belongs to the uncommon space group *Pbcn* with molecules in both general and special positions. The structure also contains many strong O—H...O hydrogen bonds and our attempts to decipher the packing by conventional methods (plots, geometrical calculations) proved unsuccessful. As an alternative strategy, we sought to develop a structural analogy between **3** and a simple inorganic structure. Now, a hydroxy group has a supramolecular valence of two, corresponding to a pair of hydrogen bonds, one donated and the other accepted. Therefore the packing of **3** should be derivable in terms of an eight-connected net. So we simplified the structure of **3** by reducing the molecules to spheres and displaying only the hydrogen bond connections. The result is shown in Fig. 3 which is easily recognisable as a *quasi*-BCC packing. If one distinguishes between the symmetry independent molecules, one could liken this structure to CsCl or, more strictly speaking, to Cr₂Al.

Supramolecular synthetic methodology amounts to a knowledge of the strength and directional characteristics of the intermolecular interactions. Much has been written and said about this topic¹ and I will merely list some of the more important interactions here. Yet, as in molecular synthesis, this is the most arduous component in the synthetic exercise, requiring much knowledge and experience. In addition to the well-understood strong hydrogen bonds of the O—H...O, N—H...O and N—H...N type, weak hydrogen bonds of the C—H...O(N) and O(N)—H... π type should also be considered. A number of other weak heteroatom interactions such as N...halogen, S...S and halogen...halogen are known to have specific effects upon crystal packing, while the more exotic organometallic interactions (O—H...M, M—H...O, Au...Au) are only now beginning to be noticed.⁶ A mention must be made of interactions in hydrocarbon systems. It is known for instance that phenyl groups pack with very specific geometries, leading to crystals that are characterised by high crystallinity and low solubility—the so called 'phenyl factor'.²⁴ In this context, it is still not clear if the C—H... π 'hydrogen bond' is an extreme case of the herringbone interaction.

The node connections in the network depiction of an organic crystal structure are of greater significance than the nodes. These connections consist of recognisable groups of inter-

molecular interactions and the term *supramolecular synthon* has been suggested in analogy to molecular synthons in organic synthesis.^{6,25} Like molecular synthons, supramolecular synthons enable a focussing of synthetic strategy and allow the synthetic chemist to attack general supramolecular targets. Supramolecular synthons incorporate both chemical and geometrical aspects of molecular recognition. In principle, a given supramolecular structure contains a very large number of supramolecular synthons. However, in the most useful and significant of these, a maximum of structural information is encapsulated within the most economically-sized unit. If information is a measure of the amount of form—*Information ist das Mass einer Menge von Form*²⁶ the most useful synthons combine smallness with form.

Consider for instance the linear ribbon structures of piperazine-2,5-dione, 1,4-benzoquinone and 1,4-dicyanobenzene. The network depictions of each of these structures are identical. The supramolecular synthons **I**, **II** and **III** are equivalent though



they are constituted with strong (**I**) and weak hydrogen bonds (**II**, **III**) respectively. A knowledge of the piperazine-2,5-dione structure and the directional properties of C–H...O and C–H...N hydrogen bonds allows an anticipation of the benzoquinone and dicyanobenzene crystal structures. Widely different substances can have the same or similar crystal structures and in this manner, supramolecular synthons may be invoked in crystal design strategies.

From network to molecular structures—retrosynthesis

Implicit in the supramolecular synthon approach to crystal engineering is the identification of a crystal as a retrosynthetic

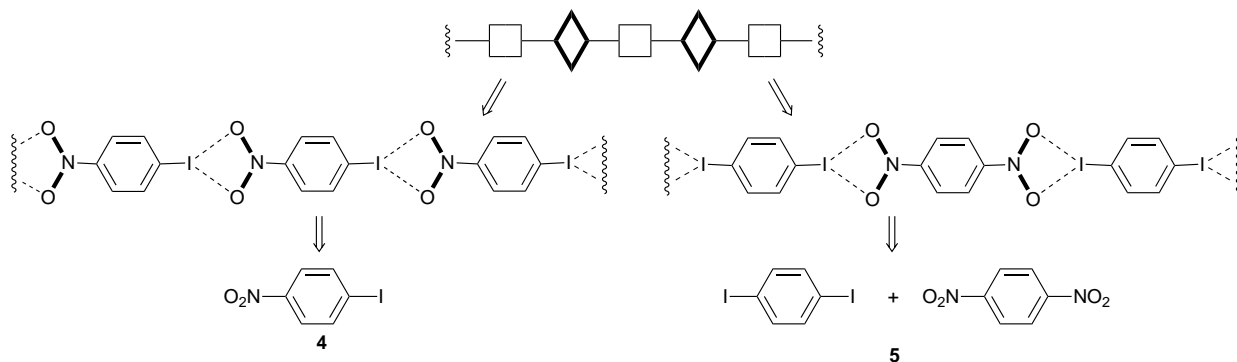
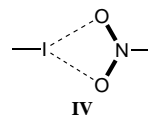


Fig. 4

target. As stated above, a target is defined in terms of a network and a typical example of supramolecular retrosynthesis is now illustrated with reference to structures based on the polarisation induced iodo...nitro synthon **IV**.^{27,28} Previous work showed that



there is a definite tendency for I atoms to make short, attractive contacts with nitro groups and a possible synthetic target is a linear ribbon (Fig. 4). If one alternates synthon **IV** with phenyl rings, 4-iodonitrobenzene **4** suggests itself retrosynthetically as a molecule that has few other crystallisation options. In the crystal structure of **4**, the desired ribbon pattern is obtained. The

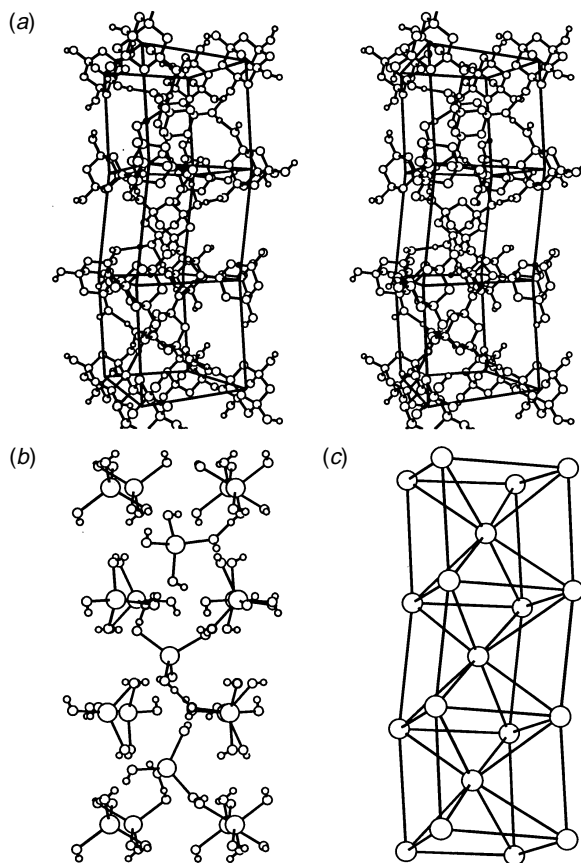


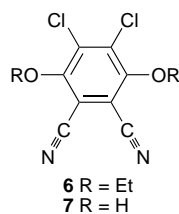
Fig. 3 (a) Stereoview of the crystal structure of 1,3,5,7-tetrahydroxyadamantane **3**; (b) same as (a), with the adamantyl skeleton reduced to a sphere; (c) same as (b) with the entire molecule reduced to a sphere and hydrogen bonds shown as lines. Notice the similarity of (c) to the CsCl structure.

strategy may be extended to the crystal structure of the 1:1 complex **5** of 1,4-diiodobenzene, and 1,4-dinitrobenzene where again synthon **IV** alternates, but in opposite senses, with the phenyl rings. Retrosynthetic analysis of the linear ribbon target shows that the crystal structures of compound **4** and complex **5** are equivalent. Such observations reiterate that distinct molecular structures M_1, M_2, M_3, \dots may in general be associated with the same crystal structure C_m .

The future—designer crystals

Crystal engineering is poised today at an exciting intersection of structural and supramolecular chemistry and combines scientific rigour with artistry and skill. If truly designer crystals are to become a reality, progress will become necessary in each of the three synthetic aspects: target identification, methodology and strategy.

Unlike in molecular synthesis, target identification (network designation) in crystal engineering is a non-trivial exercise. Progress in network theory and information science, coupled with technical advances in current database software such as the Cambridge Structural Database,²⁹ will probably become indispensable if crystal structures are to be routinely notated as networks. Consider for instance the similar networking of molecules in the 1,4-diethoxy **6** and 1,4-dihydroxy derivative **7**



of 2,3-dicyano-5,6-dichlorobenzene (Fig. 5).³⁰ In both cases, tetrameric loops are formed. In **6** the relevant interaction is the polarisation-induced $C\equiv N\cdots Cl-C$, while in **7**, conventional hydrogen bonding of the $C\equiv N\cdots H-O$ type is involved. Interestingly, the $O-H\cdots O$ bonded tetramers in α -oxalic acid and squaric acid are topologically related to **6** and **7**. It would be desirable if comparisons such as these could be generated routinely through database protocols.

Improved supramolecular synthetic methodology will consist of obtaining more accurate and reliable information on intermolecular interactions. It is clear that a very large number of precise, low temperature X-ray structure determinations will be obtained in the future. Neutron diffraction analysis will become increasingly common as a means of studying and characterising unusual types of hydrogen bonding. We have recently collaborated with Judith Howard of the University of Durham on the neutron diffraction analysis of 2-ethynyladamantan-2-ol, which contains an $O-H\cdots\pi$ hydrogen bond and have shown that the $O-H$ group points to the centre of the alkyne bond rather than towards one of the carbon atoms that form this bond.³¹ Joint studies with Dario Braga of the University of Bologna have confirmed the existence of a number of soft hydrogen bond-like interactions: $M-H\cdots O$, $O-H\cdots M$, $C-H\cdots O\equiv C-M$ and the *pseudo*-agostic $C-H\cdots M$.³² How useful all these interactions will be in a general sense remains to be seen. However, it is worthwhile to note that molecular synthesis progressed greatly with an array of novel reactions and if the molecule–supermolecule analogy continues to be a reliable predictor of future events, then it is only a matter of time before the exotic interactions begin to be exploited in crystal engineering.

Another compelling need is to be able to visualise a crystal structure in its entirety, not just look at selected intermolecular interactions which have been deemed to be important. The vast majority of organic crystal structures are best considered as an interplay between the medium range, isotropic forces and the long range, anisotropic forces. Sometimes, the directional

requirements of these forces act in consonance, at other times in conflict and it is hard in any given situation to predict if the isotropic or anisotropic forces will dominate. This variable and subtle interplay of intermolecular forces is both confusing and annoying. It is simplistic at best and grossly misleading at worst to try and analyse, even more so to try and design, crystal structures on the basis of only a single type of intermolecular interaction. The understanding of the interplay of intermolecular interactions is a major challenge in the practice of crystal engineering today because secondary and tertiary features often control structurally important attributes of a crystal, for example, the presence or absence of an inversion centre. Along these lines, we have been collaborating with Frank Allen of the Cambridge Crystallographic Data Centre in the use of an interaction display program, NIPMAT.³³ This program creates a pictorial matrix using the atoms in the molecular skeleton ($A_1, A_2, \dots, A_m, \dots, A_n$) in which the matrix element $A_m A_n$ is defined as representing the shortest intermolecular contact $A_m \cdots A_n$ in the crystal. Each matrix element is shown in terms of a grey scale. The shorter the contact, the greyer the square which represents that particular contact. Therefore, the plot obtained (see Fig. 6 for the NIPMAT plots of naphthalene and terephthalic acid) is a visual representation of *all* the intermolecular interactions *simultaneously*. These plots show the utter difference in packing in these two structures. In naphthalene, $C\cdots H$ interactions are important coupled with an overall isotropic packing. This is shown by the overall greyness of the plot. In terephthalic acid, $O-H\cdots O$ hydrogen bonding and $C\cdots C$ stacking are important and the packing is more directional. This is shown by the more black-and-white appearance of the plot.

It is in the area of new synthetic strategies that the most exciting developments may be expected. An appreciation of supramolecular synthons not only as structural units but also as

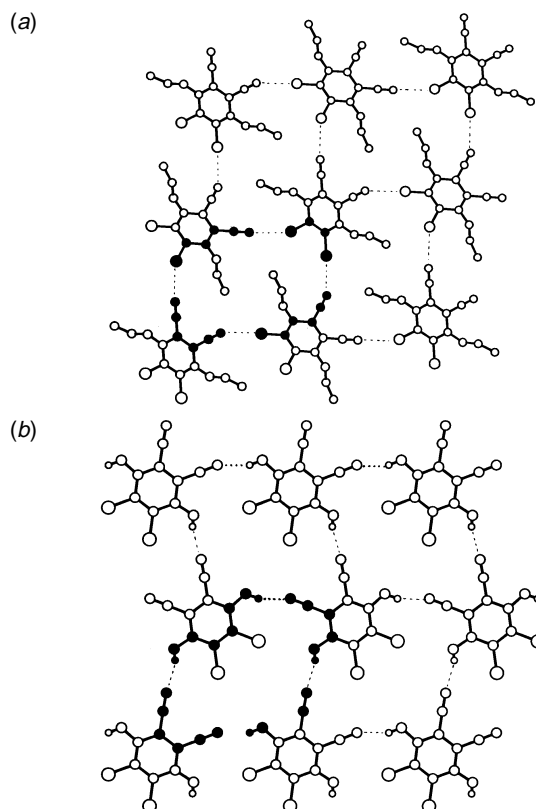
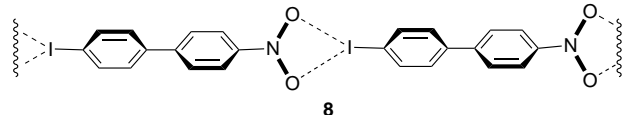


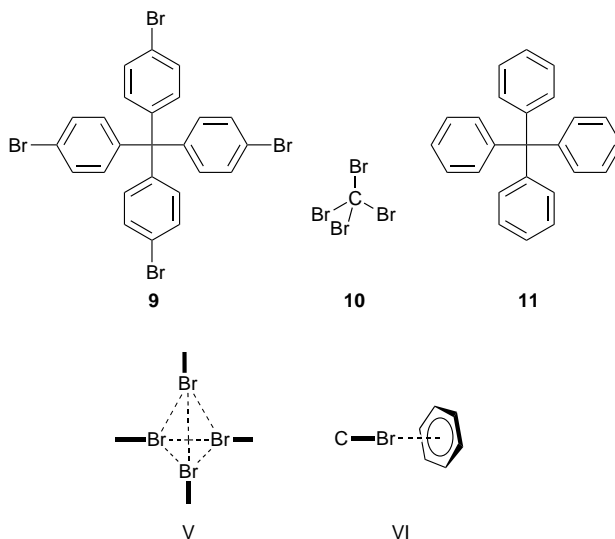
Fig. 5 Networking of molecules in (a) 1,4-diethoxy-2,3-dicyano-5,6-dichlorobenzene **6** via $C\equiv N\cdots Cl$ interactions and (b) 1,4-dihydroxy-2,3-dicyano-5,6-dichlorobenzene **7** via $C\equiv N\cdots H-O$ hydrogen bonds. These networks are topologically similar although the interactions are quite different.

being responsible for characteristic supramolecular properties may lead to novel and unexpected solid state structures. In a recent report, we have shown that the linear ribbon structure of 4-nitro-4'-iodobiphenyl **8** may be retrosynthetically derived by



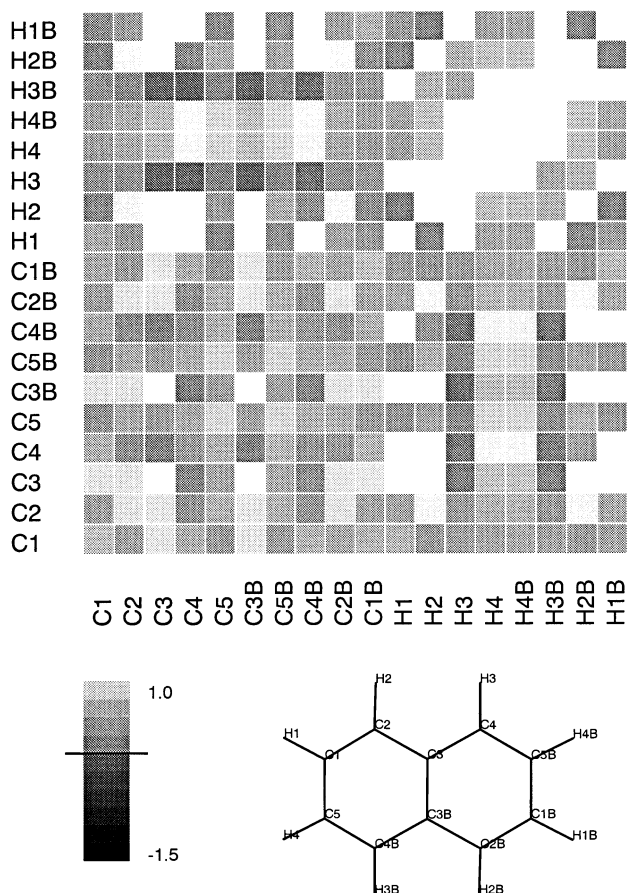
an interleaving of the iodo-nitro synthon **IV** and the twisted biphenyl molecular synthon.³⁴ The chiral ribbons that result pack in the non-centrosymmetric space group *Fdd2* and the crystals display moderate SHG activity ($\times 6$ urea). The term 'supramolecular chiron' has been suggested.³⁵ More interestingly, the calculated molecular hyperpolarisability β , of **8** is only 4.3×10^{-30} esu. This observation hints that the crystal SHG has contributions also from the polarisation-based synthons **IV**. Many useful crystal properties are a consequence of molecular *and* supramolecular structure. It is therefore not surprising that supramolecular hyperpolarisability as manifested in synthons such as **IV** are important.

A final example demonstrates the equivalence of appropriate molecular and supramolecular synthons in crystals of tetrakis-(4-bromophenyl)methane **9** and the 1 : 1 molecular complex of CBr_4 **10** and tetraphenylmethane **11** (Fig. 7).³⁶ In **9**, a diamondoid network is formed by linking the tetraphenylmethane units with the tetrahedral supramolecular synthon **V**. Four bromine atoms are arranged in a tetrahedral fashion and the distance between any two of them is 3.91 Å. If the empty centroid in **V** is considered as a phantom 'carbon' atom, then the cluster approximates to a super- CBr_4 molecule.



One can now interchange the molecular and supramolecular synthons in the structure of **9**. The Br_4 clusters **V** are connected to the tetraphenyl moieties through C-Br covalent bonds. It was expected that these Ph-Br molecular synthons could be replaced with the supramolecular synthon **VI**, which is based on the $\text{Br} \cdots \text{phenyl}$ interaction. In other words, the replacement of **V** with CBr_4 accompanied by the concomitant replacement of **9** by **11** should lead to no major structural change. In practice, co-crystallisation of CBr_4 **10** and **11** led exclusively to the formation of a complex which is nearly isostructural with **9**. In

(a) Crystal packing for CSD-NAPHTA10



(b) Crystal packing for CSD-TEPHTH

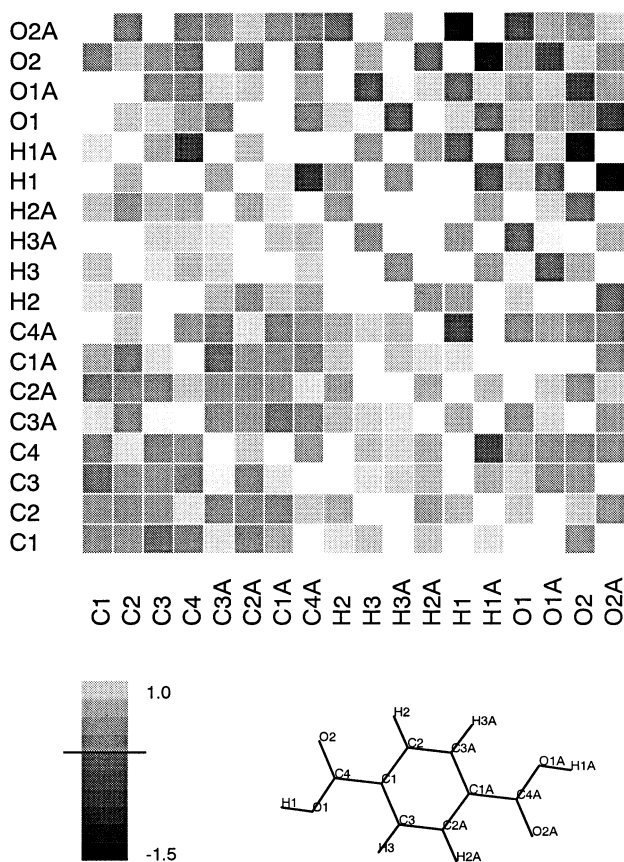


Fig. 6 NIPMAT plots of (a) naphthalene (NAPHTA10) and (b) terephthalic acid (TEPHTH). Notice that the packing in the former is of a more isotropic nature.

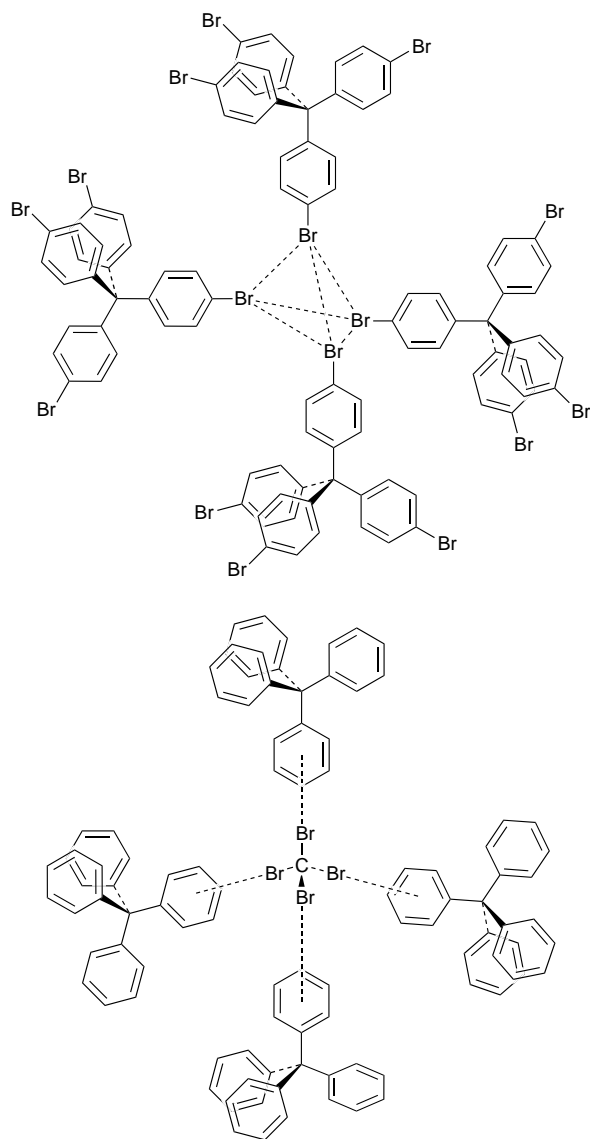


Fig. 7

the complex, four molecules of **11** are linked to a CBr_4 molecule through synthon **VI** ($\text{Br}\cdots\text{phenyl ring centre } 3.67 \text{ \AA}$). There are no major differences in the crystal structures of **9** and the complex of **10** and **11**, and both may be simplified to distorted diamondoid networks. Although these crystal structures are formed from widely different components (**9** is a one-component crystal while the complex is a two-component crystal), they have close similarities at the supramolecular level. Most intriguingly, the distance between the bromine in the tetrahedral synthon **V** is only 12% greater than the $\text{Br}\cdots\text{Br}$ distance in the CBr_4 molecule. Observations such as this almost seem to challenge Kitaigorodskii's definition of a molecular crystal as one in which the distances between certain groups of atoms (molecules) are much smaller than the distances between atoms in different groups.²¹

Crystallography and organic chemistry

The research described in this article is but another statement in the dialogue that has existed between X-ray crystallography and organic chemistry throughout this century.³⁷ This dialogue has been sometimes friendly and sometimes not, but it has always led to unexpected and fruitful developments in both subjects. Schmidt, in general, did not differentiate between these subjects when he extended the topochemical principle to organic

reactions,² nor did say Bürgi and Dunitz when they developed the idea of structure correlation.³⁸ This article began with a reference to the tremendous strides in the practice of crystallography today and it has hopefully gone on to show that with the corresponding reduction of experimental burden, the endeavours of the chemical crystallographer may profitably be harnessed towards supramolecular synthesis. Crystallographers have always been confounded by technical strides in their subject and yet have always responded successfully by redefining their subject. It was J. M. Robertson who, while commenting on new methods in crystallography in the early fifties, predicted that, 'In the future, it is to be expected that the new methods will outstrip the standard degradative procedures of organic chemistry and the energies of the chemist will then be freed to concentrate on his second major problem, that of synthesis, which *at present* lie beyond the scope of crystallography'.³⁹ It is with a keen sense of pleasure therefore that I draw the attention of the reader to how accurately Robertson was looking into the distant future, to a time when the subject of synthesis would come well within the ambit of X-ray crystallography.

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