SOME STUDIES OF INTERMOLECULAR INTERACTIONS AND SUPRAMOLECULAR SYNTHESIS: APPLICATIONS TO CRYSTAL ENGINEERING

A Thesis
Submitted for the Degree of
Doctor of Philosophy

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March 1998

To

Amma and Bapu

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of the investigations carried out by me in the School of Chemistry, University of Hyderabad under the supervision of Professor Gautam R. Desiraju.

In keeping with the general practice of reporting scientific observations due acknowledgements have been made wherever the work described is based on the findings of other investigators.

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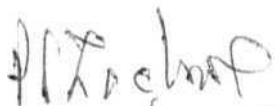
Hyderabad
March 1998

Venkateshwar Rao Thalladi

CERTIFICATE

Certified that the work 'Some Studies of Intermolecular Interactions and Supramolecular Synthesis: Applications to Crystal Engineering' has been carried out by **Venkateshwar Rao Thalladi** under my supervision and that the same has not been submitted elsewhere for a degree.



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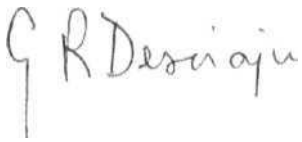

Professor Gautam R. Desiraju
Thesis Supervisor

ACKNOWLEDGEMENT

It gives me great pleasure to thank my research adviser Professor Gautam R. Desiraju for introducing me to this fascinating field of research. He has been inspiring and the discussions with him have been thought provoking.

I would like to thank Dr. Ashwini Nangia for his helpful guidance during the later stages of my Ph.D. work. It is my pleasure to thank Prof. Dr. Roland Boese, University of Essen, Germany for hosting me in his laboratories during May-July 1996, and for teaching me the principles of X-ray structure determination. My special heart-felt thanks for his concern regarding my livelihood there.

I thank Prof. P.S. Zacharias, Dean, School of Chemistry and all the faculty members of the School for their co-operation.

I would like to acknowledge the assistance of Dr. H.L. Carrell, Fox Chase Cancer Center, Philadelphia, U.S.A., Prof. J.A.K. Howard, University of Durham, U.K., and Prof. R. Boese, University of Essen, Germany for collecting the X-ray diffraction data on the compounds studied in this work, and Prof. J. Zyss, CNET, France for NLO characterisation of the compounds discussed in Chapters 5 and 6. Thanks are due to Mr. H.-C. Weiss and Dr. S. Brasselet for friendly and helpful discussions.

I thank Prof. A Krishnamurthy, Kakatiya University, Warangal for his encouragement.

I wish to thank my friendly and co-operative labmates Drs. V.R. Pedireddi, K Panneerselvam, C.V.K Sharma, B.S. Goud, D.S. Reddy, K. Biradha, P.S. Chandrakala, P. Senthivel, M. Muthuraman and Messrs. A Anthony, R. Thaimattam, K.S. Srinivasan, J.R.K Rao, P.K Thallapally, V.S.S.Kumar and Ms. N.N.L. Madhavi for the pleasant atmosphere they have extended I wish to thank all my friends in the School of Chemistry for making my stay in the School an enjoyable one. I also wish to thank all the colleagues at the University of Essen for their help during my stay in Germany.

I thank all the personnel of the School of Chemistry, COSIST building and Computer Center for their help.

I thank the UGC and the DAE for fellowship support during my research tenure, I thank the Heinrich Hertz-Stiftung des Landes Nordrhein-Westfalen, Germany for funding my visit to the University of Essen, Germany during the period May-July 1996.

A special note of thanks to Frau and Madhavi who helped me during the preparation of this thesis.

It would be too formal to thank Kittu and Santhu who have always been with me. I wish to thank Shekhar, Madhavi and Mytri for extending their timely support. My special thanks to Wiola and Marcin who made my stay in Germany an enjoyable and memorable one.

The blessings and the best wishes of my family members made me what I am and I owe my everything to them. I am at loss for words to express my gratitude to the one with whom I share all my feelings.

Venkat R. Thalladi

PREFACE

Crystal engineering involves the rationalisation and synthesis of crystal structures. An organic crystal is the ultimate supermolecule and therefore crystal engineering is a supramolecular equivalent of organic synthesis Molecular association in crystals is governed by intermolecular interactions. Supramolecular synthons are the substructural units made of intermolecular interactions and play a very important role in crystal architecture. The utility of the supramolecular synthon concept in crystal engineering is illustrated in Chapter 1 and this concept is the crux of the thesis.

Chapter 2 describes the neutron diffraction analysis of the crystal structures of 2- and 3-aminophenols. It has been shown that the molecule → crystal structure relationship does not hold as might have been expected from a functional group approach. The selectivity in the choice of supramolecular synthons is discussed.

The role of the C-F group in crystal packing is described in Chapter 3. Comparative analysis of the crystal structures of a series of hydroquinones has shown that the C-F group is indecisive in adopting a specific structural pattern dictated by either C-H or C–Cl (C-Br) groups. C-H-F interactions have been shown to exist in the crystal structures of a series of fluoro-substituted benzenes. These compounds are liquids at room temperature and the single crystals are grown using a special technique. It has been shown that C-H-F interactions have the hydrogen bonding character and that they are similar to C–H ··O and C–H···N hydrogen bonds in their nature. The F-atom has been shown to be distinctly different from rest of the halogens in that it does not form F·· F interactions.

Supramolecular retrosynthesis of linear ribbon structures based on I ··NO_2 synthons is discussed in Chapter 4. The robustness of I···NO_2 synthons has been shown and the concept of interchangeability of molecular and supramolecular synthons has been utilised.

The use of C–H···O hydrogen bonds in the construction of trigonal two-dimensional networks has been presented in Chapter 5. Retroanalysis of such networks leads to trialkyl isocyanurates as the starting materials. The carry-over of molecular symmetry into the crystal is difficult. This has been achieved, with the aid of structural insulation, in the case of trimethyl isocyanurate by complexing it with 1,3,5-trinitrobenzene. An octupolar non-linear optical crystal has been engineered based on C–H···O hydrogen bonds.

Crystal engineering of NLO active substances has been generally based or dipolar paradigm. Octupolar systems have been expected to overcome the disadvantages posed by the dipolar moieties. Supramolecular synthesis of trigonal octupolar networks in a family of triaryloxy triazines is presented in Chapter 6. Piedfort units generated from these molecules assemble into trigonal networks using herringbone interactions. The principles of crystal engineering have been used to study the effect of substitutional variation in the kind of network structure generated. Crystal engineering of trigonal and hexagonal network structures has been shown to be possible. The supramolecular retrosynthetic approach described in this chapter provides structural control in two dimensions whereas control in the third dimension still remains to be achieved in a general sense.

Salient crystallographic details of the crystal structures discussed in this thesis have been given in an appendix at the end of the thesis. A full list of atomic coordinates has been deposited with University of Hyderabad and can be obtained from Prof. Gautam R. Desiraju, School of Chemistry, University of Hyderabad, Hyderabad, India.

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Hyderabad
March 1998

CONTENTS

CHAPTER ONE

CRYSTAL STRUCTURES - RATIONALISATION AND SYNTHESIS

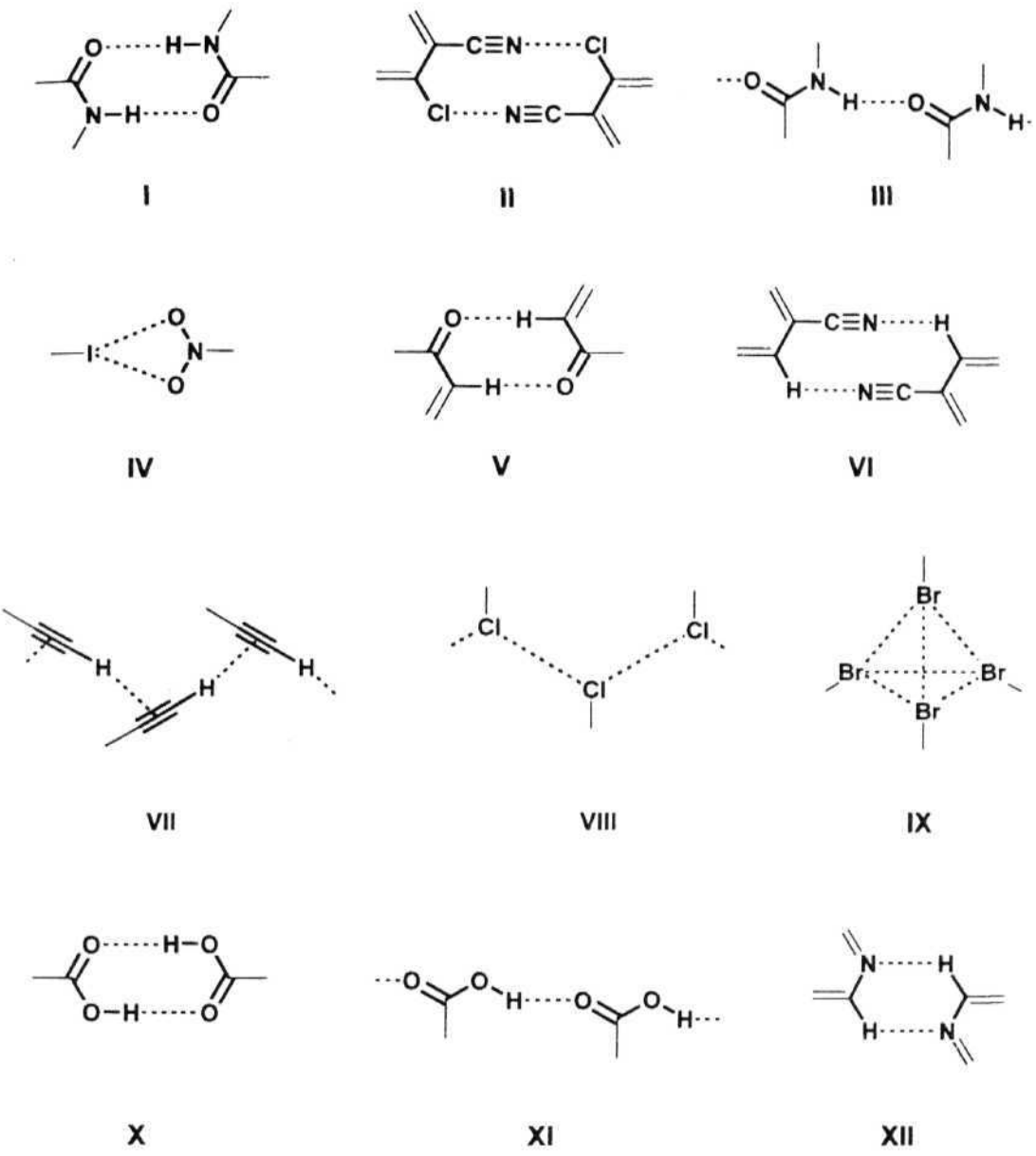
1.1 Introduction

The design of molecular solids with desired physical and chemical properties is a major endeavour of current chemical research. This constitutes what is broadly known as *crystal engineering*.[1] The ever-growing demand for functionalised materials coupled with the quest for understanding the fundamentals that govern crystal packing have been responsible for the development of crystal engineering into a mature subject.[2] An organic crystal has been recognised as a supermolecule *par excellence* wherein an infinite number of molecules are held together by intermolecular interactions.[3] Molecular association leads to the formation of supermolecules and the field of supramolecular chemistry, that is the chemistry of molecular assemblies and of the intermolecular bond, has developed into a distinct area of research.[4] Realising that the supramolecular equivalent of a molecule is a crystal, with atoms and covalent bonds being replaced by molecules and intermolecular interactions, crystal engineering has been discerned as supramolecular synthesis in the solid state.[5,6] Crystal engineering has two important components: rationalisation and synthesis. Both these aspects are discussed in the following sections. Rationalisation involves the analysis of crystal structures and the knowledge thus gained is utilised in the synthesis of new structures.

1.2 Intermolecular Interactions and Supramolecular Synthons

The mutual recognition of molecules in the crystal is governed by intermolecular interactions. An understanding of these interactions is therefore essential for crystal engineering studies. Various interactions have been identified: strong hydrogen bonds (O–H O, O–H···N, N–H···O, N-H-N), weak hydrogen bonds (C–H···O, C–H···N, O–H···π, N–H···π, C–H···π) and interactions

involving halogens and other heteroatoms such as N, O and S. Analysis of an individual crystal structure leads to the identification of intermolecular interactions pertaining to a specific structure. The Cambridge Structural Database (CSD) facilitates the analysis of a large number of crystal structures. The geometrical attributes of intermolecular interactions and their chemical characteristics can be studied reliably by statistical analysis. Implicit in the statistical approach to crystal engineering is an insight into the various ways in which the interactions can be grouped together to form substructural units. These substructural units have been variously termed as motifs, building-blocks, patterns. couplings and synthons. Supramolecular synthons are "structural units within supermolecules which can be formed and/or assembled by known or conceivable synthetic operations involving intermolecular interactions".[5] It should be noted that supramolecular synthons are designed combinations of interactions and are not identical to the interactions. The supramolecular synthon concept is flexible and permits classification over a wide range of structures. At times a single interaction may be considered as a synthon while in other cases many interactions may be implicit in a particular synthon. Accordingly, chemical and geometrical information is contained in the term 'supramolecular synthon' and in this respect this terminology is superior to other descriptors. Many substructural motifs can be identified from the dissection of a crystal structure and therefore caution should be taken in the choice of a particular supramolecular synthon (a discussion on the selectivity of supramolecular synthons is presented in Chapter 2). Scheme 1 shows various supramolecular synthons discussed in the present chapter. The utility of this concept is revealed in the following sections and in the forthcoming chapters.

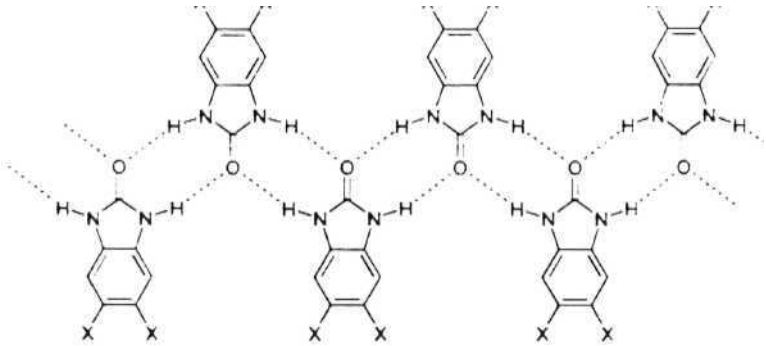


Scheme 1. Supramolecular synthons discussed in this chapter.

1.3 Comparison of Crystal Structures

Crystal structures are the starting points for crystal engineering and structural comparison has been found to be a rewarding exercise. Rationalisation of crystal structures involves such comparative analysis. In this regard, a favoured strategy has been to compare a series of closely related crystal structures that contain a

common functionality of interest and which differ slightly at the molecular level. Two variations of this strategy may be identified. One approach is to keep the basic core of the molecule constant while varying some of the functionalities or positioning them in different locations on it. In the other approach, functional groups (similar or dissimilar) of interest are consistently positioned in a particular fashion while the molecular core is varied slightly. Some gross structural patterns may be discerned in a family of structures, provided many crystal structures are studied. Such structural analysis leads to an understanding of the interplay between various kinds of interactions that exist in these structures. What is *of* interest is that robust supramolecular synthons can be identified from studies of this kind.



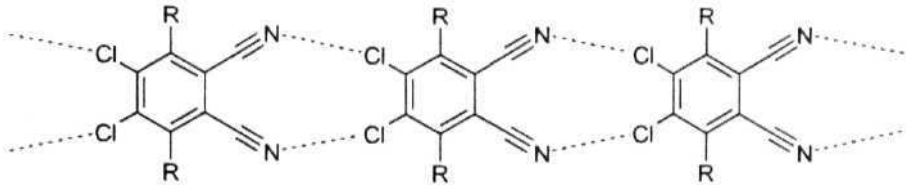
Scheme 2. Synthon I mediated linear tapes in the crystal structures of 2-benzimidazolones.

1.3.1 Fixed Molecular Core

Two recent examples illustrate the strategy of a fixed molecular core. In a study of a series of crystal structures of 2-benzimidazolones, the Whitesides group has observed two major structural patterns (Scheme 2). Four of the derivatives in addition to the parent compound form a one-dimensional tape structure based on synthon I whereas two others produce three-dimensional hydrogen bonded networks that are open variations of the linear tapes. The differences in the association of tapes in the crystal structures within the first

category, and the reasons for the formation of two structure types has been rationalised on the basis of the varied demands of different functional groups to form distinct intermolecular interactions.

A study from this laboratory (Desiraju group) has analysed a series of crystal structures of 2,3-dicyano-5,6-dichloro-l,4-dialkoxybenzenes in order to exploit the C≡N···Cl interactions in crystal engineering.[9] Two gross structural patterns, tapes based on synthon II and sheets based on tetramer synthons formed by C≡N···Cl interactions were observed (Scheme 3). The methoxy and the *n*-octyloxy derivatives and also the unsubstituted parent compound form the tape structure. The inter-tape packing is governed by C–H···N dimer formation and close-packing of the methoxy and *n*-octyloxy groups. Deviations from the tape structure lead to other structural varieties that are defined by the requirements of the alkoxy groups to form hydrophobic interactions.

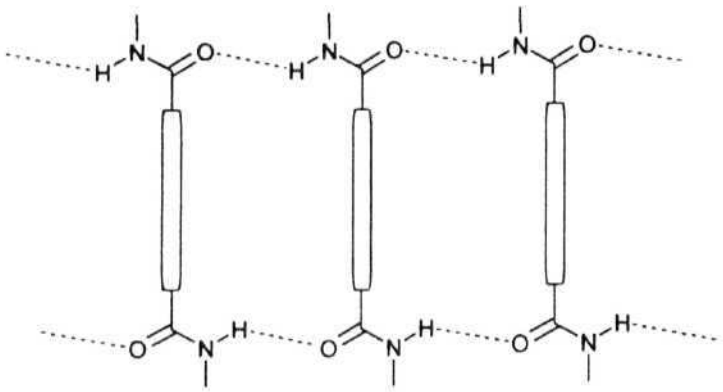


Scheme 3. Linear tapes based on synthon **II**.

13.2 Variable Molecular Core

Many studies related to this approach can be found in the literature[10] but as a representative example, a recent study by the Lewis group is presented.[11] In this study the crystal structure analysis of six secondary arenedicarboxamides has been carried out. It has been shown that four rod-like diamides produce classical one-dimensional tape structures with the separations between the successive molecules in the tape being 5 A (Scheme 4).[12] Sheet structures have been obtained from the other two diamides which are based on the naphthalene molecular core. It is important to note that synthon **III** is consistently present in both structural patterns. The differences in packing arrangements have been

attributed to the interactions between aromatic rings and to C–H···O hydrogen bonds.



Scheme 4. Classical packing pattern of secondary carboxamides based on synthon **III.** The distance between the adjacent molecular spacers is 5 A.

1.4 Discrimination Between Intermolecular Interactions

It may be observed from the previous section that while in the studies of Whitesides and Lewis the main focus has been on the strong hydrogen bonding, the work of Desiraju focuses on weaker interactions. Studies of weak intermolecular interactions are important for various reasons. Not all structures are exclusively stabilised by strong hydrogen bonds. In fact, many crystal structures are supported by weak interactions and to understand the nature of the molecular association in such structures, a better understanding of these weaker interactions is essential.[13] Often it has been observed that crystal structures are not as might have been expected from a consideration of strong hydrogen bonds alone. In such cases, it may be found that the so-called weak interactions are responsible for structural 'anomalies'. Non-appraisal of weak interactions leaves the subjects of crystal engineering and supramolecular chemistry in the dark and in such a situation many crystal structures would appear to be mysterious. It may not be always possible to design a particular target structure based completely on

strong hydrogen bonds while ignoring the contribution of weak interactions. Additionally, it is possible that strategies may be developed on the basis of weak intermolecular interactions alone.

A question that may be asked is if the strong interactions are themselves perturbed, what would be the fate of the weaker ones, and, what could possibly be the advantage of using such weak interactions in crystal engineering. This thesis attempts to answer such a question. A detailed appraisal of weak interactions is necessary to understand crystal structures. Therefore these interactions should be thoroughly studied and should not be neglected. Perhaps it may be suggested that achieving a target is important and not the kind of forces that are used. In this connection, a recent study of the Hulliger group is interesting.[14] In this study of perhydrotriphenylene (PHTP) inclusion complexes it was shown that strong hydrogen bonded synthons are less preferred compared to the more polarisable non-centrosymmetric synthons such as **IV.**

1.5 Supramolecular Synthons in Crystal Engineering

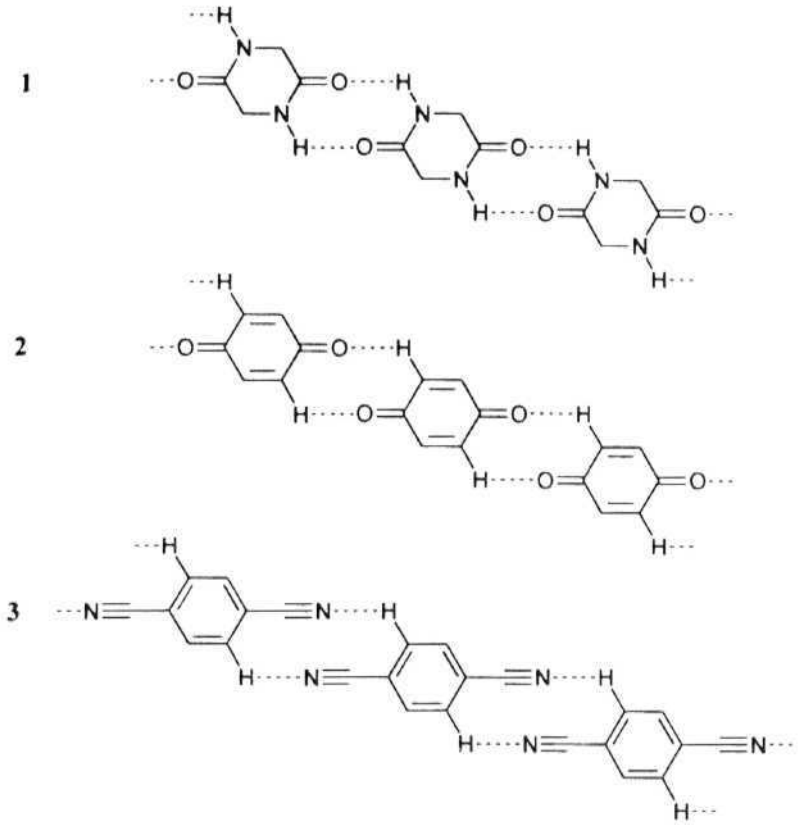
Crystals are composed of molecules. Therefore it is not surprising that the main emphasis in the approaches described in Section 1.3 has been on the variation of molecular structure and on the understanding of attendant differences in the crystal structures obtained. In order to understand what molecules *do* in crystals, one needs to look at crystal structures. It has been mentioned at the outset that crystal engineering is supramolecular synthesis in the solid state and therefore a rational design of crystal structures requires supramolecular ingenuity and a thought process beyond the molecule.[56] The supramolecular synthon concept has been developed on these grounds and has evolved to become a convenient bridge between molecular and structural chemistry. This is illustrated in the following sub-sections.

1.5.1 Synthon Transferability

The similarity between the linear tape structures found in piperazine-2,5-dione, 1, 1,4-benzoquinone, 2 and 1,4-dicyanobenzene, 3 has been outlined (Scheme 5).[15] These structures are constructed from synthons I, V, and **VI** respectively. Even though these synthons constitute interactions of different strengths, the essential topological similarity between them results in the formation of supramolecularly similar tape structures. A CSD survey revealed that synthons I, V and **VI** are not just confined to the crystal structures of 1, 2 and 3 but are also found in many other derivatives of these compounds. In spite of the variations in the molecular structures of such derivatives, these synthons are transferable between different crystal structures and this suggests their robustness. Synthon transferability strengthens the choice of these synthons as design elements in crystal engineering. For instance, the work of Jenneskens and co-workers on 2-methoxy and 2,5-dialkoxy derivatives of 2 showed that the tape structure recurs in the four crystal structures studied.[16]

1.5.2 Synthon Interchangeability

Synthon transferability suggests the possibility of synthon interchangeability. The ethynyl and chloro groups generate topologically similar supramolecular synthons **VII** and **VIII**. Both these synthons are structurally robust and exist in many crystal structures.[17] In their recent studies, Boese and co-workers have analysed the crystal structures of 1,4-diethynylbenzene, 4 and 4-chloroethynylbenzene, 6. In the context of synthon interchangeability, these two structures along with that of 1,4-dichlorobenzene, 5 present an interesting result. The structures of 4, 5 and 6 are similar to one another (Figure 1). While the structures of 4 and 5 are stabilised exclusively by synthons **VII** and synthons **VIII** respectively, the structure of 6 is stabilised by the alternating chains of synthons **VII** and **VHI.** A comparison of the latter structure with the former two suggests that the Cl···Cl synthon **VHI** is interchangeable with ethynyl synthon



Scheme 5. Generation of similar supramolecular structures from different molecular structures. Notice the topological similarity between synthons I, V and VI.

VII. It appears that similarities in shape and size of the synthons **VII** and **VHI** contribute towards the smooth exchange of these synthons between the structures of 4 and 5 to yield the structure of **6.**

1.5.3 Inter-changeability of Molecular and Supramolecular Synthons

A more intriguing possibility is suggested for the replacement of benzene ring. a molecular synthon, with the carboxy dimer supramolecular synthon X by relating the crystal structures of terphenyl and benzoic acid.[5] This idea has been successfully employed in the work described in Chapter 4 in the synthesis of a linear ribbon structure. In a recent review on 'Synthetic Supramolecular

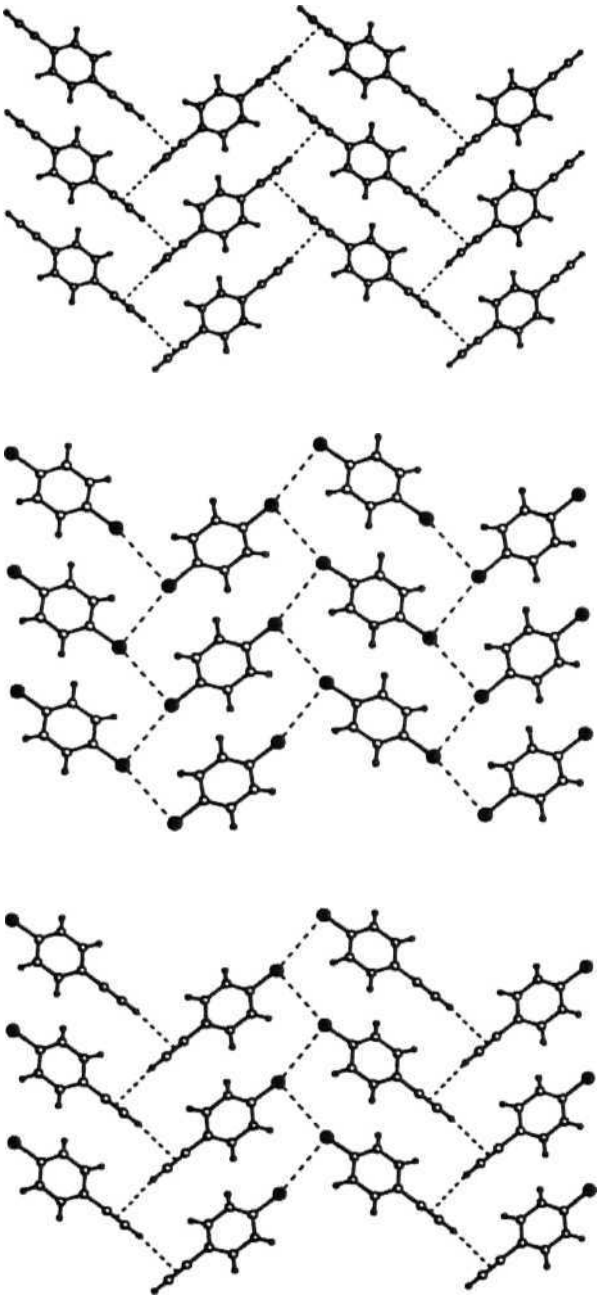


Figure 1. Illustration of synthon interchangeability in the structures of 4 (top), 5 (middle) and 6 (bottom). Notice the topological and size similarity between synthons **VII** and **VIII.**

Chemistry', Stoddart has suggested the advantages of supramolecular retrosynthetic methodology based on this and related work.[6a] An excellent example that describes the interchangeability of molecular and supramolecular synthons is found in the tetragonal crystal structures of *tetrakis*-(4-bromophenyl)methane, 7 and the 1:1 complex. 8 between tetraphenylmethane and CBr_4, studied by the Desiraju group (Figure 2).[19] Compound 7 generates a distorted diamondoid network based on alternating tetrahedral templates: the tetraphenylmethane system and synthon IX. a tetrahedral supramolecular cluster formed by four bromine atoms. If a phantom carbon atom could be imagined at the center of supertetrahedral synthon IX it would mimic a CBr_4 molecule. Such a realisation led to the crystallisation of molecular complex 8. the structure of which is similar to that of 7 at a supramolecular level. A supramolecular synthon IX is replaced by a molecular synthon CBr_4 and Br···phenyl interactions assemble the constituent molecules in the structure of complex 8. The similarities between the structures of 7 and 8 would not have been realised if one were not using the concepts of a supramolecular hierarchy. It may be reasoned that topological similarity in conjunction with similarity in size of synthons. be they molecular or supramolecular, renders synthon interchangeability possible.

1.5.4 Synthon Interference and Structural Insulation

The structural similarity between 4, 5 and 6 follows from not just synthon interchangeability but also from structural insulation. Synthons **VII** and **VIII** are well insulated from one another in the structure of 6. When such an insulation is absent or in other words when interactions interfere with one another, unexpected crystal structures could result. For example, it is shown in Chapter 2 that in the structures of 2- and 3-aminophenols, synthon interference leads to the formation of unexpected N–H···π hydrogen bonds and that the molecule → crystal structure relationship does not hold as might have been anticipated from a

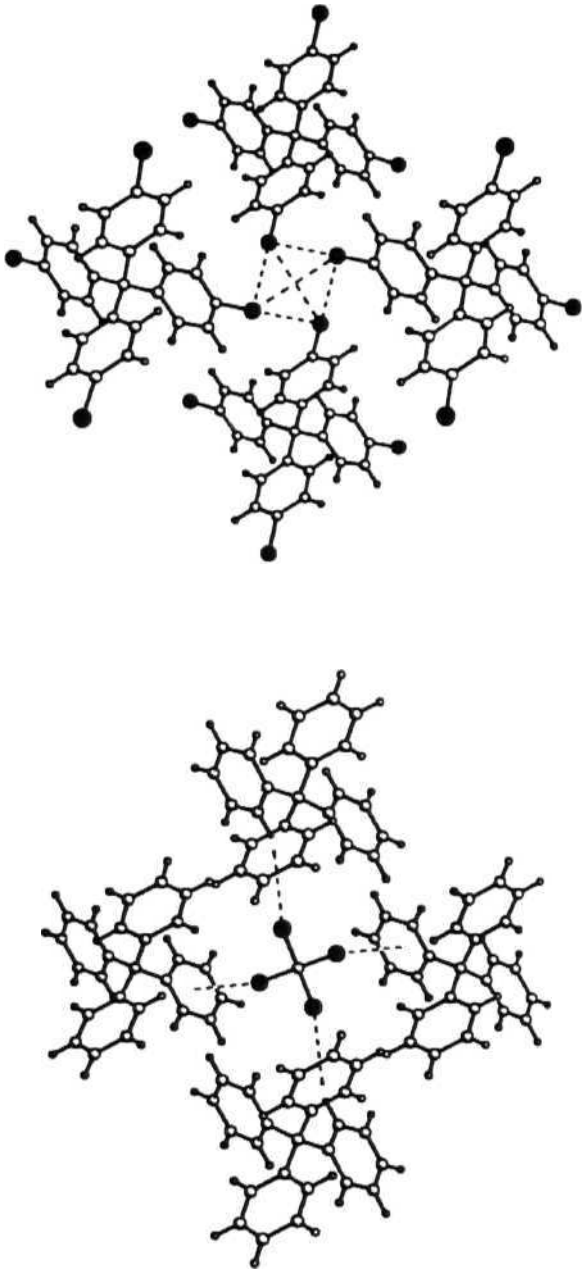


Figure 2. Interchangeability of molecular and supramolecular synthons. Notice that the supramolecular synthon IX in the structure of 7 (top) and the molecular synthon CBr_4 in the structure of 8 (bottom) have similar shape and size.

functional group approach. At times, when synthon interference is predictable, one can take advantage of this in the creation of otherwise unyielding structures. The supramolecular synthesis of a rosette structure by the Whitesides group serves as an excellent example wherein steric interference has been used to produce the desired rosette structure."[0]

1.5.5 Supramolecular Retrosynthesis

A worthwhile goal in any scientific endeavour is to derive the unknown from what is known. In the early days of crystal engineering molecular structures were thoroughly understood whereas crystal structures were very poorly fathomed. Therefore it seems reasonable that studies during that time were mostly molecule-based. Today, any study of crystal engineering is benefited by: (a) 175 000 crystal structures deposited in the CSD, a convenient tool to retrieve any crystal structure or any supramolecular fragment in an easy and efficient way: (b) results of many previous crystal engineering studies, and (c) many simplified approaches to understand complex supramolecular assemblies. Having such a background, it seems logical to derive an unknown molecular structure from a known supramolecular (crystal) structure. Accordingly, conceiving a desired supramolecular structure and working backwards to the constituents, in other words supramolecular retrosynthesis, is a very important tool in the deliberate design of crystal structures.[5] Supramolecular retrosynthesis leads to the molecular possibilities for a given supramolecular structure, and if planned with enough expertise, the chances of the unknown molecule resulting in any other supramolecular structure are diminished. Perhaps, it remains to be realised if the phenomenon of supramolecular retrosynthesis is capable of providing a logical lead to avoid polymorphism, a vexing problem in crystal design. Supramolecular retrosynthesis of one- and two-dimensional networks is illustrated in Chapters 4, 5 and 6.

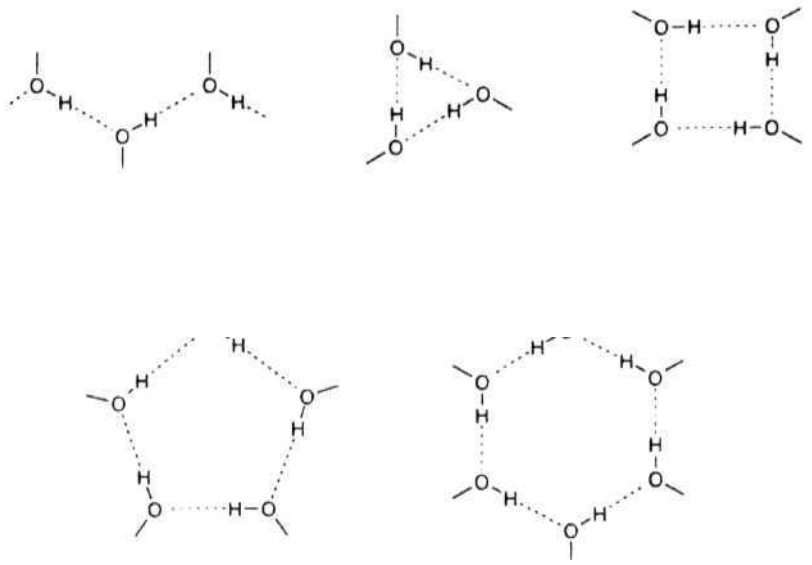
1.5.6 Property Directed Supramolecular Synthesis

Organic substances are now being thought of as materials rather than as molecules[2b] and therefore targets in crystal engineering need to be defined at a supramolecular rather than at a molecular level.[5] Thus the concepts of retrosynthesis and synthons are more appropriate in the realm of supramolecular chemistry. Crystal engineering is progressing towards applications. The goals are now set around microporous solids for selective chemical reactivity and catalysis,[21] NLO active substances for electrooptic applications and parametric oscillators,[22] nanostructured materials for information processing. for energy and charge transport[23] and organic ferromagnets.[24]

Work in the area of organic microporous solids has been in the forefront of crystal engineering. Various strategies have been developed and have been shown to be successful but an organic microporous solid that achieves the capabilities of efficient zeolites is yet to be synthesised. The ideal requirement of NLO crystals is the non-centrosymmetric assembly of molecules that have molecular hyperpolarisability, β. Various types of dipolar molecules have been developed and shown to have NLO activity.[22] An efficient way of producing polar assemblies of dipolar molecules as inclusion guests in PHTP host channels is described by the Hulliger group (see Section 1.4).[14] However, there are other disadvantages with dipolar molecules (see Chapters 5 and 6) in electrooptic configurations and a new class of compounds with attached octupolar nonlinearities have been proposed. Octupolar systems are expected to overcome many of the disadvantages posed by dipolar species and more details about octupolar crystal engineering are provided in Chapters 5 and 6. Nanoscale assemblies are of utmost importance in transport phenomenon and the principles of self-assembly have been applied to generate a range of systems from the level of supermolecules to millimeter scale objects.[4-6,23]

1.6 Polymorphism and Crystal Structure Prediction

The phenomenon by which the same substance could result in different crystal forms is called polymorphism. Polymorphism questions the underlying basis of crystal design. While there has been much progress today in understanding the existence of polymorphism in a particular substance, it should also be remembered that polymorphism is not universal.[26] Only some varieties of compounds such as polyfunctional molecules or molecules with high conformational flexibility exhibit polymorphism routinely. The concept of supramolecular synthon has also been applied to the understanding of polymorphism.[2] The ability of a functional group to form different supramolecular synthons might lead to different supramolecular (crystal) structures, that is to polymorphism. The –OH group is a typical example and forms synthons in open and cyclic variations as shown in Scheme 6.[2] Hydroquinone. for example, exists in three polymorphic forms α, β and /which consists of trimer, hexamer and linear synthons respectively. Carboxylic acids are known to assemble in dimeric and catemeric variations leading respectively to synthons X and XI. Tetrolic acid occurs in two forms, one stabilised by synthon X and the other by XI.[29] The supramolecular synthon concept has also been used in a different way to explain the possibility of polymorphism in pyrazine carboxamide.[30] The compound is capable of forming closed and open variations of synthon **XII** in many possible ways from chemically different locations on the molecule. Each of these possibilities or combinations of some of these can lead to different supramolecular structures. Several other structural reasons may be responsible for polymorphism and these are not discussed here. Polymorphism, because of its random nature, has been recurring time and again and its unexpected appearance may be taken as an advantage for further studies in crystal engineering.



Scheme 6. Various packing modes possible for hydroxy groups. These synthons are observed in closed and open variations in the crystal structures.

Polymorphism means that a molecule can have more than one crystal structure. This immediately poses the question as to which one of these structures is preferred by the molecule. The problems of obtaining single crystals suitable for X-ray diffraction together with the pharmaceutical requirements have necessitated crystal structure prediction.[31] The Polymorph Predictor program (Cerius[2]), for the *ab initio* prediction of crystal structures has been developed based on the Monte Carlo simulation technique (see Chapter 3 for further details on the use of this program).[32] Computational limits notwithstanding, success has been achieved in some cases using the Polymorph Predictor program but conformationally flexible molecules continue to pose problems.[33] One of the shortcomings with this method is that each prediction produces many energetically similar crystal structures and in the absence of any other experimental data it is difficult to select the correct structure. On the other hand, if partial data is available in the form of powder X-ray spectra or the cell and space group information a more confident prediction can be made.[34]

A far away goal of crystal engineering lies in the understanding of nucleation and crystallisation. Crystallisation is a very complex phenomenon and no proper theory or experiment has been developed to understand this process. Molecular dynamics has been evolving as a promising tool to understand the formation of molecular aggregates and is expected to shed light on crystallisation process. A recent study by Gavezzotti[29] on tetrolic acid has shown that the catemer synthon XI has 10% probability in a non-polar solution compared to dimer synthon X suggesting the possibility of polymorphism which has been experimentally found. A combined approach of molecular dynamics and crystal structure prediction has been evolving to be an ambitious goal of crystal engineering.

1.7 References and Notes

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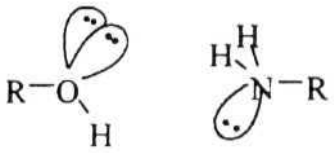
CHAPTER TWO

CORRESPONDENCE BETWEEN MOLECULAR AND CRYSTAL STRICTURES: A STUDY OF 2-, 3-AND 4-AMINOPHENOLS

2.1 Introduction

Crystal engineering of organic solids using strong hydrogen bonding interactions of the O–H···O and N–H···O types is widely practised. The strength and directionality of these interactions had conferred enormous predictability in many studies of crystal engineering.[1] The carboxyl and amide groups are the most prominent functionalities that make use of these interactions and have been exploited in the synthesis of novel supramolecular structures.[2] Utilisation of hydroxy and primary amino groups in the design of predictable structures has come into light recently.[3] The hydroxy groups have one hydrogen bond donor and two acceptors whereas the primary amino groups have two donors and one acceptor. Therefore alcohols and primary amines have been considered to be complementary hydrogen bonding functionalities both stoichiometrically and geometrically. Such complementarity has been identified simultaneously and independently by Ermer and Eling, and by Hanessian *et al.* who have shown that predictable structures can be obtained using compounds or molecular complexes containing equal stoichiometries of -OH and -NH2 groups.[3] Further, the hydroxy-amino recognition in these systems is benefited by a 50% increase in the number of hydrogen bonds when compared to either pure alcohols or primary amines and leads to tetrahedral configurations at both hetero-atoms in the hydrogen bond network. Hanessian *et al.* have shown that triple stranded helical supramolecular structures are generated from 1:1 complexes of chiral 1,2-diols and 1,2-diamines. The hydroxy-amino recognition has also been implicit in some other studies.[4] Ermer and Eling have constructed exquisite supramolecular structures based on a number of aromatic systems wherein the hydroxy and amino groups are linearly disposed. Various structural possibilities have been

envisaged by Ermer and Eling for hydroxy-amino recognition, the most important of which is the super arsenic sheet structure which could be derived either from cubic diamond (zinc blende) or from hexagonal diamond (wurtzite) lattices. Such an analogy between inorganic and organic crystal structures greatly facilitates the understanding of complex organic supramolecular systems.[5]



Alcohols and primary amines possess complementary hydrogen bond donors (hydrogen atoms) and acceptors (lone pairs).

The underlying aim of the studies of Ermer and Eling, and Hanessian *et al.* is to establish connections between molecular and crystal (supramolecular) structure. Considering the molecular basis of organic chemistry seeking such connections is only natural.[6] Therefore any rational approach that associates functional groups with crystal structure attributes is considered to be important and the hydroxy-amino recognition falls into this category. The crystal structure of 4-aminophenol, 1 (Figure 1) is an archetypal example and shows how the tetrahedral hydrogen bonded network is constructed.[3a] It is interesting to note that in the case where -OH and $-NH_2$ groups disposed linearly, super-arsenic sheet structures are always observed,[3a] whereas when these groups are in a vicinal arrangement, helical supramolecular structures are produced consistently,[3b-c] albeit with equal predictability. It therefore appears that the geometrical disposition of the -OH and $-NH_2$ groups on the molecular skeleton plays a very important role in the supramolecular structure obtained. In such an instance, rationalisation of the crystal structures of 2- and 3-aminophenols, 2 and 3. is expected to give further insight into the hydroxy-amino recognition. The structures of 2 and 3 have been determined previously using X-Ray diffraction.

In a recent study N–H···π hydrogen bonds have been proposed in these structures. The N-H ·π hydrogen bonds are uncommon and their structural characterisation requires high precision in the location of H-atom positions. Thus in this study, the crystal structures of 2 and 3 were determined using low temperature neutron diffraction.

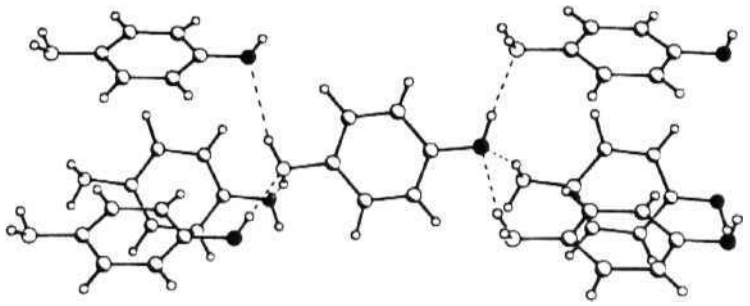


Figure 1. Tetrahedral network formed by N–H···O and O–H···N hydrogen bonds and the herringbone interactions between aromatic rings in the crystal structure of **1.**

2.2 N–H···π and C–H···O Hydrogen Bonds

The crystal structures of 2 and 3 shown in Figures 2 and 3 belong to the space groups *Pbca* (Z = 8) and $Pca2_1$ (Z = 4) respectively. The geometries of the various intermolecular interactions found in these structures are given in Table 1. In both the structures N–H···π hydrogen bonds have been observed and their formation is facilitated by electron rich aromatic rings. Two situations may be observed when an aromatic ring acts as a hydrogen bonding acceptor. Either the ring as a whole[9] or part of the ring[10] may contribute the π electrons towards hydrogen bonding. In the structures of 2 and 3, however, it is not possible to conclude definitively if a C=C bond of the phenyl ring or the ring as a whole (centroid) is more significant with respect to N–H···π hydrogen bonding. In 2 for example, the shorter approach (2.309A) to the ring centroid is the more bent one (145.0°, (d) in Table 1). A longer approach of 2.421 A to the centre of a C=C

bond is more linear (173.9°, (e) in Table 1). Similarly in 3 a short contact to ring centroid is more bent (2.409A, 148.7°. (i) in Table 1) compared to a long linear contact (2.504A, 171.8°, (J) in Table 1) to a C=C bond. The N-atoms are distinctly tetrahedral in both structures with the perpendicular distances from the basal plane to the apex of the pyramid being 0.331 and 0.358Å in 2 and 3 respectively. Inspection of Figures 2a and 3a reveals that the N–H· ·π hydrogen bonds would not be so effective if the N-atoms were planar, and perhaps this is the driving force for pyramidalisation.

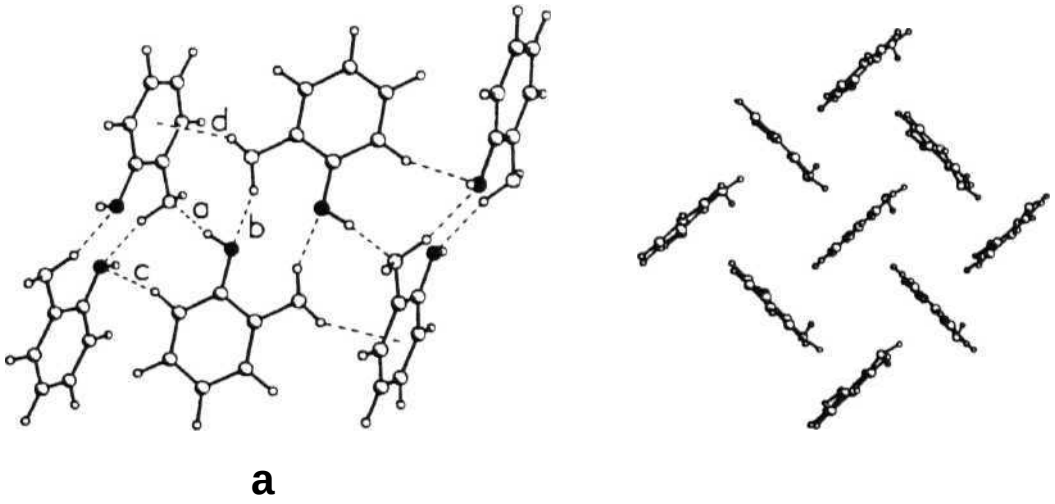


Figure 2. Crystal structure of 2 showing hydrogen bonds in (a) and herringbone interactions in (b). The arrangement of aromatic rings shown in (b) is similar to that in the structure of benzene.

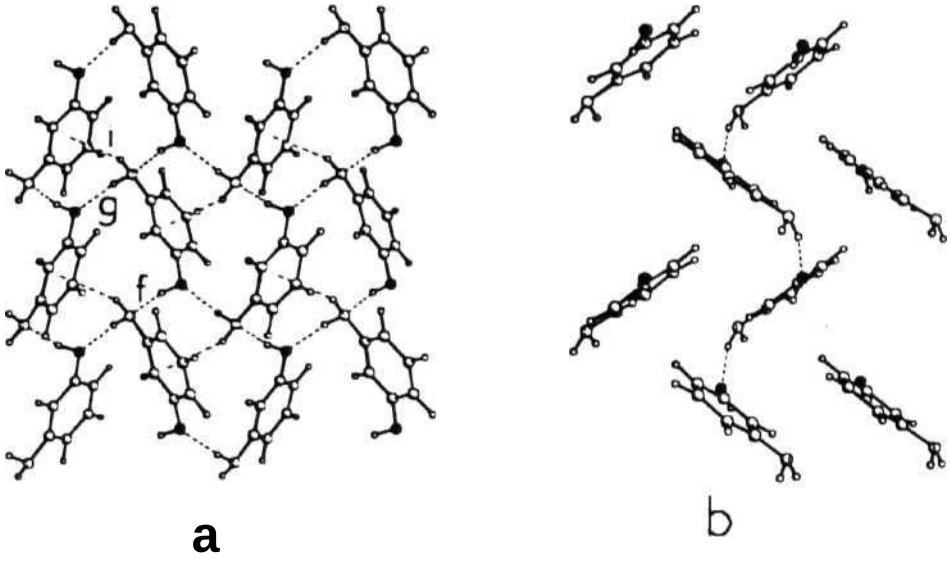


Figure 3. Crystal structure of 3. (a) View down [010] showing hydrogen bonds. (b) Perspective view showing herringbone interactions.

Surprisingly, the hydroxy-amino recognition pattern as observed elsewhere by others[3-4] is not found in these compounds In 2, the hydroxy and amino groups form a centrosymmetnc arrangement. Each -OH group donates a hydrogen bond to an $-NH_2$ group (O–H N. (a) in Table 1) and accepts one (N-H 0, (b)) from another. The fourth coordination site is occupied by a C–H···O hydrogen bond (c). Each $-NH_2$ group similarly donates (b) and accepts (a) a strong hydrogen bond. The second amino H-atom participates in the N–H···π hydrogen bond (d). Interestingly, both the O- and N-atoms have a tetrahedral environment but unlike in 1, the hydrogen bonding is not exclusively of the strong type. A very similar situation prevails in the structure of 3 with adjacent N–H···O bonded molecules related by screw axis The N-H rc hydrogen bond is again present (i) along with other interactions (f. g. h) as in 2 and the tetrahedral environment around the O- and N-atoms is maintained. The cooperative scheme of hydrogen bonds in both structures may be noted In contrast, there are no significant N-H ··π interactions in 1 and the shortest N···π distance is as long as 4.466A.

Table 1. Hydrogen bond geometries in the crystal structures of 2 and 3.

		X-Ray			Neutron		
Compound	Interaction	D(Å)	d(Å)	θ(°)	D(Å)	d(Å)	θ(°)
1	a. O–H···N	2.780	1.772	169.2	2.787	1.782	172.7
	b. N–H···O	3.114	2.221	153.4	3.113	2.141	156.6
	c. C–H···O	3.650	2.686	160.6	3.620	2.577	160.6
	d. N–H···π	3.260	2.458	146.2	3.199	2.309	145.0
	e. N–H···π	3.487	2.577	172.4	3.438	2.421	173.9
2	f. O–H···N	2.749	1.883	161.1	2.753	1.758	168.0
	g. N–H···O	3.011	1.957	153.4	3.030	2.024	165.6
	h. C–H···O	3.359	2.625	131.7	3.323	2.524	129.0
	i. N–H···π	3.341	2.410	161.9	3.328	2.409	148.7
	j. N–H···π	3.534	2.584	167.9	3.522	2.504	171.8

Interactions d and i are to the centre of the phenyl ring while e and j are to the centre of the C-C bond.

23 Are the Crystal Structures of 2- and 3-Aminophenols Anomalous?

It may be noted from Figures 2 and 3 that the structures of 2 and 3 are distinctly different from 1 and other related systems studied by Ermer and Eling. No super-arsenic sheets based on hydroxy-amino recognition are observed in 2 and 3. Thus it appears that the structures of 2 and 3 are 'anomalous' if the structures of Ermer and Eling are considered to be 'normal'. An analysis of the packing of aromatic rings in the structures of 2 and 3 is revealing. The aromatic rings are arranged in a herringbone fashion in 2 (Figure 2b) and it has been previously pointed out that this arrangement is almost identical to the arrangement of aromatic rings in crystalline benzene.[11-12] Figure 3b shows the corresponding arrangement of rings in 3. Herringbone interactions are identified by their characteristic T-shaped geometry and their importance in many organic crystal structures has been discussed repeatedly in the past[13] Accordingly, the unusual hydrogen bond network in the structures of 2 and 3 may then be understood as a

result of the need to establish herringbone arrangement. It has been stated that the N–H···π hydrogen bond is uncommon because it can occur only in acceptor-poor systems.[14] In the present context, though the acceptor atoms are present they are inaccessible because of the constraints imposed by the formation of the particular herringbone geometry. Thus the formation of weaker N–H···π and C-H ·O hydrogen bonds at the expense of stronger N–H···O bonds hints that the optimisation of herringbone interactions rather than the formation of N–H···O hydrogen bonds is the primary structural effect in these systems. Further, the aromatic hydroxy-amino systems of Ermer and Eling and the aliphatic hydroxy-amino systems of Hanessian *et al.* may now be contrasted. Despite the variation in the geometrical disposition of -OH and $-NH_2$ groups both these systems display tetrahedral supramolecular arrangements and it may be inferred that these arrangements are more likely in aliphatic systems where an N–H π hydrogen bond cannot exist. It should be noted at the same time that the deviation from linear arrangement of -OH and $-NH_2$ groups in 2 and 3 has resulted in entirely different crystal structures.

The observed crystal structures of 2 and 3 optimise several types of interactions. The structure of 2 is especially noteworthy in that the melting point difference between 2 (175°) and 1 (189°) is one of the smallest between isomeric *ortho* and *para* disubstituted benzenes. To the extent that melting points provide a measure of packing efficiency, the packing coefficients of 1. 2 and 3 are examined. These are respectively 0.714, 0.752 and 0.729. The higher values for 2 and 3 indicate that these 'anomalous' structures do not suffer from any marked packing deficiencies. Incidentally, the generality of these structures may be appreciated from the fact that 4-methyl-2-aminophenol, 4[15] (m.p. 141°) and 4-chloro-2-aminophenol[16] have structures very similar to that of 2. Figure 4 shows two views of the crystal structure of 4. The similarity between the structures of 2 and 4 extends to the same networking of strong and weak hydrogen bonds.[17] Thus 2 (and

3) belong to a structural family different from that of 1 and it is hard to decipher which one of these structures is anomalous.

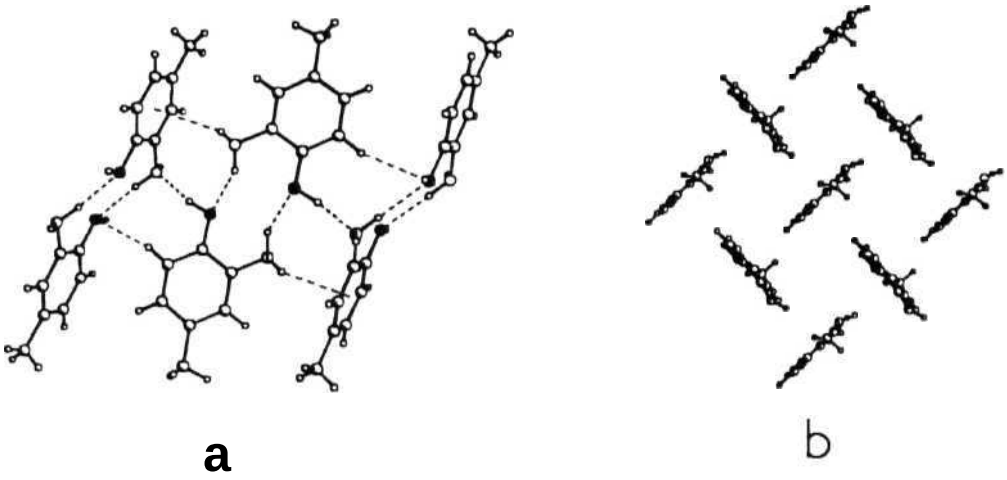
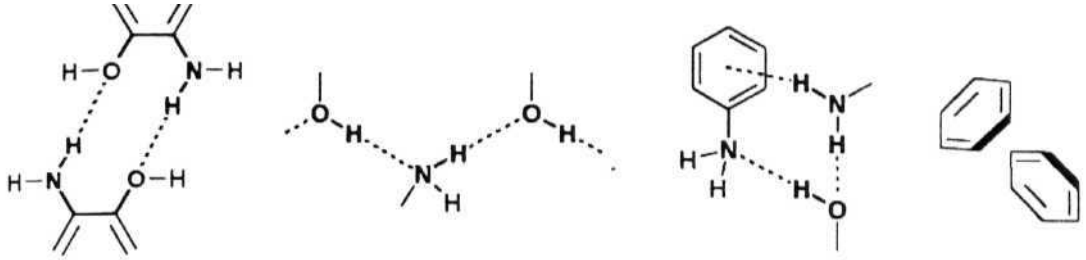


Figure 4. Hydrogen bond (a) and herringbone interactions (b) in the crystal structure of 4. Compare this with Figure 2.

2.4 Interaction Interference and Supramolecular Synthons

Crystallisation is a supramolecular event and molecular recognition is a key phenomenon during this process. Molecular recognition involves a chemical and geometrical complementarity between molecules. Since molecules approach one another in many possible ways during crystallisation, specific recognition between functional groups though useful, may not always occur. This is so because not only the chemical features of the functional groups but also their relative arrangement on the molecular skeleton has a profound role in the supramolecular structure generated. In other words, various sets of intermolecular interactions interfere with one another during crystallisation. In the case of aminophenols these sets correspond to hydrogen bonding and herringbone interactions. If the



5 6 7 8

Supramolecular synthons in the crystal structures of 2 and 3.

interactions are insulated from one another (minimal or non-interference) a direct relationship between molecular and crystal structure may be observed as in **1**. If the interference is maximum, that is when the interactions work in conflict, unexpected crystal structures could arise as in 2 and 3. This clearly indicates that the functional group approach towards the understanding of crystal structures is scarcely valid since functional groups are of molecular origin whereas the crystal structural features are supramolecular. The concept of supramolecular synthons is thus helpful These are identified as the smallest structural units that contain the maximum information necessary to transform the molecular structural features into the crystal. Molecular functional groups such as -OH and $-NH_2$ and supramolecular fragments like $-OH\cdots NH_2$ and $-N(H)H\cdots OH$ are also small structural units. that is molecular and supramolecular synthons, but they contain too little information to uniquely determine the molecule → crystal relationship. Conversely, a synthon as big as a unit cell could be imagined that consists of all the information but it is hardly useful for it is specific only for that structure. Thus the choice of a supramolecular synthon should be exercised with caution. In the present context of the crystal structures of the isomeric aminophenols, perhaps more meaningful supramolecular synthons are 5-8. These are small in size and contain a wealth of information sufficient for understanding molecular and crystal structure relationship. In other words, synthons 5-8 are the most economic

supramolecular units. A CSD[18] survey shows that the synthons 5 and 7 are specific to the title crystal structures and compound 4, whereas synthon 6 is quite general and is observed in many structures that contain hydroxy and amino groups.

2.5 Conclusions

Neutron diffraction analysis of the crystal structures of 2 and 3 has led to the unequivocal structural characterisation of N–H···π hydrogen bonds. It is shown that functional group approach to understand the arrangements of molecules in crystals may not always be useful and therefore it is not realistic to expect straightforward correspondences between molecular and crystal structures. In addition to the chemical nature of the functional groups, their relative disposition on the molecular skeleton has an intricate effect in the supramolecular architecture. Interaction interference plays a significant role during structure generation. If different interactions work in harmony, predictable structures are obtained; if not unexpected crystal structures can result. It has been shown that strong hydrogen bonding of the O–H···N and N–H···O type need not control crystal packing to the exclusion of other factors. The supramolecular synthon concept has been shown to recognise the inadequacy of present molecule → crystal transforms and provides a supramolecular basis for the description of supramolecular structures.

2.6 Experimental

Crystals of 2 suitable for neutron diffraction analysis were grown from ethanol in Hyderabad. A crystal with dimensions 4.1 × 4.1 × 3.3 mm was selected for the experiment. The neutron structure determination of 2 was conducted at the pulsed neutron source, ISIS, Oxford, on the Laue time-of-flight diffractometer, by Drs. V.J. Hoy and C.C. Wilson. Crystals of 3 suitable for neutron diffraction analysis were grown from methanol in Hyderabad. A crystal of dimensions 5.3 × 1.7 ×

0,65 mm was selected The neutron diffraction study of 3 was earned out by Drs. V.J. Hoy and G.J. Mclntyre at the Institute Laue Langevin reactor source in Grenoble using the four circle diffractometer. D19 Both the neutron experiments were carried out under the supervision of Prof. J.A.K Howard In both cases, the full anisotropic refinement was earned out using the program SHELXL-93.[19] The relevant crystallographic information is given in the appendix

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16. The crystal structure of 4-chloro-2-aminophenol has been determined to a low accuracy (S. Ashfaquzzaman, A.K. Pant, *Acta Crystallogr.,* **1979,** *B35,* 1394) and so is not discussed in any further detail.
17. Note that two of the cell edges of 2 and 4 are nearly identical. Cell parameters of 4: a = 7.780, b = 22.901, c = 7.596A, $\alpha = \beta = \gamma = 90°$.
18. F.H. Allen, J.E. Davies, J.J. Galloy, O. Johnson, O. Kennard, C.F. Macrae, EM. Mitchell G.F. Mitchell, J.M. Smith, D.G. Watson, *J. Chem. Inf. Comput. Sci.* **1991,** *31,* 187.
19. G.M. Sheldrick, SHELXL-93, A program for the refinement of single crystal diffraction data, University of Gottingen, Germany, **1993.**

CHAPTER THREE

FLUORINE ATOM INTERACTIONS IN CRYSTAL PACKING

3.1 Introduction

There has been much recent interest in the intermolecular binding ability of the C-F group, the so-called organic fluorine.[1] Such interest is, in part, motivated by concerns in bioorganic and medicinal chemistry in that some control is sought in enzyme-substrate recognition. In this respect, the C-F group has been compared not only to the C-H and C–Cl groups but also to the C–OH group.[1-2] However, a full understanding of the role of the C-F group even in far simpler supramolecular systems remains, in a general sense, elusive.[3,7] Crystal packing is governed mainly by the same principles that apply when a ligand binds to a macromolecular receptor.[8] Thus, an understanding of the packing of small-molecules containing the C-F group is expected to be of utility. Hydrogen bonds of the O–H O=C, O–H O-C N-H O=C, N-H O-C, N-H O-H and O–H···N–H type have been extensively studied and employed in crystal engmeering[9] and supramolecular chemistry.[10] In contrast, little is known about hydrogen bonds of the O–H··· F-C and N-H •F-C type. Pauling's definition of the hydrogen bond[11] would imply that F, as the most electronegative atom, should be a stronger hydrogen bond acceptor than O- and N-atoms. While the F ion is indeed one of the best acceptors and the strength of the hydrogen bond formed by the HF_2^- approximates a covalent bond,[12] it is the C-F group that does not form hydrogen bonds commensurate with electronegativity considerations, as do the C-0 and C-N groups.

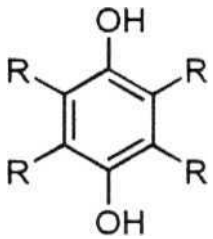
Glusker and co-workers have been in the forefront of studying intermolecular interactions of the C-F group.[5] In particular, a paper by Shimoni and Glusker[5] comments on the hydrogen bond acceptor capability' of this group. Based on the CSD studies, these authors have concluded that the C-F group is unable to compete favourably with 0- and N-atom acceptors. Recently, Howard *et al*[6] and Diinitz and Taylor[7] have undertaken database and computational studies to assess

the acceptor capabilities of the C-F group with -OH and -NH donors These studies are in general agreement with those of Glusker and show that the C-F group is a very poor acceptor hardly ever forming hydrogen bonds. However, it should be noted that in these studies of O(N)–H ··F–C hydrogen bonds, there is the unavoidable introduction of the competing, stronger 0- and N-atom acceptors.[3a]

Since C-H O and C-H N hydrogen bonds have been used in crystal engineering[13] (see Chapter 5) this raises the question as to the nature and possible utility of the C-H F-C (hereafter C–H···F) hydrogen bonds in crystal engineering. This then is the subject of the present chapter. Shimoni and Glusker[5] have stated that the poor competition of the C-F group with O- and N-atom acceptors extends to C-H donors. Therefore, in the evaluation of the acceptor capabilities of the C-F group, C-H F geometries in compounds containing only C, H and F-atoms are better candidates. This indeed was the approach adopted by Shimoni and Glusker who concluded from their CSD study[5] that though C-H F interactions are weak, they make a contribution to crystal packing. Yet, Howard *et al.*[6] state that "the predominant C–F···H–C contacts in the Database appear to have very little significance in energy terms and are essentially van der Waals complexes". The present study also attempts to characterise the C-H-F interaction: (1) Is it a specific 'hydrogen bond' type of interaction or does it merely provide van der Waals stabilisation? (2) Can this weak interaction be made a part of a useful supramolecular synthon, that is an operative fusing element in crystal architecture? (3) What are the prospects for this interaction in systematic crystal structure design?

In order to fully understand the role of the C-F group in crystal packing. two contrasting situations have been studied in the present work. First, the C-F group is taken in the presence of only strong hydrogen bonding donors (-0H groups) and no other weak donors are made available. Tetrafluorohydroquinone, 2 has been chosen for this purpose and it is identified that its crystal structure bears a close relationship to that of γ-hydroquinone, **1**.[14] Further, tetrachlorohydroquinone, **3**[1]

found to be isostructural to 1 and 2. A deeper structural analysis of 1-3 necessitated the structure determination of tetrabromohydroquinone. 4. Comparative analysis of the closely related structures of hydroquinones 1-4 provides the possibility of exploring the nature of C-F group in crystal packing when it is compelled to associate with strong hydrogen bond donors only. In the second situation, as presented in Section 3.4, the C-F group is taken with only weak hydrogen bond donors and its acceptor capabilities are evaluated.



1 R = H
2 R = F
3 R = Cl
4 R = Br

Table 1. Some important geometrical parameters in the structures 1-4.

	1[a]	2	3	4
O···O (Å)[b]	2.84, 2.83	2.82	2.92	2.95
Inclination (°)	33, 35	39	46	50
Layer separation (Å)	3.86	3.85	6.05	7.68
Layer offset (Å)	2.86	3.29	2.83	2.78
Layer plane[c]	(202)	(100)	$(10\bar{2})$	(101)

[a] Two values are given for the two symmetry independent molecules. [b] For consistency with the reported structures of 1 and 3 the values are given only to two decimal places. [c] Defined as the plane in which O–H O hydrogen bonded layers are present. The deviation of the 0-atoms from the mean plane lie in the range of 0.17-0.24Å.

3.2 Structural Description of Hydroquinones 1-4

3.2.1 Tetrafluorohydroquinone

In the crystal structure of 2 (space group $P2_1/n$, $Z = 2$), the molecules lie on inversion centres. The -OH groups of adjacent 2_1-related molecules form O–H O

hydrogen bonds (Table 1) that link the molecules in chains parallel to [010] In each chain. any -OH group participates in two hydrogen bonds, one as a donor and one as an acceptor. This is a common pattern in the crystal structures of phenols.[16] Adjacent chains associate to form layers parallel to (202), these layers being defined as the mean planes of the O-atoms (Figure 1). The aromatic rings are inclined to the layers at an angle of 39°. The perpendicular distance between layers or the interlayer separation is 3.85Å (Figure 2). The nearest aromatic rings in adjacent layers are not parallel. Additionally they are offset by 3.29A (Figure 1). The layer offset is defined in terms of the distance between the projections of centroids of non-parallel aromatic rings in adjacent layers on the mean plane. The description of ring inclination and interlayer separation is shown in Figure 2.

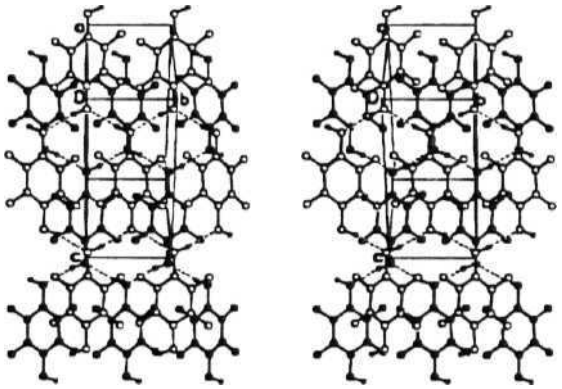


Figure 1. Stereoview of the two consecutive O–H ·O hydrogen bonded layers in the structure of 2. Note the ring inclination and layer offset. Molecular components in one layer are shown as open circles and in the other they are shaded in this Figure and in Figures 3, 5 and 7.

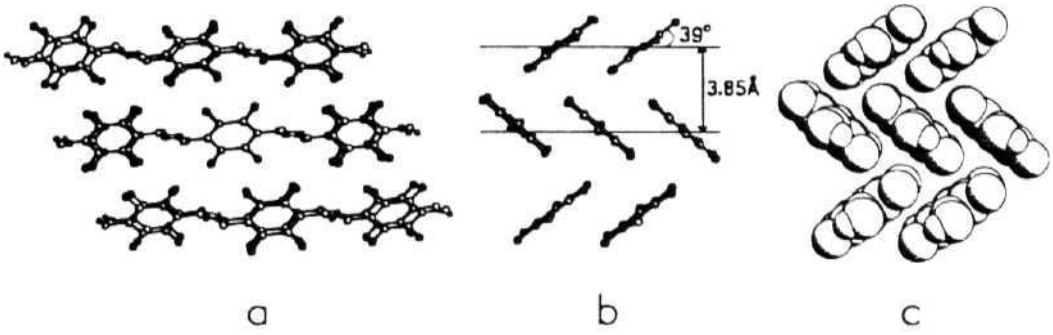


Figure 2 Crystal structure of 2: (a) View down [010] showing parallel layers. (b) Lateral view of nearest interlayer molecules showing ring inclination and interlayer separation The horizontal lines represent the mean planes of the layers. (c) Space-filling view of (b). Notice the loose packing of molecules.

3.2.2 γ-Hydroquinone

γ-Hydroquinone,[14] 1 has a structure similar to that of 2. However, there are two symmetry-independent molecules. Each forms hydrogen bonded layers as described above for 2 and alternating symmetry-independent layers are observed in the structure. Each of these layers consists of a hydrogen bond network that is topologically identical to that found in 2 (Figure 3). The ring inclination and the laser offset are less than those found in 2 (Table 1). The interlayer packing is governed by herringbone/C–H···π interactions (Figure 4) The C-H groups point towards the mid-point of the HC=CH bond rather than towards the ring centroid (C···X, H···X, C-H-X: 3.67, 2.75A. 143°; 3.64, 2.65Å, 150°. X is the mid-point of the HC=CH bond).

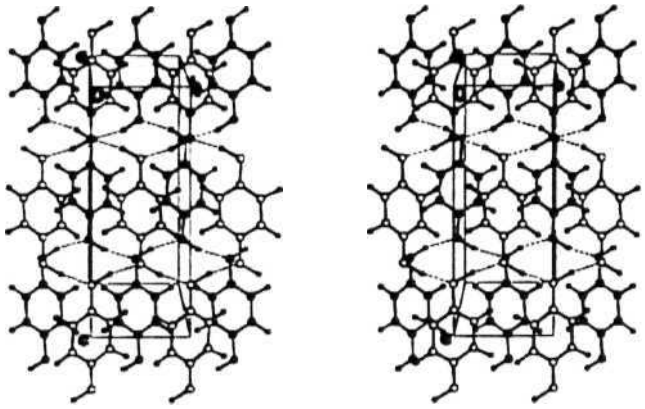


Figure **3** Stereoview of the two consecutive O–H···O hydrogen bonded layers in the structure of **1**. Note the decrease in layer offset compared to Figure 1.

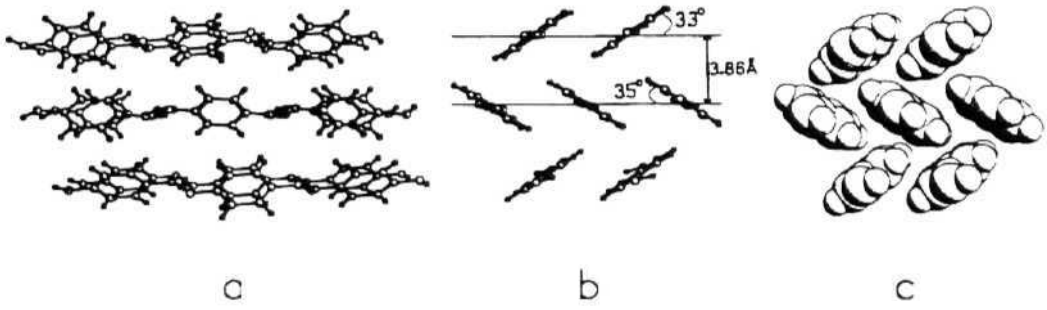


Figure 4. Crystal structure of 1: (a) View down [010] showing parallel layers. (b) Lateral view of nearest interlayer molecules showing ring inclination and interlayer separation. The horizontal lines represent the mean planes of the layers. (c) Space-filling view of (b). Notice that the C-H groups approach the mid-point of the HC=CH bond and not the ring centroid Compare this with Figure 2c.

3.2.3 Tetrachlorohydroquinone

Continuing further, tetrachlorohydroquinone,[15] 3 was also found to be structurally similar to 1 and 2 (Figure 5). Topologically similar O–H O hydrogen

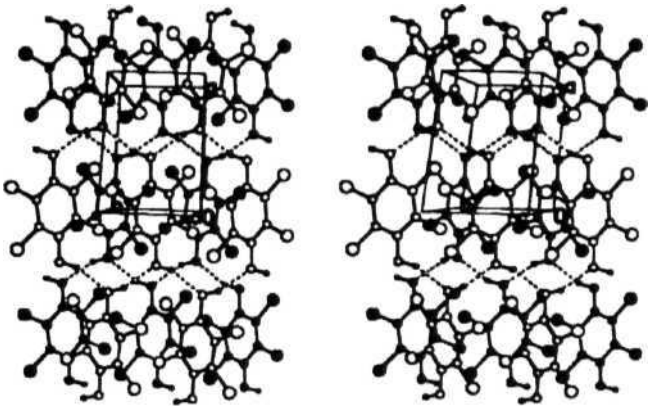


Figure 5. Stereoview of the two consecutive O–H···O hydrogen bonded layers in the structure of 3. Note the decrease in layer offset compared to Figure 1.

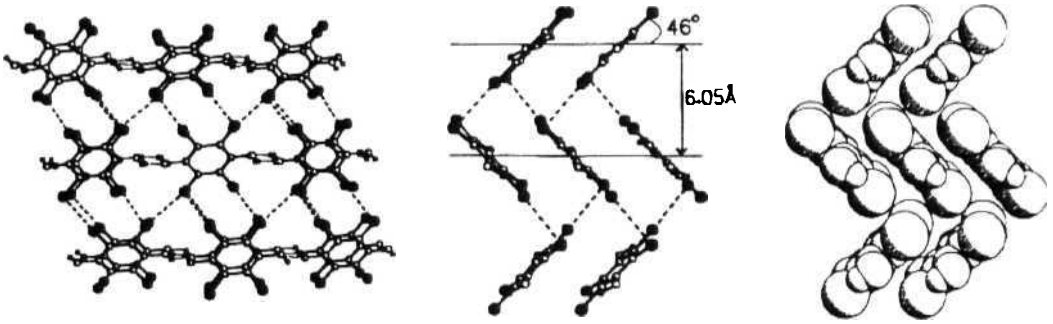


Figure 6. Crystal structure of 3: (a) View down [010] showing parallel layers. (b) Lateral view of nearest interlayer molecules showing ring inclination and interlayer separation. The horizontal lines represent the mean planes of the layers. Notice the type II Cl—Cl interactions between the layers. Compare this with Figure 2b. (c) Space-filling view of (b) Note the close approaches of Cl-atoms. Compare this with Figure 2c.

bonded layers may again be identified The aromatic rings are also inclined but at a steeper angle with respect to the layers and the layer offset is small (Table 1). Adjacent layers are interconnected with Cl···Cl interactions (Figure 6) of both type I (Cl···Cl, 3.39A; θ_1 = θ = 167°) and type II geometries (Cl—Cl, 3.44A; θ_1 = 176°, θ_2 = 81°).[17] A longer interlayer separation of 6.05A and a layer offset of 2.83 A accommodate these C1-C1 contacts.[18]

3.2.4 Tetrabromohydroquinone

The structural similarities between 1, 2 and 3 prompted the crystal structure determination of 4. the details of which are given in Figures 7 and 8. Chains of O–H···O hydrogen bonds parallel to [010] are found. The chain and layer structure is as described previously for 1-3 with type I (Br···Br, 3.55A; θ_1 - θ, 172°) and type II (Br Br. 3.58A: θ_1 = 175°. θ_2 = 88°) Br-Br interactions in the interlayer region.

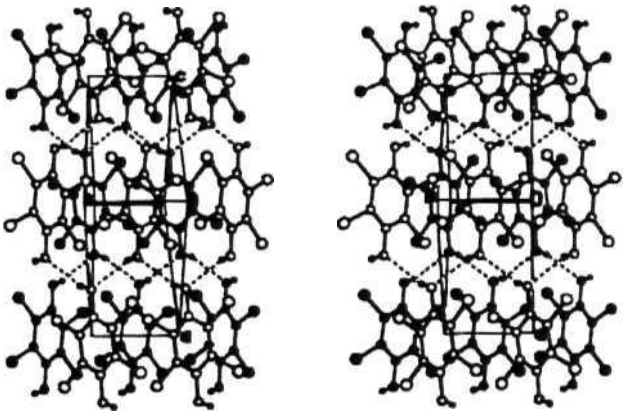


Figure 7. Stereoview of the two consecutive O–H O hydrogen bonded layers in the structure of 4. Note the smaller layer offset and longer interlayer separation.

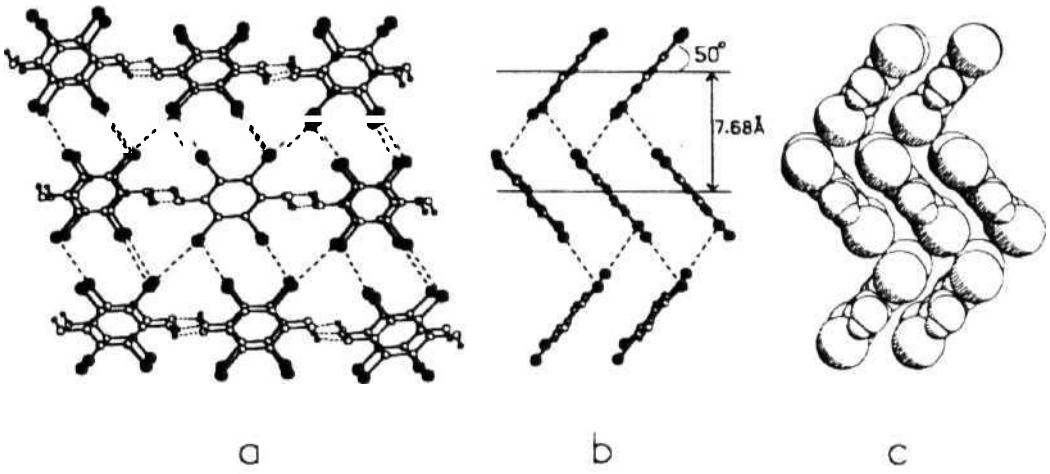


Figure 8. Crystal structure of 4: (a) View down [010] showing parallel layers. (b) Lateral view of nearest interlayer molecules showing ring inclination and interlayer separation The horizontal lines represent the mean planes of the layers. Notice the type II Br···Br interactions between the layers. Compare this with Figure 2b. (c) Space-filling view of (b). Notice the close approach of the Br-atoms. Compare this with Figure 2c.

3.3 Structural Discrimination between Hydroquinones 1-4

It may be noted that it is very unusual to find a group of crystal structures wherein replacement of a majority of the H-atoms in a molecule by F, Cl and Br successively causes no major changes in the gross structure. crystal symmetry and network features. For this reason. a more detailed comparison of these structures was deemed worthwhile.

3.3.1 Lattice Energy Calculations

A comparison of lattice energies is helpful in the analysis of structurally similar systems such as those described above though the potential for the F-atom is not known to the accuracy as might be required.[19] Lattice energy (U_{latt}) calculations with the molecular geometry held invariant gave U_{latt} values of -28.4. -20.2, -26.2

and -28.8 kcal/mole per molecule for the optimised crystal structures of **1, 2, 3** and **4** respectively.

3.3.2 Herringbone Interactions in 1 and Halogen-Halogen Interactions in 3 and 4

The invariant feature in the four structures in this study is the O–H 0 hydrogen bonded network with O 0 distances King within a narrow range of 0.13Å. The variable features are the aromatic ring inclination. the interlayer separation and the layer offset (Table 1). These three parameters are geometrically interrelated Some ring inclination is necessary given the **O-H-0** geometry and it increases with the increase in the size of substituents (H, F, Cl and Br). Consider the inclinations of 33 and 35° in 1. A steeper inclination results in a greater interlayer separation as in 3 and 4. The structure of 1 is archetypical of the herringbone packing between layers. The combination of a shallow inclination and small offset enables optimal C–H···π contacts and Figures 3b-c highlights the resemblance of this structure to the classic herringbone structure of naphthalene.[20] Indeed, it is known that such herringbone packing is compatible with the demands of O–H···O hydrogen bonding in the crystal structures of other phenols.[16b] Now consider the chloro and bromo derivatives. 3 and **4** Given the invariant O-H-0 network, these compounds opt for a steep increase in the inclination with a slight decrease in the layer offset so that halogen···halogen interactions of the so-called type II geometry are manifested (Figures 6b-c and 8b-c). It is well-known that the type II contacts are polarisation-induced and contribute actively to crystal structure stabilisation,[21] while type I contacts arise due to close-packing about an inversion centre. The structures of 3 and 4 are nearly isostructural and show the close similarity of the C–Cl and C-Br groups in forming such polarisation-induced halogen···halogen interactions. In terms of interaction insulation, one could state that the O–H 0 hydrogen bonded network is effectively insulated from the herringbone interactions in 1 as well as from the halogen···halogen interactions in

3 and 4. These situations in effect represent two distinct structural possibilities for this family of compounds.

3.3.3 Indecisive C-F Groups in the Interlayer Packing of 2

Given the above background, it is now instructive to analyse the structure of the tetrafluoro derivative 2. The ring inclination is slightly more than in 1 and less than in 3 and 4 (Table 1), and is accompanied by an increase in the interlayer offset to 3.29A. Consideration of only ring inclinations leads to the conclusion that there is a smooth structural transition from 1-4. However, consideration of layer offsets and layer separations (Table 1) shows that this is not the case and indeed accentuates the oddity of the structure of 2. The interlayer separation in 2 is almost the same as, in fact slightly less than, in 1 whereas large interlayer separations are observed in 3 and 4. An increase in layer offset and an ambivalent ring inclination in 2 precludes herringbone type interactions, say of the $C(\delta+)\cdots F(\delta-)$ type, (Figure 2)[22,23] and also halogen···halogen interactions of the F···F type. Since the geometry of the O–H···O network is fixed, the only element of variability in these structures is the torsional freedom of the aromatic ring around the C-0 bonds and the concomitant changes in layer separation and offset. Two possibilities, exemplified by 1 on the one hand, and by 3 and 4 on the other are optimal. However, the tetrafluoro derivative, 2 adopts neither possibility and the ring inclination is balanced uneasily between the two optimal orientations. The layer structure and interlayer geometry are such that the F-atoms are as distant from one another or from any other group (shortest F • F. 2.88A; shortest F C, 3.00A). This weakness in packing is quantified by crystal energy calculations. The value of U_{latt} for 2 is significantly less than that for compounds 1, 3 and 4, whilst the short O···O separation perhaps compensates in part for the deficiencies in packing elsewhere in the structure.

There has been some discussion on the existence of attractive F—F contacts.[4] Retrieval of F···F distances from the CSD in a recent study reveals many

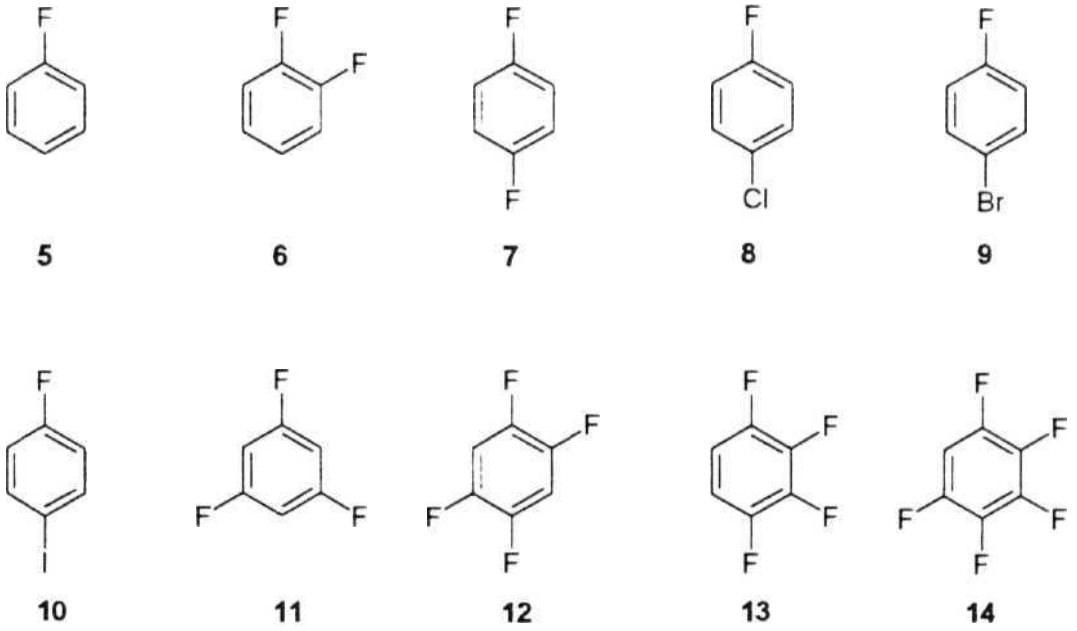
geometries in the 2.40-3 50A range.[24] Assuming a van der Waals radius of 1.47A for the F-atom.[25] many of these contacts could be described as short.[26] However, most of these have the type I geometry like the contact in compound 2. with the two F-atoms being related by an inversion centre In this context it should be noted that mere shortness of an intermolecular contact does not necessarily denote attraction and that in any crystal structure. a few repulsive contacts must co-exist with the numerous attractive contacts.[27] What is significant in 2 is that while the aromatic rings should be fully able to optimise their inclination. layer separation and offset within the constraints of the O–H O scaffolding to achieve an optimal F···F type II geometry, they fail to do so.[28] This more than any other reason indicates that the F-atom does not tend to form a polarisation-induced F···F contact. like Cl and Br

An analysis of the crystal structures of **1-4** reveals that the C-F group does not resemble either the C-H group or the C–Cl and C-Br groups in its packing characteristics and that it disfavours the structural alternatives adopted by the three latter groups. Neither herringbone type interactions. say of the C(δ+)···F(δ-) type, nor halogen···halogen interactions of the F···F type are realistic for if they were. compound 2 would resemble 1 or 3 and 4 more closely. The C-F group is also unable to adopt a distinctively stabilising packing of its own. say with a change in the O–H O pattern.[29] It is for this reason the term 'indecisive' seems appropnate in describing the supramolecular behaviour of this unique functional group at least in situations such as those found in the structure of **2.**

3.4 C–H···F Interactions in the Crystal Structures of some Fluorobenzenes

It is clear that the C-F group cannot compete with O–H groups to form 0-H ·F interactions in preference to O–H···O interactions. In order to verify the acceptor capabilities of the C-F group. C–H···F interactions are now considered As stated in Section 3.1. only compounds containing C. H and F-atoms (and no

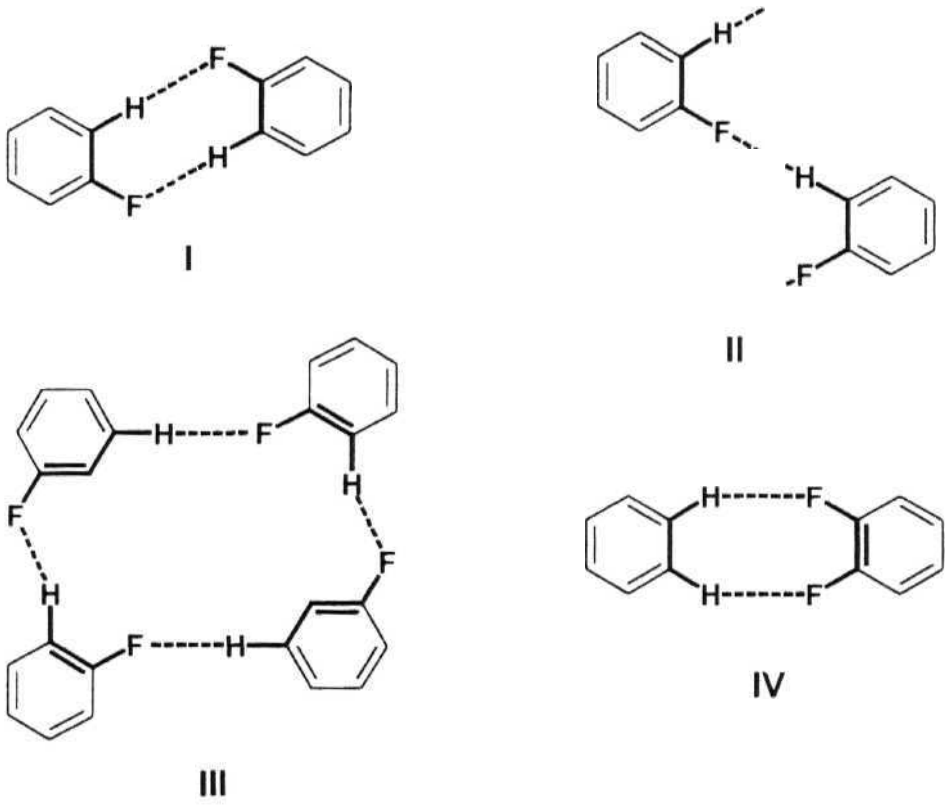
other) are appropriate Further, the dependence of the strength of the C-H X interaction on C-H group acidity[13] meant that the selected compounds should have as large a number of acidic C-H groups as possible. Thus, compounds 5-7 and 11-14 (Scheme 1) were chosen. Additionally, compounds 8-10 were identified as being closely related to 7. Fluorobenzenes 5-14 are advantageous from several viewpoints. They form a chemically homogeneous set and all of them contain just a single type of C-H group Because of the presence of the F-substituents on the benzene rings, the acidity of the C-H groups is enhanced Arguably, the acceptor ability of $C(sp^2)$–F is not as good as that of $C(sp^3)$–F [6] Still, the ease of obtaining compounds 5-14 (Aldrich) and the fact that the strength of any hydrogen bond depends more on donor acidity than on acceptor basicity led to the belief that these compounds were worthy of further structural study.



Scheme 1. Fluorobenzenes studied in this work

Reference has been made repeatedly to the presence of C–H F interactions with only limited descriptions as to what these interactions really are.[4,30] If the

C-H F interaction is of the hydrogen bond type, it should be similar at least in part to C-H 0 and C-H N interactions, the archetypes of the weak hydrogen bond.[31] An analysis of the similarities and differences between C-H-F and C-H ··O/C–H···N situations is therefore given in the following sections. Compansons have been made between the structures of fluorobenzenes 5-14 and topologically similar structures stabilised by C-H 0 and C-H N hydrogen bonds. Such comparisons are simplified by the identification of supramolecular synthons I-IV (Scheme 2).[32] These synthons, based on C-H-F interactions, are topologically similar to well-known C-H 0 and C–H···N based synthons.



Scheme 2. Supramolecular synthons based on C-H-F interactions in fluorobenzenes 5-14.

3.4.1. Fluorobenzene and Related Structures

In crystalline fluorobenzene. 5, ($P4_32_12$) molecules are bisected by the 2-fold axis (Figure 9a) and the symmetry-related *ortho*-H atoms are involved in C-H F interactions (2.474Å, Table 2). The C-F group acts as a bifurcated acceptor. In effect. each molecule is linked to four neighbours *via* mutually perpendicular C-H···F mediated helices parallel to [100] and [010]. The *meta*-H atoms form C-H···π interactions (C···π, H···π, C–H···π: 3.570, 2.728Å, 134.5°; π is the centroid of the aromatic ring) that link adjacent C-H-F helices. No short C-F or F···F interactions are found (shortest C···F and F-F distances are 3.372 and 4.727A).

In 5. the possible intermolecular contacts are C-C (stacking), C···H (herringbone). C-F (dipole···dipole), H—F (hydrogen bond) and F F (close-packing or polarisation). The only short intermolecular contacts found are the C-H···F interactions. Do these influence the crystal packing? In this context it is relevant to compare the structure of 5 with those of pyridinium fluoride (PyHF),[33] pyridine-1-oxide (PyNO)[34] and benzonitrile (PhCN).[3] These structures (Figure 9b-d) are built respectively with C–H···F , C–H···O and C-H—N hydrogen bonds and bear a close similarity to that of 5.

PyHF (Figure 9b) belongs to the space group $P4_12_12$ which is enantiomorphous to $P4_32_12$. Here too. molecules are bisected by the 2-fold axis and both *ortho*-H atoms act as hydrogen bond donors. now in C–H···F interactions[36] forming interconnected and perpendicular helices along [100] and [010]. Indeed, PyHF and 5 are isostructural (except for the difference in handedness). PyNO (Figure 9c) has been described in the space group *C222*\ with two symmetry independent molecules each bisected by a distinct 2-fold axis.[34] The H-atoms were not located in the reported structure and have been inserted in calculated positions. Here again, all the *ortho*-H atoms are involved in the formation of C–H···O hydrogen bonds with perpendicular and interlinked C–H···O mediated helices. In fact, PyNO and 5 are structurally similar as an inspection of Figures 9a and 9c will show.

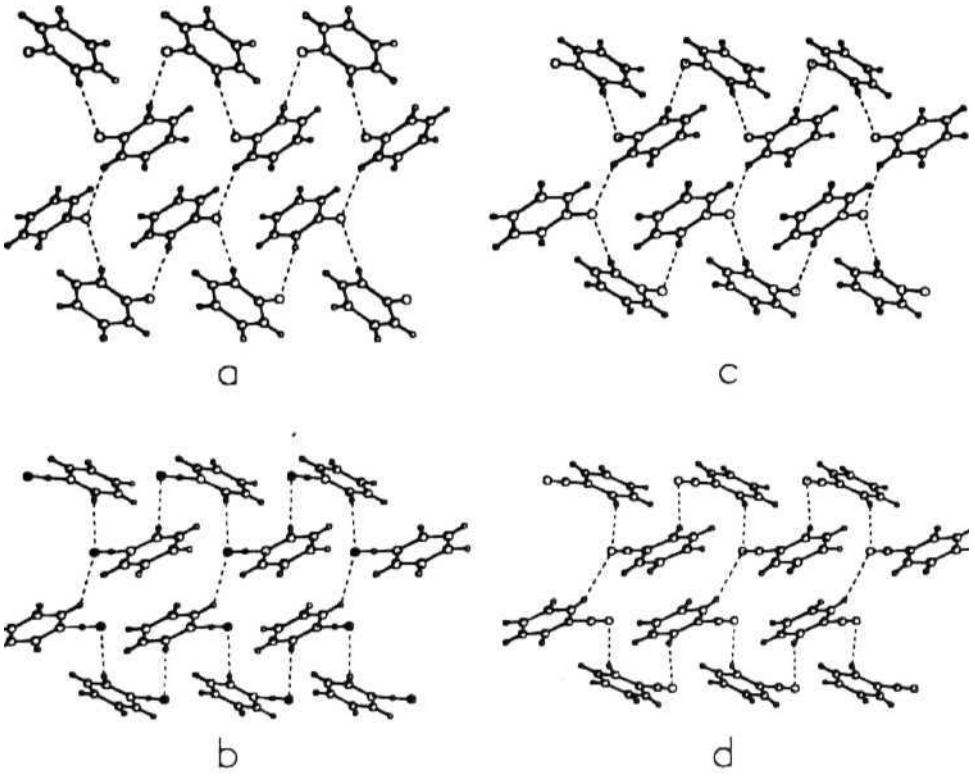


Figure 9. Structural similarity between 5 and, PyHF, PyNO and PhCN. (a) C–H···F mediated helices in the crystal structure of 5. Helices along [100] are shown horizontal. Helices along [010] are reduced to a single interaction for clarity. (b), (c) and (d) C–H···F^-, C–H···O and C–H···N mediated helices in PyHF, PyNO and PhCN respectively. Notice the similarity between (a), (b), (c) and (d).

Finally, PhCN (Figure 9d) belongs to space group $P4_12_12$ and is isostructural to 5 (except for the handedness). Here, C-H-N hydrogen bonds substitute for the C–H···F interactions.

The structural similarity at this very fine level, that is at the level of individual interactions, between 5 on the one hand and PyHF, PyNO and PhCN on the other, indicates that the nature and character of the structure-determining intermolecular interactions in these four structures are identical. There is no argument that inorganic fluoride is one of the best hydrogen bond acceptors. So the C–H···F

Table 2. C-H F interactions in the crystal structures of **5-14**.[a]

Compound	Interaction	C···F (Å)	H···F (Å)	C–H···F (°)
5	C2–H2···F1	3.376	2.474	140.33
6	C4–H4···F2	3.338	2.637	121.99
	C5–H5···F1	3.520	2.580	145.03
7	C2–H2···F1	3.569	2.681	139.23
	C3–H3···F1	3.455	2.488	148.43
8	C13–H13···F11	3.458	2.440	156.53
	C23–H23···F33	3.529	2.500	159.07
	C33–H33···F22	3.372	2.406	148.25
9	C31–H31···F12	3.541	2.501	161.27
	C32–H32···F11	3.413	2.423	151.85
10	C3–H3···F1	3.408	2.562	134.54
11	C2–H2···F1	3.396	2.624	127.82
	C2–H2···F3	3.441	2.454	151.29
	C4–H4···F3	3.422	2.501	142.66
12	C2–H2···F3	3.382	2.363	156.75
13a	C5–H5···F3	3.640	2.565	173.46
	C6–H6···F2	3.348	2.584	127.09
	C6–H6···F1	3.523	2.490	159.57
13b	C5–H1···F3	3.507	2.647	136.20
	C6–H2···F2	3.404	2.641	127.14
	C6–H2···F4	3.555	2.502	164.52
14	C6–H1···F12	3.637	2.627	155.52
	C6–H1···F15	3.565	2.864	122.70
	C6–H1···F11	3.456	2.783	120.36
	C16–H11···F4	3.568	2.641	143.49
	C16–H11···F1	3.316	2.596	123.37
	C16–H11···F2	3.653	2.729	143.38

[a] All C-H bond lengths are normalised to standard neutron distances.

interaction in PyHF is an attractive interaction and a significant hydrogen bond.[36] The nature and strength of C–H···O and C–H N hydrogen bonds is well-documented and these interactions are shown to control the crystal packing in many instances (See Chapter 5). Their respective roles in the structures of PyNO and PhCN parallel that of C–H···F^- in PyHF. It may be inferred therefore that the

C-H F interaction in 5 is likewise important in the adoption of the observed crystal structure.

It is now instructive to compare the crystal structures of 5 and chlorobenzene These packings are completely different, suggesting the varying behaviour of C-F and C–Cl groups. In chlorobenzene. Cl···Cl and herringbone interactions contribute the major stabilisation.

3.4.2 1,2-Difluorobenzene

1.2-Difluorobenzene. 6 belongs to the space group $P2_1/n$. Screw-related molecules are connected by C-H-F interactions (2.580, 2.637A, Table 2) giving catemeric chains along [010] which in turn lead to a layer structure parallel to (10 1) as shown in Figure 10a. The structure is replete with many other weak C-H-F interactions but herringbone interactions predominate and the overall packing (Figure 10b) is similar to that of benzene. just like 2-aminophenol, another *ortho*-disubstituted benzene that is discussed in Chapter 2.

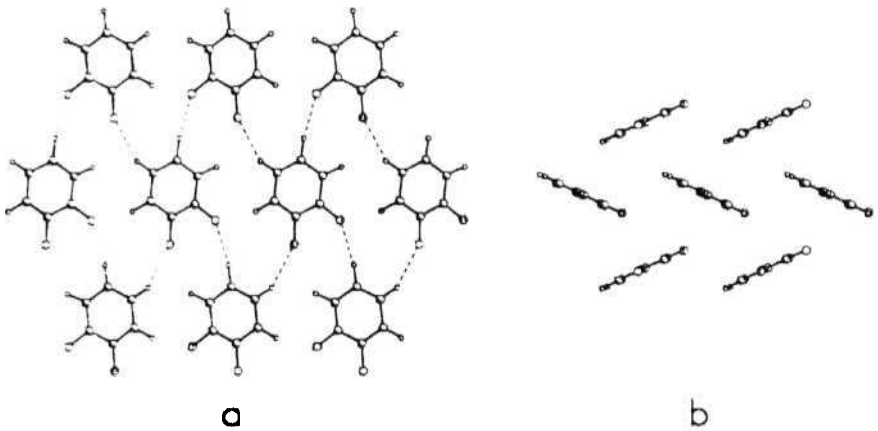


Figure 10. Crystal structure **of** 6. (a) C-H-F catemer mediated layer structure Note that alternating molecules provide C-H and C-F groups. (b) Herringbone arrangement of molecules in 6 similar to that found in benzene crystal structure.

3.4.3 1,4-Difluorobenzene and Related Structures

All the H-atoms in 1,4-difluorobenzene, 7 are involved in C–H F interactions (2.681, 2.488A, Table 2, Figure 1 la) that generate dimer and catemer synthons I and II (Scheme 1). Molecules translated along [010] are linked by synthon I and form linear tapes. Adjacent 2_1-screw axis related tapes (space group $P2_1/c$) are connected by synthon II to generate a corrugated sheet structure parallel to (10 2). These corrugated sheets are held together by weak herringbone interactions along [001] to complete the three-dimensional structure.

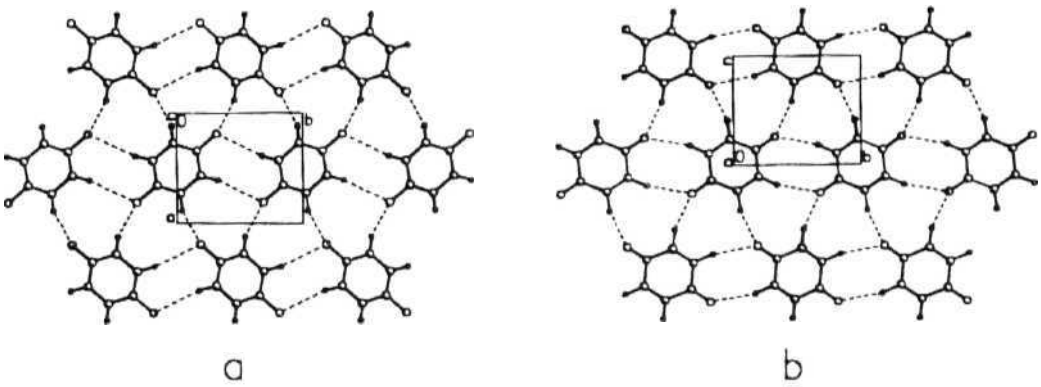


Figure 11. Structural similarity between 7 and BQ. (a) Corrugated sheet structure parallel to (001) in 3. Notice synthons I and II. (b) Flat sheets stabilised by C–H· O hydrogen bonds in the crystal structure of BQ. Notice C–H O dimer and catemer synthons.

A comparison of the crystal structures of 7 and 1,4-benzoquinone (BQ)[37] is revealing. BQ adopts space group *P2\la* (Z = 2) and C–H O mediated dimers and catemers topologically similar to I and II may be identified. C-H O dimer mediated tapes are linked by C–H···O catemers to produce a perfectly flat sheet structure (Figure 11b). It is evident from Figures 11a and 11b that C–H···F interactions and C–H···O hydrogen bonds produce similar supramolecular synthons which lead to similar supramolecular structures (tapes and sheets).

The structure of 3 may also be contrasted with those of other 1.4-dihalobenzenes. 1.4-Dichlorobenzene exists in triclinic (β-form) and monoclinic (a- and γ-forms) modifications that are stabilised by type I and type II Cl···Cl interactions respectively. The crystal structure of 1,4-dibromobenzene is isostructural to, and several forms of 1,4-diiodobenzene are closely related to the α- and γ-forms of 1,4-dichlorobenzene. All these structures are distinct from 7. which is largely stabilised by C-H-F interactions While the structures of the other 1,4-dihalobenzenes are influenced by X···X (hereafter X = Cl. Br or I) interactions, F···F interactions are not favoured in 7. With its ability to form attractive C-H-F interactions, 7 resembles BQ rather than the other 1.4-dihalobenzenes.

A comparison of the structure of 7 with those of 4-chlorofluorobenzene. 8. 4-bromofluorobenzene. 9 and 4-iodofluorobenzene. 10 is interesting.[39] The C–H F catemer synthon II is present in all these three crystal structures and is identical to that seen in 7. Figures 12a-c show that this catemer synthon is well-insulated from other halogen···halogen patterns, characteristic only of the heavier halogens So type II I···I interactions are found in 10 (Figure 12c) while both type I and type II Cl···Cl and Br···Br interactions are found in 8 and 9 respectively (Figures 12a and 12b show only the type I interactions). Notably, no short F···F contacts are observed in any of the three structures and the shortest F···F distances in 8. 9 and 10 are 3.344, 3.384 and 3.408A respectively.

Despite other variations in structures 8-10. the C–H···F based synthon II remains intact. This synthon is, in effect, sufficiently robust in the presence of the well-known type I and type Il Cl···Cl, Br ·Br and I···I interactions. It is therefore either the dominant pattern in these structures or at the least, immune to interference from the X···X interactions and the putative F···F interaction that is not seen at all. Though there is enough possibility for the existence of such an interaction in compounds 7-10, its absence shows that it cannot compete with the

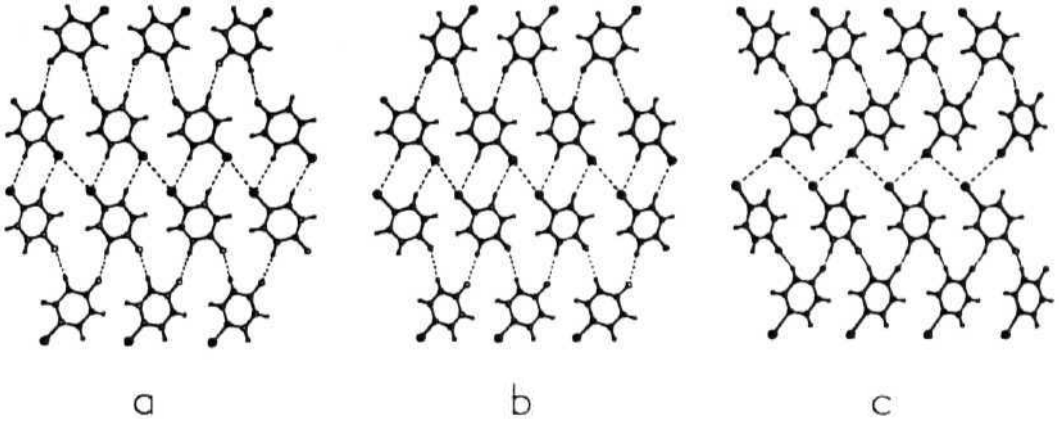


Figure 12 Crystal structures of 8. 9 and 10. (a) Sheet structure in 8. Two such symmetry independent sheets are observed. (b) Sheet structure in 9. C–H···F catemer synthons II. alternate with C–H···Br dimers and type I Br···Br interactions. Compare this with (a). (c) Alternating C-H-F catemer synthons II, and type II I I interactions in the corrugated sheet structure of 10.

C-H-F interaction. The demonstration of such a viability of the C–H···F interaction in these compounds indicates an attractive nature of C-H-F interactions. Hints along these lines were obtained a decade ago[40] but the present study offers direct experimental evidence for the importance of the C-H-F interaction and of synthons based on this interaction.

3.4.4 Structural Similarity between 1,3,5-Trifluorobenzene and 1,3,5-Triazine

The molecule of 1,3,5-trifluorobenzene, **11**, (*I*2/*a*) is bisected by the 2-fold axis. Each H- and F-atom is involved in the formation of two C–H • F interactions, or in other words, bifurcation occurs at every atom. Each molecule is connected to six neighbours through synthon I. This extends to three cross-linked, synthon I mediated tapes, two of which are shown in Figure 13a. In effect, the three-dimensional structure is extensively stabilised by C-H-F interactions (2.454,

2.501. 2.624A).[41] It may be noted that as one moves along the series **5-14** towards the more F-rich molecules, the relative importance of C-H-F interactions increases and in **11**. for instance, this is mostly the only interaction of significance. The structure of **11** is clearly understood then as a result of the enhanced C-H acidity brought about by increasing number of F-substituents and of the availability of a matching number of C-F acceptors. In this light. it is not at all difficult to appreciate the close similarity between **11** and the classical structure of 1.3.5-triazine[42] (*R 3 . Z = 3:* Figure 13b) wherein each molecule is linked to six neighbours through C–H ·N dimers Here too. three cross-linked. now C-H-N dimer mediated. tapes may be identified. Specifically, the following similarities may be noted between **11** and *sym*-triazine: (i) both have similar molecular features in terms of the number and relative disposition of hydrogen bond donor and acceptor groups: (ii) these groups are utilised in the same manner and twelve short hydrogen bond type interactions (C–H···F. C-H-N) per molecule are observed in both cases; (ni) each molecule is connected to six neighbours through topologically similar supramolecular synthons and in an identical manner; (iv) anti-parallel stacking of molecules is seen in both the structures This fine similarity between **11** and *sym*-triazine indicates that the C-H-F interactions in **11** and the C–H·· N hydrogen bonds in *sym*-triazine play a very similar role in supramolecular assembly in the respective cases. In an early review on weak hydrogen bonding. Bernstein. Cohen and Leiserowitz[43] emphasised that for such interactions. it is the repetitiveness of a certain pattern that is more significant than the geometrical attributes. As illustrated in Chapter 1 such repetitiveness indicates the transferability of synthons.

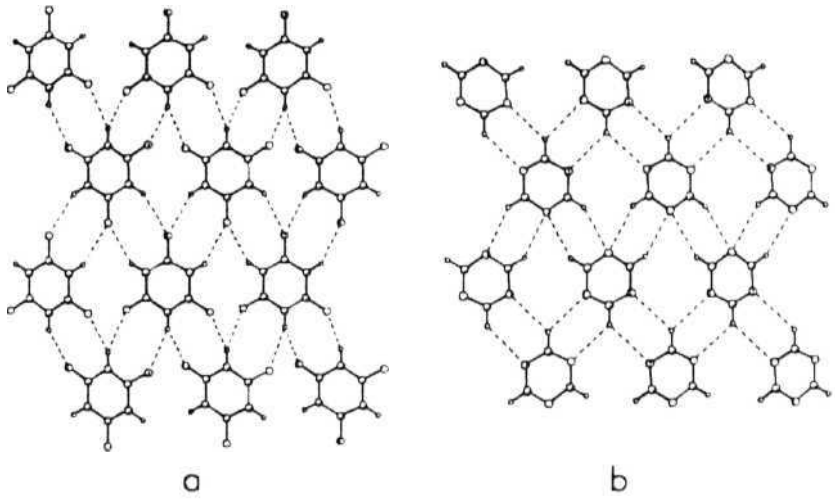


Figure 13. Structural similarity between 11 and 1,3,5-triazine. (a) Two cross-linked synthon I mediated tapes in the crystal structure of **11**. The third tape is not shown for clarity. Notice the bifurcation at H- and F-atoms. (b) C–H···N dimer mediated cross-linked tapes in the structure of triazine. Notice the similarity between the two structures.

3.4.5 Isostructurality of 1,2,4,5-Tetrafluorobenzene and 1,2,4,5-Tetrazine

The molecule of 1,2,4,5-tetrafluorobenzene, 12 lies on an inversion centre ($P2_1/c$. Z = 2) and the two symmetry-related H-atoms form very short C-H-F interactions (2.363A). Each molecule is thus connected to four neighbours as shown in Figure 14a. This defines synthon HI that mediates in the formation of corrugated sheets roughly parallel to (10 2).[44] The close-packing of these sheets leads then to the three-dimensional structure. As was observed for **11** and 1,3,5-triazine. the structures of 12 and 1,2,4,5-tetrazine[45] (Figure 14b) are very similar, indeed isostructural. Corrugated sheets based on C-H-N interactions are seen in the tetrazine and are topologically similar to those found in the structure of 12.[46] This lsostructurality further strengthens the argument that C-H F interactions determine crystal packing as do C-H-N interactions and in this respect, provides more evidence for their description as weak hydrogen bonds. Along these lines, it should be noted that the C-H-F interaction in the structure of 12 is the shortest

among those found in this study. This is as might have been expected if the strength of a C–H ·F interaction increases with increasing acidity and hardness of the H-atom. In general, C–H 0 and C–H N hydrogen bonds are considered to arise from the interactions between a soft donor (C-H) and a soft acceptor (0 or N). The F-atom in the C-F group is, however. a hard acceptor and this could be one of the reasons why it does not form very effective C–H···F hydrogen bonds The hardness of the H-atoms in compounds 5-14 (in addition to their acidity) could well promote the formation of short C-H ·F hydrogen bonds in this structural family.

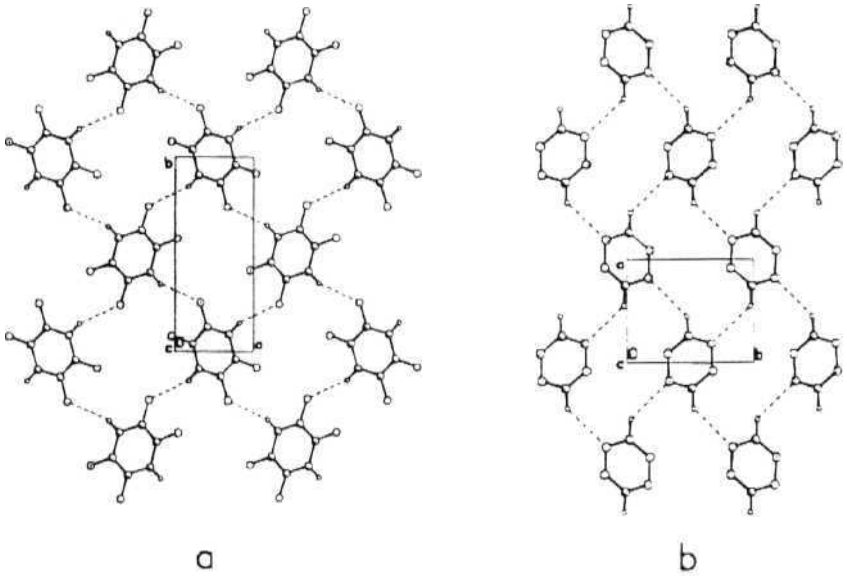


Figure **14** Structural similarity between 12 and 1.2.4.5-tetrazine. (a) Corrugated sheet structure formed by synthon III in 12. (b) Similar sheet structure formed by topologically similar synthons made of C-H N hydrogen bonds in tetrazine.

3.4.6 Polymorphism in 1,2,3,4-Tetrafluorobenzene

Crystals of 1,2,3,4-tetrafluorobenzene, 13 were grown from the pure liquid as described in Section 3.6.1 and were found to belong to space group *Cllc* (Z = 8).

This form is labelled **13a.** Another form has been found, **13b.** ($P2_1/n$, Z = 4)[47] that has been grown from 1:3 toluene-pentane at 195 K Interestingly. C–H F interactions are important in both polymorphs. Sheets parallel to (30 T) are observed in **13a** (Figure 15a). Both H-atoms in the molecule. one of them bifurcated, participate in C–H· F interactions (2.490, 2.565. 2.584Å) Molecules translated along [010] are connected by synthon IV to form tapes Adjacent *c*-glide related tapes are held together by synthon II to give a pair of tapes Successive pairs of tapes are inversion related (but not connected with C–H ··F interactions) to generate the sheet. Stacking along [100] gives the three-dimensional structure. In **13b,** anti-parallel stacking of the molecules lead to stacked diads (Figure 15b). The packing of tliese diads in a sandwich herringbone fashion produces a layer[48] and the interlayer packing is governed by C-H-F interactions. Here too, both the H-atoms are involved in C-H-F interactions with one of them bifurcated (2.502, 2.641, 2.647A). Synthon IV mediated tapes are again identified with successive 2_1-screw axis related tapes being linked by C-H-F interactions.

In terms of C-H-F synthons, structures **13a** and **13b** provide essentially the same information and suggest the overall structural influence of C-H-F interactions. Synthon IV is identified in both the forms and linear tapes based on this synthon constitute a significant portion of the respective structures. Though the packing of these tapes is different in the two forms, it is the C–H F interactions that are utilised for this purpose. All in all, the C-H-F interactions seem to play an important and similar role. This similarity arises from the fact that the same synthons are seen in both cases, though the final structures are different.

In order to further gauge the significance of these structures. *ab initio* structure predictions were attempted with the Polymorph Predictor module in the Cerius^2 program.[49] The prediction was carried out in each of the observed space groups and in each case, a structure was obtained that closely matched the experimental

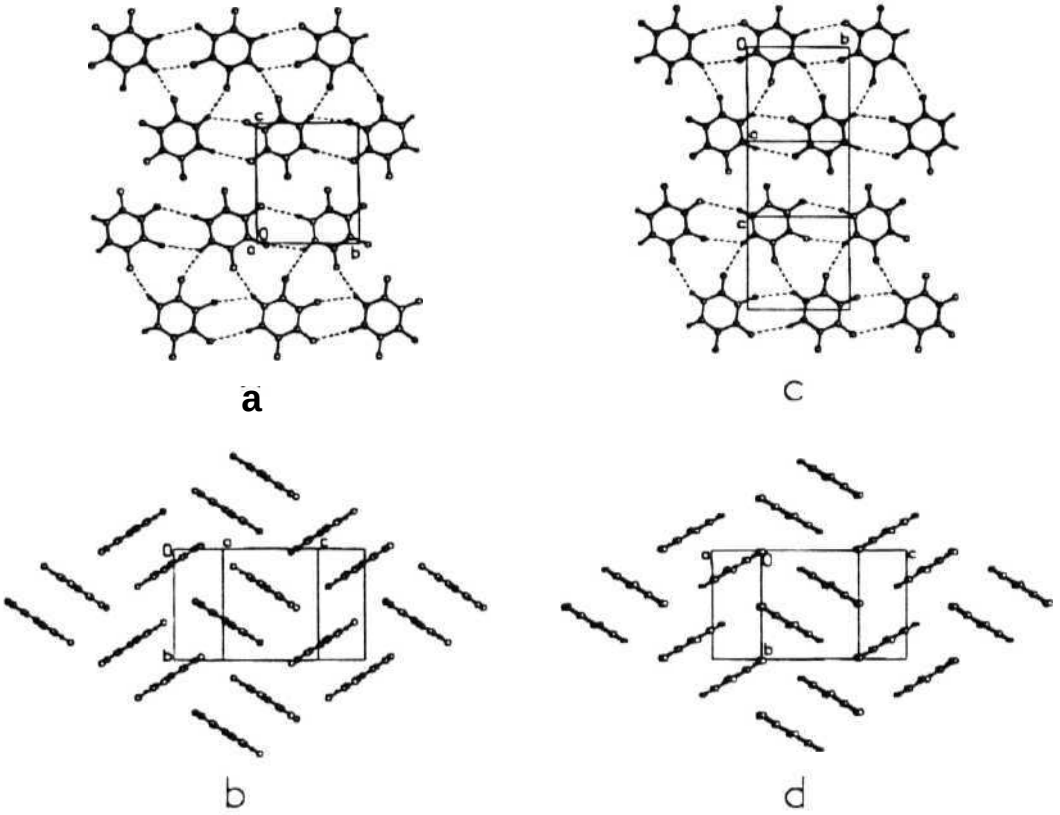


Figure 15 Polymorphism in 13. (a) and (c) Flat sheet structure based on synthons II and IV in experimental and predicted structures in $C2/c$ space group. Notice the similarity between the two structures. (b) and (d) Sandwich herringbone packing seen in experimental and predicted structures in $P2\backslash ln$ space group. Notice the similarity between the two structures.

structure. These predicted structures are shown in Figures 15c (form **13a)** and 15d (form **13b).** Both the predicted structures contain synthon IV mediated tapes. The prediction in *Cllc* resulted in perfectly flat layers as observed in **13a,** with the packing of molecules within and between layers identical to that found in the experimental structure. The prediction in $P2\backslash ln$ reproduced the diads and the sandwich herringbone packing seen in **13b.** The minor difference between the experimental and predicted structures is the relative mutual orientation of these

diads within the sandwich herringbone pattern. These two prediction sequences illustrate the ability of the Polymorph Predictor software in the *ab initio* prediction of crystal structures and also show that the experimental structures are not unrealistic. The polymorphism that is obtained in this system could arise from the fact that the temperatures of crystal growth were different in the two cases.

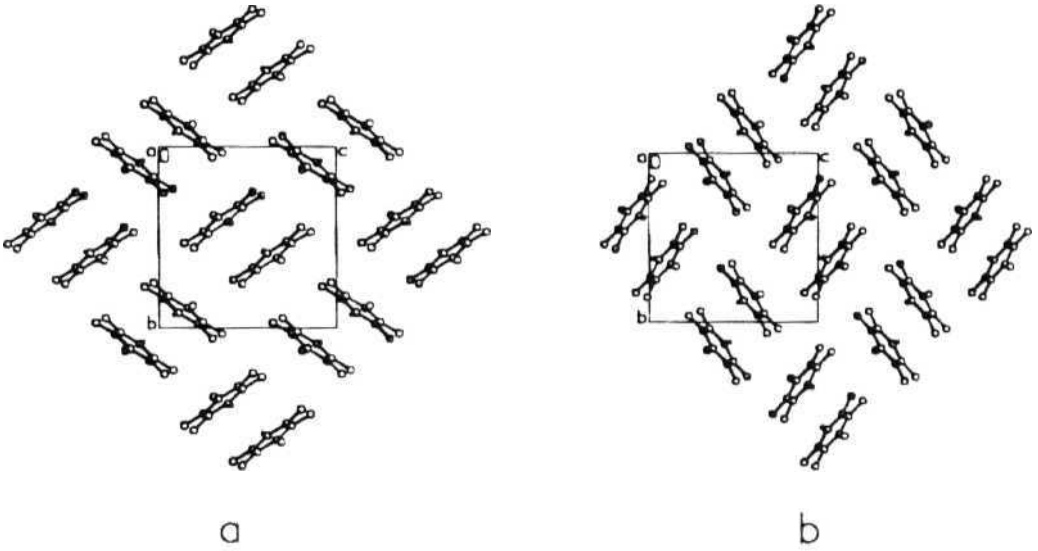


Figure 16. Crystal structure of 14 showing sandwich herringbone packing of molecules. Symmetry independent molecules form alternating independent layers at different heights along the *a*-axis. The layers shown in (a) and (b) are present at [100] and [200] respectively.

3.4.7 Pentafluorobenzene - Sandwich Herringbone Packing

In F-rich pentafluorobenzene. **14** the C-H group is trifurcated between three C-F groups. There are two symmetry-independent molecules ($P2_1/c$, Z=8) and each forms a centrosymmetric diad as in **13b** (Figure 16). The assembly of 2_1-related diads in a sandwich herringbone fashion leads to alternating, symmetry-independent layers parallel to (100). Interlayer packing is stabilised by C–H • F interactions (2.596-2.864Å). In hindsight, **13b** and 14 seem to adopt the same

cnstal structure because their large dipole moments favour the anti-parallel diad as the primary structural motif.

3.4.8 Hydrogen Bond Nature of the C–H···F Interactions in 5-14

As mentioned in the Introduction, the C-H-F interaction is generally weak and does not play a significant structural role in crystal packing because of the presence of acceptors that are stronger and more polarisable than the C-F group A set of compounds that contains only C-. H- and F-atoms is therefore more appropriate to assess the viability of this interaction. Accordingly, the cnstal structures of 5-14 have been determined and analysed. It is now pertinent to compare the C–H F interactions in these crystal structures with all the others in the CSD that contain only C-. H- and F-atoms. Figures 17a and 17b are scatterplots of H···F distances, *d versus* C-H F angles. *6* (H-atom positions normalised). Interactions between all types of C-H and C-F groups are shown in Figure 17a while Figure 17b includes only interactions between $C(sp^2)$–H and $C(sp^2)$–F groups. There is no real difference between these scatterplots. Generally, there is some kind of inverse correlation between length and angle but there are many points in the top right hand corner of these plots that simply add to the crystallographic noise. Some of these correspond to bifurcated interactions but no specific conclusion may be drawn on this or any other basis. In contrast, Figure 17c which is the corresponding *d-9* scatterplot for the compounds in this study shows a strong negative correlation that is very characteristic of hydrogen bonding. The top right hand corner is now completely empty, suggesting definitely that when a C-H-F geometry is present in these compounds, it is there for a specific chemical reason. Table 2 shows that the H···F distances decrease systematically with increasing C-H group acidity. Compounds 11 and 12 are especially noteworthy in this regard. An inspection of plots 9a-c reveals that only when the carbon acidity is enhanced to the levels of the compounds in the present

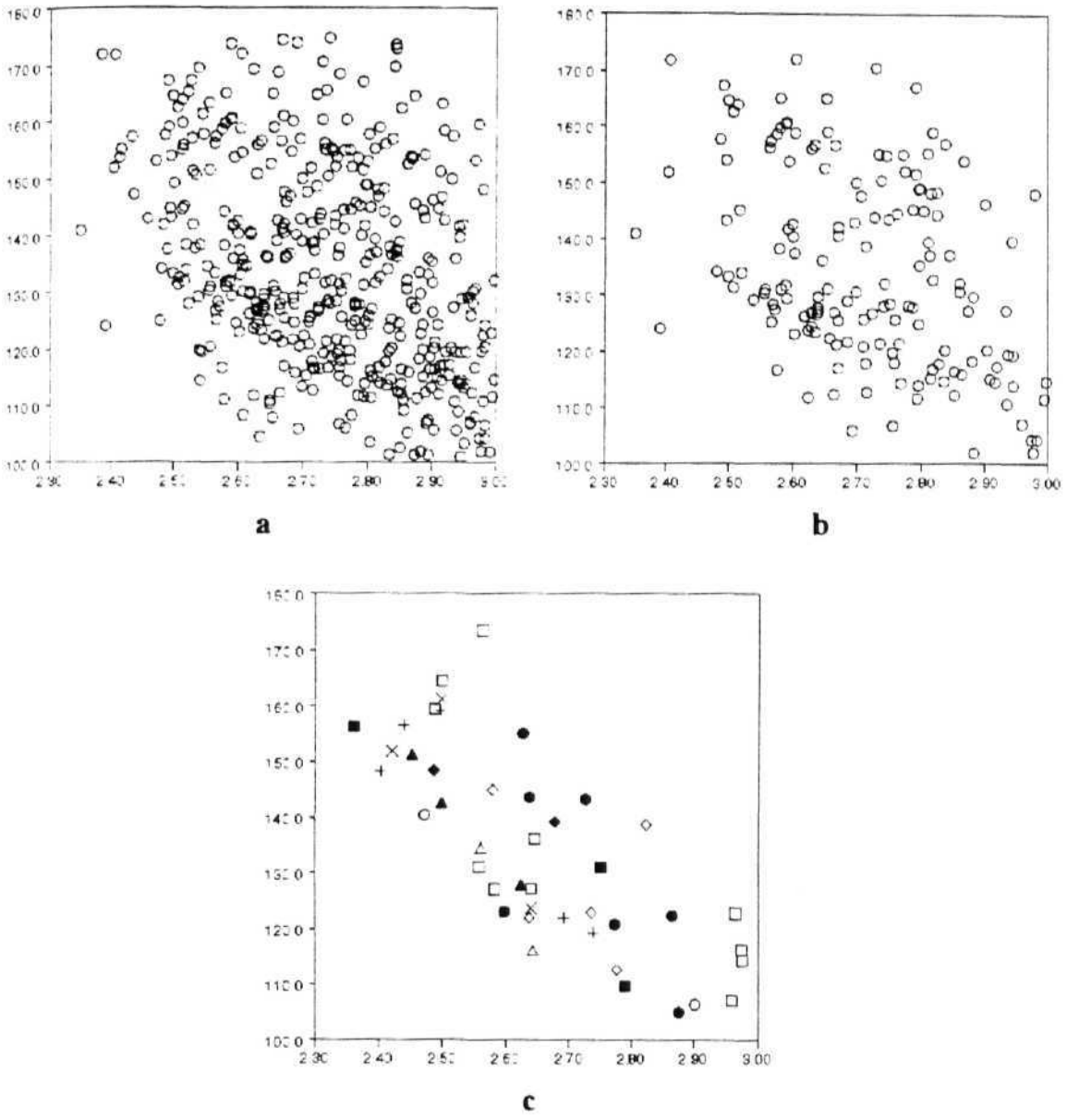


Figure 17. Scatterplots of H···F distance *versus* C–H···F angles for the C–H···F interactions. (a) Interactions between any C–H and any C–F found in CSD. (b) Interactions between $C(sp^2)$–H and $C(sp^2)$–F found in CSD. (c) Interactions found in the present study (O:**5**, ✧:**6**, ◆:**7**, Δ:**8**, ×:**9**, ✚:**10**, ▲:**11**, ■:**12**, □:**13**, ●:**14**) Notice the broad scattering of points in (a) and the narrow band in (c).

study and only in the absence of competing acceptors is the hydrogen bond nature of the C~H F interaction even revealed Selection of specific compounds is not new to the study of weak hydrogen bonds. The C-H-F interaction is not likely to manifest itself easily. In addition to the absence of competing acceptors, the relevant C-H acidities must be sufficiently high. Once these conditions are met. however. C-H-F geometries seem to display all the characteristics of weak hydrogen bonds. In particular they resemble the C–H···O and C–H···N hydrogen bonds in their structure-directing properties and in this respect, they could be possibly used in crystal engineering strategies.

3.5 Conclusions

A comparative analysis of the crystal structures of hydroquinones **1-4** reveals the supramolecular behaviour of the C-F group when it is compelled to associate only with strong hydrogen bonding donors and acceptors. The O–H···O hydrogen bonds are dominant in these structures and consistently produce a rigid framework. The C-F group does not compete with the -OH group to form hydrogen bonds of the O–H···F type This study also reveals that the C-F group does not resemble either the C-H group or the C–Cl and C-Br groups in its packing charactenstics and that it disfavours the structural alternatives adopted by the three latter groups

The acceptor capabilities of the C-F group are expected to be revealed in the absence of competing acceptors such as O- and N-atoms and the crystal structure analyses of compounds **5-14** confirms the existence of significant **C-H-F** interactions. It has been shown that C-H-F interactions can be as important as C–H O and C–H···N hydrogen bonds in stabilising specific crystal structures. A comparison of the fluorobenzene structures **5-14** with the corresponding chloro. bromo and iodo structures unequivocally proves that F behaves distinctly different from the other halogens. F would form C-H-F interactions rather than F···F contacts, whereas the heavier halogens seem to prefer the formation of

halogen···halogen interactions Supramolecular synthons based on C–H···F interactions and that are topologically similar to well-known C–H···O and C-H · N synthons may be identified. Such synthons can in principle be used in the design of novel and functional crystals. The general influence of C–H F interactions has been shown to be the same in the pol>Tnorphic modifications **13a** and **13b**. other differences notwithstanding. Having established the nature of these newer interactions one could then proceed to the *ab initio* prediction of crystal structures. Monte Carlo simulation based crystal structure predictions of **13** in the experimentally observed space groups \ield structures that are very closely related to the experimental ones. An inverse *d-6* correlation with little scatter for the C–H···F interactions in compounds **5-14**, shows that these interactions have the characteristics of weak hydrogen bonds.

3.6 Experimental

3.6.1 General Procedure for Crystal Growth

Single crystals of 2 were selected from the Aldrich sample as received. Single crystals of 4 were obtained by slow evaporation of a $CHCl_3$ solution. All the fluorobenzenes (**5-7** and **11-14**) were commercially available (Aldrich) and were used for crystal growth as received Since all these compounds are liquids, a special crystal growth technique described below was followed.[50] The experimental setup consists of an X-ray diffractometer with an attached low-temperature device for cooling the sample. An IR laser source is setup in such a way that the sample can be irradiated with the laser. The liquid sample was loaded into a capillary and then the capillary was perfectly sealed. After placing the capillary onto the goniometer, the sample was cooled slowly below its melting point. The cooling had to be done carefully so as to ensure that the liquid becomes poly-crystalline but not glassy (getting a single crystal just by cooling is almost impossible). The IR laser was then applied at such an intensity where it just melts the poly-crystalline compound. The laser beam was applied on a very tiny portion

and was scanned along the length of the capillary very slowly while the temperature was kept constant. The rate of scanning depends on the nature of the sample and this can only be identified by the experiment. After few cycles of scanning the poly-crystalline sample transforms and anneals into a single crystal. At this stage, the quality of the crystal was checked by X-ray rotation photographs and the laser experiment was repeated with varying intensities and varying scan speeds till an X-ray quality single crystal was obtained.

Collecting the data just below the melting point of the sample was obviously difficult and once the single crystals suitable for X-ray data collection were obtained the temperature was gradually decreased. The data was then collected at low temperatures (see appendix). The integrity of the crystal was checked at regular intervals during cooling through standard X-ray routines. It must be mentioned that in several instances getting a single crystal itself was difficult (sometimes innumerable attempts were required). Maintaining the integrity of the crystal during cooling was equally difficult and this was the reason why the data were collected at different temperatures. In each instance the data was collected at the best possible temperature.

3.6.2 X-Ray Crystallography

The X-ray data were collected at the University of Essen, Germany by the candidate and by Mr. H -C. Weiss and Mr. D. Blaser under the supervision of Prof. R. Boese. An empirical absorption correction based on equivalent reflections was applied for 4 (Seimens-SADABS), the structure solutions and refinements were carried out using the SHELXS-86[51] and SHELXL-93[52] programs built-in with the Siemens SHELXTL (Version 5.03) package. In contrast to 2, where the hydrogen atom could be located and refined without constraints, the hydrogen atom for 4 had to be treated as rigid group because of the high absorption of the Br-atoms. In the structures of all the fluorobenzenes (5-7 and 11-14) the H-atoms were located from difference Fourier maps and were refined isotropically. Further

details of the X-ray data collection, structure solution and refinement are given in the appendix.

3.6.3 Crystal Energy Calculations

Lattice energy calculations on 1-4 were carried out using the Cerius^2 program.[49] The electrostatic potential (ESP) charges were obtained by single-point AM1 (MOPAC6) calculations on the molecular geometry as found in the crystal structure. Since energy minimisations can vary the C–O–H torsion angles and produce totally different calculated geometries, these molecular geometries were not optimised further. The molecules were assigned AM1 ESP charges and the lattice energy, U_{latt} calculated using the Dreiding 2.21 force field in the Crystal Packer module. The evaluation of Coulombic interactions was done using the standard Ewald summation technique; van der Waals interactions were truncated at 8()A separation O–H···O hydrogen bonds were included in the calculations and repulsive van der Waals interactions from H-atoms were excluded. The search for hydrogen bonds in the Crystal Packer module also loads O–H F-C hydrogen bonds, but based on the current knowledge that these interactions are very weak,[6-7] they were not included in the calculations. The energy of the crystal was then minimised until the gradient in energy was below 0.01 kcal/mol.

3.6.4 Polymorph Prediction

Polymorph predictions on 13 were carried out using the Polymorph Predictor (PP) module in the Cerius^2 program[49,53] Initial molecular minimisation was carried out with the AM1 Hamiltonian in Mopac 6.0. ESP charges were assigned using Mopac 6.0. Dreiding 2.21 force field was used for all PP calculations. The Ewald long-range summation method was used for electrostatic interactions. The number of molecules in the asymmetric unit was specified. Monte Carlo packing simulation technique at the fine level (the program provides three levels, fine, medium and coarse) was followed for each of the space groups in which the

structure was to be predicted. The following are the sequence of events that were carried out by the PP module during the prediction. Large numbers of unoptimised structures were produced for each space group Only low energy structures were taken for further analysis. Many of these structures were very similar and may be grouped into clusters. Cluster analysis was then performed at fine level to obtain low energy representative of each cluster based on a modified Patterson function. This reduces the number of structures to a large extent and outputs low energy cluster representatives that were still energetically unrefined. A full energy minimisation with respect to all degrees of freedom was carried out on each of these structures. A final cluster analysis was performed on these energy minimised structures and the lowest energy' structures were considered for further study. The whole polymorph prediction sequence was repeated twice to check its reproducibility from different starting points This is considered to be an advisable procedure.

3.6.5 Retrieval of C-H-F Geometries

The October 1997 release of the CSD[54] consisting of 175 093 entries. was used to retrieve C-H-F interactions in crystal structures. A database subset was made for error and disorder free structures with R < 0.10 consisting of the elements C. H and F only. Duplicate entries with higher R-values were removed. Subsequent searches were made on this database subset. The C-H bond lengths were normalised to the standard neutron distances. The H F distances < 3.0Å were retrieved within a C-H-F angle range of 100-180°.

3.7 References and Notes

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CHAPTER FOUR

SUPRAMOLECULAR SYNTHESIS BASED ON IODO···NITRO SYNTHONS

4.1 Introduction

By organic synthesis has meant, till recently, the construction of molecular systems using covalent bonds. A combination of the huge volume of work done over more than a century in the making of these bonds along with chemical intellect has culminated in the synthesis of molecules as complex and as intricate as Vitamin B_{12},[1] palytoxin[2] and taxol[3] to name a few. Nevertheless, molecular synthesis has found its limits, since there is a need for fast and convenient production of nanosystems that have applications as functional materials and practical devices.[4] The inability of molecular synthesis to cope with such demands has necessitated the development of a new form of synthesis, namely *supramolecular synthesis*, which deals with the construction of multicomponent supramolecular assemblies utilising intermolecular interactions.[5] Indeed, supramolecular chemistry, the chemistry beyond molecule, has been developed into a highly interdisciplinary area of research.[5b] A crystal of an organic compound consists of millions of molecules held together by intermolecular interactions and has been recognised as a perfect example of supermolecule, a supermolecule *par excellence*.[6] Systematic crystal engineering,[7] the design of crystal structures, is therefore a supramolecular equivalent of organic synthesis.[5a]

Targets in molecular synthesis are defined in terms of covalent bond connectivity with an appreciation of the accompanying stereochemistry. Any crystal structure may be depicted as networks with molecules acting as nodes and the supramolecular synthons as node connectors. Taking advantage of such simplification of complex organic structures, targets in crystal engineering may now be conveniently defined in terms of networks with due attention to the chemical and geometrical characteristics of intermolecular interactions. The fundamental difference between molecular and supramolecular synthesis is that

while the targets are constructed in a stepwise and sequential manner in the former, self-assembly results in the formation of targets in a single step in the latter. Various targets may now be discerned at a supramolecular level *viz.* ribbons, tapes, sheets, layers, channels, tubes, cavities and a variety of two and three-dimensional networks. The target in the present work is a linear ribbon and the possibility of constructing such a ribbon, based on the iodo···nitro synthon, I formed from two convergent, polarisation-induced I ···O interactions, is explored further in this chapter.[8] Synthon I has been observed in this laboratory and symmetrical and unsymmetrical variations of these synthons have been identified from a CSD study.[9] In this work, the crystal structures of 4-iodonitrobenzene, 1 and the 1:2 complex, 2. of 1,4-dinitrobenzene and 4-iodocinnamic acid have been determined. These structures along with that of the 1:1 complex, 3, of 1,4-dinitrobenzene and 1,4-diiodobenzene, reported previously,[10] illustrate the utility of the supramolecular synthon concept in developing strategies for systematic and general crystal engineering as is described in the following sections.

I II

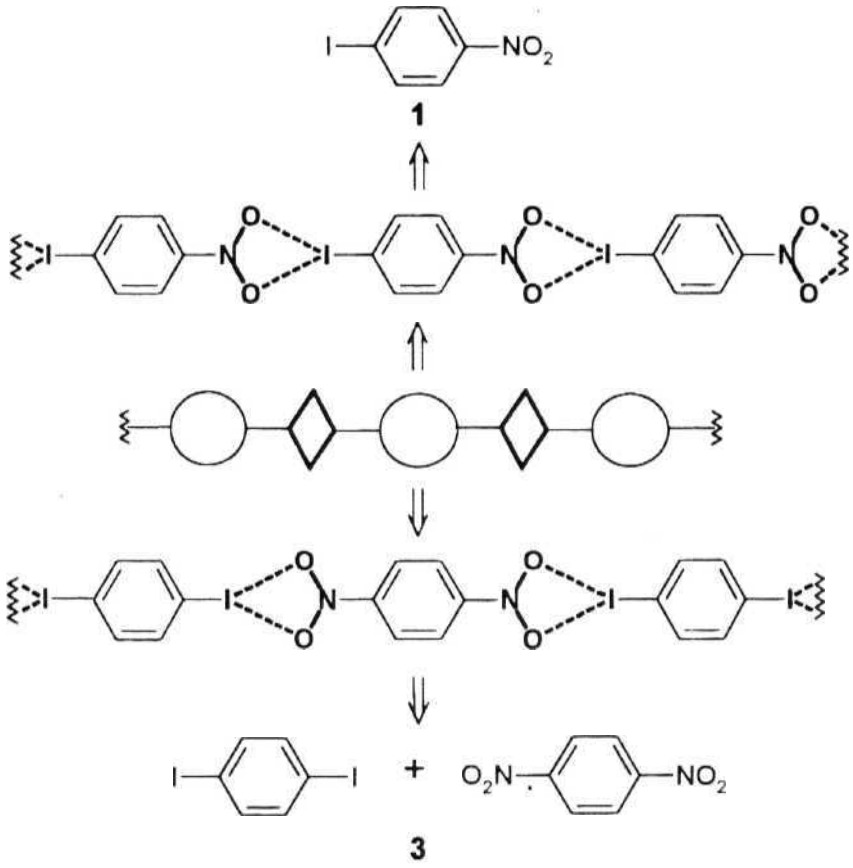
4.2 Supramolecular Retrosynthesis

Retrosynthesis in the realm of synthetic organic chemistry involves the logical dissection of complex molecular structures into simpler components *via* synthetic intermediates which contain the essential information in the targets. These intermediates are termed synthons. Inherent in retrosynthesis is a certain structural simplification and this phenomenon is naturally expected to be of greater utility in crystal engineering since the targets here are much more abstract. Retrosynthesis is thus applied to supramolecular (crystal) structures, conveniently conceived as networks, resulting in the supramolecular intermediates, that is the supramolecular

synthons, which comprise the vital intermolecular information necessary for building up the entire structure. The final step is the identification of the constituents. The general supramolecular retrosynthetic plan may then be described as networks (crystal structures) ⇒ supramolecular synthons ⇒ constituents (molecules). Scheme 1 illustrates the supramolecular retrosynthesis of a linear ribbon structure. The strategy involves the alternation of molecular and supramolecular synthons each of which have linear ditopic connectivity. Phenyl rings and I synthons are considered for this purpose and there are two ways of alternating these synthons. Synthon 1 is intrinsically polar and if the successive synthons are related by translation a polar ribbon structure results and compound 1 is the end point of the retrosynthesis. The crystal structure of 1 is shown in Figure 1 and it may be observed that the desired ribbon pattern is obtained. If the successive supramolecular synthons are inversion related, a centrosymmetric ribbon structure is generated as observed in the crystal structure of complex 3 (Scheme 1). It is seen from the structures of 1 and 3 that though the constituent supramolecular synthons are the same and appear at the same location in the linear ribbon, their relative mutual orientation leads to varying molecular components in the retrosynthetic analysis. Implicit here is the anisotropy (polarity) of the supramolecular synthons. This may be readily appreciated if one considers the centrosymmetric carboxyl synthon, II. Alternating synthon II with phenyl rings in a linear ribbon leads to only one molecular possibility-, namely terephthalic acid.

4.3 Robustness of Iodo···Nitro Synthons

The transferability of I synthons between the above structures is revealed by their presence in compound 1 and in complex 3 and suggests the robustness of these synthons. Such robustness may further confirmed by introducing other relatively strong synthons (such as II) into the supramolecular structure. Structural simplification assisted by retrosynthesis allows for the planning of a



Scheme 1. Retrosynthetic analysis of the linear ribbon pattern leading to compound 1 or alternatively to complex 3. Supramolecular synthons are shown as heavy lines.

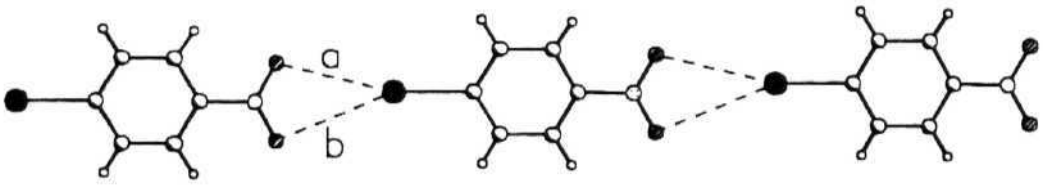
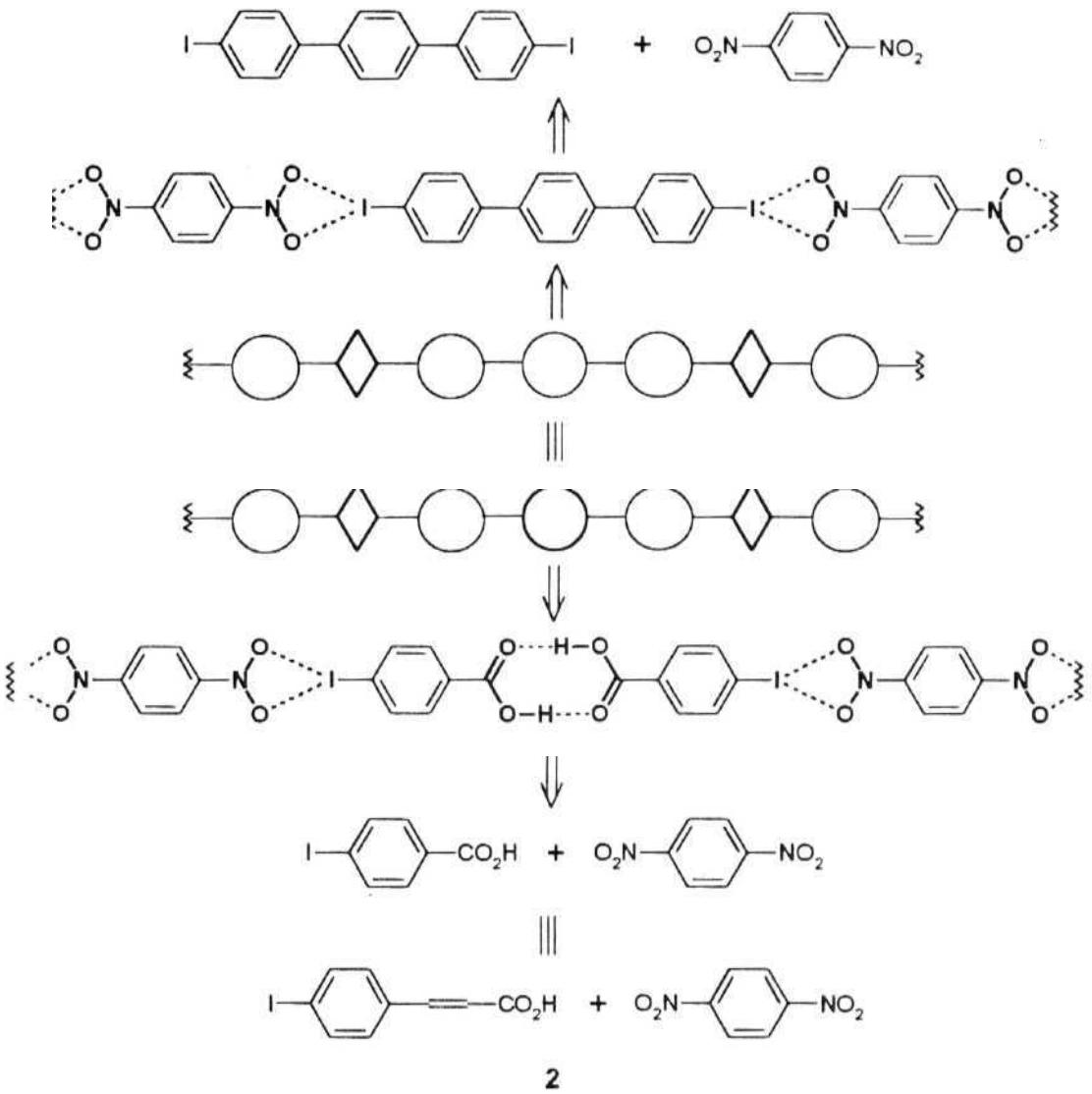


Figure 1. Linear ribbon in the crystal structure of 1. The I···O interactions are indicated: a I···O 3.327Å, C–I···O 163.8°; b I···O 3.466Å, C–I···O 157.9°. Compare this with. Scheme 1.



2

Scheme 2. Retrosynthetic analysis for the extended linear ribbon pattern leading to complex of 4,4"-diiodo-*p*-terphenyl and 1,4-dinitrobenzene (hypothetical structure) or to complex 2 (observed structure). Supramolecular synthons are shown as heavy lines.

synthetic strategy towards a new or modified target network. In order to test the robustness of I synthons, extension of the linear ribbon network shown in Scheme 1 is planned by introducing spacer groups (Scheme 2). A possible spacer is a phenyl ring and a possible target crystal structure is that of the 1:1 complex

between 4,4"-diiodo-*p*-terphenyl and 1,4-dinitrobenzene. However, the effect of a phenyl spacer may be achieved more easily by using the carboxyl synthon, **II.** as a surrogate for the phenyl ring. This strategy derives from the close similarity between the crystal structures of benzoic acid and *p*-terphenyl. The carboxy dimer ring in the benzoic acid crystal structure is viewed as the supramolecular equivalent of the central phenyl ring in the *p*-terphenyl molecular structure.[5a,11] Accordingly, co-crystallisation of a complex from a 1:2 mixture of 1,4-dinitrobenzene and 4-iodobenzoic acid (Scheme 2) was attempted. For solubility reasons, this combination proved unsatisfactory and 4-iodocinnamic acid was substituted for 4-iodobenzoic acid. Complex 2 was then obtained and its crystal structure is shown in Figure 2. In this structure, the now elongated supramolecular diiodo moiety is able to link to 1,4-dinitrobenzene molecules. The robustness of the iodo···nitro synthon, I with respect to the manipulations involving (the presumably more reliable) carboxyl synthon **II** may be noted. Synthons I and **II** may thus be used in a modular fashion without mutual perturbation and interference and such synthon robustness is always a desirable situation in crystal engineering.

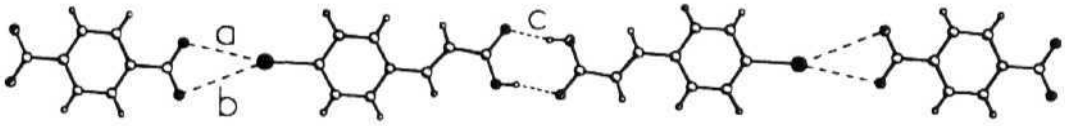


Figure 2. Linear ribbon pattern in the crystal structure of 2. The I—O interactions and O-H-0 hydrogen bonds are indicated: a I···O 3.306Å, C–I O 169.9°; b I···O 3.655A, C–I···O 154.7°; c **0 - 0** 2.649A. O–H···O 167.8°. Compare this with Scheme 2.

It should be noted that the retrosynthetic strategy described in this work is for the supramolecular synthesis of one-dimensional networks mediated by iodo-nitro synthons, I. Real, that is three-dimensional crystals are mediated by three-

dimensional arrangements of supramolecular synthons. In the present case, the linear ribbons in Figures 1 and 2 are further linked laterally *via* C–H···O hydrogen bonds and C-H I interactions as observed previously[10] and further *via* stacking interactions to complete the three-dimensional structure (Figure 3). The strategy outlined here can. in principle, therefore be extended to the entire three-dimensional structure

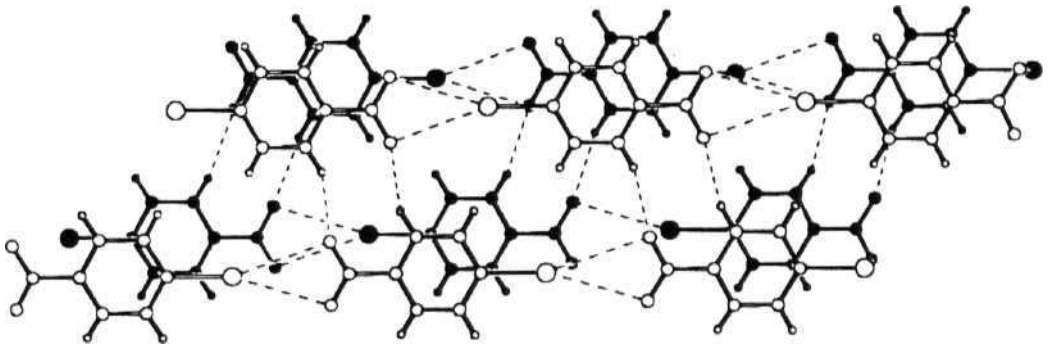
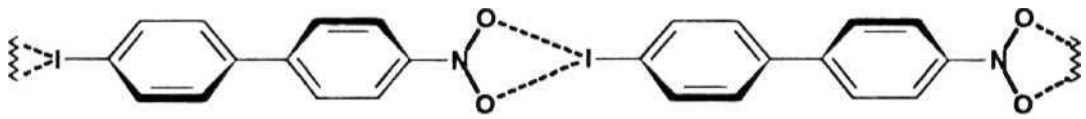


Figure 3. Inversion stacking of linear ribbons in the crystal structure of **1**. Ribbons on the top and at the bottom are drawn open and shaded respectively. Note that the ribbons are also related by an inversion centre laterally. I···Oand C-H O interactions are indicated as dashed lines

4.4 Design of an SHG Active Crystal

Having established the robustness of the synthon I, one may then proceed to use these synthons in the design of crystal structures with specific properties. Further work has shown that I may be alternated with biphenyl groups that are chiral at the molecular level to produce a non-centrosymmetric ribbon structure as in **1**.[12] These polar nbbons are inverted in the crystal structure of 1 (Figure 3) to favour the anti-parallel stacking. However, the chirality at the molecular level has apparently helped the parallel alignment of polar ribbons in the crystal structure of 4-iodo-4'-nitrobiphenyl (Scheme 3) ultimately leading to an SHG (Second Harmonic Generation) active crystal.



Scheme 3. Linear ribbon pattern observed in the crystal structure of 4-iodo-4'-nitrobiphenyl. Notice the twisted molecular conformation.

4.5 Conclusions

It is shown that the principles of retrosynthesis may be applied to supramolecular networks using the supramolecular synthon concept. Iodo···nitro synthons I have been shown to be useful in the construction of linear ribbon structures with a high degree of predictability. These synthons have also been shown to be robust and can be used in a modular fashion with carboxyl synthons in supramolecular synthesis. This study is also supported by the observation that synthons 1 can be crafted on to a chiral molecular species to produce an SHG-active crystal. The supramolecular synthesis of one dimensional network (ribbon) structures is thus achieved. The supramolecular synthesis of higher dimensional structures is presented in Chapters 5 and 6. A recurring theme in crystal engineering is that quite different molecular structures can still result in similar supramolecular (crystal) structures. This study shows that molecular and/or supramolecular fragments with similar sizes, shapes and topologies have similar effects on crystal structures (see Chapter 1). Such a generalisation is more useful because it recognises the interchangeability of molecular and supramolecular synthons within a particular family of crystal structures.

4.6 Experimental

Compound 1 and 4-iodocinnamic acid were prepared according to literature procedures.[13] Single crystals of compound 1 suitable for X-ray diffraction were grown from the slow evaporation of a dioxane solution. Dark yellow crystals of complex 2 (m.p. 240°) were obtained from a 1:1 solution of EtOAc and EtOH

containing 1,4-dinitrobenzene and 4-iodocinnamic acid in 1:2 molar proportions The X-ray data for 1 and 2 were collected at the University of Durham. U.K. by Dr. V.J. Hoy under the supervision of Prof. J.A.K. Howard. The structures were solved using SHELXS-86[14] and all the non H-atoms were refined anisotropically using SHELXL-93.[15] Empirical absorption corrections were applied for both the structures. The relevant crystallographic information is given in appendix.

4.7 References and Notes

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CHAPTER FIVE

C–H···O HYDROGEN BONDS IN CRYSTAL ENGINEERING

5.1 Introduction

Pauling's definition of hydrogen bond would appear to suggest that it is formed only between two electronegative atoms.[1] The low electronegativity of C-atoms, together with the lower acidity of C-H groups, delayed the realisation that these groups could form hydrogen bonds with electronegative atoms such as 0 and N. The presence of C–H···O attractive forces was hinted as early as in 1937 by Glasstone,[2] though the structural study of Sutor has been recognised as the first attempt to charactense these interactions.[3] The existence of these hydrogen bonds has been questioned by Donohue based on an assumption that the outer limit for H···O contacting distance for a hydrogen bond is only 2.2 A.[4] However, several spectroscopic studies have provided convincing proof for C-H 0 hydrogen bonds in solids.[5] The C-H groups are ubiquitous in organic compounds and most of the functional groups contain O- and/or N-atoms and it is quite natural that many organic solids contain C–H···O(N) interactions.[6] Statistical characterisation of these hydrogen bonds has been possible because of the large body of crystallographic data deposited in CSD. The CSD study of Taylor and Kennard of 113 crystal structures determined by neutron diffraction has unequivocally proved the existence of these interactions in crystals and has also confirmed that these interactions are electrostatic in nature [7]

In a study of C–H···O hydrogen bonds formed by chloroalkyl compounds Desiraju has shown that these bonds are attractive even at distances much longer than the van der Waals sum.[8] This again indicates that C-H ·O hydrogen bonds are electrostatic and not van der Waals interactions. Surprisingly however, Cotton *et al.* in a recent communication[9] have questioned the hydrogen bond nature of C–H···O(N) interactions and claimed that many of the reported C–H···O(N) hydrogen bonds are just van der Waals interactions. Such claims have been shown

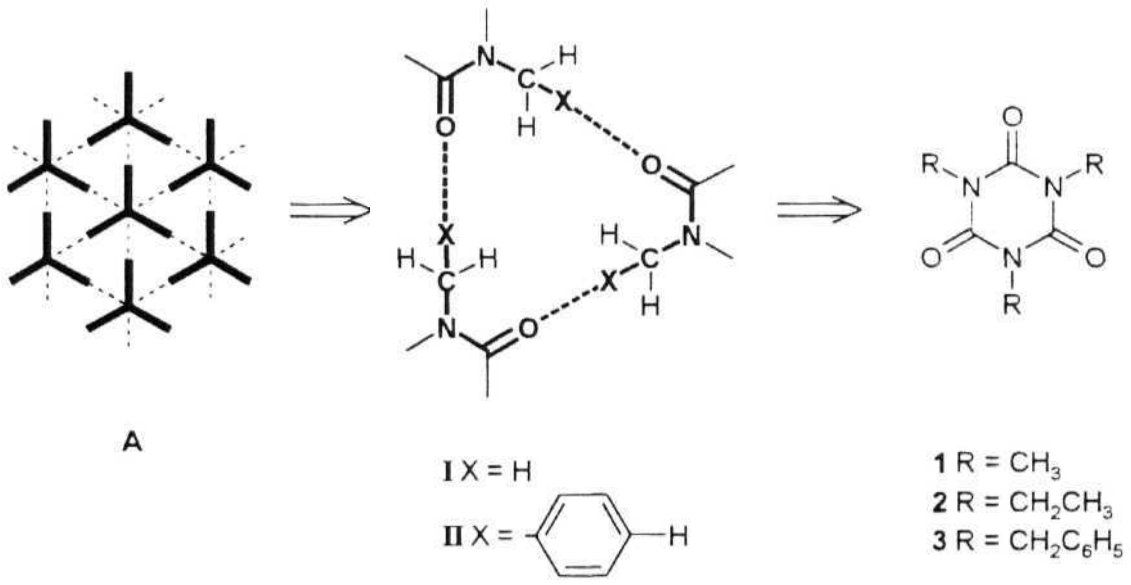
to be erroneous by Steiner and Desiraju[10] since their statistical analysis revealed that directionality behaviour of *any* kind of C–H 0 interaction is distinctly different from C–H···H–C contacts. The former prefers linear geometries reflecting its electrostatic character whereas the latter lack any angular specificity and hence are van der Waals interactions. Such attractive C-H 0 bonds play a very important role in the stabilisation of crystal structures.[6] Understanding these interactions is also important for they have been found to contribute to the stability of many biological systems.[11]

The significance of C-H-0 interactions in the crystal structures of dimethyl oxalate[12] and α,β-unsaturated carboxylic acids[13] has been pointed out very early and a detailed account of the importance of these interactions in many quinonoid compounds has appeared.[14] Use of C–H···O hydrogen bonds in molecular recognition and crystal engineering has been emerging as an active area of research.[6,15] C-H O equivalents of N–H···O synthon based supermolecules have been observed[16] and have been deliberately synthesised which substantiates their use in further studies.[17] C–H···O hydrogen bonds have been used in combination with carboxy dimer synthons to produce a one-dimensional linear tape structure.[18] Higher dimensional networks based exclusively on C–H 0 hydrogen bonds have not been reported. In this chapter, the synthesis of C–H···O mediated trigonal supramolecular networks is presented. These networks arc aesthetically pleasing and also exhibit supramolecular octupolar non-linearities.

5.2 C–H···O Mediated Trigonal Networks

Supramolecular chemistry has been generally involved with the synthesis of lower dimensional finite aggregrates.[19] Later developments have shown that self-assembly helps in the generation of infinite arrays of molecules leading eventually to crystals, liquid crystals or thin films.[2r] Associated with these infinite systems are interesting properties and the subject in this sense is more challenging for the goal is two-fold: successful synthesis of network structures with attendant

properties. Retrosynthetic analysis need not be restricted to one-dimensional networks as has been described in the previous chapter and may be extended to higher dimensional systems.[21] Supramolecular synthesis of higher dimensional networks is much more intriguing and the principles of crystal engineenng may profitably applied for these systems. The targets in this study are the trigonal networks and the interactions chosen for the generation of these networks are C-H 0 hydrogen bonds. Scheme 1 shows the supramolecular retrosynthesis of a two-dimensional trigonal network based on C–H···O hydrogen bonds leading to trialkyl isocyanurates as the starting materials. The success in this synthesis thus depends on the ability to produce the trigonal supramolecular synthons such as I and II.



Scheme 1 Retrosynthetic analysis of the trigonal network A based on supramolecular synthons I and II leading to trialkyl isocyanurates as the starting materials.

5.3 Failure of Symmetry Carry-over from Molecule to Crystal

Symmetry in the crystals indicates symmetrical networking of molecules Symmetrical networks have been generated from symmetrical as well as from unsymmetrical molecules. In case of unsymmetrical molecules it is the symmetry of the supramolecular synthons. which hold the molecules in crystal, that is responsible for the symmetry of the networks and therefore of the crystal. Typical examples are symmetrical synthons formed by -OH groups such as trimers, tetramers and hexamers which lead to similarly symmetrical space groups for these systems.[22] Symmetrical molecules when used to produce similarly symmetrical networks generally use a combination of rigid molecular core with strong linear supramolecular synthons.[23] However, it should be noted that not all symmetrical molecules retain their molecular symmetry in the crystals. In general, carry-over of molecular symmetry into the crystal is not trivial. Inversion centre is the only molecular symmetry that is routinely transformed into the crystal as it facilitates the close-packing of molecules.[24] Since the targets in this work arc trigonal networks, trigonal molecules were the obvious choice but most of these molecules adopt lower symmetry crystal systems (trinitrobenzene. triphenylbenzene, cyanuric acid, melamine. trihalobenzenes to name a few). Such a situation seems reasonable as there is no restriction that the symmetry of the supramolecular synthons formed is the same as that of these molecules. Thus the successful strategy to produce trigonal networks from trigonal molecules should also ensure that the synthons compatible with trigonal symmetry are formed. Accordingly trialkyl isocyanurates were chosen for the present study.

Trimethyl isocyanurate. 1 has the essential molecular features as required by the retrosynthetic scheme shown above and it seemed that this substance could be used to generate the tngonal network A. But, as with many other trigonal molecules the molecular symmetry of 1 was not preserved in the crystal.[25] The structure is replete with a large number of C-H 0 hydrogen bonds with two

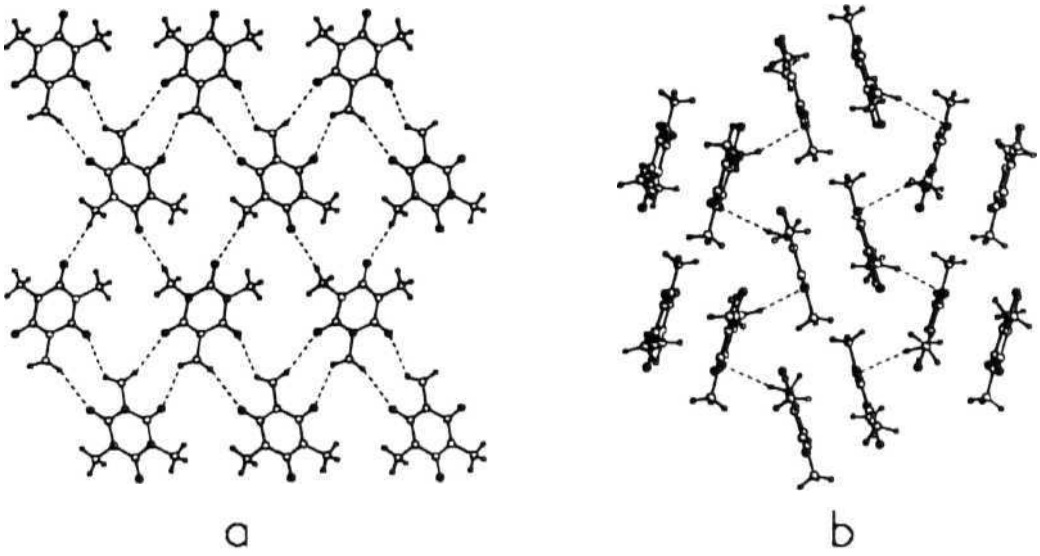


Figure 1. Crystal structure of 1. (a) Corrugated layer structure of B molecules perpendicular to [001]. [010] is vertical. The C-H O hydrogen bonds are indicated. (b) Close-packing of C diads.

molecules in the asymmetric unit. These are referred to hereafter as B and C. The B molecules are assembled into a corrugated layer parallel to (001) as shown in Figure 1a. Each molecule of B is connected to four screw-axis related neighbours along [010] through C-H ·O hydrogen bonds (Table 1). Adjacent, inversion related B layers are linked by additional C-H O hydrogen bonds along [001] to give a bilayer structure. These B bilayers are separated by other layers comprised of stacked diads of C molecules (Figure 1b). C-H O hydrogen bonds link the C diads within the layer and also link them to B molecules in the adjacent layer. Bilayers of B and layers of C alternate along [001] to complete the structure.

Table 1. Geometrical parameters for C–H O hydrogen bonds[8] found in the structures of 1, 2. 3 and 5.

	C···O (Å)	H···O (Å)	C–H···O (°)
1	3.230	2.538	120.83
	3.680	2.660	156.75
	3.662	2.742	142.55
	3.437	2.721	123.31
	3.362	2.463	139.61
	3.513	2.899	116.11
	3.185	2.707	106.28
	3.726	2.725	153.48
2	3.350	2.489	135.62
	3.299	2.528	127.31
	3.305	2.600	122.02
	3.340	2.665	129.96
	3.493	2.811	120.89
3	3.426	2.504	142.37
	3.907	2.968	145.26
5	3.422	2.736	120.97
	3.816	2.812	154.20
	3.731	2.836	140.00

[a] All the C-H distances are normalised to the standard neutron lengths along the C-H vector.

5.4 Structural Insulation

The crystal structure of 1 has a three-dimensional networking of C-H 0 hydrogen bonds whereas the desired trigonal network is two-dimensional Therefore reduction in dimensionality is required so as to synthesise the trigonal network from 1. Many interactions interact with one another in crystals and crystal structures are a result of a subtle balance between these interactions. An important strategy in crystal engineering is to dissect and isolate different kinds of intermolecular interactions so that consequences of any one kind are easier to predict and control. Such structural insulation minimises the interference between

interactions and is a convenient device to reduce the dimensionality of a crystal.[26] jt is necessary that these exercises are carried out; otherwise general three-dimensional structural control is very difficult to achieve It is pertinent here to note that the three-dimensional crystal structure of 1,3,5-tricyanobenzene has been reduced to two dimensions through π···π complexation with hexamethylbenzene.[27] In this complex. C–H···N interactions and methyl···methyl close-packing control the two-dimensional aggregation of molecules in different layers, while π···π stacking interactions assemble the layers in the third dimension. Following these lines. an equimolar complex 5 between 1 and 1,3,5-trinitrobenzene, 4 was

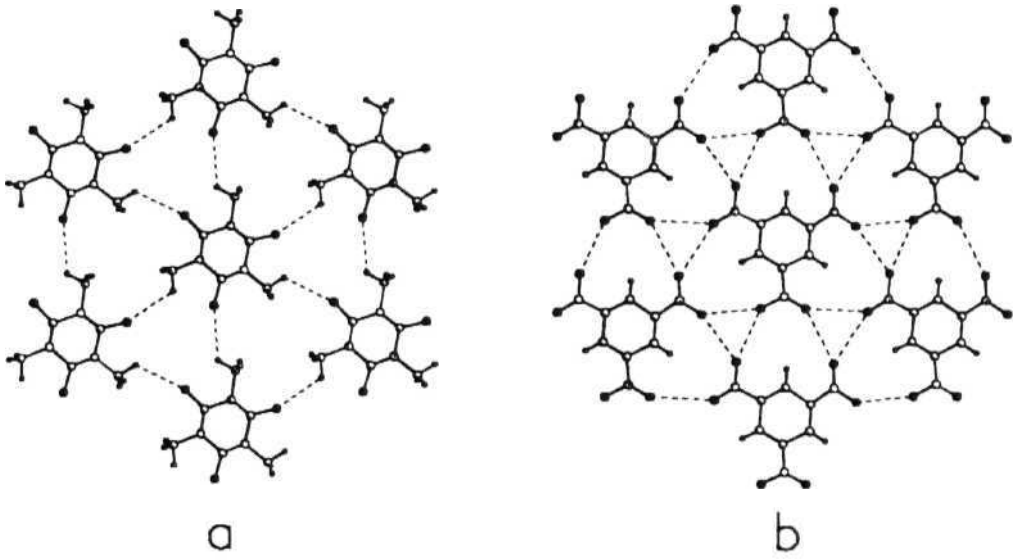


Figure 2. Crystal structure of complex 5 shown perpendicular to [001]. (a) Trigonal network of 1 molecules based on synthon I. The C-H 0 hydrogen bonds are indicated as dashed lines. (b) Layer consisting of 2 molecules. Two symmetry independent O···O van der Waals contacts are shown.

crystallised. Compound 4 is trigonal like compound 1; and the complexation of these two was expected to reduce the dimensionality of structure of 1 to the one in

which the molecular symmetries are preserved If compound 4 were not to bc of trigonal symmetry. even if the structural insulation ıs achieved. the mismatch of the symmetry would have collapsed the complex into a less symmetrical system

The crystal structure of complex 5 consists of alternating and perfectly flat layers of 1 and 4 molecules. These layers are shown separately in Figures 2a and 2b. Figure 2a shows that molecules of 1 lie on three-fold rotation axes and are connected by C-H-0 (Table 1) hydrogen bonded I synthons to generate a trigonal supramolecular net. Interestingly. the symmetry of the molecules and the symmetry of the supramolecular synthons are implicitly linked here and produce networks with the same symmetry as the constituents. Figure 2b shows that the molecules of 4 which lic on a second set of three-fold axes. are likewise networked ın a trigonal manner *via* O O close-packing (2.891. 3.083Å). The following structural features of the layers of 4 are noteworthy: (i) there are no C-H 0 bonds within the layers. (ii) such a layer is seen neither in the crystal structure of pure 4 which (like pure 1) is three-dimensionally linked with C–H···O bonds[28] nor ın the many molecular complexes formed by 4. (iii) there is an unusually large number of intralayer O···O van der Waals contacts. The 3.083A contact is similar to that found in hexanitrobenzene (3.07A). This latter structure ıs of historical interest because it was used by Kitaigorodskii to estimate the value of the O-atom van der Waals radius.[24a]

Examination of Figure 2 shows that the structural insulation of 1 and 4 molecules ıs effective. Each of these components forms three-dimensionally close-packed crystals when taken individuallv. but ın the complex. molecules of 1 and 4 form separate layers (two-dimensional packing) which fully utilise their molecular symmetry. Complex formation ıs undoubtedly favourable because the packing coefficients of complex 5. pure 1 and pure 4 are respectively 0.71. 0.68 and 0.65. So the interlayer association ıs also of interest and ıs shown ın Figure 3. In the alternating layers. molecules of 1 and 4 are staggered and in projection yield an

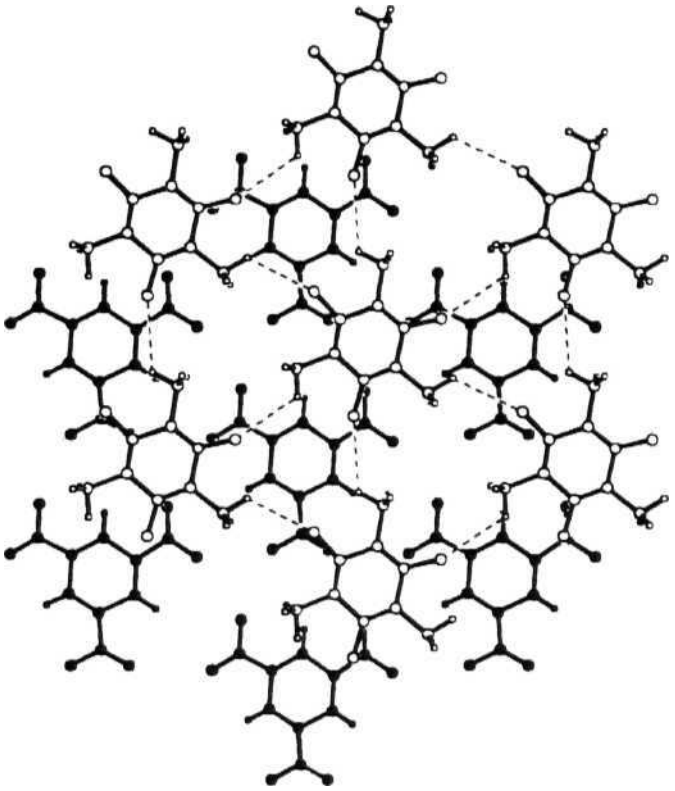


Figure 3. Arrangement of alternate layers of 1 (open) and 4 (shaded) molecules in the structure of complex 5. Notice the honeycomb arrangement.

interesting honey comb structure with the centres of the voids coinciding with the third set of three-fold axes. The interlaver interactions are restricted to weaker C-H 0 bonds (Table 1). To the extent that these very weak interactions arc viable. the layers are not completely insulated from each other. Thus structural insulation seems to be an efficient tool to reduce the dimensionality of the crystal and alleviates the engineering problems to lower dimensional systems.

5.5 From Aesthetics to Properties

Interest in compound 1 was primarily motivated by its symmetry and the probable symmetrical networks that can be produced from it and related derivatives. Accordingly, aesthetically pleasing trigonal networks of 1 molecules have been synthesised in complex 5. At this stage, the importance of these networks as being relevant in octupolar non-linear systems was realised.[2] Crystal engineering is increasingly turning towards functional materials. Traditional crystal engineering strategies towards SHG (second harmonic generation) active materials have been based on dipolar molecules. Large dipole moments in these molecules tend to favour the anti-parallel alignment of dipoles and preclude the formation of non-centrosymmetric crystals.[15] High anisotropy in these molecules has also been found to limit their application to electrooptic configurations.[31] Recently a new class of SHG-active substances, octupolar molecules, have been proposed and been shown to display significant NLO (non-linear optical) behaviour at the molecular level.[2] Supramolecular octupolar materials have not yet been synthesised. While the molecular engineering of octupolar systems requires alternating trigonal arrangements of donor and acceptor groups, the engineering problem at the supramolecular or crystalline level amounts to steering the structure of an appropriately substituted trigonal molecule towards the trigonal, non-centrosymmetric network A shown in Scheme 1.

Of course, as illustrated in the structure of pure 1, many trigonal molecules do not retain their symmetry in the crystal. Though such trigonal networks are identified in complex 5, single component crystals are preferred to molecular complexes for NLO applications in general. This is because pure compounds are easier to handle than molecular complexes by considerations of material purification, crystal growth and optical characterisation in both solution and solid state. Therefore attention was turned to the symmetrical isocyanurates all of which have alternating C-H O donors and acceptors in the molecular structure. Such an alternation is a prerequisite for the formation of network A.

5.6 Triethyl Isocyanurate

In the crystal structure of triethyl isocyanurate, 2 molecular symmetry is not preserved as in pure **1**. The molecular geometry of 2 in the crystal shows that while two ethyl groups project in one direction with respect to the central heterocyclic ring, the third projects in the opposite direction. Molecules related by translation along [010] and [100] are connected by C–H···O bonds (Table 1) involving methylene and methyl groups respectively (Figure 4). The target trigonal network A is based solely on C–H···O hydrogen bonds and perhaps the feeble acidity of the C-H groups in 2 is the reason for the non-adoption of the desired structure.

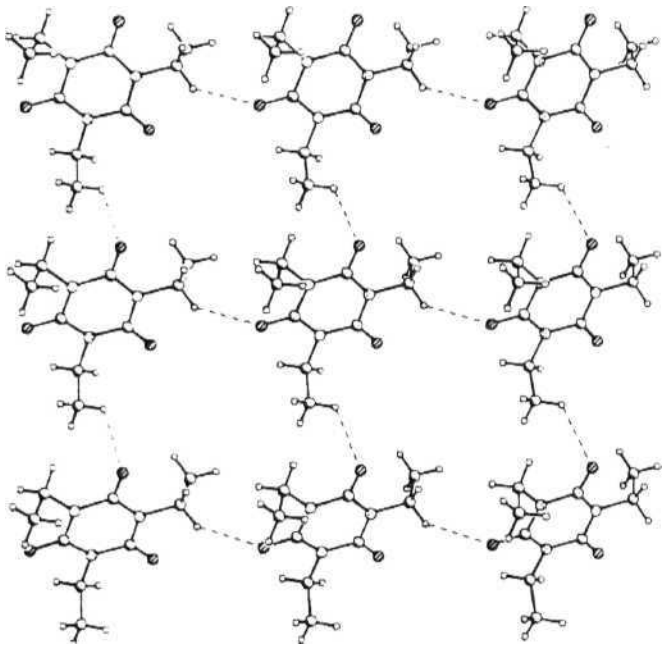


Figure 4. Crystal structure of 2. C-H-0 interactions are indicated as dashed lines.

5.7 Tribenzyl Isocyanurate - An Octupolar Non-linear Optical Crystal

It is by now clear that the C-H O bond strength increases with the acidity of C-H groups.[33] Compound 2 consists of $C(sp^3)$–H groups which are weakly acidic. Aromatic C-H groups are more acidic compared with $C(sp^3)$–H groups and hence the crystal structure of tribenzyl isocyanurate. 3 was examined. Compound 3 consists of aromatic rings which allow the charge transfer for the purposes of increased NLO activity and in this respect some molecular engineering is also involved in the choice of 3. Figure *5* shows that 3 is far from planar. With respect to the central heterocyclic ring, two benzyl groups point in one direction while the third points in the other. leading to an overall chair shape. Molecules arc networked into a trigonal layer structure as shown in Figure 6. These networks are characterised by synthon II. which is the tris phenylogous extension of synthon I. The layer structure in 3 is corrugated with two distinct intralayer C-H ·O hydrogen bonds (Table 1). Molecules translated along [001] are connected by the interactions designated j in Figure 6 to form chains. Adjacent chains are *n*-glide related and are connected by interactions k. The chains are additionally interconnected by herringbone interactions (dotted lines in Figure 6). The corrugated layers are stacked along [010] while weak C–H ··π interactions complete the structure.

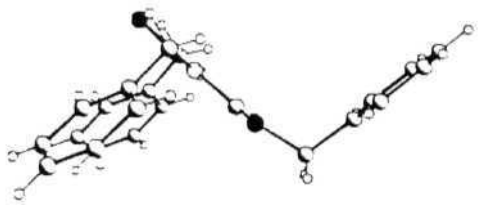


Figure 5. View of an individual molecule of 3 to show its non-planar character. Notice the overall chair shape of the molecule.

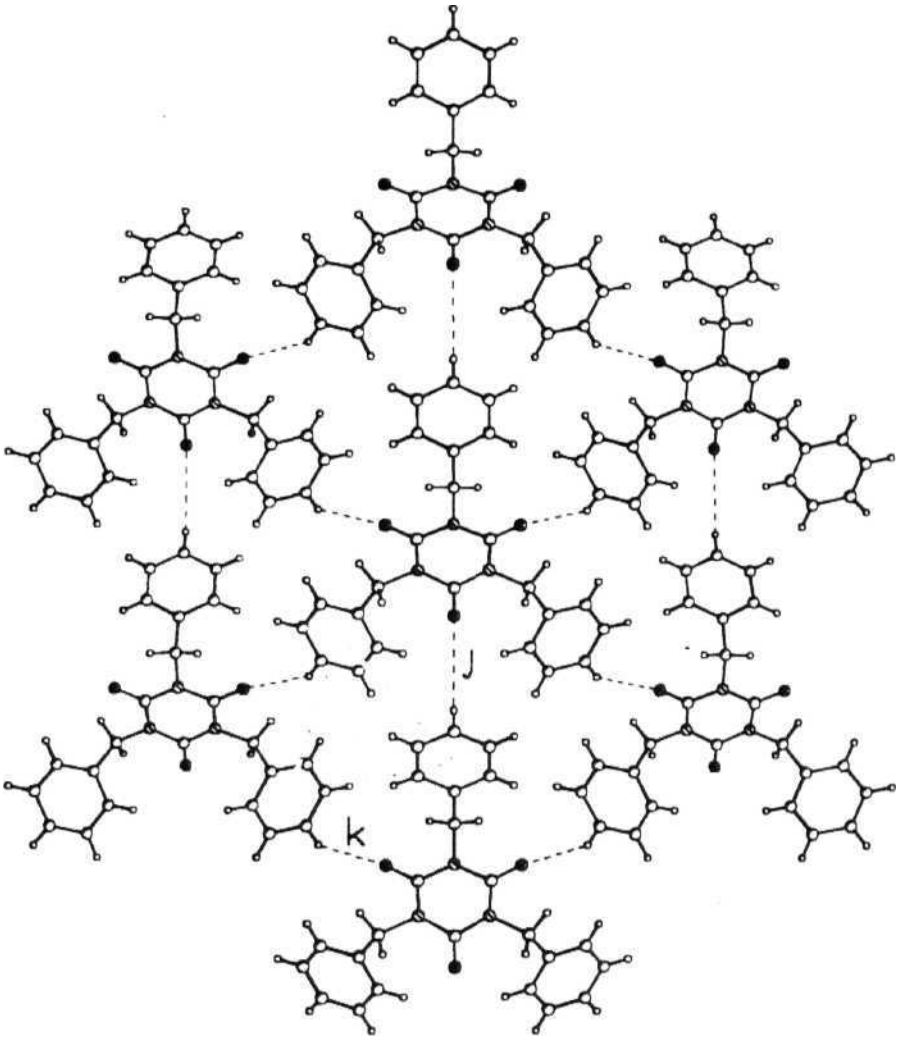


Figure 6. A view of the crystal structure of 3 down [010] to show the trigonal network structure. C–H···O hydrogen bonds are indicated as j and k, while herringbone interactions are indicated as dotted lines. Notice the occurrence of supramolecular synthon II and the overall non-centrosymmetry of the network.

The non-centrosymmetric nature of crystalline 3 was confirmed by a visible SHG-powder signal at 1 064 μm of the order of one tenth that of urea and exhibits a molecular hyperpolarisability, β equal to (10±2) ® 10^{-30} e.s.u. This is

comparable to that of the classical dipolar *para*-nitroaniline molecule under the same measurement conditions. One of the relevant properties of 3 is that it is completely transparent in the visible region. This is important in the context of absorption of the 2ω beam by the sample itself a problem of nuisance value for some coloured materials. Since the methylene groups prevent the conjugation between the peripheral and central rings, the weak second harmonic signal of 3 can be ascribed to poor charge transfer. The octupolar structure of 3 is confirmed by a HLS (harmonic light scattering) depolarisation measurement[34] and the depolarisation ratio $D = 0.65$ is close to the theoretical value of 2/3 for purely octupolar structures.[35] The theoretical crystalline non-linear coefficient was inferred from the molecular hyperpolansability using the oriented gas model. From the geometry of the unit cell, the overall norm of the macroscopic coefficient is found to be 96 ® 10^{-9} e.s.u.

5.8 Conclusions

This work shows that C-H-0 hydrogen bonds can be used for crystal engineering and supramolecular construction Carry-over of molecular symmetry into the crystal is not a trivial issue and the crystal structures of pure 1 and 2 do not show trigonal supramolecular assembly. Structural insulation has been shown to be an effective device to reduce the dimensionality of crystal structure of 1 and the transfer of molecular symmetry into the crystal is achieved Symmetry of the molecules and supramolecular synthons inextricably link in complex 5 to produce the networks of similar symmetry. Considerations of the acidity of the C-H groups resulted in the successful application of the supramolecular retrosynthesis of an octupolar non-linear crystal and illustrate that network structures can be developed with C–H···O hydrogen bonds.

5.9 Experimental

5.9.1 X-Ray Crystallography

Trialkyl isocyanurates, **1-3** were prepared by refluxing a mixture of corresponding alkyl halides and potassium isocyanatc in DMF according to literature procedures.[36] Single crystals of compounds 1. 2 and 3 suitable for X-ray diffraction were grown from slow evaporation of EtOH and $CHCl_3$ solutions respectively. Light yellow crystalline needles of complex 5 (m.p. 110-112 °C) were obtained from a $CHCl_3$ solution containing equimolar quantities of 1 and 4. Hexagonal tablets were obtained from a solution in CCl_4. The data were collected on both types of crystals but these were seen to correspond to the same crystal form. The X-ray data for 1 were collected at RSIC, Madras, and for 2 and 5 were collected at Fox Chase Cancer Center. Philadelphia. U.S.A. by Drs A.K. Katz. C.J. Carrell and H.L. Carrell. The data for 4 were collected by the candidate at the University of Essen. Germany under the supervision of Prof. Roland Boese. The structures were solved using SHELXS-86[3] and all the non H-atoms were refined anisotropically using SHELXL-93.[38] The relevant crystallographic mfonnation is given in appendix.

5.9.2 NLO Measurements

The lack of a permanent dipole moment in 4 makes the classical Electric Field Induced SHG (EFISH) experiment unsuited to the determination of molecular nonlinearity, β. Therefore the measurements in solution were performed by use of the HLS experiment[34] by Dr. S. Brasselet under the supervision of Prof. J. Zyss at CNET, Bagneux. France.

5.10 References and Notes

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CHAPTER SIX

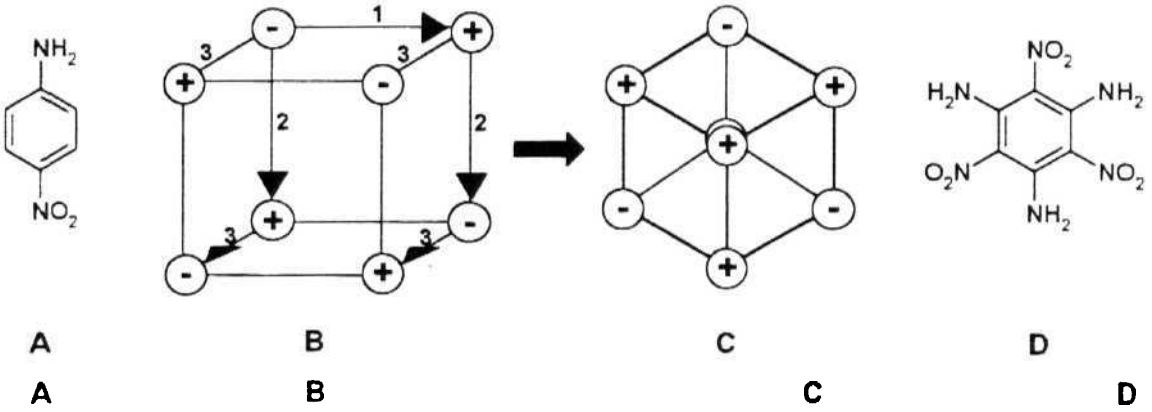
TOWARDS FUNCTIONALISED SOLIDS

6.1 Introduction

Crystal engineering has as its goals the design and synthesis of functional materials for practical applications.[1] Solids exhibiting high second harmonic generation (SHG) for non-linear optical (NLO) applications such as electrooptic modulation, optical frequency conversion have attracted much interest.[2-3] Traditional crystal engineering studies have been exclusively based on dipolar paradigm wherein electron donor and acceptor groups interact through a conjugated π-system. Typical examples are *p*-nitroaniline (pNA) analogues,[4] disubstituted stilbenes and push-pull polyenes.[6] However, these dipolar systems have some disadvantages towards NLO applications:[7] crystallisation of long, linear molecules has been found to be difficult: the high ground state dipole moment in these molecules tends to favour their anti-parallel alignment leading to centrosymmetry; high anisotropy in these molecular structures has limitations towards electrooptic configurations. The main aim in the crystal engineering of dipolar species has been therefore to ensure that the non-centrosymmetric assembly of the dipoles is established. Such exercises have been carried out with the help of chiral handles[8] or using directed hydrogen bonds.[9] Reducing the ground state dipole moment while preserving the molecular hyperpolarisability, β had been a long sought goal and was achieved in the push-pull structure of 3-methyl-4-nitropyridine-1-oxide (POM).[10]

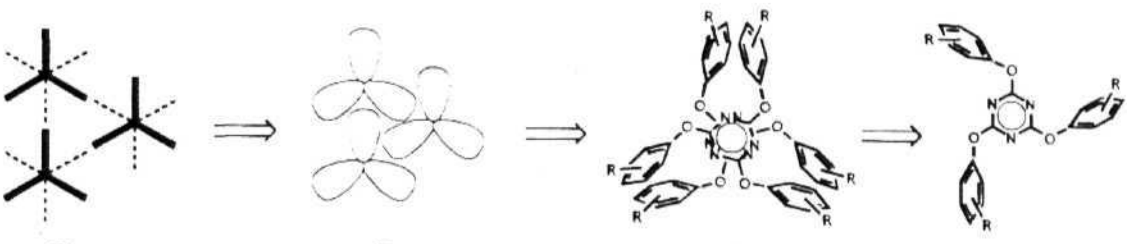
It has been pointed out that the studies involved with one-dimensional dipolar objects has ignored a wealth of possibilities available from two and three-dimensional self-assembly.[7] Thus the quest for non-dipolar molecules with non-zero β has led to the identification of more symmetrical molecules with attached octupolar non-linearities.[7,11] Of course, a non-centrosymmetnc assembly of these isotropic molecules is required in order that these substances may be used in NLO

applications. The transition from dipoles to octupoles may be effectively presented as illustrated in Scheme 1,[12] by considering dipolar pNA and its trigonal analogue, octupolar 2,4,6-triamino-1,3,5-trinitrobenzene (TATB).[13] SHG measurements on the powder sample of TATB showed that it possesses a finite β.[14] Since TATB has a planar trigonal symmetry the dipolar feature is lost in this molecule. The seeming contradiction between these two situations was resolved by Zyss.[7] Seeking explanations for the existence of a finite β in such systems Zyss had shown, on the basis of group theoretical analysis, that in general the β may contain contributions from odd-order multipoles.[7] It was also shown that the octupolar part of the β has many more components than the dipolar part and in this sense it expresses a higher non-linear dimensionality. In particular, molecules with trigonal and tetrahedral symmetries have been expected to show octupolar responses. It may be noted that,



Scheme 1. From dipoles to octupoles. A pNA, a model dipolar molecule. B. An Octupole represented in a cube with eight point charges. It can be generated by successive operations invoking translations and inversions of signs of point charges: First, second and third operations lead to a dipole (2^1), a quadrupole (2^2) and an octupole (2^3) respectively. C. Projection of the cube B along a body diagonal transforms a three-dimensional object with tetrahedral symmetry to a two-dimensional species with trigonal symmetry. The charges on the projected diagonal coincide and cancel out. D. TATB, a model octupolar molecule.

as revealed from the studies of Zyss. objects with symmetries higher than those sustained by octupoles do not possess a finite β.[7] Thus, octupolar symmetry presents an advantageous situation: it is high enough to have a zero dipole moment, but not so high that it cannot allow a finite β. Octupoles are non-dipolar yet non-centrosymmetric. Octupolar non-linearity has been experimentally demonstrated in molecular systems,[15] and this far, its demonstration in supramolecular, that is crystalline, systems has remained a challenge.

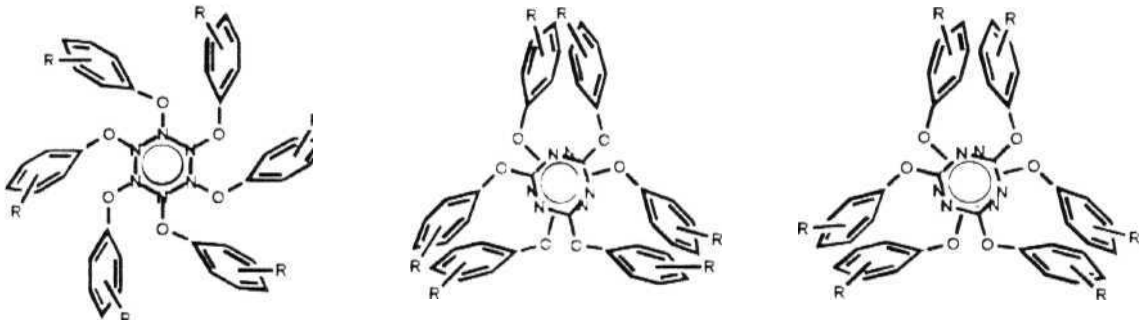


Scheme 2. Retrosynthesis of a trigonal octupolar network. E Trigonal network. F. Recognition of trigonal species G. Stacked molecular diads of triazines. H. 2,4,6-Triaryloxy-1,3,5-triazine

6.2 Octupolar Networks - Trigonal Symmetry

As illustrated in Chapter 5, a typical symmetry pattern that leads to crystalline octupolar non-linearity is the trigonal network E constituted with trigonal molecules (Scheme 2). This two-dimensional network is non-centrosymmetric and arises from specific attractive interactions between structural elements that are schematically represented by bold and dashed lines.[14] The main task in the crystal engineering of such a structure lies therefore in identifying the complementary elements and eventually a molecule that contains these elements in appropriate locations. This is not trivial. The carry-over of molecular symmetry into crystal symmetry (or even pseudosymmetry) is not expected from Kitaigorodskii's theory of close-packing[16] and a majority of trigonal molecules routinely adopt close-packed crystal structures of low symmetry. As detailed in Chapter 5, the symmetry of supramolecular fragments may not coincide with the symmetry of the molecules

and this inevitably leads to low s\Tnmetry crystal structures. Therefore, the strategy is to ensure that the s>Tnmetry of the supramolecular synthons[17] is tuned to the symmetry of the constituents and therefore to the networks. Obviously, it is also necessan" to sec that the non-centrosymmetry of the two-dimensional trigonal network E is extended to the third dimension. The work described in this chapter. however. concentrates on non-centrosymmetric two-dimensional lamellar structures. Three-dimensional structural control is far more difficult to achieve and for a new family of potential octupolar NLO compounds. even this more limited goal of dissecting out critically large two-dimensional non-centrosymmetric substructures is useful.[18] It is shown that such trigonal networks arc a common structural feature in the family of structures described here even when the overall crystal structures are centrosymmetric in the third dimension.



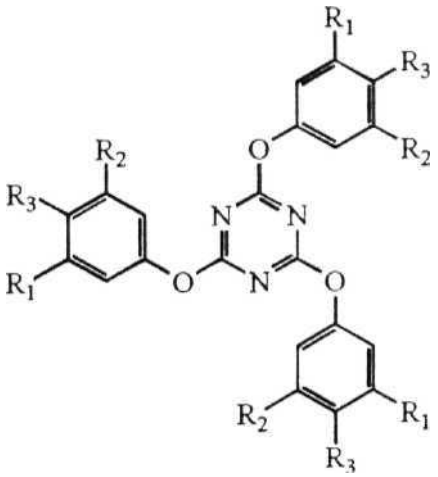
C_{3i}-PU **C_3-PU** **D3-PU**

Scheme 3. Piedfort units with three-fold symmetry

6.3 Supramolecular Retrosynthesis and Piedfort Units

Supramolecular retrosynthesis[17] of the network E based on shape recognition leads to synthons such as F. Herringbone interactions between aromatic rings have been considered for the purpose of shape recognition and yielded the supramolecular species G. Crystalline triaryloxy substituted 1.3.5-triazines form stacked diads called Piedfort units (PUs).[19] Here we use the PU, which in itself is a supramolecular species **G**, as the starting point for the generation of higher level

supramolecular assemblies Further retrosynthesis leads to substituted 2.4.6-tnphenoxy-l,3,5-triazines H as starting materials Retrosynthetic analysis shown in Scheme 2 although follows from Chapter 5 it is distinctly different While the isocyanurate molecules discussed in Chapter 5 self-assemble in one step to the trigonal network, the triazines chosen here do the same in two steps First, the **H** molecules, with the help of intermolecular interactions, form a finite supramolecular species G which then generates the desired two-dimensional trigonal network E through self-assembly. Such multi-stage supramolecular synthesis has been recently described.[20] PUs possessing C_{3i}, C_3 and D_3 symmetry (hereafter C_{3i}-PU, C_3-PU and D_3-PU) have been identified[2] (Scheme 3) though only C_3-PU and D_3-PU are relevant in the generation of the network E. In summary, the successful transformation of H to E requires that only those combinations of intermolecular interactions in consonance with the symmetry of H be optimised and many others which would lower the s\Tnmetry be suppressed at each level of the supramolecular synthesis. In this work the crystal structures of the s}Tnmetrical 2,4,6-triaryloxy-1,3,5-triazines **1-8**, have been investigated and the effects of substitution on the network structures obtained are analysed.



1 $R_1 = R_2 = R_3 = H$
2 $R_1 = Cl, R_2 = R_3 = H$
3 $R_1 = Br, R_2 = R_3 = H$
4 $R_1 = CH_3, R_2 = R_3 = H$
5 $R_1 = R_2 = Cl, R_3 = H$
6 $R_1 = R_2 = CH_3, R_3 = H$
7 $R_1 = R_2 = H, R_3 = Cl$
8 $R_1 = R_2 = H, R_3 = Br$

6.4 Triazine 1 - A Non-Centrosymmetric Crystal

6.4.1 C–H· O and C–H···N Hydrogen Bonds in D_3-PU

2,4,6-Triphenoxy-1,3,5-triazine, 1 crystallises in the non-centrosymmetric space group *Ia*.[22] D_3-symmetric Piedfort units (D_3-PUs) formed by an assembly of two molecules of 1 may be identified (Figure 1). The two molecules in the D_3-PU are related by an *a*-glide and are held together by π···π stacking interactions between triazine rings and also by C-H O and C–H N hydrogen bonds. One of the molecules in the D_3-PU donates three C–H···O hydrogen bonds to the other which in turn donates three C-H N hydrogen bonds back to the first. The molecules of 1 use *ortho* H-atoms of the phenoxy groups for such hydrogen bonding. In effect, a D_3-PU is stabilised by π···π interactions and six weak (C-H···O and C–H···N) hydrogen bonds. The geometrical parameters for these interactions are given in Table 1.

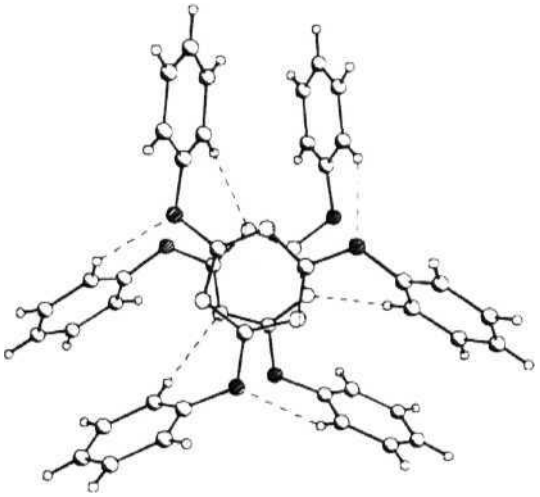


Figure 1. View down [100] showing a D_3-PU in 1. C–H···O and C-H ·N bonds are shown as dashed lines. Molecules related by *a*-glide form D_3-PUs.

Table 1. Geometrical parameters for the intermolecular interactions in the structure of **1**.

Interaction[a]	D[b] (Å)	d[c] (Å)	θ[d] (°)
ortho-C–H···O	3.455	2.509	145.63
ortho-C–H···O	3.544	2.603	145.20
ortho-C–H···O	3.566	2.618	146.14
ortho-C–H···N	3.541	2.535	154.57
ortho-C–H···N	3.449	2.401	163.23
ortho-C–H···N	3.468	2.461	154.70
para-C–H···X[e]	3.556	2.699	135.96
para-C–H···X	3.924	3.289	118.67
para-C–H···X	3.968	3.341	118.24
meta-C–H···X	3.759	2.936	133.29
meta-C–H···X	3.805	2.994	132.27
$\pi\cdots\pi$[f]	3.301		

[a] All the C-H distances are normalised to the standard neutron lengths along the C-H vector. [b] D is the distance between C and the acceptor (O, N or nng centroid). [c] d is the distance between H and the acceptor (O, N or nng centroid). [d] θ is the angle at H in C-H X (X = O, N or nng centroid). [e] Herringbone interactions are expressed as **C-H-X,** where X is the centroid of the aromatic ring acting as the C-H acceptor. [f] For $\pi\cdots\pi$ interactions. D is the perpendicular stacking distance.

6.4.2 Herringbone Interactions - Octupolar quasi-Trigonal Networks

The mean plane of the D_3-PU is almost parallel to (100) and makes an angle of 4.2° with it. A layered structure parallel to (100) anses from the orthogonal geometry of the herringbone interactions between the phenyl groups (Figure 2. Table 1). All the *para* H-atoms on the phenyl groups and two of the *meta* H-atoms are engaged in these herringbone interactions and thus play a very important role in the generation of the tngonal layer structure. It may be noted that the D_3-PUs in 1 are only approximately D_3-symmetric and hence the network generated is quasi-trigonal and not perfectly tngonal.

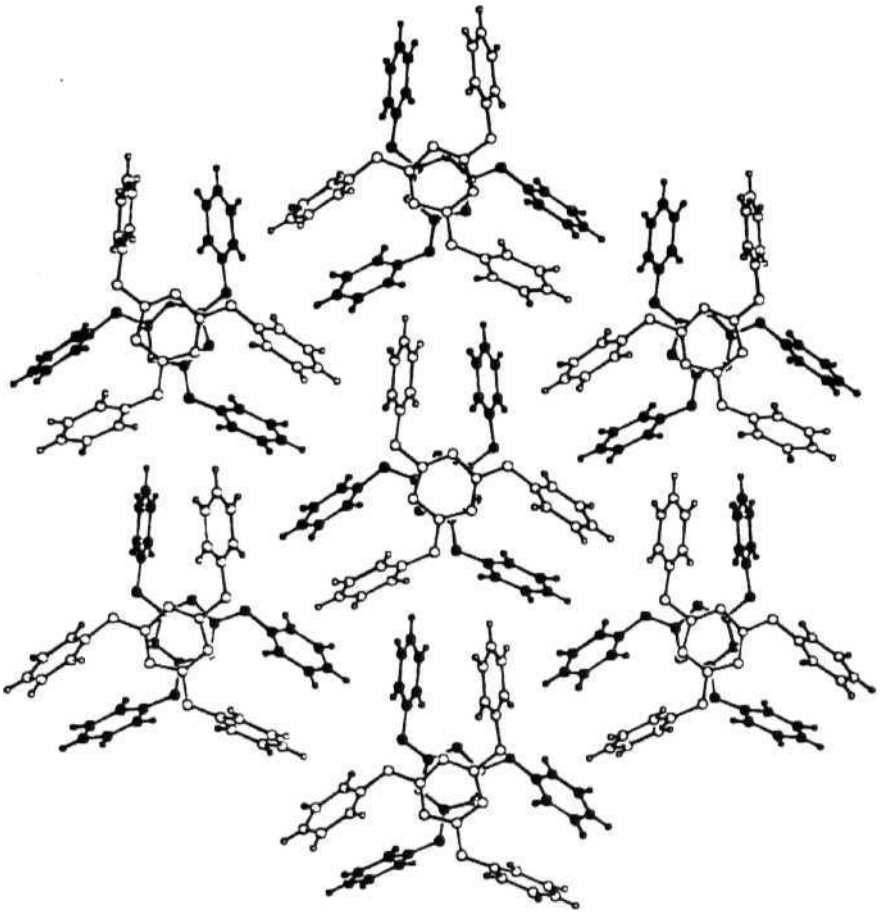


Figure 2. View down [100] showing the trigonal layer structure in 1. Molecules at different heights along [100] are respectively unshaded and shaded The packing of D_3-PUs within the layer is governed by herringbone interactions. Note that the D_3-PUs are translation related along [001] whereas they are related by body centering along [010].

6.4.3 Eclipsed Stacking of D_3-PUs - Bulk Non-Centrosymmetry

The D_3-PUs are translationally stacked along [100] in an eclipsed manner and produce a columnar structure. Significantly, all the C–H O bonds run in the [100] direction whereas all the C-H N bonds run in the opposite [1 00] direction.

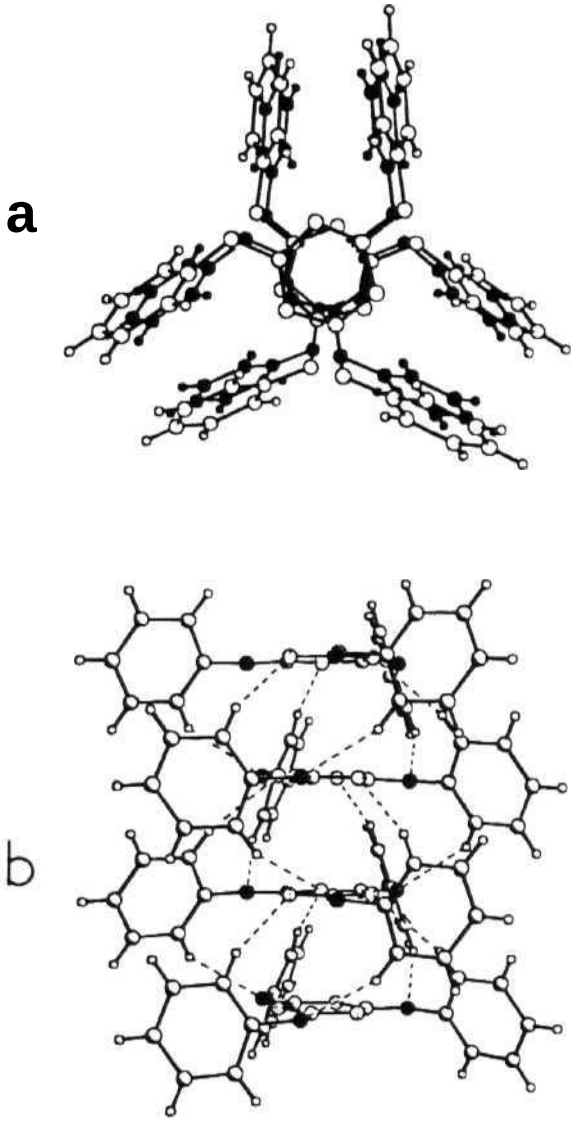


Figure 3. Two views of eclipsed stacking of D_3-PUs m **1**. (a) View down [100]. The unshaded D_3-PU is above the shaded one. (b) Side view of the same stacked pair of D_3-PUs. C–H···O and C–H N bonds are indicated as dashed lines. The sense of these hydrogen bonds maintains the polarity. The shading scheme adopted is: C - crescent. H - unshaded. N - dotted, O - hatched. The same shading scheme is followed in the remaining figures.

Since these C–H O and C-H N hydrogen bonded strands are polar, such translated stacking results in overall non-centrosymmetry with a macroscopic non-linear coefficient one-tenth that of urea (see Section 6.9). Three-dimensional structural control is a major endeavour in crystal engineering today and it is realised here serendipitously but also because the herringbone and hydrogen bonding interactions occur in roughly orthogonal directions (Figure 3) The supramolecular synthesis of octupolar network E (Scheme 2) leading to the crystal structure of SHG active 1 underscores the importance of logic-driven supramolecular retrosynthesis in the quest for target networks with specific properties.

6.4.4 Topological Similarity between the Structures of 1 and 9

A comparison of the structure of 1 to that of *cis,cis*-cyclohexane-1,3,5-*tris*(α-picolin-6-yl)carboxamide, 9 is pertinent.[23] The structure of 9. wherein successive molecules are interconnected by three N-H ·O hydrogen bonds between amide functionalities. shows a supramolecular columnar structure similar to that found in 1. In the non-centrosymmetric structure of 9, the hydrogen bonds run along a polar direction (as they do in 1); 9 has a trigonal octupolar network structure similar to 1 and it has an SHG activity of 0.06 x urea. While the columnar structure in the triamide is stabilised by three strong (N–H O) hydrogen bonds, the structure of 1 is stabilised by six weak (three C–H O and three C-H N) hydrogen bonds. Thus, a C-H O/C–H N topological equivalent of an N–H O based supramolecular structure is serendipitously produced. This indicates that when weak hydrogen bonds are employed collectively they can work as effectively as their stronger counterparts.

Table 2. Geometrical parameters for various interactions found in the structures of **2-6**.

		D_3-PU			C_{3i}-PU		
	Interaction[a]	D[b] (Å)	d[c] (Å)	θ[d] (°)	D[b] (Å)	d[c] (Å)	θ[d] (°)
2	*o*-C–H···O	3.655	2.682	149.64	3.344	2.685	118.96
	o-C–H···N	3.738	2.892	135.33	3.640	2.672	148.98
	p-C–H···X[e]	3.720	2.760	147.92			
	m-C–H···Cl	3.847	2.767	178.37			
	π···π[f]	3.557			3.567		
3	*o*-C–H···O	3.636	2.644	152.50	3.373	2.668	122.42
	o-C–H···N	3.791	2.972	132.94	3.685	2.702	151.21
	p-C–H···X	3.835	2.846	153.10			
	m-C–H···Br	3.910	2.835	173.58			
	π···π	3.620			3.618		
4	*o*-C–H···O	3.691	2.735	147.39	3.410	2.755	118.88
	o-C–H···N	3.727	2.829	140.64	3.689	2.726	148.64
	p-C–H···X	3.810	2.840	149.50			
	m-C–H···CH_3	4.160	3.230	178.96			
	π···π	3.569			3.627		
5	*o*-C–H···O	3.850	2.853	152.53	3.600	2.837	127.66
	o-C–H···N	4.030	3.119	142.63	3.920	2.882	161.23
	p-C–H···X	4.049	3.038	156.03			
	Cl···Cl[g]	3.120					
	π···π	4.025			3.948		
6	*o*-C–H···O	3.860	2.813	163.28	3.634	2.874	127.51
	o-C–H···N	4.022	3.106	143.00	3.945	2.934	155.91
	p-C–H···X	4.067	3.081	156.03			
	CH_3···CH_3[h]	3.478					
	π···π	4.029			3.970		

[a] All the C-H bonds are normalised to the standard neutron lengths. [b] D is the distance between C and the acceptor (O, N, Cl, Br, Methyl C-atom or centroid). [c] d is the distance between H and the acceptor. [d] θ is the angle at H in C–H···Y (Y = acceptor). [e] Herringbone interactions are expressed as C-H X, where X is the ring centroid. [f] For π···π interactions D is the stacking distance. [g] For Cl···Cl interactions D is the distance between Cl-atoms. [h] For methyl-methyl close-packing, the distance between two C-atoms is expressed as D.

6.4.5 Substitutable *meta* Position

The following points emerge from an analysis of the structure of **1**: 1) Such a compound may be a good starting point for producing PUs; 2) The aggregation of PUs is governed by a combination of π···π stacking and C-H O/C–H • N interactions and indicates that *ortho* H-atoms must be available as hydrogen bond donors: 3) The herringbone interactions are critical for the trigonal layer structure and involve participation of all the *para* and a third of the *meta* H-atoms. The trigonal network is thus expected to be very sensitive to substitution in the *para* position: 4) The only site on the phenoxy group that appears not to disrupt formation of the D_3-PUs and also the trigonal network is the *meta* position. Thus, the attention is turned towards triazines **2-6**

6.5 Triazines 2, 3 and 4 - Isostructural Systems

6.5.1 Perfectly D3-Symmetric Piedfort Units

The structures of 2,4,6-*tris*-(3-chlorophenoxy)-1,3,5-triazine, 2, 2,4,6-*tris*-(3-bromophenoxy)-1,3,5-triazine, 3 and 2,4,6-*tris*-(3-methylphenoxy)-1,3,5-triazine, 4 are discussed together because of their structural similarity. Triazines 2. 3 and 4 crystallise in the trigonal space group *P* 3 *c*1 and are isostructural. The molecules lie on three-fold axes and D_3-PUs, assembled from two stacked molecules related by a 32-axis, are found in these structures (Figure 4a) as in 1. Unlike the D_3-PUs in **1**, the PUs found in 2-4 maintain perfect D_3 symmetry. The two molecules in the D_3-PU are related by π···π stacking interactions of the central rings as well as by C-H-0 and C–H···N hydrogen bonds. The geometrical parameters for various interactions found in these structures are given in Table 2. Each molecule in the D3-PU donates and accepts three C–H···O bonds *via* one of the two symmetry independent *ortho* H-atoms. The same *ortho* H-atom is also involved in the formation of a longer, bifurcated C-H N hydrogen bond with the N-atom of the

central triazine ring. Effectively, each D_3-PU is stabilised by stacking interactions and twelve weak hydrogen bonds, six C–H O and six C-H N bonds

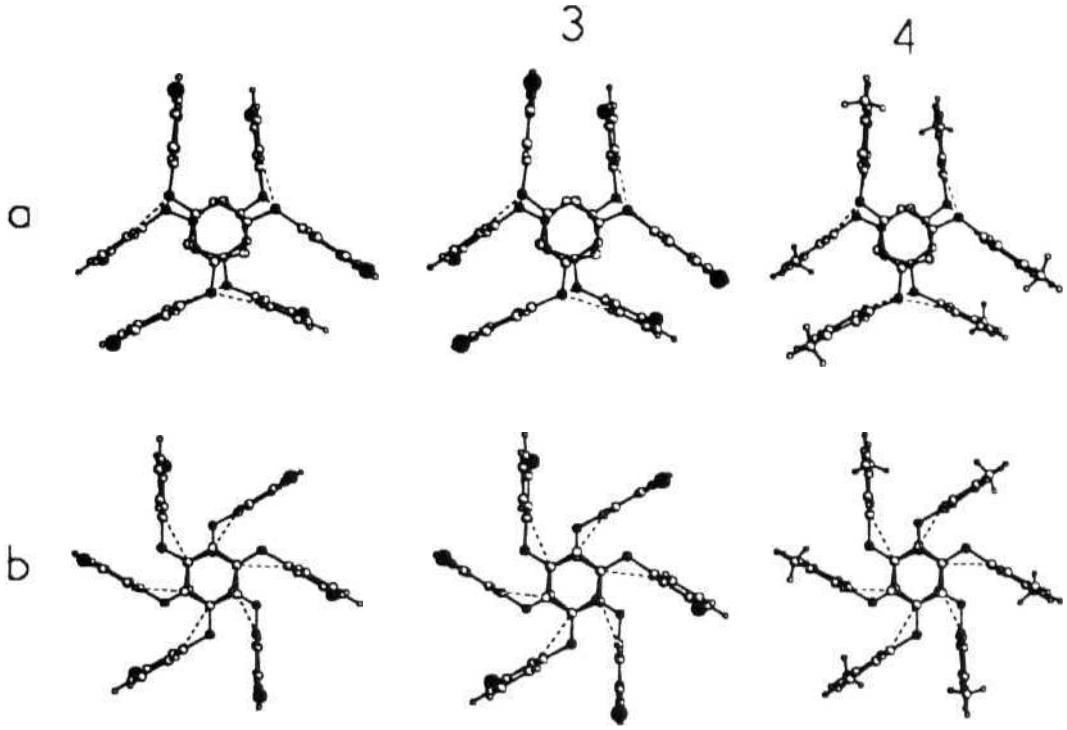


Figure 4. View down [001] showing the Piedfort units in 2, 3 and **4** (a) D_3-PUs. C–H···O bonds are indicated as dashed lines. (b) C_{3i}-PUs. C-H···N bonds are indicated as dashed lines. Bifurcation is shown in neither case. Halogen atoms are shown as cross hatched circles.

6.5.2 Herringbone Interactions - Octupolar Trigonal Networks

The mean planes of the D_3-PUs in **2-4** are constrained by crystallographic symmetry to be parallel to (001) Unlike in 1 where three *para* and two *meta* hydrogen atoms are involved in herringbone interactions, only the *para* H-atoms are involved in 2-4 and therefore the octupolar networks found in these tnazines are ideally trigonal (Figure 5). This is reflected in their macroscopic, crystallographic three-fold symmetry. Each D_3-PU in Figure 5 is connected to six

neighbours within the layer through twelve herringbone interactions. Since the D_3-PUs in **2-4** are strictly D_3-symmetric the trigonal network structure is also D3-symmetric.[24]

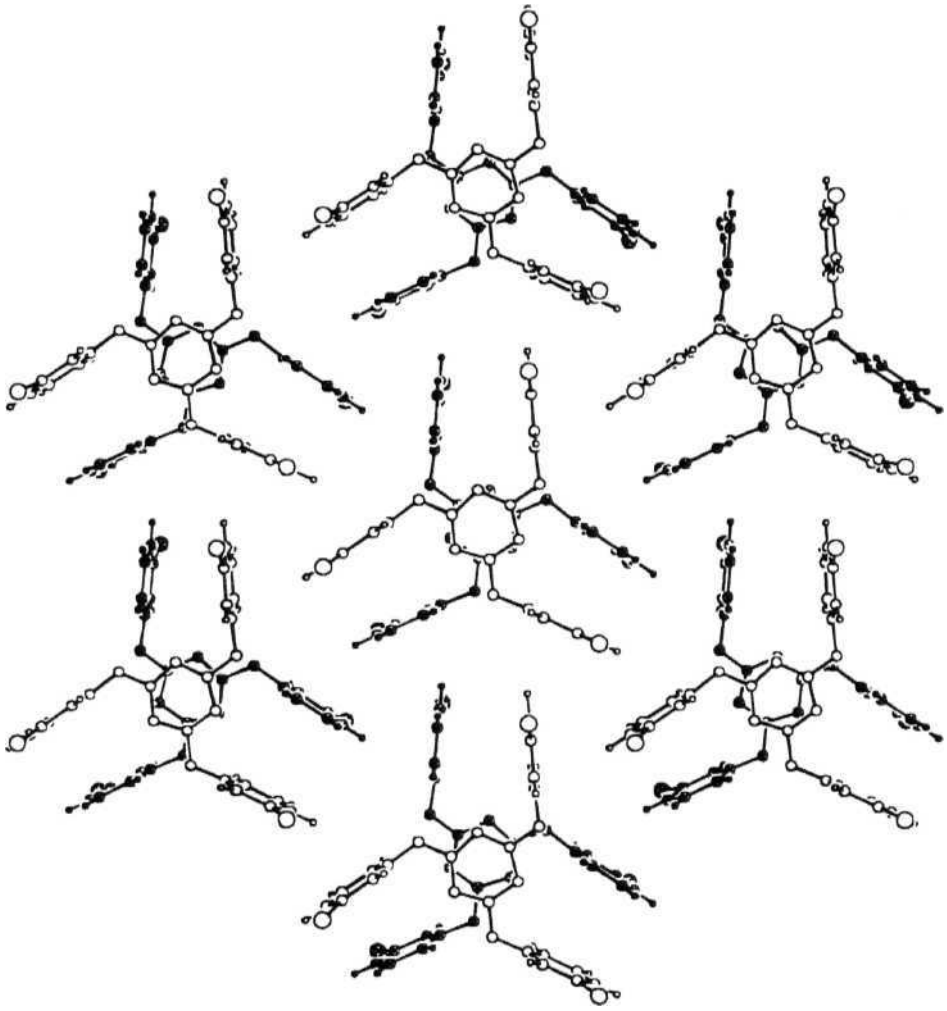


Figure 5. View down [001] showing the trigonal layer structure in 2. Molecules at different heights along [001] are respectively unshaded and shaded The packing of D_3-PUs within the layer is governed by herringbone interactions. The D_3-PUs are translation related parallel to (001) Contrast this with Figure 2.

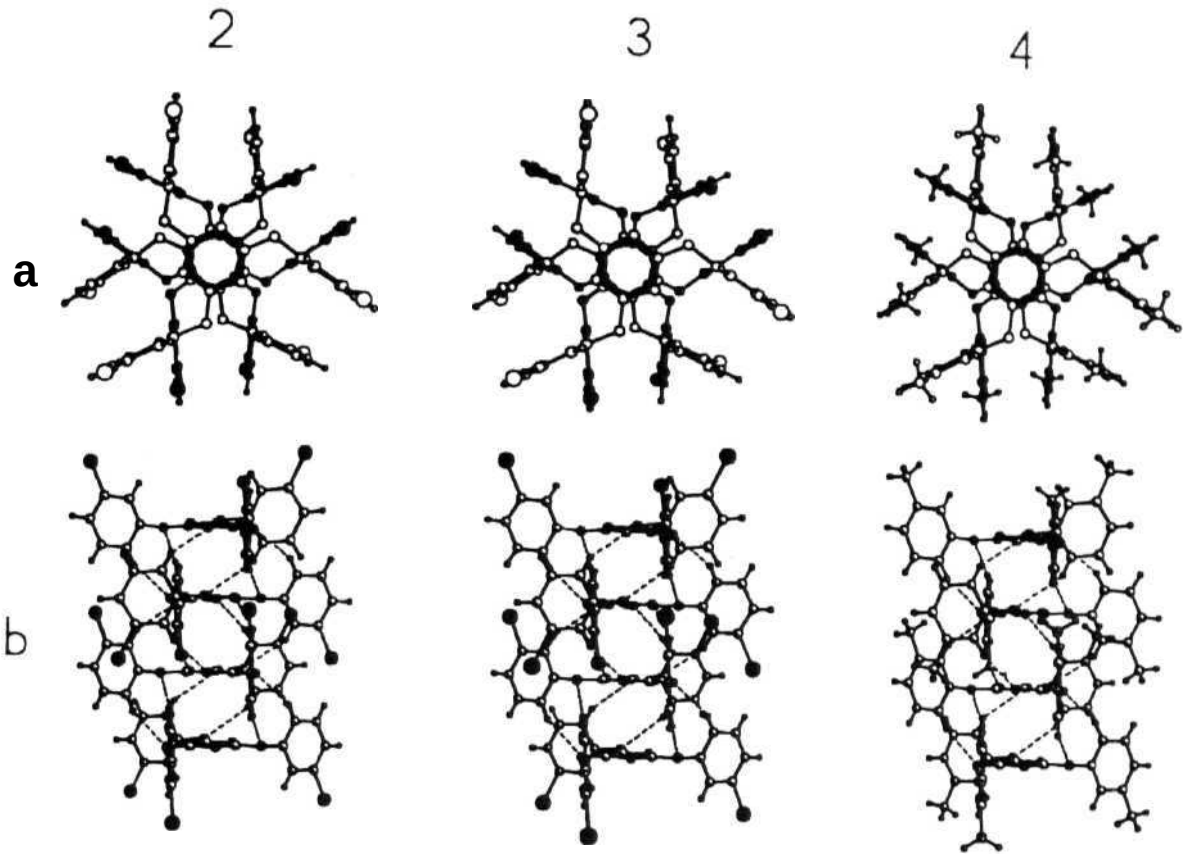


Figure 6 Two views of staggered stacking of D_3-PUs in 2, 3 and **4** (a) View down [001]. The unshaded D_3-PU is above the shaded one. (b) Side view of the stacked pair of D_3-PUs. C-H O and C–H N bonds are indicated as dashed lines. Contrast these with Figure 3.

6.5.3 Staggered Stacking of D_3-PUs Leading to C_{3i}-PUs

The successive D_3-PUs in 2-4 stack along [001] in a staggered manner because eclipsed stacking, as in **1**, would lead to unfavourable stenc interactions with the *meta* substituents. Two views of the staggered stacking of the 3 axis related D_3-PUs are shown in Figure 6. Such a staggered stacking of the D_3-PUs alleviates stenc interactions between the bulky *meta* substituents on the phenoxy groups. The isostructural nature of 2, 3 and 4 illustrates the similar stenc demand of chloro, bromo and methyl groups. Incidentally, the staggered stacking of D_3-PUs

defines a new PU with C_{3i} symmetry in these structures Piedfort units of C_{3i} symmetry (C_{3i}-PUs) result if the lower molecule of the upper D_3-PU and the upper molecule of the lower D_3-PU are selected from a staggered stacked pair of D_3-PUs Figure 4b shows the C_{3i}-PUs found in the structures of 2-4.

The two 3 -related molecules in the C_{3i}-PU are held by $\pi\cdots\pi$stacking and also by C–H···O and C-H-N hydrogen bonds One of the two symmetry independent *ortho* H-atoms is involved in bifurcated C–H···O and C-H-N hydrogen bonding between D_3-PUs. The other symmetry independent *ortho* H-atom on the phenoxy group is bifurcated between C-H-0 and C-H-N hydrogen bonds between the two molecules in the C_{3i}-PU. The data in Table 2 shows that C-H-N bonds arc relatively stronger than C-H-0 bonds in C_{3i}-PUs while the trend is the opposite in D_3-PUs. Thus, the O- and N-atoms arc responsible for effective hydrogen bonding in the alternating D_3-PUs and C_{3i}-PUs. In contrast it may be noted that bifurcation is absent in 1 which has better C-H-0 and C-H-N bonds.

6.5.4 Role of *meta* Substituents in the Inversion of Layers

The continuous, staggered stacking of D_3-PUs along [001] in 2, 3 and 4 produces a supramolecular columnar structure wherein the C-H-0 and C-H-N hydrogen bonded strands do not maintain structural polarity as in 1. This is because the successive D_3-PUs are staggered such that inversion related molecules are stacked. Accordingly, successive tngonal octupolar layers are inversion related in 2-4 and the structures are centrosymmetric.

Such stacking inversion could be a result either of attractive C–H Cl/Br interactions or of the space filling demand of the bulky *meta* substituents. If attractive C–H···Cl/Br interactions are structure determining, the crystal structures of 2 and 3 should be different from the methyl derivative 4 because C–H···Me contacts are not attractive.[26] That 2. 3 and 4 are isostructural and the fact that the intermolecular contacts involving *meta* substituents are long (Table 2) indicates that layer inversion is a consequence of the similar space demand of these

groups [27] To further examine the endurance of this structure type towards *meta* substitution. the structures of 5 and 6 were determined.

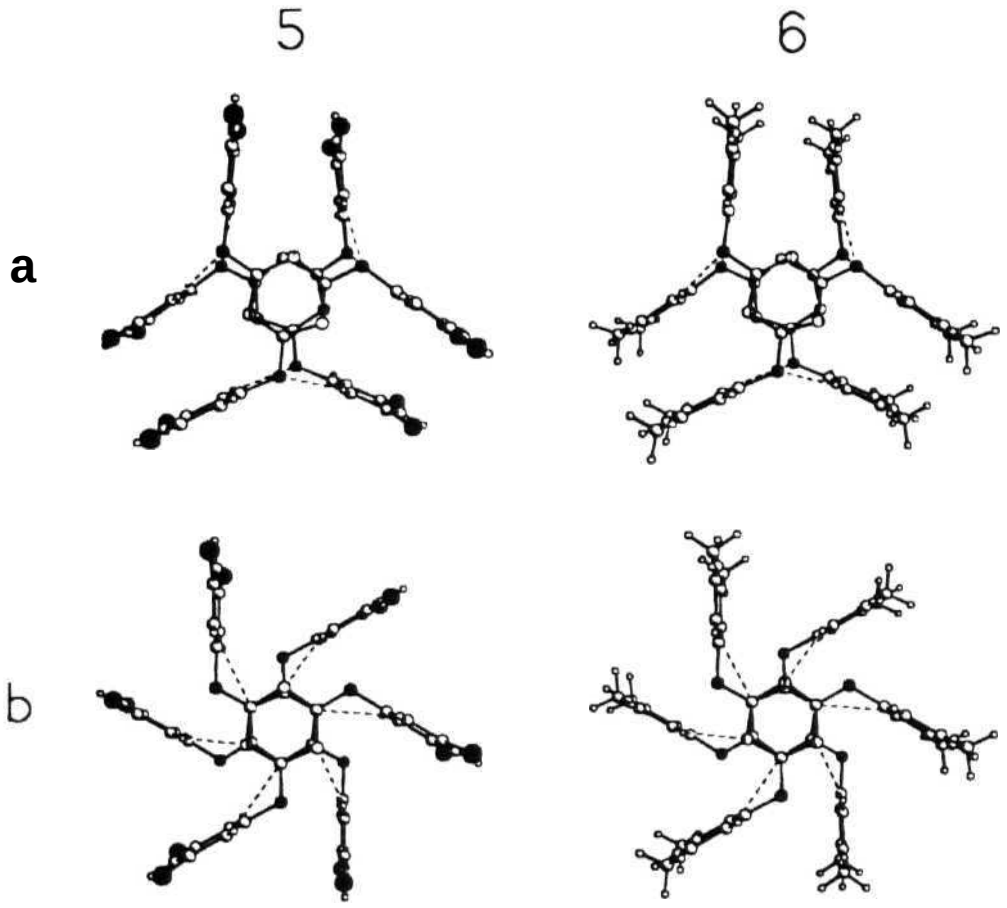


Figure 7. View down [001] showing the Piedfort units in 5 and 6. (a) D?-PUs. C–H O bonds are indicated as dotted lines. (b) C_{3i}-PUs. C-H···N bonds are indicated as dotted lines. Bifurcation is shown in neither case.

6.6 Triazines 5 and 6 - Chloro···Chloro and Methyl ·Methyl Close-Packing

The structures of 2,4,6-*tris*-(3,5-dichlorophenoxy)-1,3,5-triazine, 5 and 2,4,6-*tris*-(3,5-dimethylphenoxy)-1,3,5-triazine, 6 are isostructural to 2-4 and belong to the same trigonal space group *P* 3 *c*1. In these structures too the triazine molecule sits on a three-fold axis and D_3-PUs and C_{3i}-PUs are identified (Figures 7 and 8). The π···π stacking separations and C-H O/N distances in 5 and 6 are longer when compared with the corresponding distances in triazines **2-4** (Table 2). A supramolecular columnar structure is obtained by the staggered stacking of D_3-PUs along [001] (Figure 9)

The successive trigonal layers in 5 and 6 are inversion related and this reduces the repulsive interactions between the *meta* substituents. Interestingly in 5, the inverted layers are related by short Cl Cl geometries between the two symmetry independent Cl-atoms (Cl···Cl: 3.12 A). Usually, short Cl···Cl interactions have a structure influencing effect[26,28] and in such cases the corresponding methyl analogue has a different structure.[29] When the Cl-atom merely has a space-filling role. the chloro and methyl groups (volumes: 20 and 24 A^3 respectively) can be interchanged without much variation in the structure. That 5 and 6 are isostructural suggests that the chloro group is not involved in specific, attractive Cl Cl interactions.[30] The short Cl-Cl separation in 5 is rationalised as a repulsive contact that is forced to accommodate itself within the extremely robust trigonal packing. This is corroborated by the almost linear C-C1-C1-C geometry (type I) and *not* the distinctive mclined geometry (type II) that is characteristic of the polarisation-induced and stabilising Cl···Cl contact.[31]

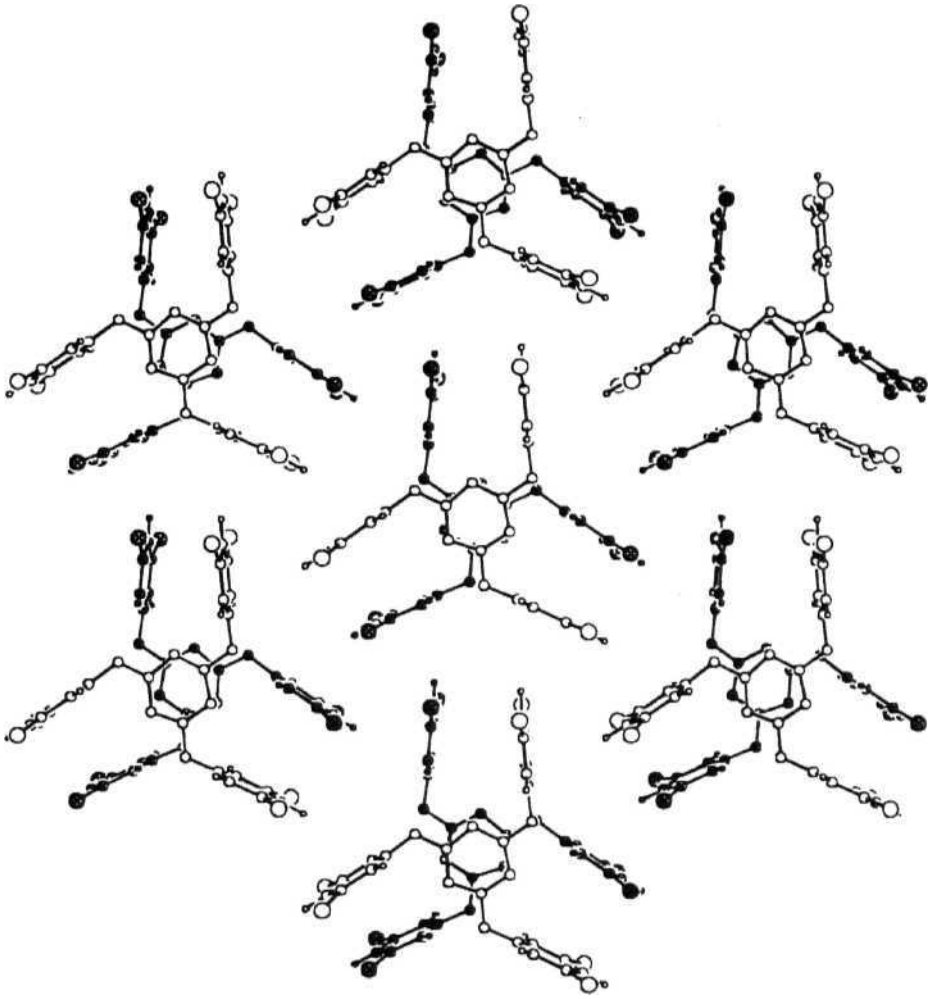


Figure 8. View down [001] showing the trigonal layer structure in 5. Molecules at different heights along [001] are respectively unshaded and shaded. The packing of D_3-PUs within the layer is governed by herringbone interactions. The D_3-PUs are translation-related parallel to (001). Compare this with Figure 5.

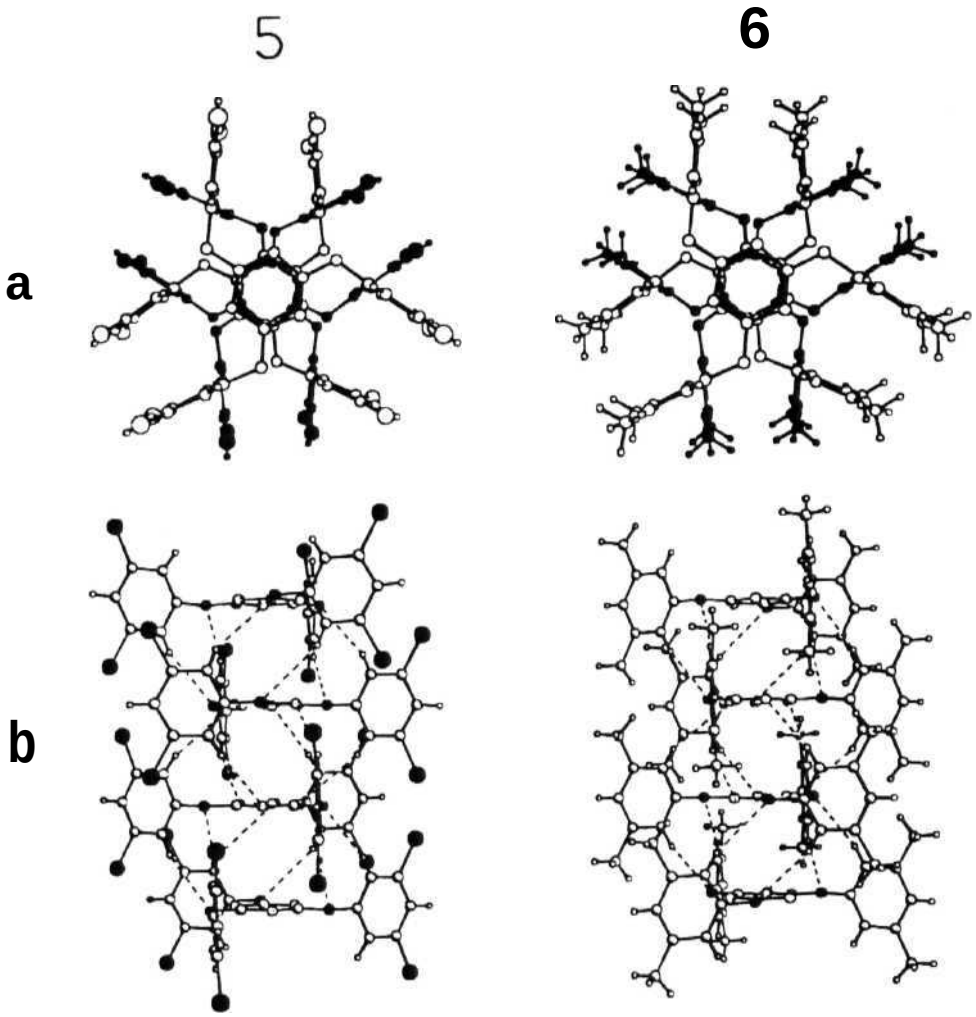


Figure 9 Two views of staggered stacking of D_3-PUs in 5 and 6. (a) View down [001]. The unshaded D_3-PU is above the shaded one. (b) Side view of the stacked pair of D_3-PUs C–H 0 and C-H N bonds are indicated as dashed lines. Compare this with Figure 6.

6.7 **Structural Comparison between 1 and 2-6**

It is now instructive to compare the crystal structure of 1 with those of 2-6. Tnazine 1 vields a polar arrangement of monoclinic symmetry *Ia*. The molecules, are related by translation within non-centrosymmetric layers and are stacked along [100] and related by *a*-glide symmetry. Substitutional variation at molecular level

gives **2-6** which produce non-centros\Tnmetric layers similar to 1 but the molecules are stacked along [001] and are related by 3 and 32 symmetry in the centrosymmetric space group *P* 3 *c*\. Though 1 is monoclinic. it has quasi-trigonal octupolar layers comparable to the perfecth' D_3-symmetric layers in 2-6 (compare Figures 2. 5 and 8). Herringbone interactions between the D_3-PUs in these layers are found in 1 as well as in **2-6**. The stacking distances vary linearly with size and this is attributed to the space demand of the *meta* substituents: the shortest and the longest stacking distances are found in 1 and 6 respectively (Tables 1 and 2). The similarities and differences between the network in 1 compared to those in 2-6 may be visualised by the stacked unshaded-shaded D_3-PU molecular diads in Figures 2, 5 and 8 While the herringbone interactions within and between the linear arrays are different in 1. unshaded-to-unshaded and shaded-to-shaded within a linear array and unshaded-to-shaded and shaded-to-unshaded between the linear arrays (Figure 2) they are all same in 2-6, always unshaded-to-unshaded and shaded-to-shaded (Figures 5 and 8). This differentiates the quasi and perfect D_3 symmetry of the tngonal networks in 1 and 2-6 respectively. Two-dimensional supramolecular octupolar non-linearities are well demonstrated in thc structures of 2-6 and all these tnazines are excellent examples of two-dimensionally chiral systems.[18] The main difference between 1 and 2-6 lies in the mode of stacking of D_3-PUs: eclipsed stacking is observed in 1 while staggered stacking is observed in 2-6. This leads to the following differences between the structure of 1 and those of 2-6: a) the absence and presence of C_{3i}-PUs. b) the absence and presence of interactions between the *meta* substituents, c) the absence and presence of inversion between layers. d) the presence and absence of bulk non-centrosymmetry.

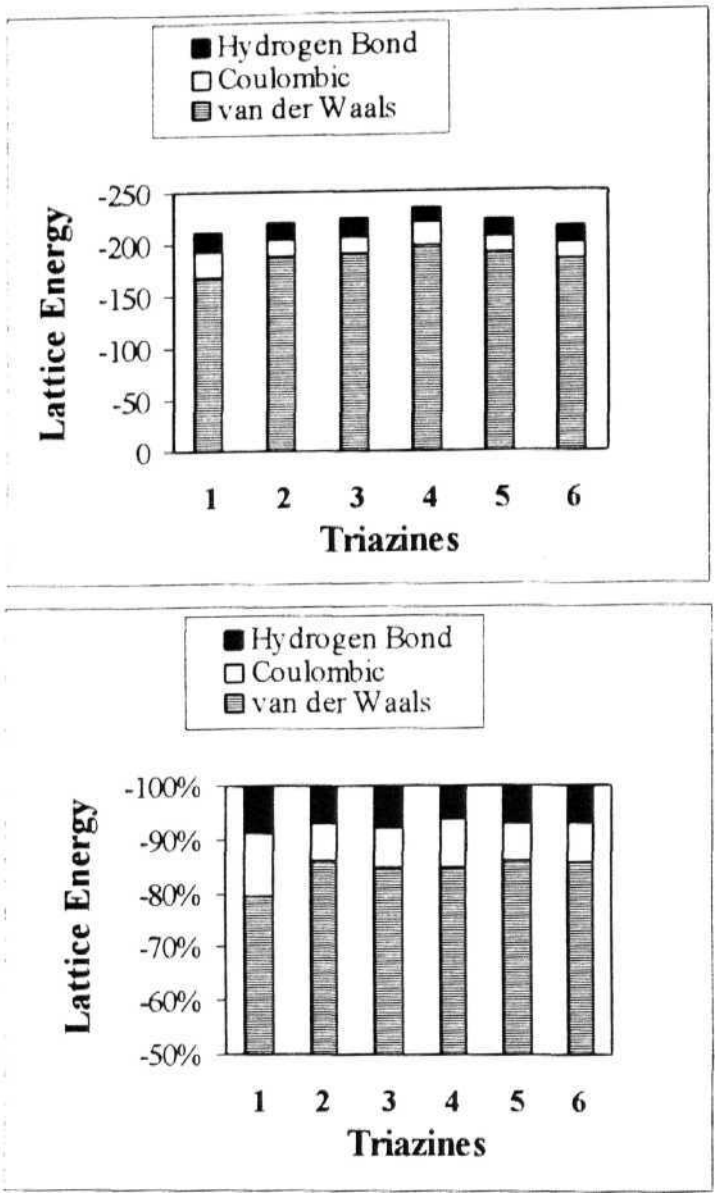


Figure 10 Calculated lattice energies for triazines 1-6 showing hydrogen bonding. Coulombic and van der Waals components. Top: Energy expressed in kcal/mol. Bottom; Energy terms expressed as percentage contributions.

6.8 Lattice Energy Calculations on Triazines 1-6

Computational quantification of various components of lattice energy helps in the understanding of the contributions from these components. Lattice energy'

calculations were performed on triazines **1-6** using the program Cerius[2]. The absolute and percentage contributions from van der Waals. Coulombic and hydrogen bond energies in triazines 1-6 are shown in Figure 10. Inspection of the absolute and percentage contributions of different energy types to the structures reveals the following: a) Triazine 1 is distinctly different from others and is stabilised with a higher contribution from weak hydrogen bonds; b) The van der Waals contributions are the least in 1 as might be expected; c) The contributions from the van der Waals energy is similar in 2. 3 and 4 and the latter one is least stabilised by hydrogen bonding; d) The percentage contribution from the three types of energies are alike in 5 and 6, indicating their gross structural similarity; e) Between triazines 2-5 the smaller van der Waals contribution in 6 indicates that it is somewhat loosely packed, relative to others. These examples show the supporting role of lattice energy calculations in crystal engineering studies and reveal similarities and differences within this particular family of structures.

6.9 Triazines 1-6 - Molecular and Crystal Non-Linear Characterisation

The molecular non-linear coefficients, $\sqrt{\langle\beta^2\rangle}$ of compounds **1-6** determined from HLS measurements at $1.064\mu m$ are given in Table 3. The molecular hyperpolarisability of these compounds is of the same order of magnitude as that of the classical dipolar pNA molecule ($\sqrt{\langle\beta^2\rangle} = 10 \times 10^{-30}$ esu) implying that there is a comparable, moderately efficient charge transfer in these molecular structures. The depolarisation ratio $D = \langle\beta^2_{zxx}\rangle/\langle\beta^2_{xxx}\rangle$ is about 0.63 for these compounds and confirms their octupolar symmetry since the calculated D value for pure octupolar symmetry is 0.67.[32] Assuming a planar octupolar structure for these compounds, the resulting β tensor components reduce to the two β_{yyy} and β_{yxx} coefficients with $\beta_{yyy} = -\beta_{yxx}$, y lying along one of the three charge transfer axes.

After isotropic averaging, the microscopic β_{yyy} values can be inferred from the orientational averaging relation[32] $\langle\beta^2\rangle = 8/21\beta^2_{yyy}$ (Table 3).

Table 3. Microscopic tensorial coefficients for triazines **1-6** from HLS measurements.

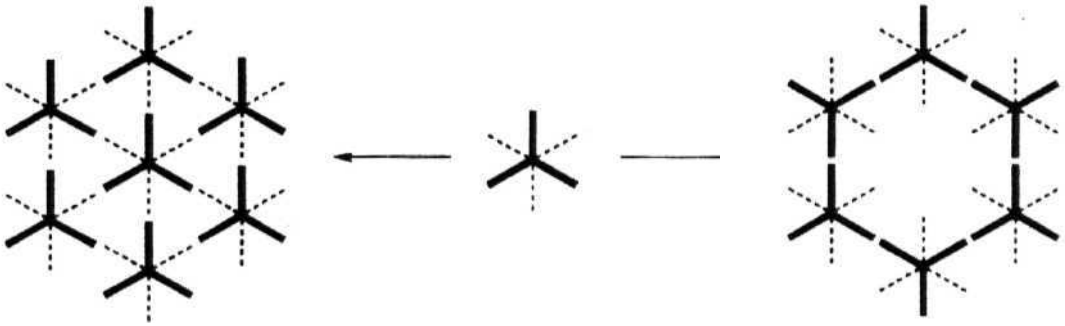
	1	2	3	4	5	6
$\sqrt{\langle\beta^2\rangle}$ (10^{-30} esu)	18±2	19±2	20±4	15±2	22±5	21±3
β_{yyy} (10^{-30} esu)	29.2	30.7	32.4	24.3	35.6	34

An estimation of the non-linear efficiency of crystalline **1**, using the oriented gas model, was performed since it is the only compound in the series that crystallises in a non-centrosymmetric structure. Triazine 1 exhibited an SHG powder signal measured as one tenth that of the urea powder signal. Triazines 2-6 that crystallise in centrosymmetric structures did not show any measurable SHG signal.

6.10 Triazines 7 and 8 - Hexagonal Networks

The similarity between the structure types exemplified by 1 and by **2-6** is the trigonal network stabilised by herringbone interactions between the *para* H-atoms and the phenyl rings. To better understand the role of the *para* H-atoms in establishing the trigonal networks, the crystal structures of triazines 7 and 8 were determined 2,4,6-*tris*-(4-Chlorophenoxy)-1,3,5-triazine, 7 and 2,4,6-*tris*-(4-bromophenoxy)-1,3,5-triazine, 8 are isostructural and crystallise in the hexagonal space group $P6_3/m$. Crystals of 7 and 8 grow as solvates from chloroform, dichloromethane, ethyl acetate, benzene and toluene. X-ray diffraction was carried out on crystals grown from benzene for both 7 and 8, with the expectation that one could take advantage of the hexagonal molecular symmetry of benzene in the analysis. However, the crystals readily loose their solvent of recrystallisation and become opaque when taken out of the mother liquor. Also, they could not be

cooled without destroying them The structural results at room temperature are of low accuracy and the solvent molecule could not be located.



I J

Scheme 4. Trigonal and hexagonal networking of trigonal molecules. The approach of unlike groups leads to trigonal packing (I) and that of like groups to hexagonal packing **(J).**

6.10.1 Centro- and Non-Centrosymmetric Packing Modes of Trigonal Molecules

Molecules with three-fold symmetry may assemble in one of the two modes depicted in Scheme 4.[14] A non-centrosymmetric trigonal lattice is obtained if unlike groups approach each other, that is solid-to-dashed lines as shown in I. This is found in the structures of triazines 1-6 where D_3-PUs serve as the trigonal species, with the edges and the faces of the phenyl rings behaving as the unlike groups. The hexagonal centrosymmetric lattice is obtained if like groups approach one another as depicted by the solid-to-solid or dashed-to-dashed lines in J. The structures of triazines 7 and 8 belong to the centrosymmetric hexagonal type

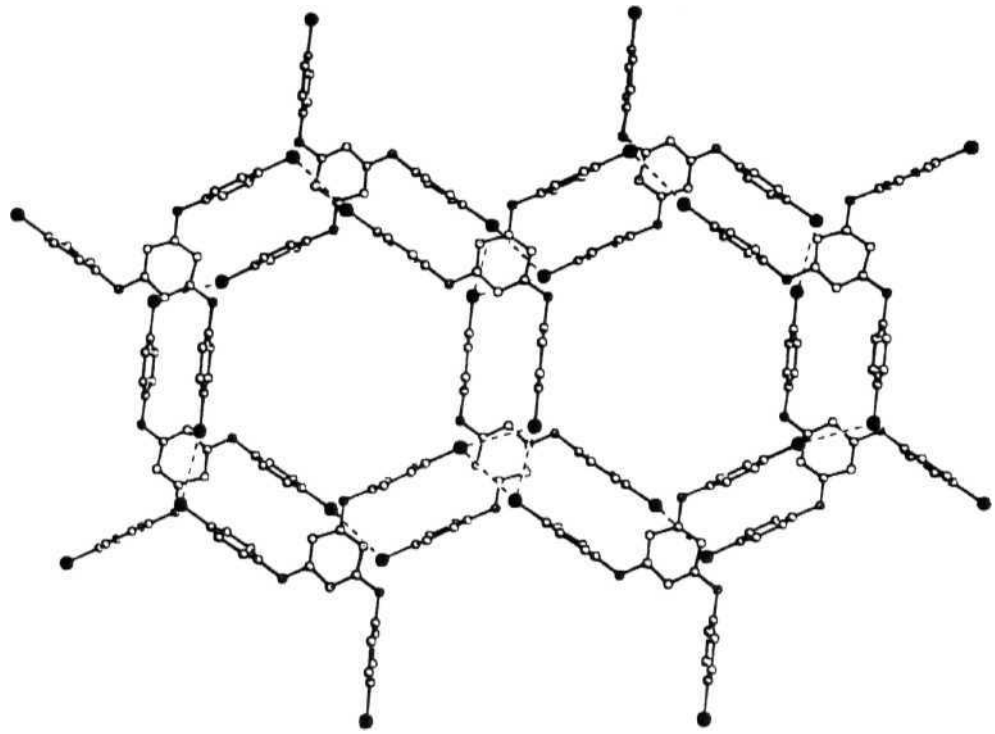


Figure 11 Hexagonal networks in the crystal structure of 7. Notice that molecular synthons (triazine ring) and supramolecular synthons (CU trimer) alternate to produce the hexagonal sheet structure.

6.10.2 Trimer Cl_3 and Br_3 Supramolecular Synthons

The crystal structure of triazines 7 and 8 have large hexagonal cavities of area 94 and 99Å^2 (Figures 11 and 12). The *para* halogen atom (Cl or Br) forms intermolecular contacts with two other symmetry related atoms through trimeric X_3 (X = Cl or Br) supramolecular synthons (Figure 13). These synthons are structurally equivalent to the well known $(OH)_3$ trimer synthon.[33] Halogen···halogen contacts have two preferred geometries.[34] type I and type II as detailed in Chapter 3. While space filling type I contacts are found in the structure of 5. the contacts present in 7 and 8 correspond to the polarisation-induced type II category as evidenced from the geometrical data in Table 4. The trimer X_3

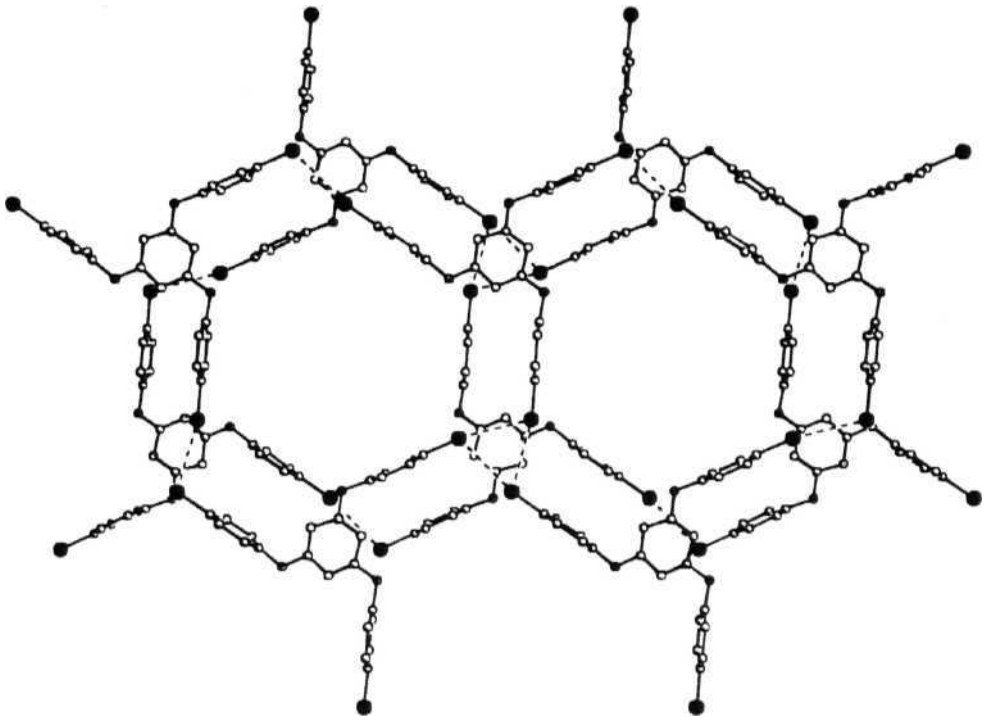


Figure **12**. Hexagonal networks in the crystal structure of 8. Notice that molecular synthons (triazine ring) and supramolecular synthons (Br_3 trimer) alternate to produce the hexagonal sheet structure. Compare this with Figure 11

synthons are cyclic and each halogen is appropriately polarised, behaving both as a donor and an acceptor. Such cooperativity effects could enhance the strength of the X· X interactions. A search for the occurrence of these synthons in CSD has revealed that such trimeric and cooperative type II halogen •halogen contacts are present only in three other structures.[3] The strength of these halogen trimer synthons and their attractive character was appreciated when several attempts to crystallise the *para*-methyl derivative were unsuccessful. The methyl groups obviously cannot form trimer synthons similar to the halogen atoms. Yet the Cl-group in 5 could be exchanged with the methyl group in 6 keeping the structure invariant This underscores the fact that the X_3 trimer synthons are the crucial

fusing elements in the structures of 7 and 8. Apart from the X X interactions, other weak intermolecular interactions are also possible in these structures but they are not analysed because of the low accuracy in structure determination

Table 4. Type II halogen···halogen interactions in the crystal structures of 7 and 8.

	7	8
X···X[a]	3.467	3.500
θ_1	171.0	169.6
θ_2	111.0	109.6

[a] X = Cl and Br in 7 and 8 respectively.

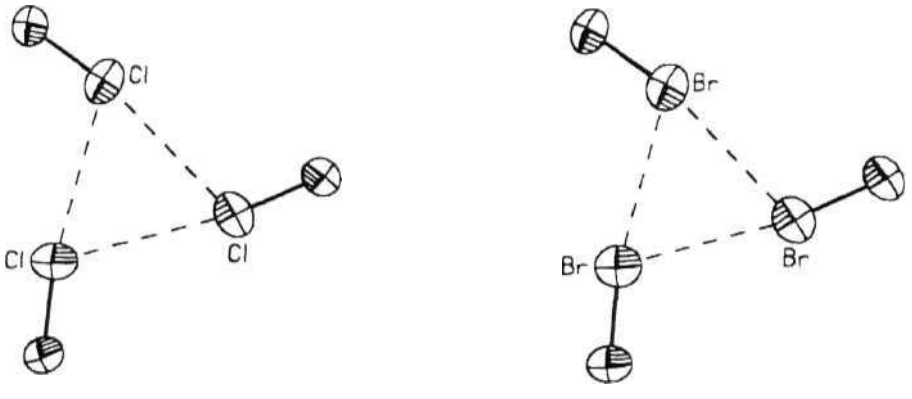
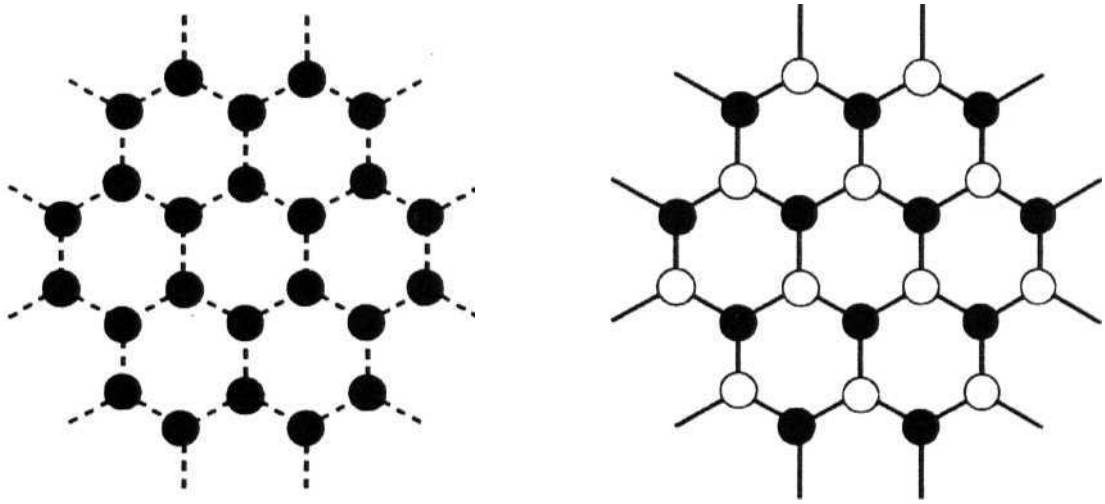


Figure **13.** ORTEP diagram showing the Cl_3 and Br_3 supramolecular synthons in 7 and **8.**

6.10.3 Hexagonal Networks - Molecular **and** Supramolecular Nodes

In general hexagonal networks may be generated by connecting tngonal nodes. The usual strategy is therefore to select molecular precursors with self-complementary functionalities positioned trigonally on the molecular framework[36] (as in J, Scheme 4) or to co-crystallise molecular species with complementary'

subunits located trigonally.[37] Such a strategy produces a hexagonal network in which the molecules act as the nodes and the supramolecular synthons are the node connectors. Here, a supramolecular synthesis is described which is quite different from the traditional assembly of a hexagonal network. The synthesis of the hexagonal networks shown in Figures 11 and 12 is achieved by alternating the molecular (triazine ring) and the supramolecular synthons (X_3 trimer). Thus, the hexagonal networks described here are produced by alternating the molecular and supramolecular nodes (**L**, Scheme 5) as opposed to the conventional systems which contain only molecular nodes (**K**, Scheme 5).[36] The hexagonal layered networks observed in the structures of 7 and 8 are parallel to (001) and successive layers are 2\ related. This results in alternate stacking along [001] of tnazme rings and X_3-trimers, that is molecular and supramolecular synthons.



K **L**

Scheme 5. Two ways of generating hexagonal networks. K. Trigonal molecular nodes (solid circles) interconnected by supramolecular node connectors (dashed lines). L. Alternating molecular (solid circles) and supramolecular (open circles) trigonal nodes are interconnected by molecular node connectors (solid lines).

In summary, it is clear that adoption of a particular structure type in the tnazine family is very sensitive to substitution at the *para* position on the phenox> groups So long as the *para* H-atom is intact, a robust polar trigonal layer results A *para*-halogen substitution results in a hexagonal layer structure The supramolecular retrosynthetic approach descnbed in this chapter provides excellent structural control in two dimensions even as it may be realised that control in the third dimension still remains to be achieved in a general sense.

6.11 Conclusions

Studies in crystal engineering towards the applications of non-linear optics reveals that the intersection of these fields has been growing to be a fertile area of research. In particular, this work shows that octupolar NLO substances may be realised not only at the molecular level but also at the supramolecular level. Octupolar systems offer advantages over dipolar systems with regard to manipulation of packing characteristics because they can be expressed as higher dimensional networks and as such a greater proportion of the structure is amenable to retroanalysis. Reduction in dimensionality through interaction insulation is of key importance in structural control. In the present work, such insulation is achieved by dissecting apart the layer and stack structures Retros\nthetic applications to supramolecular systems has been successfully exploited to yield target trigonal networks in the crystal structures of six triazines Multi-stage supramolecular synthesis has been descnbed in triazines 1 -6 and the desired two-dimensional octupolar networks have shown to be generated from a finite supramolecular species, namely the Piedfort unit. The carry-over of molecular symmetry into the crystal has been observed, without fail, in the crystal structures of 1-6 and indicates the usefulness of the retrosynthetic approach Both structural mimicry and structural diversity may be manipulated at will in the tnazine family of structures. A new modular approach, that is by alternating

molecular and supramolecular synthons has been developed to synthesise hexagonal supramolecular networks.

6.12 Experimental

6.12.1 General Procedure for the Synthesis of Triazines 1-8

Commercially available cyanuric chloride and the appropriate phenols were used as received without further purification Reagent grade solvents were used for extraction and distilled solvents were used for all recrystallisations. Cyanuric chloride (10 mmol) was heated with a small excess of the appropriate phenol (35 mmol) at 185-210° C for 5 h under a reflux air condenser.[38] HC1 gas evolved vigorously during the first few hours. The crude reaction product was extracted with boiling EtOH leaving a residue of crude triaryloxytriazine. This residue was then recrystallised from $CHCl_3$ to give the pure crystalline product in 80-90% yield. All the triazines were characterised by their IR and NMR spectra.

6.12.2 X-Ray Crystallography

Single crystals suitable for X-ray diffraction were grown from common organic solvents (see appendix). Data for 1 were collected at Fox Chase Cancer Center, U.S.A. by Drs. A.K. Katz and H.L. Carrell. Data for 2-8 were collected at University of Essen by the candidate under the supervision of Prof. R. Boese. The structure solutions and refinements were carried out using the programs SHELXS-86[39] and SHELXL-93[40] built-in with the Siemens SHELXTL package. The relevant crystallographic information is given in appendix.

6.12.3 Energy Calculations

The Cerius[2] program from Molecular Simulations was used for all the calculations.[41] The experimental crystal coordinates served as the starting point in these calculations. The AM1 Hamiltonian in MOPAC6 was used to calculate the electrostatic potential (ESP) charges. The molecular geometries were not

optimised as this would lead to a loss of molecular symmetry. The molecule with assigned ESP charges was used to build the appropriate crystal system in Cerius[2]. The lattice energy was calculated using the Dreiding 2.21 force field in the Crystal Packer module of Cerius[2] with ESP charges from M0PAC6. The Ewald summation technique was used for the Coulombic interactions and the van der Waals interactions were truncated at 8.0 A separation. C-H O and C-H N hydrogen bonds were included in the calculations. The repulsive van der Waals contributions from the H-atoms involved in the weak hydrogen bonds were excluded. The energy of the crystal was then minimised till the gradient in energy was less than 0.01 kcal/mol The values of lattice energy were calculated from this minimised crystal and the contributions from the van der Waals, Coulombic and hydrogen bond interactions were analysed.

6.12.4 NLO Measurements

The lack of a permanent dipole moment in the molecules studied here makes the classical Electric Field Induced SHG (EFISH) experiment unsuited to the determination of molecular non-linearities. β.[42] Therefore the measurements in solution were performed by use of the HLS experiments.[43] These experiments were carried out by Dr. S. Brasselet under the supervision of Prof. J. Zyss at CNET, Fiance.

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22. The X-ray diffraction on the crystals of 1 yielded an initial triclinic cell with dimensions a = 6.601(2). b = 12.426(6). c = 12.649(4) A. α = 118.23(2). β = 97.93(5) and γ = 101.22(3)° The structure was solved and refined in the space group *P*\. with two molecules in the asymmetric unit. During the refinements two of the C-atoms became non-positive-definite. It was identified from an analysis of the refined structure that the two symmetry independent molecules are stacked along [100] and they could be related by an *a*-glide perpendicular to [010]. This and the pseudo-hexagonal packing of the structure led us to search for the higher symmetry in the crystal. It was found that a higher symmetry space group is indeed possible and this is the one discussed in this chapter.

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APPENDIX

Table 1. Salient crystallographic details of the compounds discussed in this thesis.

	Chapter 2		*Chapter 3*
	2	**3**	**2**
Emp. formula	C_6H_7NO	C_6H_7NO	$C_6H_2F_4O_2$
Formula wt.	109.00	109.00	182.08
T (K)	100(2)	100(2)	298(2)
Crystal system	Orthorhombic	Orthorhombic	Monoclinic
Space group	*Pbca* (61)	$Pca2_1$ (29)	$P2_1/n$ (14)
a (Å)	19.655(2)	11.226(2)	6.5542(6)
b (Å)	7.157(2)	6.101(2)	4.8843(4)
c (Å)	7.770(2)	8.282(2)	10.1501(8)
α (°)	90	90	90
β (°)	90	90	107.990(6)
γ (°)	90	90	90
Z	8	4	2
V (Å^3)	1093.0(4)	567.2(3)	309.05(5)
D_{calc} (Mg/m^3)	1.325	1.276	1.957
F (000)	288	144	180
2θ range	3.76 - 41.62	4.49 - 49.95	6.60 - 59.92
Index ranges	$0 \le h \le 48$	$-15 \le h \le 16$	$-9 \le h \le 9$
	$0 \le k \le 14$	$-9 \le k \le 9$	$-1 \le k \le 6$
	$0 \le l \le 19$	$-4 \le l \le 13$	$-14 \le l \le 13$
$R1$	0.0634	0.0504	0.0405
$wR2$	0.1439	0.0612	0.1143
Gof	1.243	1.477	1.051
N-total	2368	2532	2176
N-independent	2046	2037	901
N-observed	2045	1227	664
Variables	136	136	59

Table **1**. *continued*..

Chapter 3			
4	**5**	**6**	**7**
$C_6H_2Br_4O_2$	C_6H_5F	$C_6H_4F_2$	$C_6H_4F_2$
425.72	96.10	114.09	114.09
298(2)	123(2)	123(2)	215(2)
Monoclinic	Tetragonal	Monoclinic	Monoclinic
$P2_1/n$ (14)	$P4_32_12$ (96)	$P2_1/n$ (14)	$P2_1/c$ (14)
8.8907(2)	5.799(2)	7.4806(11)	5.809(2)
4.7316(1)	5.799(2)	5.9608(9)	6.530(2)
11.0612(3)	14.530(7)	11.725(2)	7.190(2)
90	90	90	90
92.167(1)	90	103.815(11)	101.89(2)
90	90	90	90
2	4	4	2
464.98(2)	488.6(4)	507.68(13)	266.88(14)
3.041	1.306	1.493	1.420
388	200	232	116
5.78 - 56.36	3.78 - 30.04	2.94 - 30.01	3.58 - 25.03
$-11 \le h \le 11$	$-8 \le h \le 0$	$-10 \le h \le 4$	$-6 \le h \le 6$
$-6 \le k \le 6$	$0 \le k \le 8$	$-8 \le k \le 8$	$-7 \le k \le 7$
$-14 \le l \le 14$	$0 \le l \le 20$	$0 \le l \le 16$	$-8 \le l \le 5$
0.0665	0.0407	0.0344	0.0443
0.1431	0.1056	0.1051	0.1139
0.929	1.060	1.055	1.144
4829	858	2395	1614
1130	718	1231	476
709	637	1119	378
56	44	90	45

Table 1. *continued*..

Chapter 3			
11	**12**	**13a**	**14**
$C_6H_3F_3$	$C_6H_2F_4$	$C_6H_2F_4$	C_6HF_5
132.08	150.08	150.08	168.07
130(2)	135(2)	123 (2)	200(2)
Monoclinic	Monoclinic	Monoclinic	Monoclinic
*I*2/*a* (15)	$P2_1/c$ (14)	*C*2/*c* (15)	$P2_1/c$ (14)
6.160(2)	4.4719(11)	19.171(3)	12.380(3)
11.909(3)	10.285(2)	6.9496(12)	9.910(2)
7.504(2)	6.342(2)	9.207(2)	9.880(2)
90	90	90	90
95.47(2)	107.97(2)	116.187(13)	102.50(3)
90	90	90	90
4	2	8	8
548.0(3)	277.46(13)	1100.7(4)	1183.4(4)
1.601	1.796	1.811	1.887
264	204	592	656
3.22 - 27.46	3.92 - 29.92	2.37 - 30.12	1.68 - 27.43
$-1 \le h \le 7$	$-5 \le h \le 5$	$-26 \le h \le 25$	$-13 \le h \le 13$
$-15 \le k \le 15$	$-14 \le k \le 14$	$0 \le k \le 9$	$0 \le k \le 10$
$-9 \le l \le 9$	$-8 \le l \le 0$	$-1 \le l \le 12$	$-12 \le l \le 0$
0.0419	0.0424	0.0433	0.0344
0.1092	0.1112	0.1241	0.0912
1.055	1.085	1.070	1.055
1422	1567	1872	1467
628	761	1608	1409
538	692	1336	1099
49	51	99	208

Table 1. *continued..*

Chapter 4		*Chapter 5*	
1	**2**	**1**	**2**
$C_6H_4INO_2$	$C_{24}H_{18}N_2I_2O_8$	$C_6H_9N_3O_3$	$C_9H_{15}N_3O_3$
249.00	716.20	171.15	213.24
150(2)	150(2)	298(2)	298(2)
Triclinic	Triclinic	Monoclinic	Orthorhombic
$P\bar{1}$	$P\bar{1}$	$P2_1/a$ (14)	$P2_12_12_1$ (19)
7.545(2)	7.719(2)	8.142(1)	7.835(2)
7.802(2)	9.246(2)	13.393(1)	8.144(1)
6.599(1)	9.988(2)	14.822(1)	16.820(5)
91.43(3)	111.43(3)	90	90
92.03(3)	107.76(3)	100.88(7)	90
66.00(3)	94.03(3)	90	90
2	2	8	4
354.6(1)	618.5(2)	1587.2(3)	1073.3(4)
2.332	1.923	1.433	1.320
232	346	720	456
5.72 - 64.90	5.18 - 50.00	4.14 - 49.96	5.56 - 57.62
$0 \le h \le 11$	$-9 \le h \le 9$	$-4 \le h \le 9$	$0 \le h \le 10$
$-10 \le k \le 11$	$0 \le k \le 10$	$-4 \le k \le 15$	$0 \le k \le 11$
$-9 \le l \le 19$	$-11 \le l \le 11$	$-17 \le l \le 17$	$0 \le l \le 22$
0.0183	0.0269	0.0528	0.0380
0.0452	0.0605	0.1524	0.0963
1.127	1.066	1.088	1.074
2725	2313	2754	6916
2560	2165	2508	1568
1654	1894	1814	1380
108	196	218	136

Table **1**. *continued..*

Chapter 5		*Chapter 6*	
3	**5**	**1**	**2**
$C_{24}H_{21}N_3O_3$	$C_{12}H_{12}N_6O_9$	$C_{21}H_{15}N_3O_3$	$C_{21}H_{12}N_3O_3Cl_3$
399.44	384.28	357.36	460.69
298(2)	298(2)	298(2)	298(2)
Orthorhombic	Hexagonal	Monoclinic	Trigonal
$Pmn2_1$ (31)	$P\bar{6}$ (174)	*Ia* (9)	$P\bar{3}c1$ (165)
18.986(3)	8.708(1)	6.6010(13)	12.957(2)
4.5738(8)	8.708(1)	20.903(4)	12.957(2)
11.421(2)	6.084(1)	12.649(3)	14.193(2)
90	90	90	90
90	90	97.93(3)	90
90	120	90	120
2	1	4	4
991.8(3)	399.54(9)	1728.6(6)	2063.6(5)
1.338	1.597	1.373	1.483
420	198	744	936
4.16 - 50.84	5.40 - 54.82	6.50 - 55.12	3.62 - 44.78
$-22 \le h \le 3$	$0 \le h \le 11$	$-8 \le h \le 0$	$-1 \le h \le 12$
$-5 \le k \le 5$	$-9 \le k \le 0$	$-27 \le k \le 27$	$-13 \le k \le 1$
$-11 \le l \le 11$	$-7 \le l \le 7$	$-15 \le l \le 16$	$-1 \le l \le 15$
0.0526	0.0919	0.0832	0.0692
0.1330	0.2391	0.2033	0.1546
1.108	1.177	1.126	1.156
1889	613	3685	2226
1442	339	2044	902
1196	325	1431	747
156	57	244	96

Table 1. *continued.*

Chapter 6			
3	**4**	**5**	**6**
$C_{21}H_{12}N_3O_3Br_3$	$C_{24}H_{21}N_3O_3$	$C_{21}H_9N_3O_3Cl_6$	$C_{27}H_{27}N_3O_3$
594.07	399.44	564.01	441.52
298(2)	298(2)	298(2)	298(2)
Trigonal	Trigonal	Trigonal	Trigonal
$P\bar{3}c1$ (165)	$P\bar{3}c1$ (165)	$P\bar{3}c1$ (165)	$P\bar{3}c1$ (165)
13.1205(7)	13.023(2)	13.2925(6)	13.2987(13)
13.1205(7)	13.023(2)	13.2925(6)	13.2987(13)
14.4265(9)	14.334(3)	15.9132(9)	15.962(2)
90	90	90	90
90	90	90	90
120	120	120	120
4	4	4	4
2150.8(2)	2105.3(6)	2435.0(2)	2444.8(4)
1.835	1.260	1.538	1.200
1152	840	1128	936
3.58 - 44.98	3.62 - 44.98	3.54 - 51.26	3.54 - 44.94
$-1 \le h \le 13$	$0 \le h \le 11$	$-15 \le h \le 15$	$0 \le h \le 13$
$-14 \le k \le 1$	$-10 \le k \le 11$	$-15 \le k \le 14$	$-14 \le k \le 1$
$-1 \le l \le 15$	$-9 \le l \le 19$	$-19 \le l \le 19$	$-1 \le l \le 17$
0.0448	0.0748	0.0956	0.0507
0.1034	0.1624	0.2738	0.1320
1.070	0.996	1.111	1.009
2330	2263	9070	2437
947	920	1452	1072
694	346	1140	697
96	96	104	106

Table 1. *continued*..

Chapter 6	
7	**8**
$C_{21}H_{12}N_3O_3Cl_3$	$C_{21}H_{12}N_3O_3Br_3$
460.69	594.07
298(2)	298(2)
Hexagonal	Hexagonal
$P6_3/m$ (176)	$P6_3/m$ (176)
15.364(3)	15.602(2)
15.364(3)	15.602(2)
6.855(2)	7.0500(14)
90	90
90	90
120	120
2	2
1401.3(6)	1486.2(4)
1.092	1.327
468	576
3.06 - 49.98	3.02 - 45.00
$-1 \le h \le 15$	$-1 \le h \le 14$
$-18 \le k \le 1$	$-16 \le k \le 1$
$-1 \le l \le 8$	$-1 \le l \le 7$
0.1221	0.1077
0.3165	0.2944
1.278	1.090
2352	1853
898	719
823	463
58	57

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