POLYMORPHISM, PSEUDOPOLYMORPHISM AND NETWORKS IN ORGANIC CRYSTALS

A Thesis
Submitted for the Degree of
Doctor of Philosophy

By
V. S. SENTHIL KUMAR

School of Chemistry
University of Hyderabad
Hyderabad 500 046
India

November 2002

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To
My Parents

STATEMENT

I hereby declare that the matter embodied in this thesis entitled '**Polymorphism, Pseudopolymorphism and Networks in Organic Crystals**' is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad under the supervision of Prof. Ashwini Nangia.

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.

V. Senthil Kumar

Hyderabad
November 2002

V. S. Senthil Kumar

CERTIFICATE

Certified that the work '**Polymorphism, Pseudopolymorphism and Networks in Organic Crystals**' has been carried out by **V. S. Senthil Kumar** under my supervision and that the same has not been submitted elsewhere for a degree.

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Thesis Supervisor

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PREFACE

Modern organic chemistry finds itself at the onset of a fascinating new period, in which interest is directed towards the construction of organised systems of co-operative molecules, that is supramolecular systems in which each molecule has its distinct location and specific role. Crystal engineering has emerged as an important cross-disciplinary field of basic and applied endeavour, offering routes to the rational design of functional solids.

An organic crystal is the ultimate supermolecule and therefore crystal engineering is a supramolecular equivalent of organic synthesis. Crystal engineering deals with synthesis and rationalisation crystal structures. The supramolecular synthon concept plays a key role in crystal architecture. Visualising each crystal as a network structure, with molecules acting as nodes and the supramolecular synthons as node connectors, simplifies the understanding of crystal structures. The utility of synthon concept is highlighted in Chapter 1.

Polymorphism is an important phenomenon for both fundamental and applied reasons. Chapter 2 describes crystal structures of four polymorphic modifications of 4,4-diphenyl-2,5-cyclohexadienone that exhibit concomitant polymorphism, conformational polymorphism and conformational isomorphism, with 19 symmetry-independent molecules. A gearing of the geminal phenyl groups in the molecule leads to conformational changes from structure to structure that result in different crystal packing arrangements. Their formation is characterised by the alternative arrangements of C–H···O hydrogen bond synthons.

The design and assembly of new crystalline clathrates and nanoporous solids with desired motifs and architectures is a challenging goal in solid state supramolecular synthesis. In Chapter 3, the importance of weak C–H···O mediated benzoquinone tape motif in the synthesis of a clay mimic organic host is highlighted. Generality of the bilayer framework for guest inclusion is demonstrated.

Carboxylic acid group is the most studied hydrogen-bond functionality in crystal engineering. The crystal packing patterns of various carboxylic acids have been examined in depth and thus they are considered as the most important building block in crystal design. Binary crystallization of carboxylic acids with spacer ligands containing complementary hydrogen bonding groups such as 4,4'-bipyridine, phenazine and 2-pyridone have been achieved to get the desired architectures, where the ligands act as spacers in between acid dimers. In chapter 4, an addition to the family of spacer ligands, *trans*-1,4-dithiane-1,4-dioxide, a molecule that forms molecular complexes with carboxylic acids *via* O–H···O and C–H···O hydrogen bonds is discussed.

Current research into the chemistry of molecular assemblies and crystal engineering illustrates our increased ability to direct the construction of novel structures. The brick wall and hexagonal networks formed by an organic T-shaped molecule 5-nitrosalicylic acid and its adducts are the subject of discussion in Chapter 5.

Salient crystallographic details of the crystal structures discussed in this thesis have been given in Apendix-II at the end of the thesis. A full list of atomic coordinates has been deposited with the University of Hyderabad and is available upon request from Prof. Ashwini Nangia (ansc@uohyd.ernet.in).

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V. S. Senthil Kumar

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CHAPTER ONE

CRYSTAL ENGINEERING

1.1 Introduction

Organic chemists have been studying chemical reactions in a systematic manner for more than a century. The main stream of synthetic organic chemistry is involved in the synthesis of molecules that can be regarded as collection of atoms joined by high energy covalent bonds. A high degree of control over the formation and breaking of covalent bond have been achieved during the last century. Any complex chemical transformations can now a days be achieved in the laboratory, thanks to the development of new synthetic methods and sophisticated reagents. This renders the total synthesis of very complex molecules with molecular weights < 1000 Da, such as taxol, epothilone, palytoxin, calichearubicins and brevetoxin, possible.[1-5] But the chemistry of the covalent bond has its own conceptual limits. The synthesis of molecular structures with molecular weight > 1000 Da through the traditional covalent bond stepwise methods poses a difficult challenge. For example, the giant molecule palytoxin weighs 2680 Da with 65 dissymmetric carbons and 10^{21} possible isomers. The total synthesis of this complex macromolecule took almost 10 years and involved more than 100 researchers. The branch of chemistry referred to as "Non-covalent synthesis[6] or synthetic supramolecular chemistry" deals with the self-assembly of supermolecules using non-covalent interactions. In supramolecular synthesis, supermolecules are synthesized through the self-assembly of a large number of intermolecular interactions in a single step whereas covalent synthesis of complex molecules requires many sequential steps. According to Lehn's analogy[7] "*supramolecules are to molecules and the intermolecular bond what molecules are to atoms and the covalent bond*".

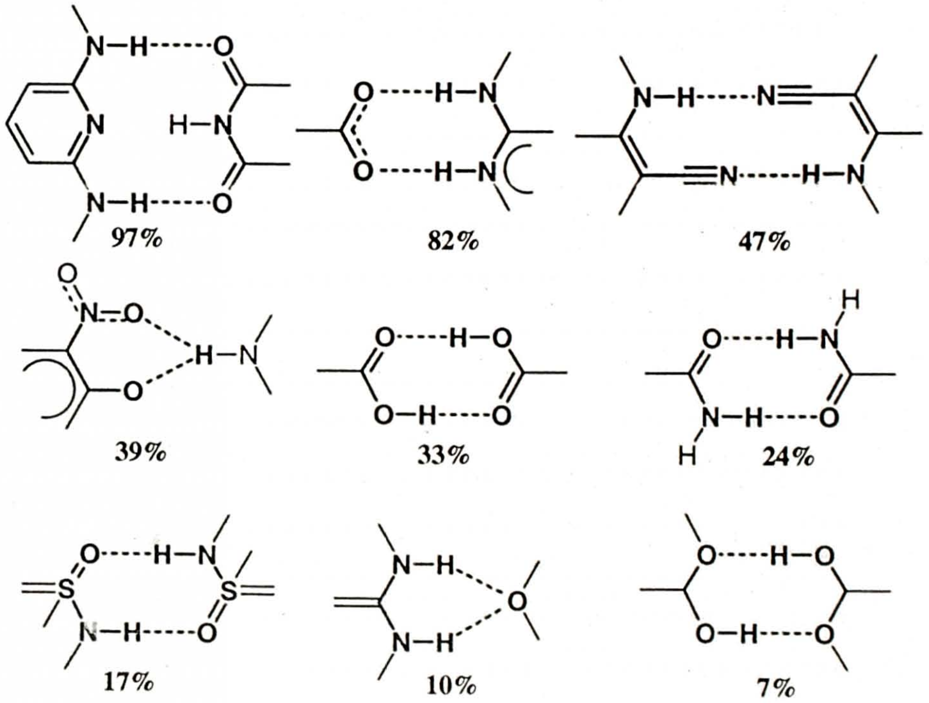
Supramolecular chemistry is the chemistry beyond the molecule and is the designed chemistry of intermolecular interactions. The ultimate aim of supramolecular chemistry is to become the "science of informed matter". Investigations on the assembly of small organic molecules in solution and the solid state are important in expanding these ideas for the assembly of well-defined supramolecular architectures. Thus supramolecular chemistry has two facets - the study of supermolecules in solution and in the solid state. Much of the early work in supramolecular chemistry was performed in solution. The study of supermolecules in solution is termed, as molecular recognition and those in the solid state is known as crystal engineering.[8] Solid-state supramolecular chemistry has taken advantage of X-ray crystallography even as it is well recognised that a crystal is a supermolecule *par excellence*.[9] The systematic strategies by which useful solid state structures are produced give the definition for crystal engineering. Schmidt first coined the term crystal engineering in connection with his work on the topochemical reactions of crystalline cinnamic acids.[10] The scope of the term was extended by Desiraju who defined crystal engineering as "*the understanding of intermolecular interactions in the context of crystal packing and the utilization of such understanding in the design of new solids with desired physical and chemical properties*".[11]

The aim of crystal engineering is to establish rigorous connections between molecular structure and supramolecular structure *via* intermolecular bonding tools. Rationalisation, analysis, design and prediction[12] are the key elements in crystal engineering. Rationalisation involves the examination of various non-covalent forces that control the crystal packing. Analysis of crystal structures deposited in the Cambridge Structural Database (CSD)[13] gives an idea of statistical trends and probability of interaction patterns. Crystal design is utilizing the knowledge base of interaction patterns in the synthesis of new structures. The recent huge stimulus of crystal engineering owes to its applications[14] in non-linear optics, catalysis, microporous materials, electronic materials and sensors, molecular modelling and drug design.

1.2 Intermolecular interactions and supramolecular synthons

The mutual aggregation of molecules in the solid state is directed by intermolecular interactions. Hence, crystal engineering studies mainly depend on understanding the nature of different intermolecular interactions. Intermolecular interactions have been regarded as synthetic vectors in designing new solids. There are several types of intermolecular interactions, which involve electrostatic forces of some kind or other. While intermolecular interactions have been classified in different ways, the most meaningful criteria are their distance dependence and their directionality. Intermolecular interactions in organic solids are of two types: medium-range isotropic forces and long-range anisotropic forces.[15] Isotropic forces that define molecular shape, size and close packing, include C···C, C···H and H···H interactions and long range anisotropic interactions, which are electrostatic, include ionic interactions, conventional hydrogen bonds (O–H···O, N–H···O),[16] weak hydrogen bonds (C–H···O, C–H···N, C–H···π)[17] and other forces such as halogen···halogen contacts.

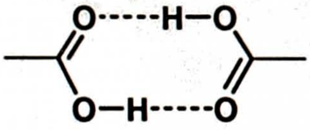
Study of an individual crystal structure leads to the identification of intermolecular interactions related to a specific crystal structure. The geometrical attributes of intermolecular interactions and their chemical characteristics can be studied reliably by statistical analysis. Implicit in the statistical approach to crystal engineering is an insight into the various ways in which the interactions can be grouped together to form substructural units. These sub structural units have been variously termed as motifs, patterns, building blocks and supramolecular synthons. The supramolecular synthon is defined as "*a structural unit within supermolecules, which can be formed and /or assembled by known or conceivable synthetic operations involving intermolecular interactions*".[18] Supramolecular synthons are designed combinations of interactions and not identical to the interactions. At times a single interaction may be considered as a synthon while in other cases many interactions may be implicit in a particular synthon. The repeating array in a crystal structure may be a single interaction, a small pattern, or a larger pattern. The subjective distinction between a pattern and a supramolecular synthon is based on its frequency of occurrence and is thus related to its reliability as an indicator of crystal packing. In this context, Allen et. al.[19] have classified bimolecular supramolecular synthons comprising ≤ 20 atoms formed with O–H···O, O–H···N, N–H···O and N–H···N interactions in organic structures archieved in the CSD. The synthons are ranked according to their frequency of occurrence and according to their probabilities of formation. Some examples of supramolecular synthons with their probabilities of formation are shown in Scheme 1. Steiner[20] carried out a similar study on the heterosynthons formed by carboxylic acids. This study shows that aggregation of O–H group of carboxylic acids with heteroatoms (N, S=O, P=O, N^+–O^-) to form heterosynthons are prefered compared to self aggregation.



Scheme 1. Examples of some supramolecular synthons with their occurrence frequencies.

1.3 Molecular complexes

The formation of a molecular complex is favoured when the intermolecular interactions between molecules of different components is stronger than those in the homomeric crystal. The molecular complex can be defined as the electrically neutral material, which consists of different molecular species that are held together by intermolecular interactions. In general, it is thermodynamically favourable to assemble similar molecules in crystal compared with the corresponding process of packing dissimilar molecules. In cocrystal, the competition to associate with another molecule to have an energetically favourable final crystal structure depends on entropic and enthalpic factors. In the crystal formation, each and every level of molecular recognition is controlled by intermolecular interactions and the recognition mechanisms are highly specific. For example the specificity of carboxylic acid-hetero atom recognition has been extensively studied through many binary crystallization experiments.[21] Zaworotko[21a] cocrystallized 4,4'-bipyridine with trimesic acid to extend the acid dimer **I** linearly to **II** without changing the network topology. The molecular complex forms a triply interpenetrated 3D structure. This is shown in Figure 1. In urea derivatives, N–H···O mediated 1D α-network is the common pattern.[22] Lauher and Fowler[23] demonstrated examples of layered structures that were formed with chains of ureas and acid-pyridine heterosynthon through cocrystallization experiments (Scheme 2). Some of these aspects are highlighted in Chapter 4.



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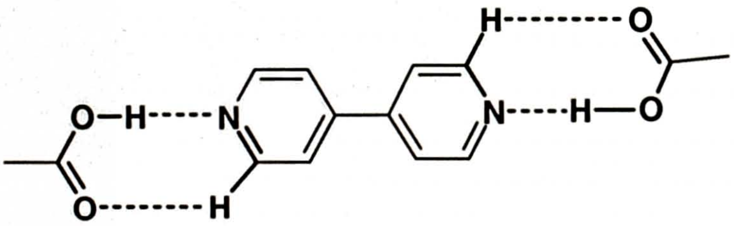

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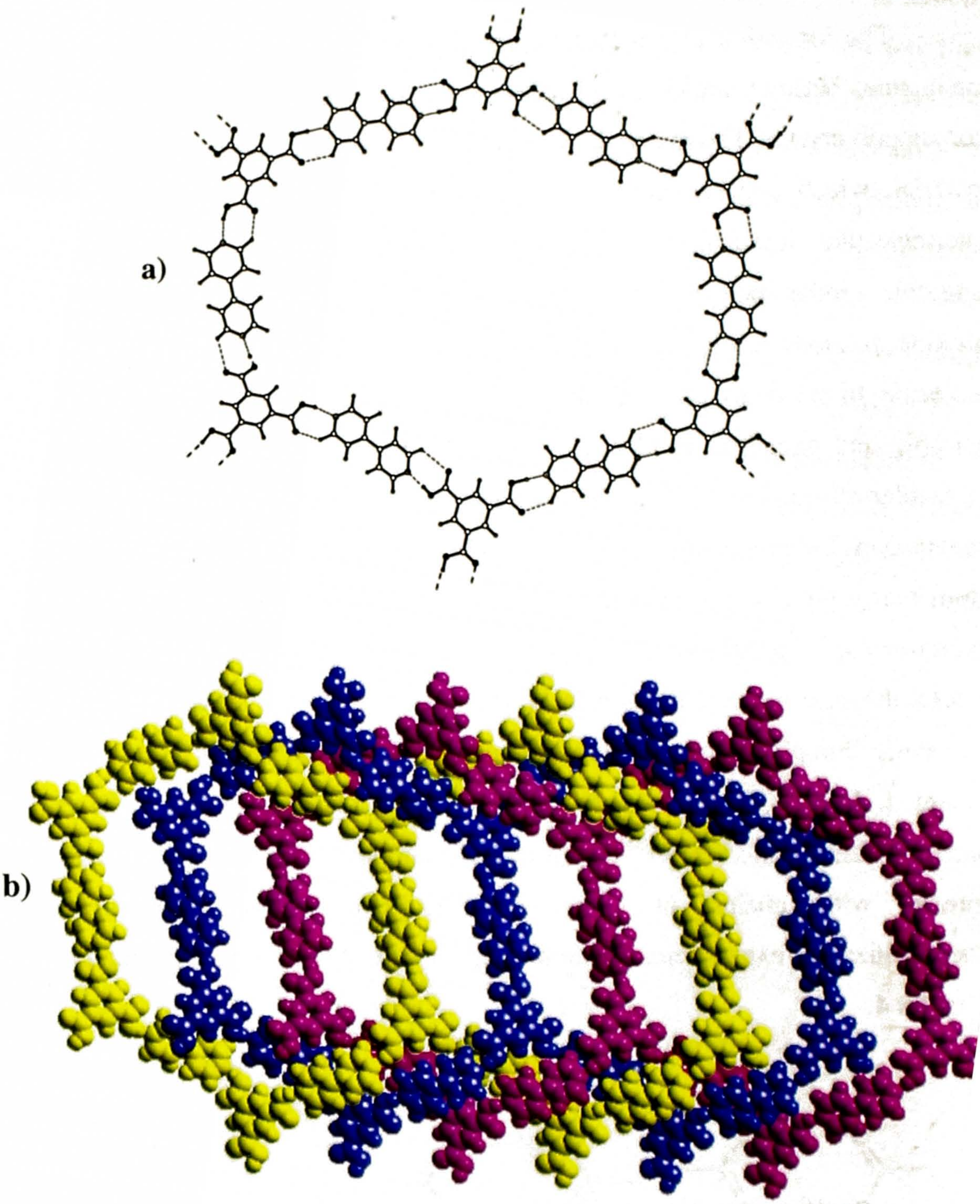
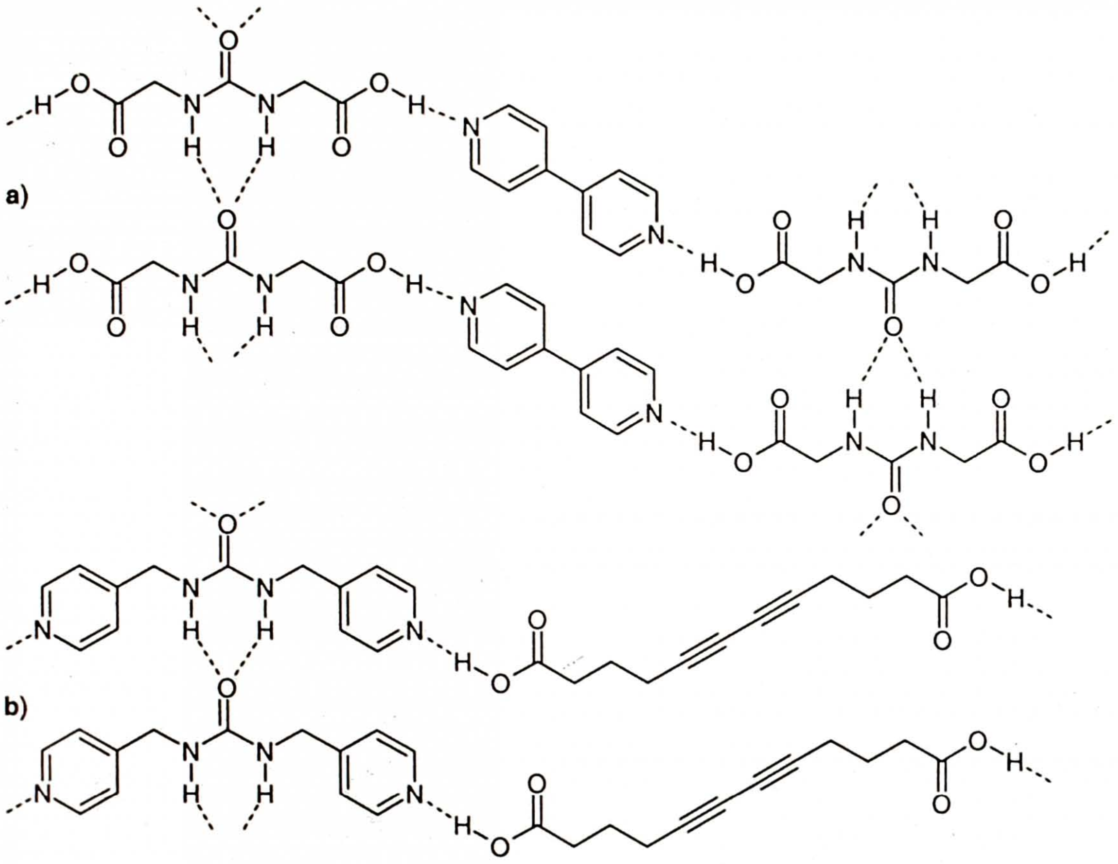


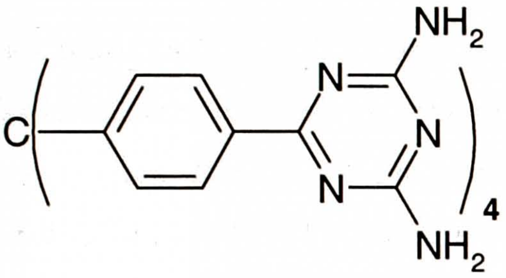
Figure 1. Crystal structure of the molecular complex of trimesic acid and 4,4'-bipyridine. a) hexagonal void of 35 X 26 Å^2 and b) triply interpenetrated network.



Scheme 2. Layered structures of (a) ureylene dicarboxylic acid and 4,4'-bipyridine and (b) pyridyl derivative of urea cocrystallized with a dicarboxylic acid.

1.4 Porous solids

Porous solids are crystalline or amorphous materials that permit the reversible passage of molecules through holes in their structure. Among the current aims of crystal engineering, there is considerable interest in the design of new host-guest systems with a view of obtaining porous solids.[24] The natural and synthetic inorganic zeolites are the classical examples of microporous materials with widespread use in industry.[25] The search for stable microporus organic networks that exhibit reversible guest exchange and possibly selective catalytic activity is of special interest. A fascinating aspect in organic microporous solids is the potential to control the host-guest chemistry of the framework by tailoring the building blocks by including binding properties of functional groups. In this context, the tetraphenylmethane derivative **1** forms an example of an organic zeolite structure.[26] Hulliger and coworkers[27] have recently reported phospazine **2**, which forms a hexagonal channel where iodine molecules are included as shown in Figure 2. The iodine molecules form molecular chains in the channels and the chains show electrical conductivity. Similarly organic based zeolite analogue has been synthesised by Ripmeester and coworkers recently.[28] Atwood and coworkers[29] have utilized calix[4]arene host cavity to trap gases methane and freon and the inclusion adducts exhibit high thermal stability. The hexagonal close-packed arrangement of calix[4]arene contains lattice voids. Methane and freon gas molecules fill the voids. These host-guest complexes are stable at high temperature and low pressure. Various methods have been developed to design microporous solids. These methods are based on the crystal engineering strategies using hydrogen bonds or metal coordination bonds that lead to open frameworks. One of the main difficulties in the design of open frameworks is that they tend to interpenetrate.[30] New approaches have been identified to overcome the problem of interpenetration. One approach has been to use molecules with clumsy shape that cannot close pack. Supramolecular wheel-and-axle[31] and dumb-bell-shaped hosts[32] with acetylene axle were shown to form porous structures. Many approaches are reported to overcome the problem of interpenetration and to fill the cavity in the crystal structure of trimesic acid. Zimmerman and coworkers[33] have used relatively larger guest molecules, such as pyrene, which has been incorporated in the cavity of trimesic acid. Ward's group has shown the utility of the dense 2D sheets of guanidinium cations and sulfonate anions arranged in puckered parallel layers; the alkyl groups act as pillars.[34] Zaworotko[35] has used similar approach in constructing open networks in the crystal structure of complexes of trimesic acid with many secondary amines. Some of these aspects are discussed in Chapter 3.



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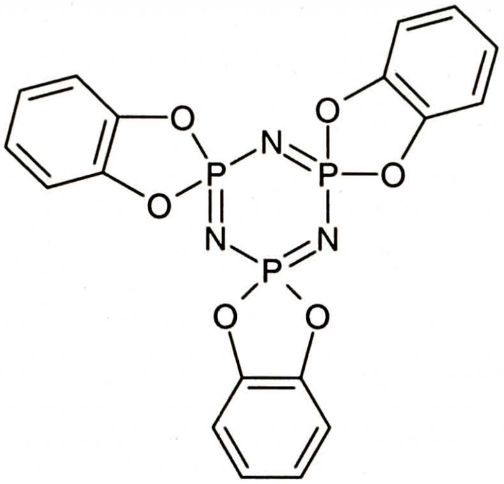

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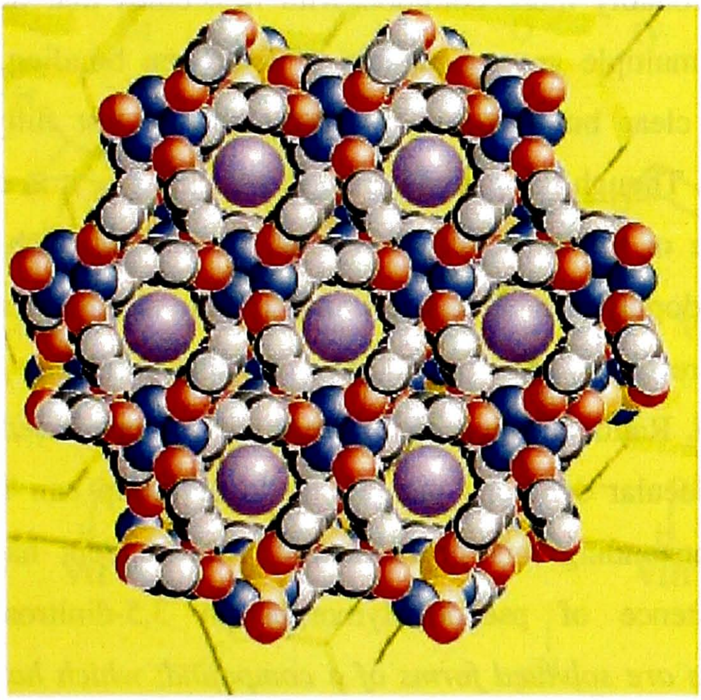
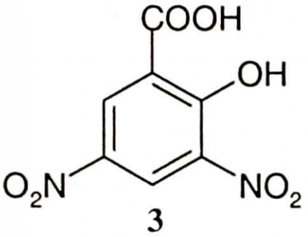


Figure 2. The structure of an organic zeolite **2**. Iodine molecules are incorporated in the cavity.

1.5 Polymorphism

Theoretically, the packing of a molecule can be arranged in many ways in the crystal in a given symmetry and polymorphism is a reflection of alternative ways in which molecules in a crystal strive towards a free energy minimum. Polymorphism is defined as the phenomenon wherein the same chemical substance exists in different crystalline forms.[36] Analysis of the crystal structures pose a challenge in understanding why molecules would adopt more than one crystalline arrangement. According to McCrone "*the number of forms known for a given compound is proportional to the time and money spent in research on that compound*".[37] However the generality of McCrone's statement remains unclear despite indications that polymorphism is more general than expected from the CSD. For example, Desiraju and Sarma[38] demonstrated that the frequency of occurrence of polymorphic modifications is not necessarily uniform in all categories of substances and the phenomenon is probably more common with molecules that have conformational flexibility and/or multiple groups capable of hydrogen bonding. The relevance of polymorphism is clear but remains a subject that is not fully understood at a fundamental level. Though the phenomenon is well known, it is difficult to define it rigorously because of the existence of several sub-classes, such as conformational polymorphs, pseudopolymorphs and tautomeric polymorphs. As a result, there is considerable interest towards the study of polymorphism in scientific and technological field. Rationalisation of different polymorphs based on the number of possible supramolecular synthons that a functional group can form is a practical approach to understanding this phenomenon. This concept has been utilized to explain the existence of pseudopolymorphs in 3,5-dinitrosalicylic acid **3**.[39] *Pseudopolymorphs are solvated forms of a compound, which have different crystal structures and/or differ in the nature of the included solvent.* The compound **3** forms seven pseudopolymorphs. Four of them are 1,4-dioxane solvates, two are hydrates and the last one is a *t*-butanol solvate. The structures of the pseudopolymorphs have been rationalised in terms of alternative arrangements of supramolecular synthons

III-IX (Scheme 3). Some aspects of conformational polymorphism and pseudopolymorphism are highlighted in forthcoming chapters.



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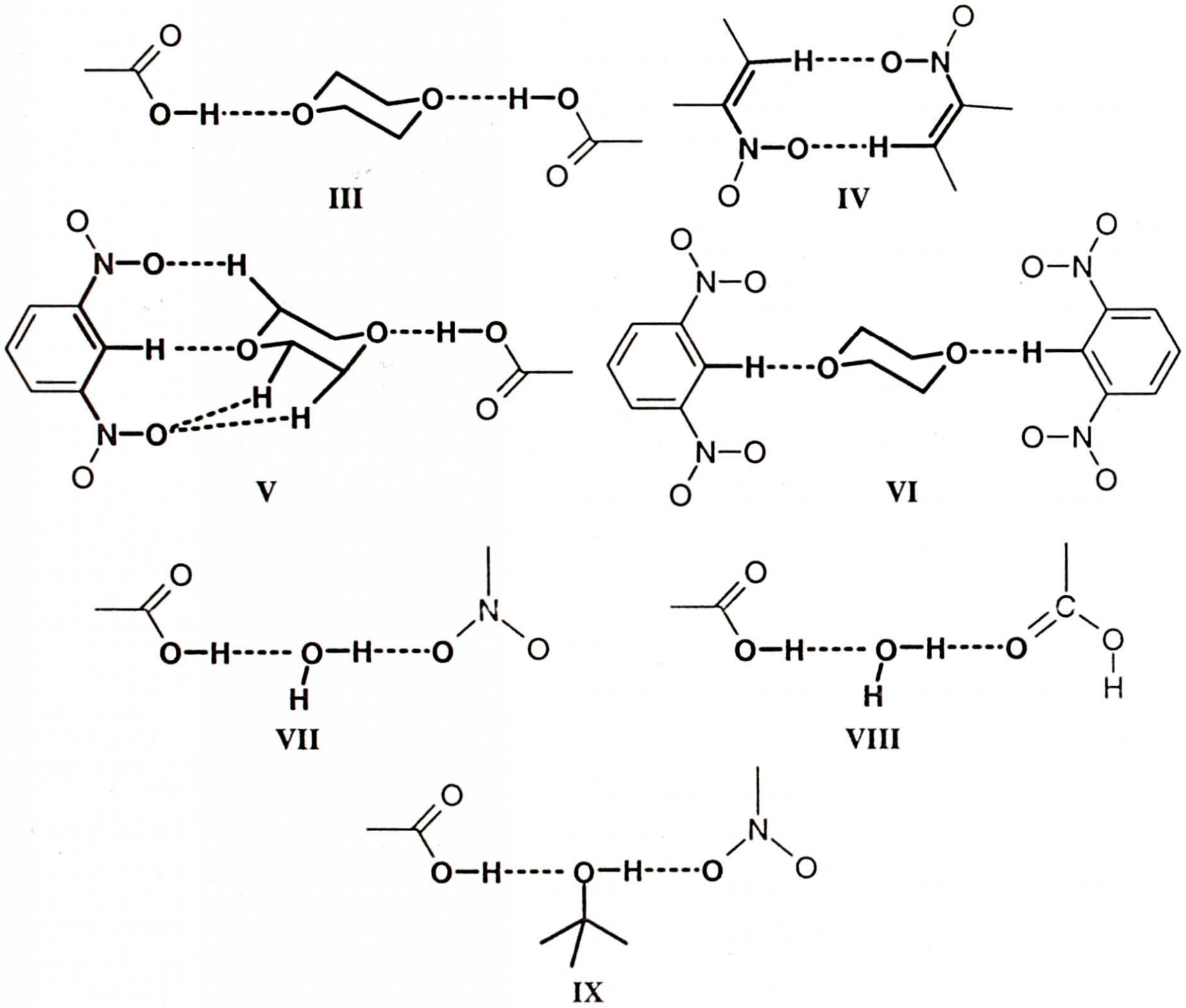
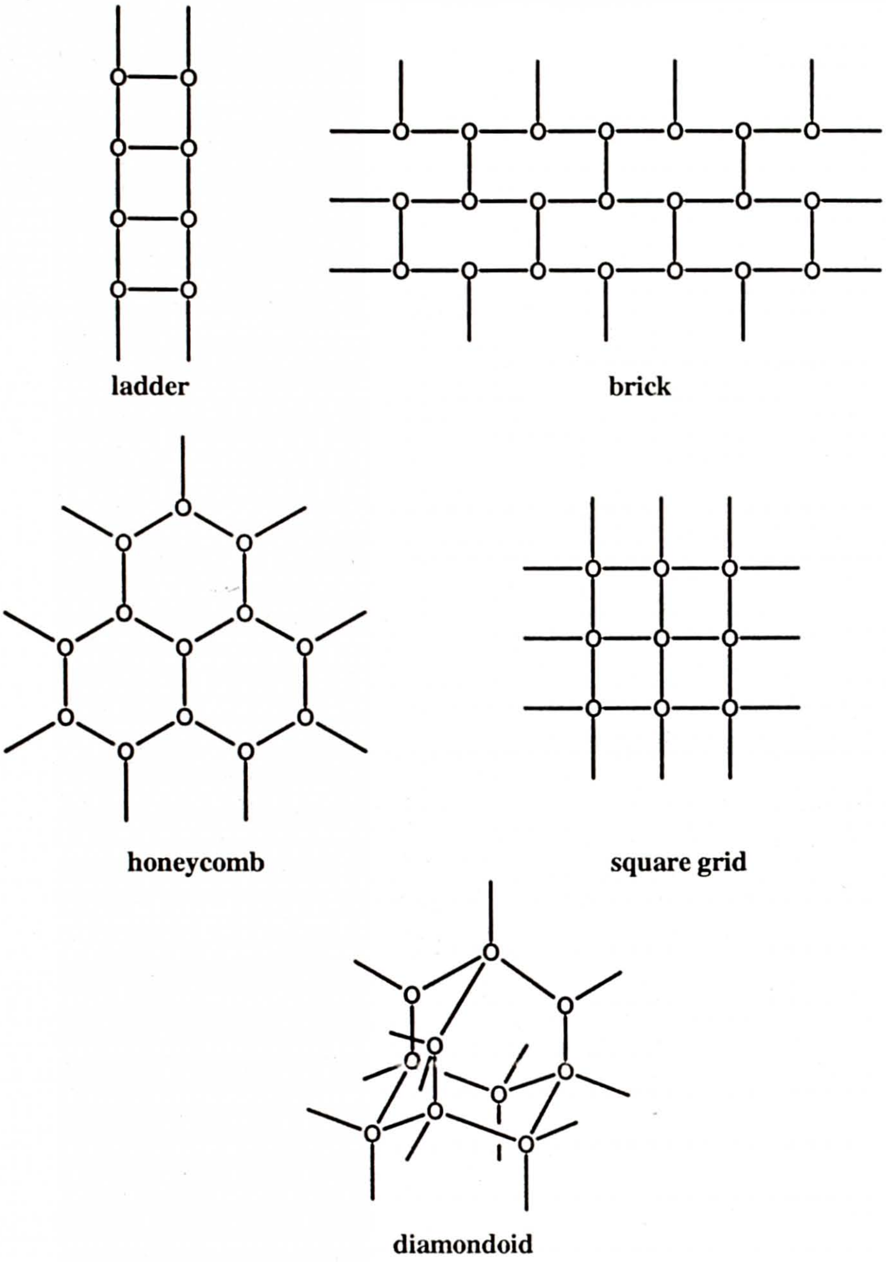


Scheme 3. The supramolecular synthons observed in the pseudopolymorphs of **3**.

1.6 Network structures

Designing of network structures is an advantageous exercise in crystal engineering.[11] Such networks are characteristic of porous solids and have potential applications in materials science.[40] One conceptual approach to building networks can be carried out by representing molecules as points or nodes and the intermolecular interactions connecting the molecules as node connectors.[41] Inorganic solids provide a wealth of information about various network architectures.[42] Various types of network architectures of contemporary interest are illustrated in Scheme 4. The topology of simple 2D networks are represented using general symbol (*n*,*p*), where *n* is the number of nodes in the smallest closed circuits in the net and *p* is the number of connection to the neighbouring nodes that radiate from any node.[30] Examples of infinite 2D nets are those given in the symbols (6,3) and (4,4). In coordination polymers, metal-ligand coordination bond is used as design element. The network topology can be designed by the metal-ligand geometry in coordination polymers. The strong metal-ligand coordination bonds impart robustness to the design strategy while the intermolecular interactions give a degree of flexibility. Ladder, brick wall, herringbone and bilayer networks built from three connected T-modules are popular targets in coordination polymers.[43] But these architectures are rare in organic structures.[44] The exercise of generating organic structures by choosing examples of inorganic solids can improve design strategies. Organic network solids make use of the molecular symmetry in the generation of network structures. Honeycomb networks have been constructed from C_3 symmetric precursors (trisubstituted benzene, triazine and cyclohexane scaffold).[45] Conventional hydrogen bonds like O–H···O and N–H···O have been extensively used to generate three-dimensional network structures because of their strength and directionality. For example, the acid dimer synthon was utilized in the construction of diamondoid networks in the structures of adamantane-1,3,5,7-tetracarboxylic acid and methane tetracarboxylic acid.[46] Wuest utilised the amide dimer in the construction of diamondoid networks.[47] Some of the aspects in constructing organic networks are highlighted in Chapter 5.



Scheme 4. Schematic representation of various types of network architectures of contemporary interest.

1.7 Crystal engineering– strategies and difficulties

Strategies for crystal engineering needs some means of connecting neighbouring molecules into predictable aggregates. There are several different approaches to design functionalised solids. Desiraju[18a] has drawn a parallel between organic synthesis and crystal engineering in an attempt to identify molecular recognition patterns in solids. Stoddart[6] has also discussed some approaches to synthetic supramolecular chemistry of nanosystems. Zaworotko[21a,46c] has shown that crystal synthesis can be carried out through binary crystallization. More frequently, structural chemists observe the repetition of certain supramolecular synthons that are robust and reliable. Molecules that contain these synthons tend to crystallize in specific energetically favourable arrangements. In this way by identifying these synthons, and with the aid of CSD, it is possible to work backwards and retrosynthetically formulate empirical rules about the recognition patterns of various functional groups.[18a] Thus crystal engineering strategies involve the following steps: i) searching the molecule with desired molecular skeleton; ii) search for reliable and robust supramolecular synthon formed by the particular functional moiety and iii) study the modes of crystallization through an analysis of crystal structures.

The large number of possible orientations of a molecule in a crystal, inaccuracies in estimating the energies, and the unexpected inclusion of solvents in crystal make the crystal engineering exercise so difficult. While polymorphism gives an idea about various ways in which the same molecule can produce different crystal structures, it is a serendipitous phenomenon, which is both beneficial and challenging aspect of crystal engineering.

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CHAPTER TWO

CONFORMATIONAL POLYMORPHISM AND CONFORMATIONAL ISOMORPHISM IN 4,4-DIPHENYL-2,5-CYCLOHEXADIENONE

2.1 Introduction

Polymorphism is the existence of the same chemical substance in at least two different crystalline arrangements of molecules in the solid state.[1] Polymorphism is currently the subject of both experimental and theoretical interest.[2] Polymorphs have different crystal structure and hence different physical and chemical properties.[3] The question of how similar the same molecule must be and how dissimilar the different packing arrangements must be in order to qualify as polymorphs goes to the origin of our understanding of the organic solid state. The existence of polymorphism implies that kinetic factors are important during crystal nucleation and growth.[4] Virtually all classes of molecular materials have been found to exhibit some degree of polymorphism. Polymorphism occurs when a slightly different balance of subtle intermolecular interaction is recognized. The discovery of new polymorphic substances is often serendipitous.[5] A recent survey[6] of the CSD shows that only 5% of compounds are classified as polymorphic. Polymorphism in crystals has been studied using thermochemical analysis, powder and single crystal X-ray diffraction, synchrotron radiation, solid-state NMR, and FT-IR.[7] A proper understanding of this enigmatic phenomenon is essential because the unexpected occurrence of a new crystalline form may demolish a well-planned crystal design strategy.[8] One of the challenges in crystal engineering is our ability to understand and control polymorphism. Polymorphism can be both beneficial and problematic. For example, oxotitanium phthalocyanine exists in four polymorphic forms. Among the four forms, one form is used as photosensitive charge generation material and the other form is inactive.[9] Getting the right polymorph is of the utmost importance in drugs, pharmaceuticals, explosives, dyes, pigments, flavors and confectionery products.[10] Thanks to studies in polymorphism, progress has been made in *ab initio* crystal structure prediction, structure determination from powder X-ray data, and in the stabilization of metastable forms.[11] A better understanding of this phenomenon will improve the design strategies in crystal engineering. Rationalization of different polymorphic forms based upon the number of possible supramolecular synthons[12] that a particular functional group can form is a practical approach to understanding polymorphism. The analysis of alternative hydrogen bonding patterns in different polymorphs provides a better understanding of crystal packing motifs, and hence in our ability to rationalize known structures and also forecast new forms.

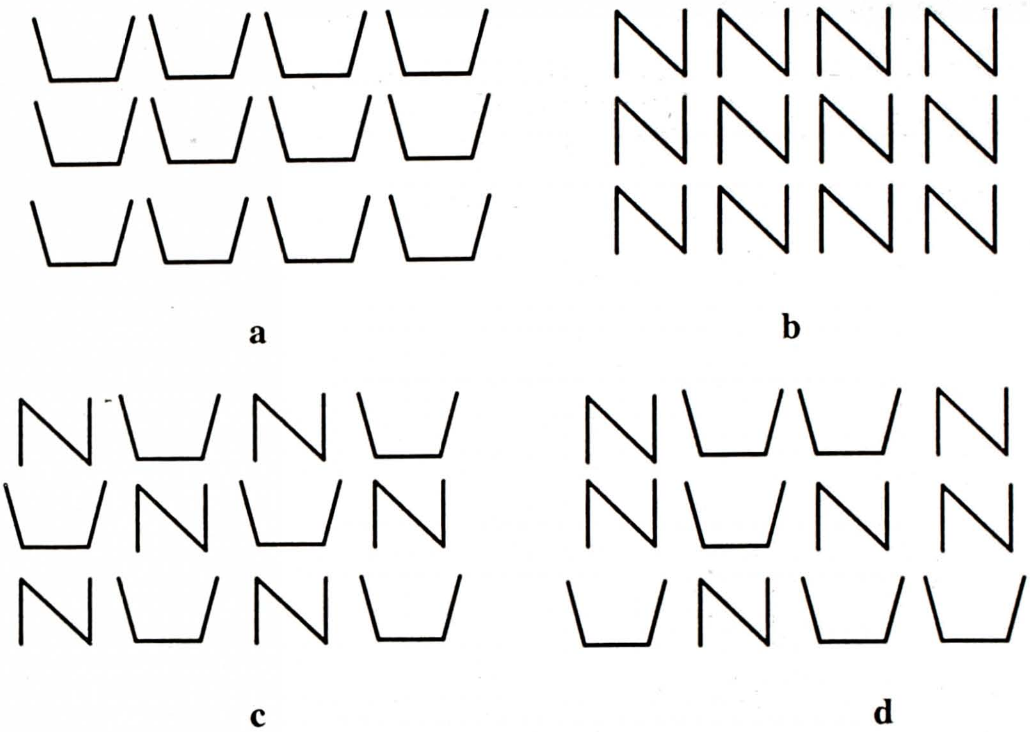
The existence of polymorphism implies that free energy differences between different crystalline forms are small (< 2 kcal mol^{-1}).[13,1b] Alternative supramolecular synthons with comparable hydrogen bond energy contribute to the stability of polymorphic structures. Polymorphs are of interest because they represent special situations for the study of structure–property relationships[14] with minimum number of variables. The conformation, hydrogen bonding and lattice energy of the same molecule in different crystalline environments can be compared in polymorphic structures.[15]

When polymorphs crystallize simultaneously in the same flask under identical crystal growth conditions from the same solvent; they are termed as concomitant polymorphs.[16] This phenomenon occurs when there are many metastable forms with almost similar energies that crystallize together. In principle, the metastable forms convert themselves to stable forms when they are allowed to stand for a period of time.[11b] This well known occurrence of concomitant polymorphism have been studied systematically both in organic as well as in organometallic systems.[17] But still this phenomenon deserves a more careful study because it is very uncommon.

2.2 Conformational polymorphism and conformational isomorphism

The differences between the lattice energies of different polymorphic modifications of an organic compound may be expected to be in the range of 1-2 kcal/mol when non-bonded interactions dominate the structure. From the estimates of the magnitudes of intermolecular interactions, this difference in lattice energies observed between polymorphic forms is comparable with the energy range required to bring about the changes in the molecular torsional parameters about single bonds, but not sufficient to perturb bond angles and bond lengths. Hence, different polymorphic modifications of a molecule that possess torsional degrees of freedom may exhibit different molecular conformations. This is the phenomenon known as conformational polymorphism.[18] Thus conformational polymorphism can be defined as the existence of different conformers of the same molecule in different polymorphic modifications. The conformational energy differences between two forms are comparable. However, there is a report[15a] where the energy difference between the two crystallographic conformations is of the order of 10 kcal mol^{-1} (6-31 G** basis set). For this particular system, the total energy difference between two observed polymorphic forms is about 6 kcal mol^{-1}.

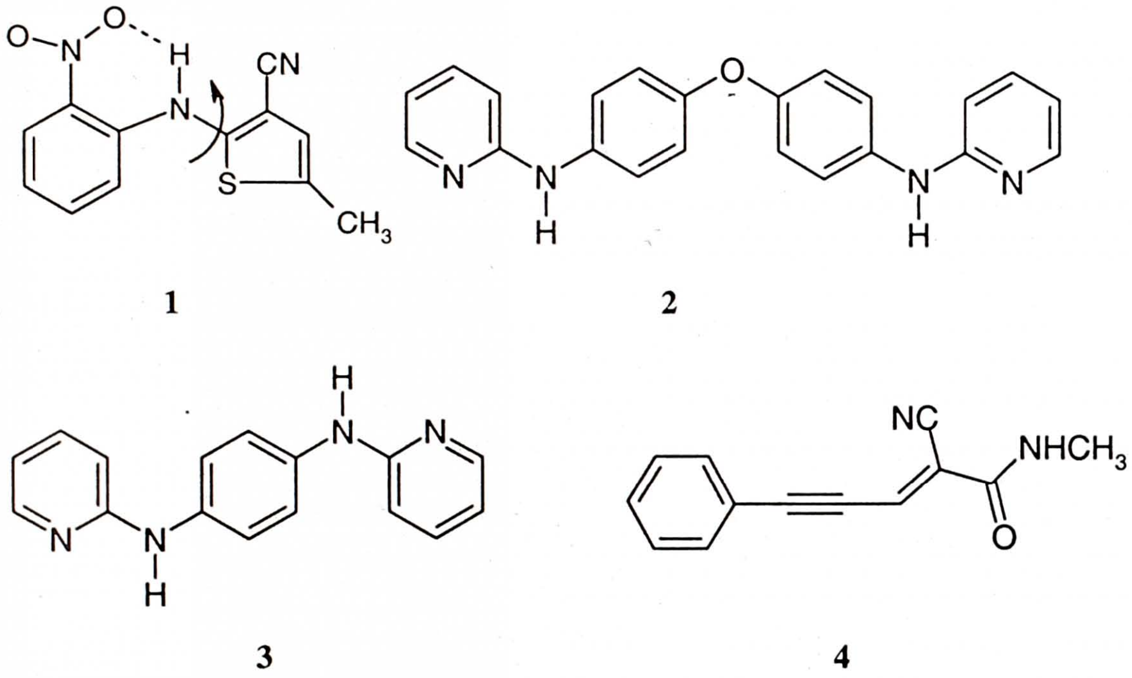
Apart from conformational polymorphism, there are two more occurrences that result from the torsional degrees of freedom in a molecule. They are conformational isomorphism and conformational synmorphism.[18a] The former describes the existence of different conformers of the same molecule in the same crystal structure and the latter explains the situation in which different conformers of the molecule are distributed randomly throughout the crystal lattice. These situations are illustrated in Scheme 1.



Scheme 1. Schematic illustration of different arrangements of conformers of the same molecule in the crystal. (a) and (b), conformational polymorphism; (c) conformational isomorphism and (d) conformational synmorphism (taken from ref. 18a).

2.3 Recent reports on conformational polymorphs

Conformationally flexible molecules have many degrees of freedom compared to rigid molecules and hence, there is a greater scope for their polymorphic occurrence. More recently, the flexible molecule 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile **1** was shown to form six different conformational polymorphs that result from the free rotation of thiophene ring in which the degree of rotation alters the degree of conjugation between thiophene ring and phenyl ring and thus result in the different colors for different polymorphic modifications.[19] The crystal structures of a family of *N*,*N*'-bis(2-pyridyl)aryldiamines were investigated.[20] The 2-arylaminopyridine systems can adopt either *Z* or *E* conformations depending on the C-N rotation, which lead to conformational polymorphism in the case of molecules **2** and **3**. In molecule **4** the degree of rotation of phenyl ring results in the change in conformation and thus lead to the formation of two conformational polymorphs.[21] The occurrence of polymorphism in flexible systems continues to be reported regularly, with the special aspects of conformational changes being highlighted.[22]

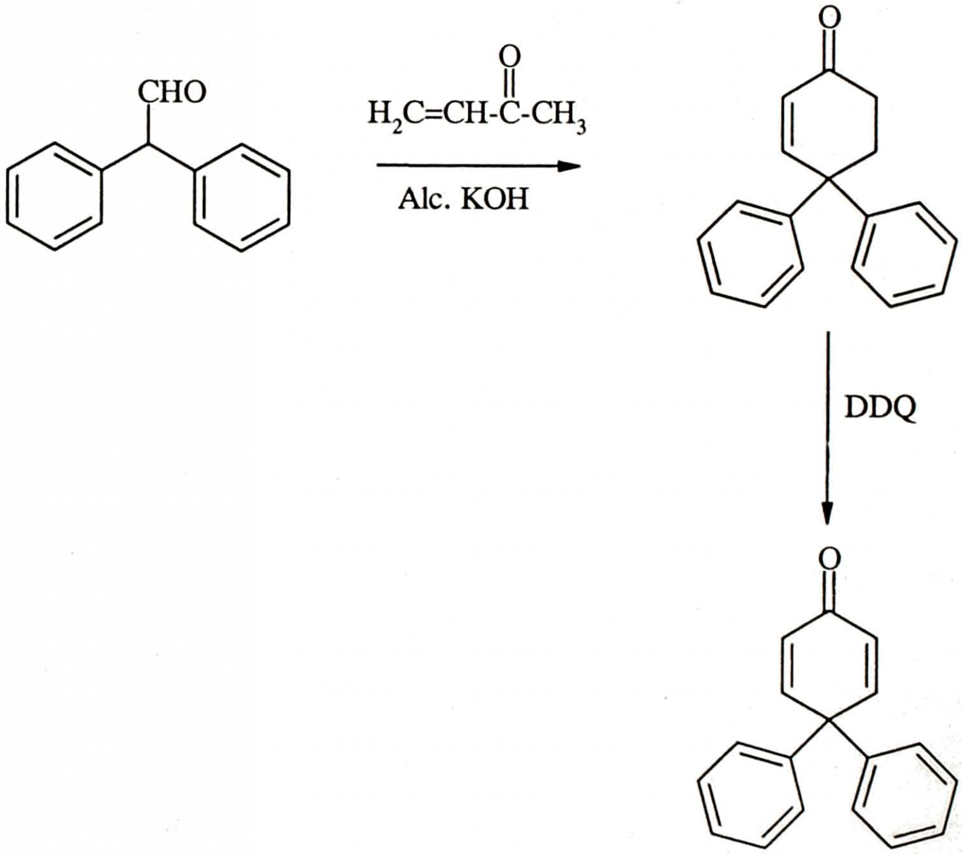


Scheme 2 Some examples of the recently reported molecules with conformational polymorphism

2.4 Polymorphism in 4,4-diphenyl-2,5-cyclohexadienone, 5

As a part of an ongoing study, 4,4-diphenyl-2,5-cyclohexadienone **5** was investigated in the expectation of obtaining the archetypal benzoquinone-type C–H···O tape motif. The compound was synthesized[23] from diphenylacetaldehyde and methylvinylketone in two steps as shown in Scheme 3. Initially, recrystallization of **5** from EtOAc–hexane appeared to have afforded three concomitant polymorphs as characterized by single crystal X-ray diffraction. A monoclinic form **A** in space group $P2_1$ (Z = 2), and a triclinic form **B** with four molecules in the asymmetric unit ($P\bar{1}$, Z

= 8).[24] The third one **C** has a larger triclinic cell ($P\ \bar{1}$, $Z = 24$) with 12 molecules in the asymmetric unit. Crystal data of **C** could not be refined better than R 0.11 despite a moderate data/parameter ratio of 7.5. When recrystallization was attempted from EtOAc/hexane/CH_2Cl_2 mixture, a new polymorph in space group *Pbca* (Z = 16) crystallized from the solution. Yet another polymorph of **5** (**D**) had been discovered. A fifth disappearing monoclinic polymorph was obtained from EtOH/CH_2Cl_2. The new form was confirmed by its cell determination (Table 1), but it changes to form **B** immediately and therefore it was difficult to collect the data. The crystallographic details for the tetramorphs and approximate cell dimensions of the fifth disappearing form are given in Table 1.

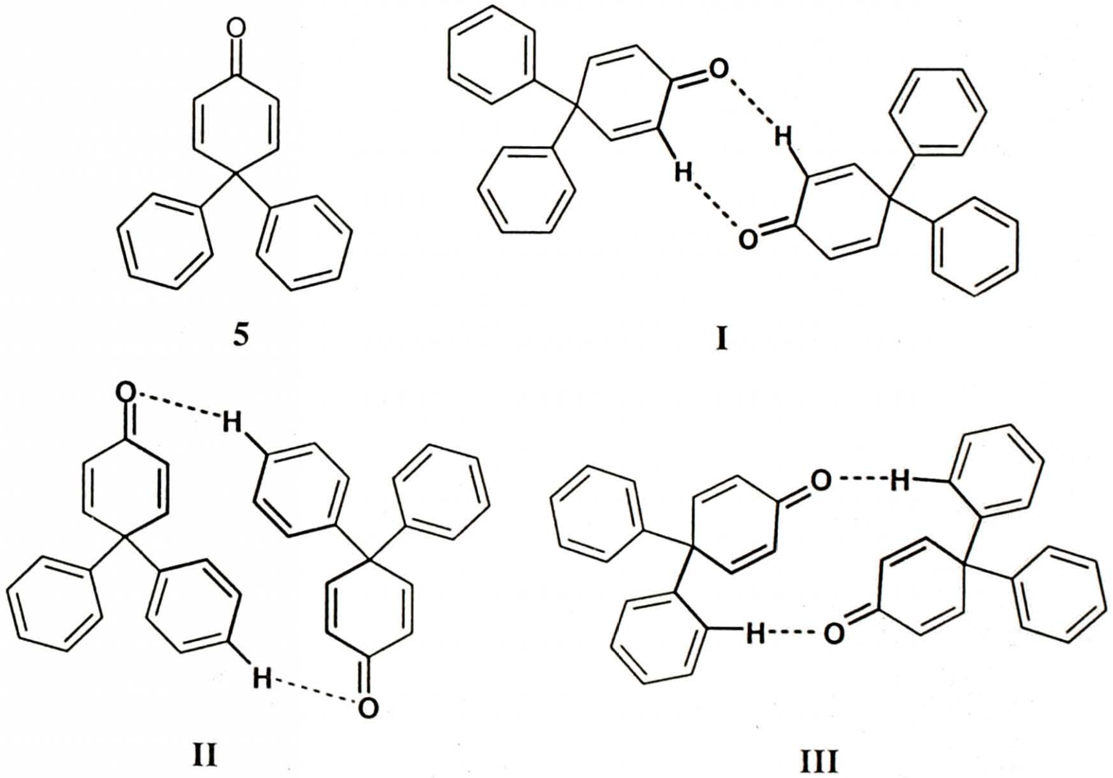


Scheme 3.

Table 1. Crystallographic data of polymorphs of **5**

	A	**B**	**C**	**D**	Fifth form
Space group	$P2_1$	$P\bar{1}$	$P\bar{1}$	$Pbca$	
a [Å]	7.9170(6)	10.0939(2)	18.3788(4)	10.7921(6)	8.39
b [Å]	8.4455(6)	16.2592(3)	19.9701(4)	17.4749(12)	14.56
c [Å]	10.3086(9)	16.2921(4)	24.4423(5)	27.9344(19)	26.80
α [deg]	90	88.257(1)	95.008(1)	90	90.36
β [deg]	105.758(2)	85.338(1)	111.688(1)	90	90.02
γ [deg]	90	83.645(1)	105.218(1)	90	90.03
Z	2	8	24	16	
R_1 [$I>2\sigma(I)$]	0.0508	0.0682	0.1121	0.0589	

There are only three examples known of systems with four polymorphs: pyrazinamide,[25] sulfapyridine[26] and pimelic acid[27] in the literature of organic crystals. The difference between the two extreme values of Z' ($\Delta Z' = 11$) in the tetramorphs of **5** is the highest known to date. In CSD, there is one polymorphic system[28] with $\Delta Z' = 5.5$ and there is no polymorphic system with $\Delta Z' > 5.5$. A novel feature of polymorphism in **5** is that these structures may be further classified as concomitant polymorphs, conformational polymorphs and conformational isomorphs. A total of 19 crystallographic independent molecules have been characterized in the four polymorphic crystal structures. While a trimorphic system[29] with seven molecular conformations and a hexamorphic system[19] with six molecular conformations are reported in the literature, molecule **5** provides the first example with 19 crystallographic independent molecular conformations in the tetramorphic cluster of structures. The polymorphs **A**, **B** and **C** may be classified as concomitant polymorphs because these crystals have been obtained from the same flask and same solvents under identical conditions. Form **A**, **B**, **C** and **D** may be termed as conformational polymorphs because different conformers of the compound **5** are present in different polymorphic forms. Forms **B**, **C** and **D** may be classified as conformational isomorphs because different conformers of the same compound are present in the same crystal. There are examples wherein only one of these phenomena occurs for a particular system.[30] For example, sulfathiazole, *o*-acetamidobenzamide and some diaryl amines form conformational polymorphs[15] and carbazole-substituted pyridinium iodide salt exhibits conformational isomorphism.[30b] But these are not concomitant polymorphs. The simultaneous occurrence of these three related phenomena in the same system established by X-ray diffraction is very rare. There are examples of polymorphism in the thermomicroscopy literature[31] and in Groth's collection,[32] but these are examples of transient phases observed in heating or cooling without crystallographic confirmation.



5 **I**

II **III**

Scheme 4. Centrosymmetric supramolecular synthons observed in the tetramorphic cluster of **5**.

2.4.1 Crystal structure of form A

Form **A** consists of linear chains of C–H···O hydrogen bonds from distinct (Ph)C–H donors to the O-atom of quinone ring (C–H···O hydrogen bond: donor – acceptor geometry; H···O distance d, C–H···O angle θ:143.9°; 2.63 Å, 129.9°) such that each molecule of **5** (A_i) is hydrogen bonded to four of its screw-axis related neighbour molecules along [101] as shown in Figure 1a. Curiously, the activated quinonoid C–H groups do not participate in any C–H···O network similar to benzoquinone.[33] Instead the *β*-hydrogen of quinonoid ring forms a chain of translation related molecules mediated by C–H···π interactions, which reinforce the C–H···O chains. This is shown in Figure 1b.

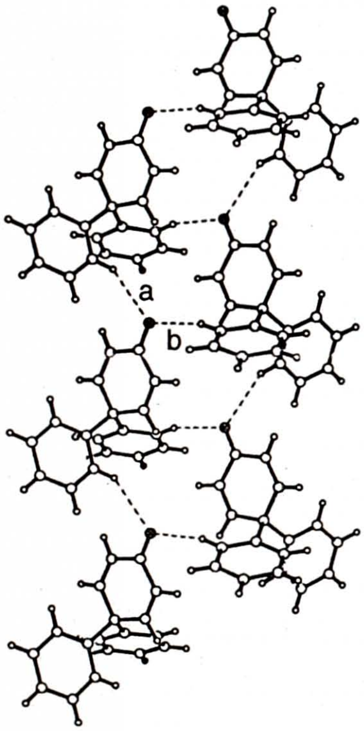


Figure 1a. Linear pattern of C–H···O hydrogen bonds between 2_1 related molecules in form **A**. See Table 2 for interaction geometry in Forms **A**, **B**, **C** and **D**.

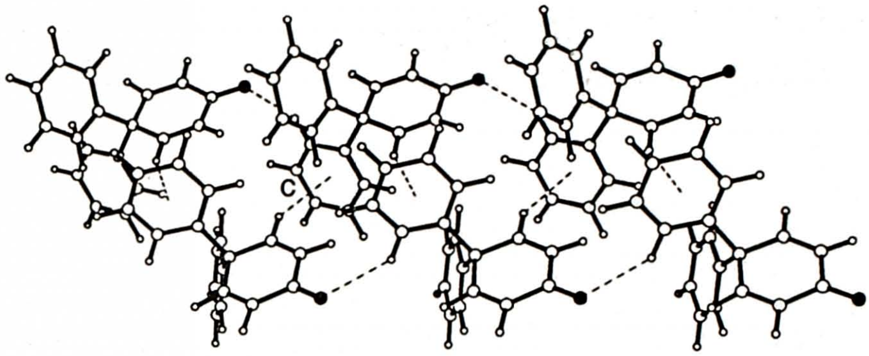


Figure 1b. Chain of C–H···π interactions between translation related molecules in form **A**.

2.4.2 Structural similarities between Form B and Form C

There are four symmetry-independent molecules in the crystal of form **B**. The crystal structure is shown in Figure 2. From the conformation point of view, each independent molecule of **B** (represented as B_i - B_{iv}) adopts a new conformation. All the four molecules engage in inversion related dimer formation. Two symmetry independent molecules (B_{ii} and B_{iii}) form centrosymmetric C–H···O dimer synthon **I** with the quinone moiety (C–H···O 2.33 Å, 169.2°; 2.49 Å, 123.4°), while the other two molecules (B_i and, B_{iv}) form centrosymmetric (Ph)C–H···O synthon **II** (2.64 Å, 137.9°; 2.75 Å, 121.5°) through the *para*-hydrogens. Auxiliary C–H···O hydrogen bonds connects the symmetry independent molecules. Polymorph **C** has a complex and intricate crystal packing, with 12 symmetry independent molecules in the asymmetric unit (C_i , C_{ii} ... C_{xii}). The crystal packing pattern resembles the crystal structure of form **B**. Symmetry variations of both the benzoquinone type C–H···O dimer synthon **I** and the dimer synthon **II** with overlapped quinonoid and phenyl rings are the recurring patterns in this structure. Molecules C_v and C_{xi} form synthon **I** with their inversion related molecules. Symmetry independent molecules C_{iv} and C_{vii} are also connected to C_{vi} and C_x respectively, through synthon **I**. Molecules C_{iii} and

C_{viii} involve in the formation of centrosymmetric dimer **II** while independent molecules C_i and C_{ix} are connected to C_{ii} and C_{xii} respectively through symmetry variations of same synthon. Auxiliary C–H···O hydrogen bonds between symmetry independent molecules further stabilize the overall structure in form **C**.

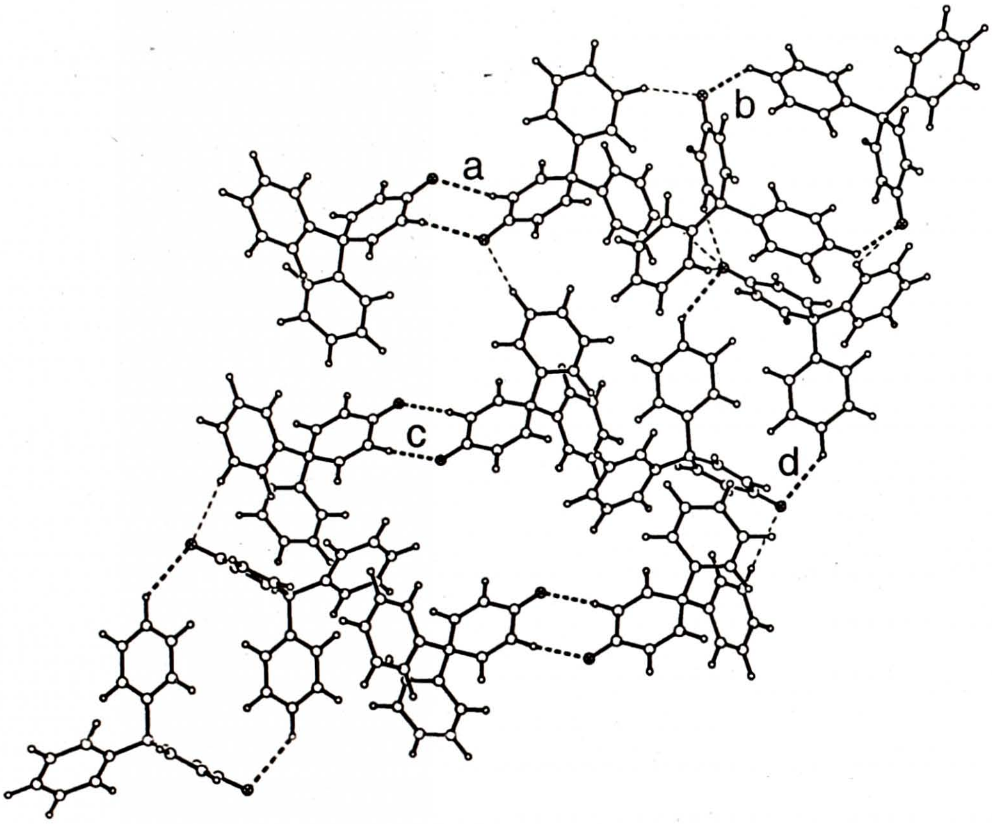


Figure 2. Centrosymmetric C–H···O synthons **I** (B_{ii} and B_{iii} molecules) and **II** (B_i and B_{iv} molecules) in form **B** are shown as bold dotted lines. C–H···O interactions are shown as normal dotted lines. The metrics of hydrogen bonds a, b, c and d are given in Table 2.

2.4.3 Structure of Form D

The orthorhombic form **D** has two symmetry-independent molecules (D_i and D_{ii}) in the asymmetric unit. D_i molecules related by translation and screw-axis are connected by C–H···O hydrogen bonds (C–H···O 2.36 Å, 138.0°; 2.55 Å, 166.9°) along [100] as shown in Figure 3a. D_{ii} type molecules are connected as centrosymmetric dimers with *ortho*-(Ph) C–H···O hydrogen bonded motifs **III** (C–H···O 2.57 Å, 144.6°), and such dimers are connected to *b*-glide related molecules by C–H···O bond (C–H···O 2.76 Å, 145.2°). Figure 3b shows the centrosymmetric dimer formed by D_{ii}. Chains of D_i and D_{ii} molecules are connected by C–H···O and C–H···π interactions (2.63 Å, 131.4°; 2.80 Å, 147.7°). This is shown in Figure 3c. D_i and D_{ii} of form **D** adopt new conformations of the compound **5**.

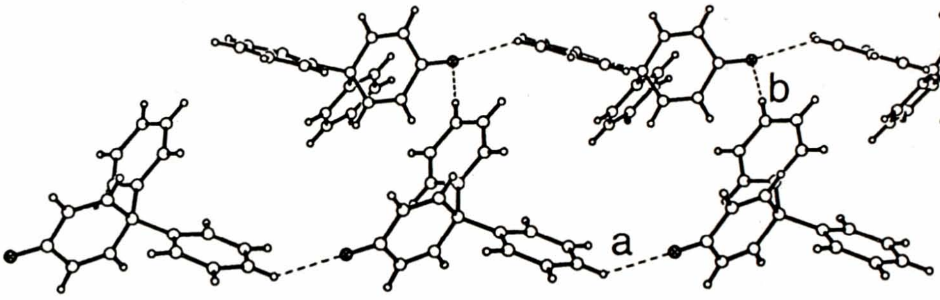


Figure 3a. Translation (left-right) and screw axis (bottom-top) related D_i molecules in form **D**.

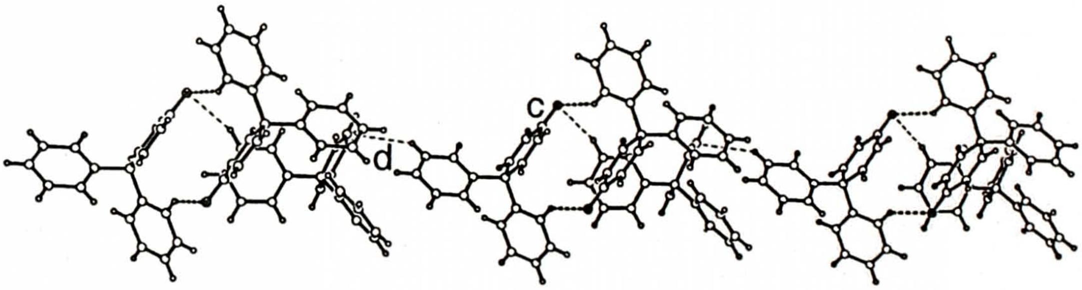


Figure 3b. Centrosymmetric C–H···O synthon **III** between D_{ii} molecules (bold dotted lines) and C–H···O interactions (normal dotted lines) in form **D**.

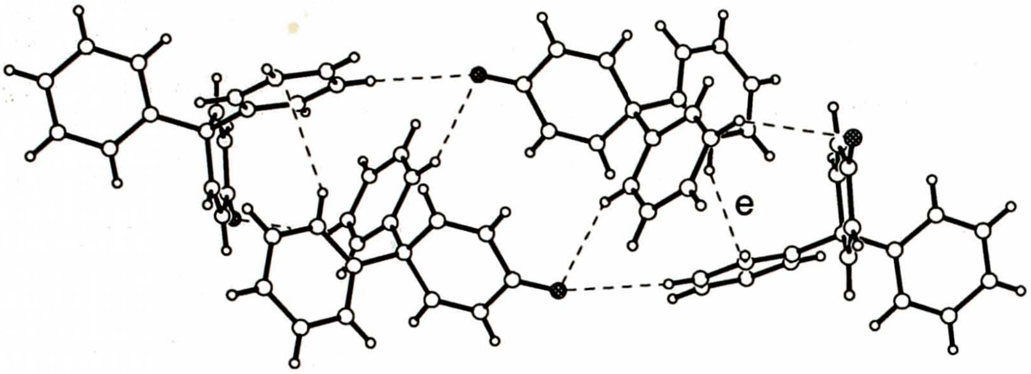


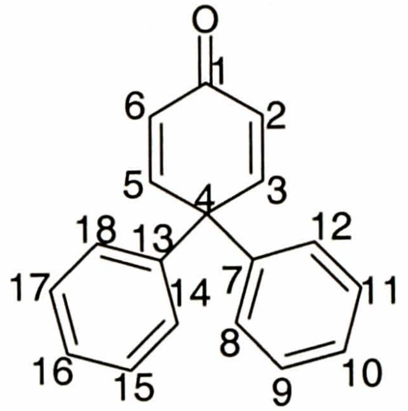
Figure 3c. C–H···π and C–H···O interactions between the two symmetry independent molecules in form **D**

Table 2. Geometrical Parameters of C–H···O and C–H···π hydrogen bonds.

Form	Interaction[a]	d (Å)	D (Å)	θ (deg)
A	a) C–H···O	2.52	3.602 (8)	163.9
	b) C–H···O	2.61	3.402 (7)	129.9
	c) C–H···π[b]	2.80	3.659	152.3
B	a) C–H···O	2.33	3.405 (4)	169.2
	b) C–H···O	2.64	3.524 (4)	137.9
	c) C–H···O	2.49	3.225 (4)	123.4
	d) C–H···O	2.75	3.443 (4)	121.5
D	a) C–H···O	2.36	3.247 (2)	138.0
	b) C–H···O	2.55	3.613(3)	166.9
	c) C–H···O	2.57	3.517 (2)	144.6
	d) C–H···O	2.76	3.701 (2)	145.2
	e) C–H···π[b]	2.80	3.646	147.7

[a] All C–H distances are neutron normalized (1.083 Å). [b] π denotes the centroid of phenyl ring.

2.5 Conformational analysis of polymorphism in 5



τ_1 = C3-C4-C7-C8

τ_2 = C3-C4-C7-C12

τ_3 = C3-C4-C13-C14

τ_4 = C3-C4-C13-C18

τ_5 = C5-C4-C7-C8

τ_6 = C5-C4-C7-C12

τ_7 = C5-C4-C13-C14

τ_8 = C5-C4-C13-C18

Scheme 5. Definition of torsion angles τ_1-τ_8 in **5**

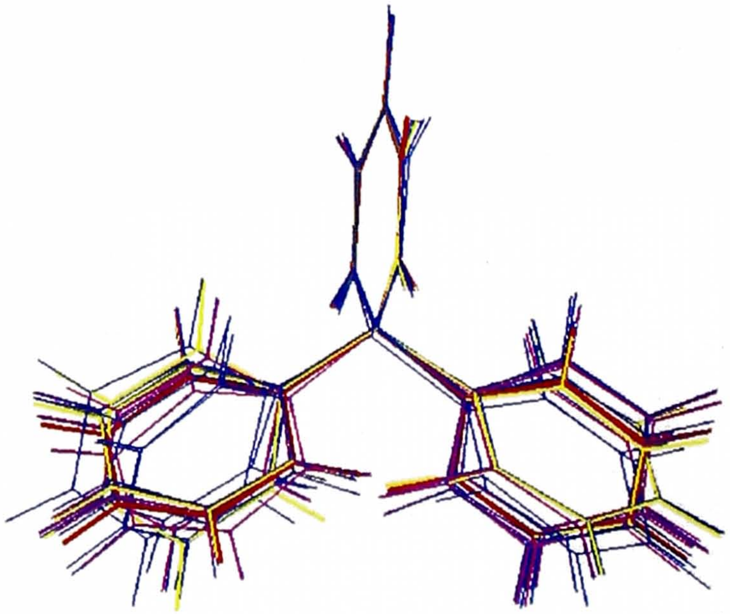


Figure 4. Overlay diagram of 19 crystallography independent molecules of **5**. Red = form **A**, molecule A_i; Magenta = form **B**, molecules B_i, B_{ii}, B_{iii} and B_{iv}; Blue = form **C**, molecules C_i, C_{ii}.....C_{xii}; Yellow = form **D**, molecules D_i and D_{ii}.

Table 3. Conformation of 19 symmetry-independent molecules in tetramorphs of **5** (forms **A**, **B**, **C**, and **D**).

Polymorph space group	Torsion angle		Crystallographic molecule	Hydrogen bond synthon
	ι_1 (°)	ι_8 (°)		
A ($P2_1$)	12.6	12.5	A_i	C–H···O chain
B ($P\bar{1}$)	11.5	17.7	B_i	II
	12.3	16.0	B_{ii}	I
	14.9	23.6	B_{iii}	I
	19.1	31.8	B_{iv}	II
C ($P\bar{1}$)	20.1	31.5	C_i	II
	20.9	30.8	C_{ii}	II
	18.4	32.3	C_{iii}	II
	12.1	22.7	C_{iv}	I
	15.2	22.0	C_v	I
	18.3	28.2	C_{vi}	I
	12.8	16.0	C_{vii}	I
	14.0	16.7	C_{viii}	II
	10.2	21.0	C_{ix}	II
	14.9	15.1	C_x	I
	11.9	16.7	C_{xi}	I
	11.5	17.4	C_{xii}	II
D (*Pbca*)	18.5	36.8	D_i	C–H···O chain
	8.4	16.5	D_{ii}	III

The 19 crystallographically independent molecules of **5** differ in the rotation about the C–C bonds between the quinone and the phenyl rings. The overlay diagram of the nineteen conformations is shown in Figure 4. These different conformations may be classified through eight possible torsion angles (τ_1, τ_2, ... τ_8). τ_1 and τ_8, taken from a single asymmetric unit of the 8-dimensional torsion angle space, have been selected as the torsion parameters to map the conformational surface in these 19 molecules (Figure **5**). Similar scatter plots are obtained if other appropriate pairs of torsion angles are used. There are two populations of conformers in Figure **5**: τ_1 = 8.0–16.0°, τ_8 = 12.0–24.0° and τ_1 = 18.0–22.0°, τ_8 = 27.0–38.0°. Structure correlation methods for mapping the conformational surface have been carried out by Mislow[34] many years ago. The motion of phenyl rings in the conformations of **5** is correlated, i.e. a change in the conformation of one phenyl ring leads to a conformational change in the second ring. Such a gearing of geminal phenyl rings has been noted in the crystal structures of benzophenones.[35] Notwithstanding that conformational change about a C–C single bond is a flexible (soft) parameter and that small difference in torsion parameters (2–3°) may not be chemically meaningful, it is clear that in **5** there are two populations of conformers with mean values of $\tau_1 = 12°$, $\tau_8 = 18°$ and $\tau_1 = 20°$, $\tau_8 = 32°$. There is a smooth geared rotation of phenyl rings in the nineteen conformations.

The emphasis in this analysis is on the structural attributes of C–H···O hydrogen bonding.[36] The tetramorphic crystal structures of **5** are stabilized by alternative arrangements of C–H···O hydrogen bond synthons **I**, **II** and **III**. There is a many-to-one relationship between the conformation of the molecule and the supramolecular synthon in the crystal (Table 3, Figure 5). However, a particular conformation is associated with only one particular hydrogen bond synthon even if the molecules are present in different polymorphs. For example, B_i and C_{xii} molecules have near identical conformations and they engage in synthon **II** in their respective crystal structures. The question whether the conformation of the molecules in the crystal structures is controlled by intermolecular interactions or *vice versa* is a difficult question to address, particularly in flexible molecules.[37] Similarly, other conformations in forms **B** and **C** that are part of the same cluster in the $\tau_1 - \tau_8$ scatter plot engage in synthons **I** and **II**. All this suggests that each of these conformations play a specific structural role during self-assembly. These two forms provide snapshot pictures at two stages of crystallization, from an evolving array of ordered molecules in a metastable form (form C, $Z' = 12$) to a compact and stable crystal lattice (form B, $Z' = 4$). The similarity in the two triclinic forms of **5** is also revealed in their calculated Powder X-ray diffraction spectra. The calculated powder X-ray diffraction spectra (Cerius^2) for the tetramorphic structures are shown in Figure 6.

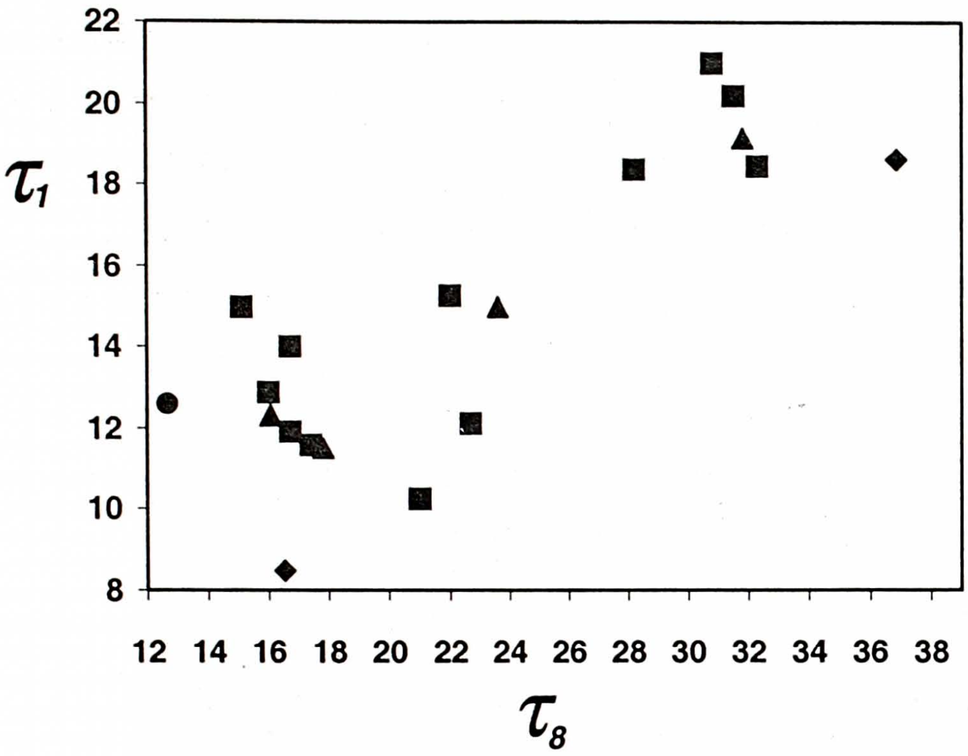


Figure 5. Conformational map (τ_1 vs τ_8) for the nineteen crystallographic independent conformations of molecule **5**. Note the two clusters of conformations. Symbols for polymorphs: A= ●, B = ■, C= ▲ D= ♦

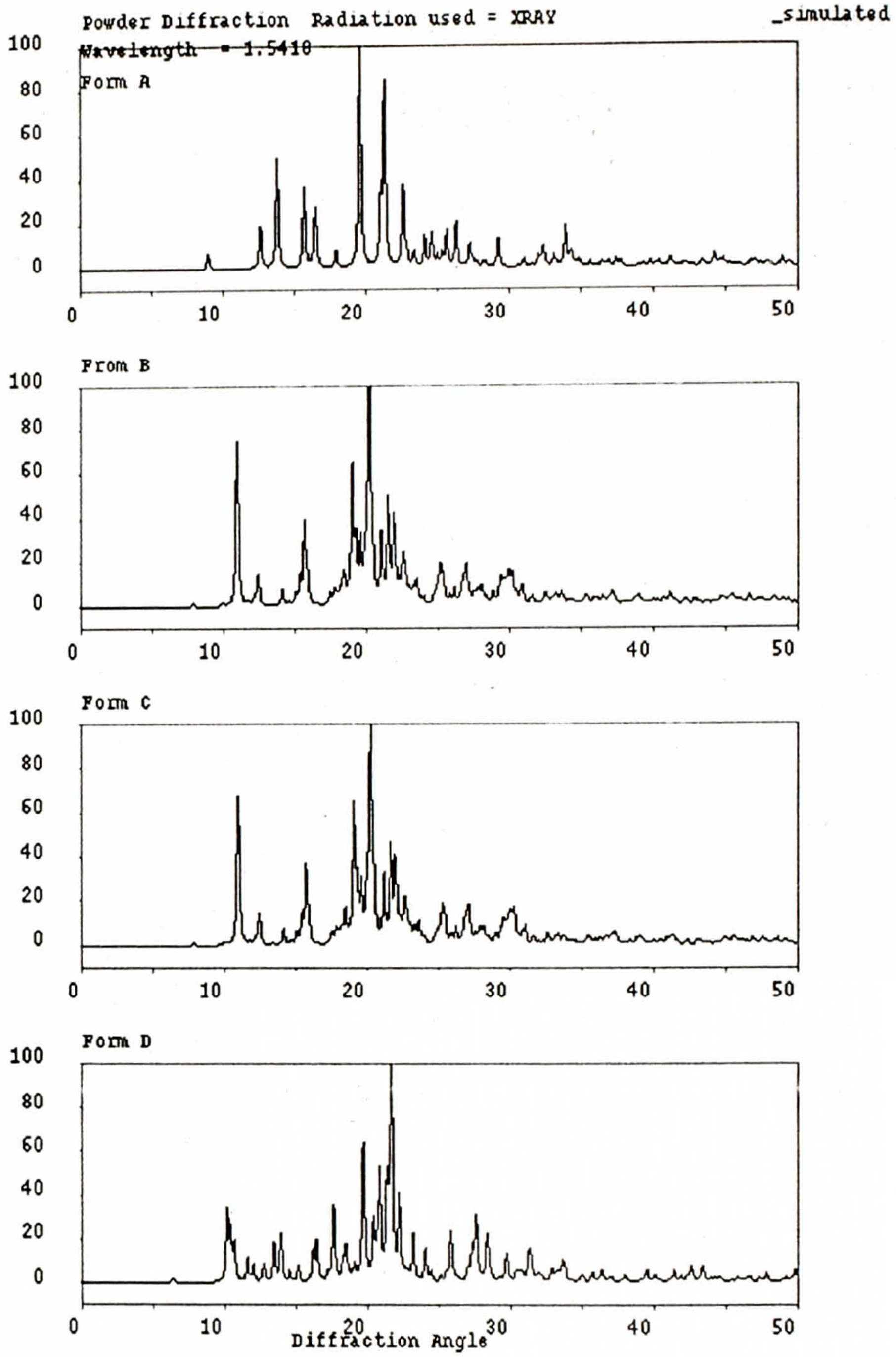


Figure 6. Calculated powder X-ray diffraction pattern (Cerius^2) for tetramorphs of **5**.

2.6 Lattice energy calculations (Cerius^2) on polymorphs of 5

The tendency to attain close packing is achieved with equal efficiency in the different polymorphic forms of **5** since their lattice energies, densities and packing coefficients are comparable. The total energy per molecule and the contributions from van der Waals, Coulomb and hydrogen bonding are listed in Table 4 along with their calculated densities and packing coefficients. The lattice energies were computed for the tetramorphs of **5** with Cerius^2 program by energy minimisation of the experimental crystal structures. The energy per molecule in the four crystal structures are 42.14, 39.66, 43.23 and 42.42 kcal/mol indicating that the various polymorphic forms have energies within a narrow kcal/mol range. Since the constituents of each form are the same, a more useful and meaningful parameter is the energy contributed from hydrogen bonding. The hydrogen bonding energies of the four forms are in the same range (1.85, 2.01 2.10 and 2.74 kcal/mol). A likely reason for the simultaneous occurrence of concomitant polymorphism and conformational polymorphism is that the differences in energy scale of crystal forms and conformational variations are comparable. Despite the loss in crystal symmetry, there is no compromise in crystal compactness because the packing coefficient is about the same. (1.23-1.25 g/cm^3) for the four forms.

Table 4. Calculated energies of the tetramorphs, corrected for number of molecules in unit cell.

	Form A	Form B	Form C	Form D
Total (kcal/mol)	-42.14	-39.66	-43.23	-42.42
van der Waals (kcal/mol)	-27.78	-27.22	-29.67	-27.19
Coulombic (kcal/mol)	-12.51	-10.43	-11.46	-12.49
Hydrogen-bonding (kcal/mol)	-1.85	-2.01	-2.10	-2.74
calculated density (g/cm^3)	1.233	1.236	1.247	1.242
% space filled	69.9	68.1	68.8	68.9

2.7 Database analysis

The next exercise was to examine the polymorphic occurrence in organic crystal structures archieved in Cambridge Structural Database (CSD). For this study a search was carried out on the CSD (ConQuest 1.4, April 2002, 257 162 entries) similar to that reported by Gavezotti and Filippini,[13] on all organic compounds with "form" or "polymorph" in the qualifier, with no disorder, 3D coordinates determined, no errors, no ions and not polymeric. Atomic species considered were C, H, N, O, F, Cl and S in any combination. The results were sorted out manually and the entries with only one polymorphic form listed, hydrates and solvates were not included. A group of two or more polymorphs for the same compound will be called as a cluster. A total of 469 clusters were found to be polymorphic. Among them, there are 422 with two, 42 with three, three with four, one with five and one with six partners, for a total of 993 organic crystal structures. It is clear from this study that the organic molecules that adopt four or more polymorphs are rare. Only five organic crystal systems (pyrazine carboxamide, sulfapyridine, pimelic acid, sulfathiazole and 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile) have four or more polymorphs in the quarter of a million or so crystal structures deposited in the CSD. Table 5 illustrates the database search results obtained in the previous (Gavezotti and Filippini[13] and Yu et. al.[19a]) and present study. The list of 469 reference codes of the polymorphic compounds found in this study is given in Appendix-I.

Table 5. Database search results on polymorphic occurrence.

	No. of clusters identified by Gavezotti and Filipini[13]	No. of clusters identified by Yu et. al.,[19a]	No. of clusters identified in the present study
total no. of clusters	163	321	469
two forms	147	291	422
three forms	13	27	42
four forms	3	3	3
five forms	none	none	one
six forms	none	none	one

2.8 Conclusion

Polymorphism in 4,4-diphenyl-2,5-cyclohexadienone **5** is significant for several reasons. This is the first example of four polymorphs with 19 different crystallographic conformations of the same molecule characterized by low-temperature X-ray diffraction, the highest value in any system of conformational polymorphs. The tetramorphic crystal structures of **5** are stabilized by alternative arrangements of C–H···O hydrogen bonds. The results show that the structural variety of possible supramolecular synthons results in the polymorphic occurrence. The flexible conformations of **5** result in alternative hydrogen bond synthons **I**, **II** and **III**, which in turn may be traced as the cause of concomitant polymorphism. In addition to concomitant polymorphism, **5** also exhibits conformational polymorphism and conformational isomorphism. Such systems may serve as an accurate benchmark for the refinement of atom–atom potentials in crystal structure prediction programs. The formation of closely related polymorphic structures re-emphasizes the importance of structure-defining interactions during crystallization. This study also highlights the subtle nature of molecular features that induce polymorphism. Further studies on temperature/pressure-mediated phase transition, kinetic and thermodynamic data, the search for new polymorphs and their morphology are in progress.

2.9 Experimental Section

4,4-Diphenyl-2,5-cyclohexadienone **5** was synthesized from diphenylacetaldehyde and methylvinylketone in two steps as reported in the literature.[23] To a mixture of diphenyl acetaldehyde (1.68 ml, 9.4 mmol) and methylvinylketone (0.86 ml, 28 mmol) in 30 ml dry ether, was added 0.5ml of 3N alc. KOH solution at 0 °C. The mixture was stirred at 0 °C for 2 hr and at room temperature for 2 hr. Then the reaction mixture was neutralized with 20% HCl

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solution and 5ml of benzene was added to dissolve the solid residue. The two phase mixture was extracted with EtOAc, washed with water twice, washed with brine solution, dried over sodium sulphate and the solvent was evaporated to obtain crude product. Purification of the crude material through column chromatography yielded pure 4,4-diphenyl-2-cyclohexenone. To the product of the first step (992 mg, 4 mmol), in 1,4-dioxane was added DDQ (3.632 g, 16 mmol) and catalytic amount of *p*-toluenesulfonic acid and the reaction mixture was refluxed for 72 hr. Then the reaction mixture was filtered through celite and the filtrate was diluted with EtOAc, washed thrice with 30 ml of 10% NaOH solution, washed with water and brine, dried over sodium sulphate and solvent was evaporated under vacuum. The crude product was purified through column chromatography to obtain pure 4,4-diphenyl-2,5-cyclohexadienone **5**. m.p. 122–124 °C. ^{1}H NMR (δ, $CDCl_3$): 6.45 (d, 2H), 7.25-8.15 (m, 12H). IR (KBr): 3057, 1651, 1624, 1449, 1446 cm^{-1}

X-ray crystallography

The polymorphic forms **A**, **B** and **C** were crystallized from 5% EtOAc/*n*-hexane at ambient temperature. Form **D** was crystallized from CH_2Cl_2/EtOAc/*n*-hexane. A disappearing fifth polymorph was crystallized from CH_2Cl_2/EtOH. DSC (scan rate 20 °C min^{-1}) of the bulk material shows two endotherms at 118 and 122 °C. The experimental PXRD spectrum of the bulk material matches with the simulated spectrum (*Cerius*^{2}) of the **A** form. Moreover, crystallization at low temperature yielded only form **A** suggesting that it may be the stable form. Data on polymorph **A**, **B** and **C** were collected at the University of Canterbury, New Zealand by Dr. R. Kadirvelraj and Prof. W. T. Robinson and on form **D** were collected at University of Durham, U.K. by C. K. Broder and Prof. J. A. K. Howard, on Bruker SMART diffractometer in the ω-2θ scan mode. The incident radiation used for both the data is Mo-Kα X-ray (λ = 0.71073 Å). The structure solutions and refinements of these crystal structures were performed with the SHELX97.[38] All the geometrical analysis were carried out with PLATON[39] on Silicon Graphics computer.

Cerius^2 Calculations

Lattice energy calculations were carried out in the *Cerius*^{2} suite of programs (Version 4.2). Using the experimental crystal structures as input, the electrostatic potential (ESP) charges were determined (AM1, MOPAC). The geometries were not optimised, as it would lead to loss of molecular symmetry. ESP charges were assigned to the molecules and the lattice energies were calculated on the minimised structures (Table 4.). All calculations were performed using standard program default parameters.

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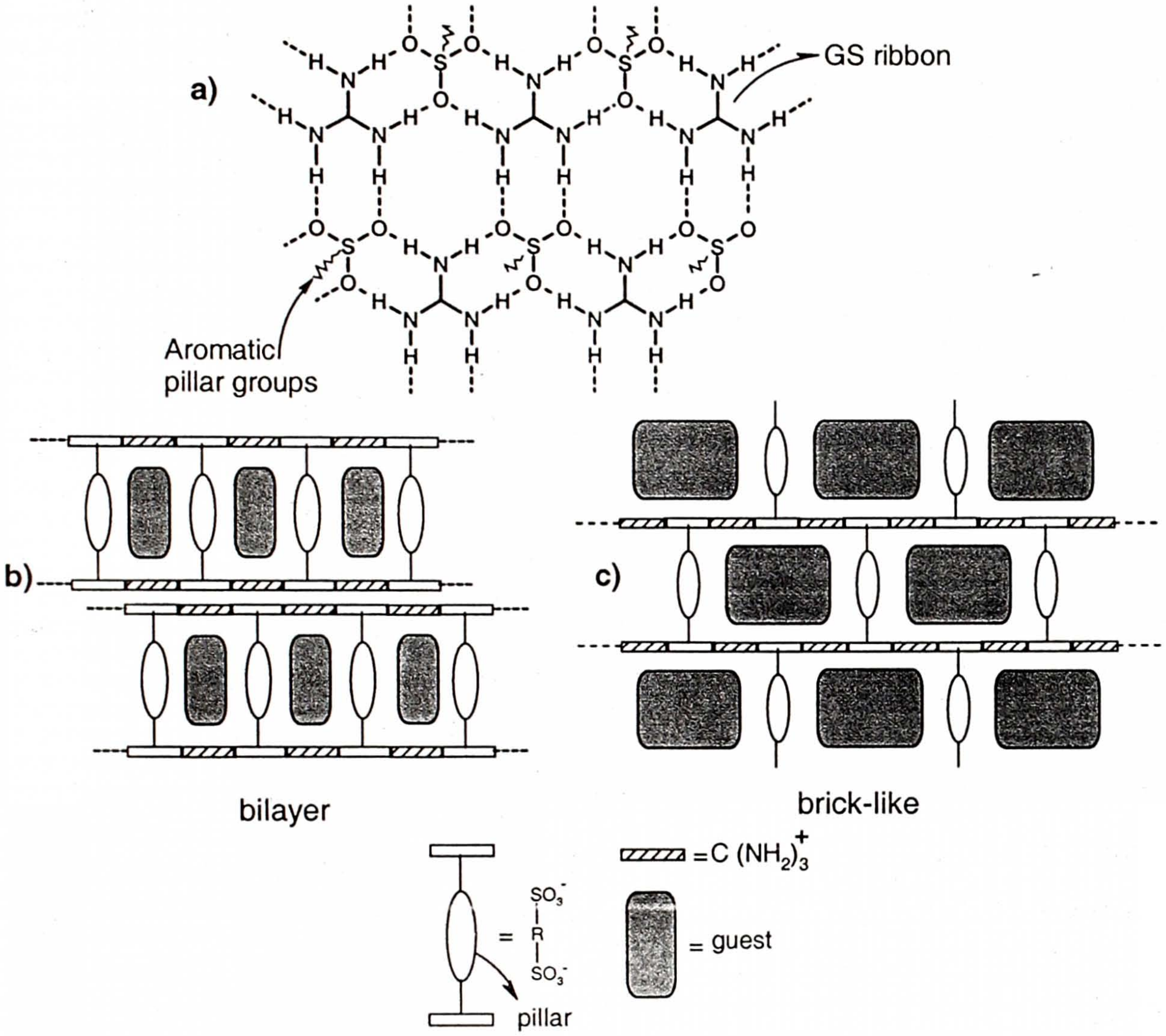
CHAPTER THREE

SUPRAMOLECULAR SYNTHESIS OF A CLAY MIMIC HOST

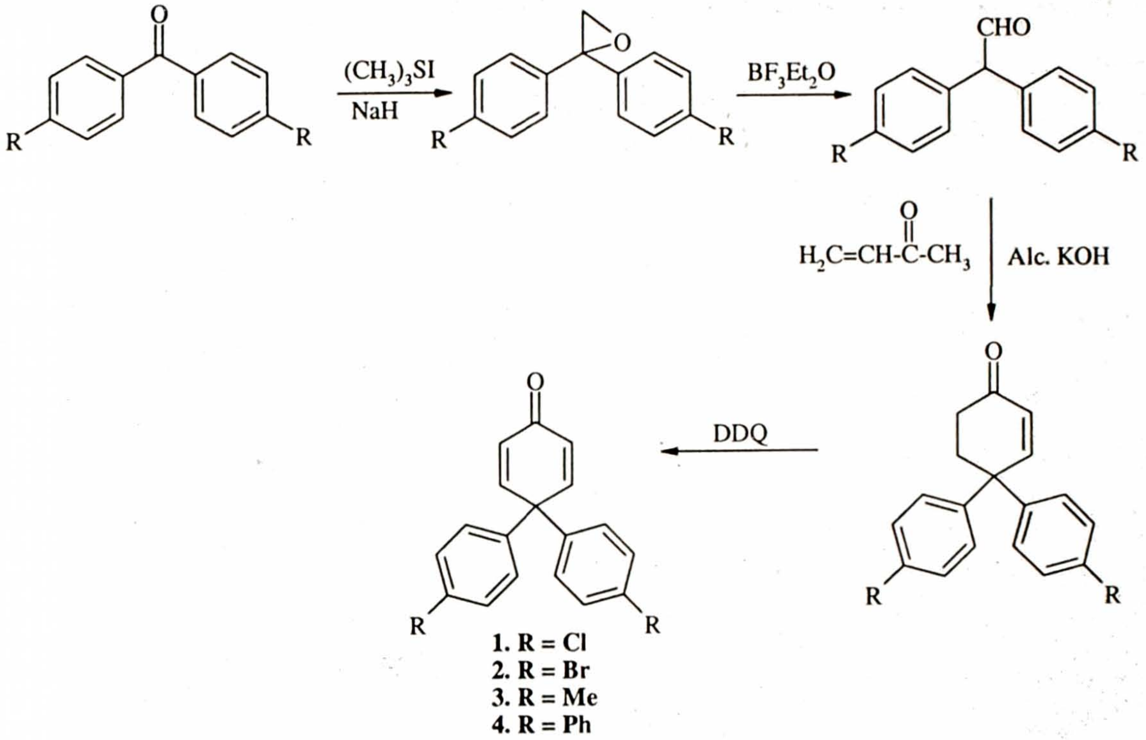
3.1 Introduction

The development of property-directed synthetic concepts is a major challenge in synthetic supramolecular chemistry.[1] Self-assembly of tailored molecular building blocks results in an ever increasing number of interesting crystal structures. Crystal engineers aim to design and synthesize solid-state host-guest structures by using functional building blocks. Inclusion compounds[2] and binary crystals are important topics in supramolecular chemistry, owing to their great promise in understanding molecular recognition and also in practical applications. Molecular host frameworks that include guest species provide a unique opportunity to study the fundamental physicochemical phenomena associated with molecular recognition and ordering.[3] The promise of these materials in chemical separations, catalysis, optoelectronics, and magnetism has prompted efforts to develop crystal engineering strategies for the synthesis of open host frameworks.[4] These strategies rely mainly on the planned self assembly of host frameworks through carefully designed hydrogen bonds between complementary groups. Organic molecule based inclusion compounds can be synthesized with various topologies such as 1D channels, 2D lamellar galleries and 3D porous networks through functionalized scaffolds.[3,5] Despite numerous attempts for rational design of open frameworks, the prediction of inclusion crystal structures is still elusive and success can frequently be serendipitous.[6] Recent trends indicate that host frameworks can be synthesized based on the placement of appropriate functional groups on a molecular skeleton that optimizes their chemical and topological complementarity. In this context, O–H···O hydrogen bonding between alcohols[7] and phenols has been used by Bishop to design helical host lattices from C_2 symmetric diols. Halogen···halogen and nitro···nitro interactions in *para*-substituted triphenoxy triazines[8] have been utilized by Nangia for the design of hexagonal host frameworks.

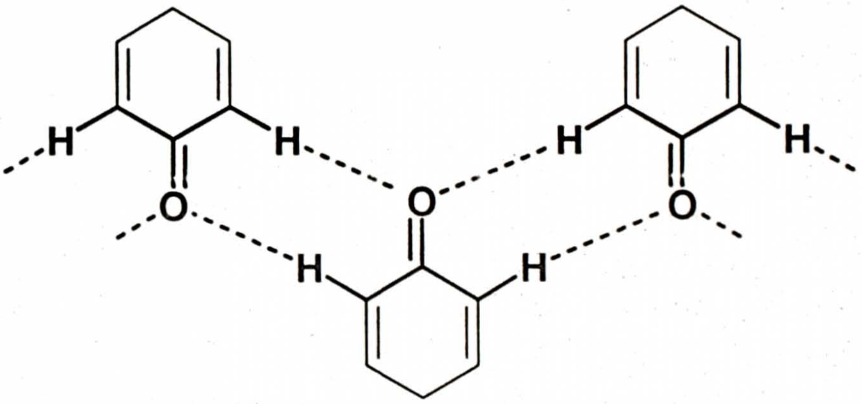
Among the diverse inclusion compounds, channel-type host architectures are attractive because they produce a one-dimensional environment to probe a specific phenomenon or to manifest a particular property. In this context, synthesis of lamellar host materials that mimic the layered architectures of naturally occurring clay is crystal engineer's current theme of interest.[5a,b] This can be attained by constructing molecular 2-D scaffolds using hydrogen bonded sheets, which are further separated by organic components.[9] In organic clay mimics, the soft hydrogen bonds replace the coordination or metal-ligand bonds and the hydrophobic organic groups replace the ions or water molecules found in clays. Ward's group has shown the utility of the dense N–H···O hydrogen bonded 2D sheets formed by the topological and chemical complementarity in guanidinium cations (G) and organic sulphonate anions (S) in the construction of clay mimic architectures.[5b] Aromatic pillars further separate the 2D sheets (GS) and guest molecules are included in the aromatic pillar regions as shown in Scheme 1. The host architectures adopt either a bilayer arrangement or a brick architecture depending on the nature of the guest included (Scheme 1). The complex of trimesic acid and *N,N*-dibenzylamine forms a clay mimic host architecture with a 2D layer that is stabilized by rigid hydrogen bonding between trimesate anions and ammonium cations and the benzyl groups act as pillars.[9c] In this chapter, the importance of weak C–H···O hydrogen bonds in the non-covalent synthesis of clay mimic host material is described.



Scheme 1. The clay mimic host architecture observed in Guanidinium sulfonates: (a) A view of honeycomb two-dimensional GS layer (2D scaffold) b) bilayer arrangement c) brick architecture.



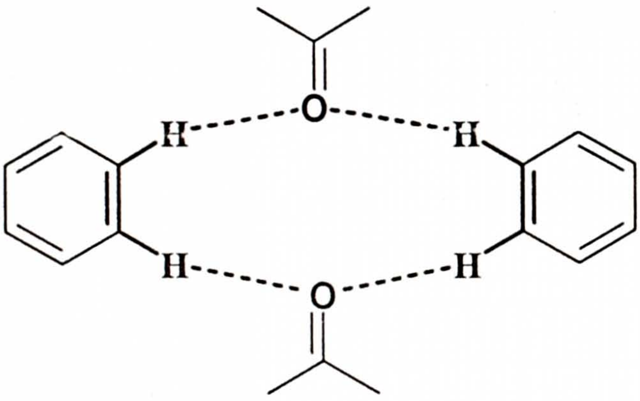
Scheme 2



I

As a part of an ongoing study in the design and synthesis of a clay mimic host architecture, archetypal benzoquinone tape motif **I** was considered as a design element. For this study, 4,4-diaryl-2,5-cyclohexadienone with geminal aryl groups were chosen as tecton.[10] One of the main difficulties in constructing open networks is that the open frameworks tend to interpenetrate.[11] Guest inclusion competes with interpenetration and the former occurs in only ca. 15% cases as noted in a recent CSD survey.[12] It was expected that cyclohexadienone ring will self-assemble *via* C–H···O mediated synthon **I** and the aryl rings will constitute the pillars in third dimension to form an open architecture. To implement the above molecule to supermolecule design strategy, the crystal structures of 4,4-bis(*p*-chlorophenyl)-2,5-cyclohexadienone **1**, 4,4-bis(*p*-bromophenyl)-2,5-cyclohexadienone **2**, 4,4-bis(*p*-tolyl)-2,5-cyclohexadienone **3** and 4,4-bis(*p*-biphenylyl)-2,5-cyclohexadienone **4** were analyzed. The compounds were synthesized by using reported procedures in four steps as shown in Scheme 2.[13] Although the crystal structures of the halogen and methyl substituted compounds **1**, **2** and **3** do not have the tape motif, the biphenyl analogue **4** forms the open architecture with expected benzoquinone tape synthon **I** and guest species are included in the interlayer region.

3.2 Crystal structure of 4,4-bis(*p*-chlorophenyl)-2,5-cyclohexadienone 1



II

The compound crystallizes in monoclinic space group *C2/c*. The structure is extensively stabilized by C–H···O interactions. The most relevant pattern is based on the ten membered centrosymmetric synthon **II** which connects two hydrogens of a phenyl ring with *c*-glide and 2-fold rotation related molecules through C–H···O hydrogen bonds. The cyclohexadienone ring and one phenyl ring form a *zigzag* sheet like structure in (011) where the synthons are arranged in a herringbone fashion. The sheet like structure is shown in Figure 1a. The other phenyl ring acts as a spacer between two such inversion related sheets by connecting the sheets through C–H···π interactions (Figure 2a). Inversion related sheets are also connected by C–H···Cl interactions[14] (Figure 2b). The quinonoid hydrogens are participating in C–H···π and C–H···Cl interactions. There is a polarization induced type II Cl···Cl contact (3.56 Å, 175.0°, 102.2°) between chlorine atoms as shown in Figure 2c.[15] The metrics of the intermolecular interactions are given in Table 1.

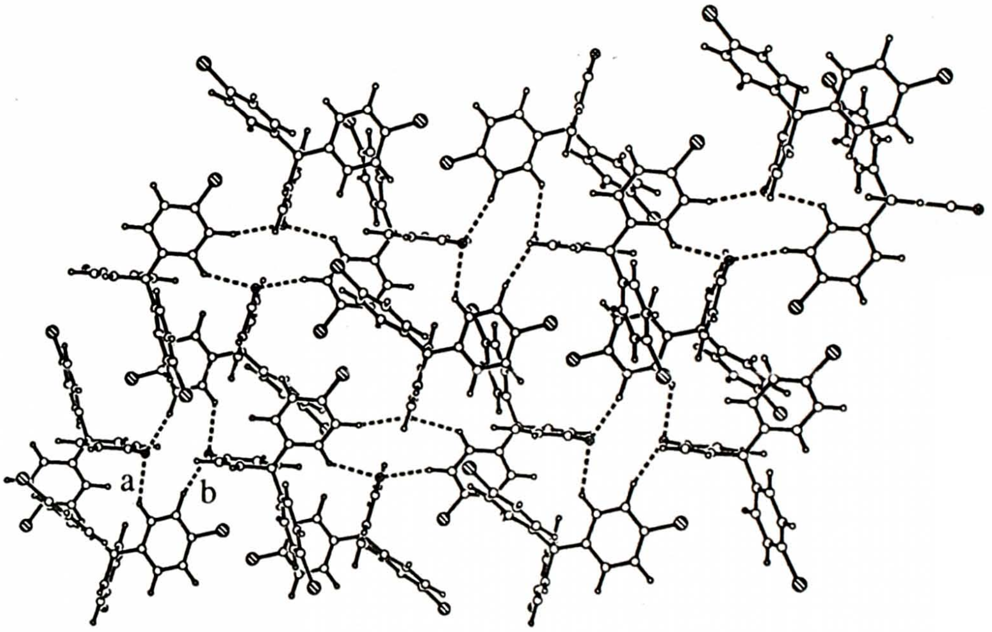
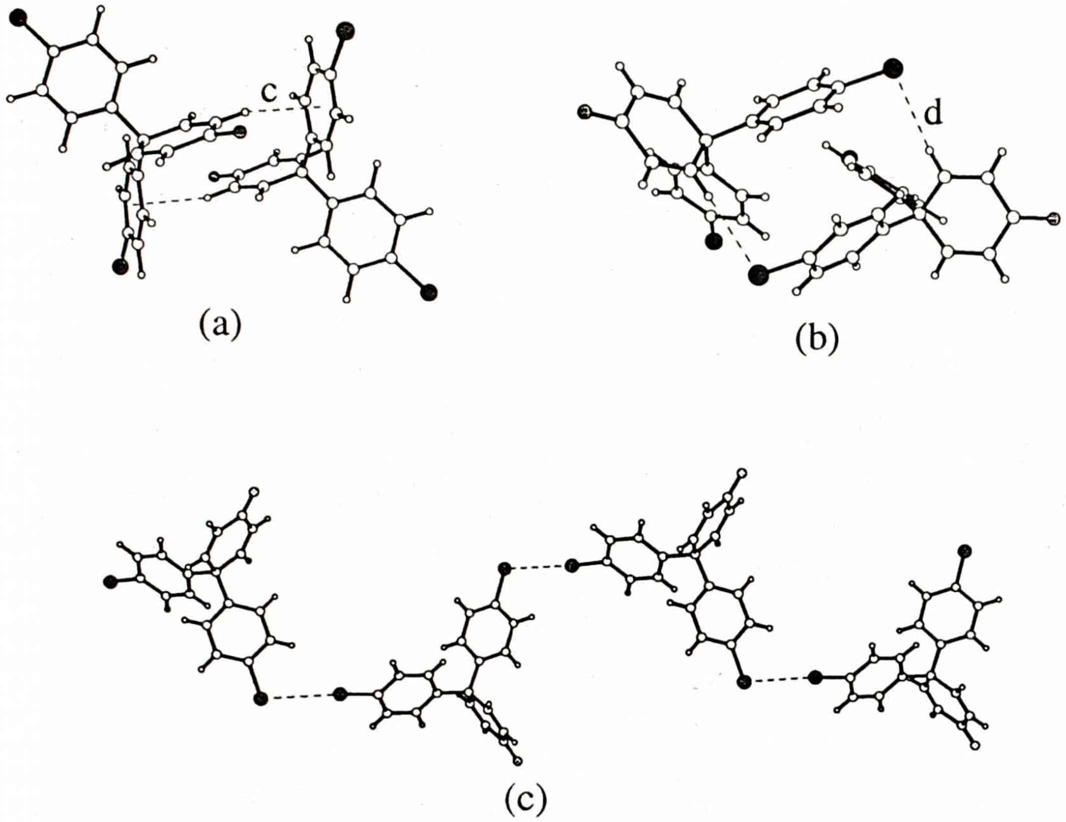


Figure 1. The crystal structure of 4,4-bis(*p*-chlorophenyl)-2,5-cyclohexadienone **1**. Notice the synthons are arranged in a herringbone fashion.



(a) (b)

(c)

Figure 2. Centrosymmetric C–H···π (**a**) and C–H···Cl (**b**) patterns observed in the crystal structure of **1**. **Figure 2c.** Polarization induced type II Chlorine···Chlorine contact.

3.3 Crystal structure of 4,4-bis(*p*-bromophenyl)-2,5-cyclohexadienone 2

The structure of 4,4-bis(*p*-bromophenyl)-2,5-cyclohexadienone in space group C2/c is isomorphous with the corresponding chloro structure. The synthon **II** observed in the chloro compound is seen in this structure also. The structural changes caused by the substitution of chloro group by the bromo group are almost negligible in this family of cyclohexadienones. The crystal structure of **2** is shown in Figure 3 and the metrics of the intermolecular interactions are given in Table 1. The structure is also extensively stabilized by the formation of centrosymmetric C–H···π and C–H···Br dimers. The metrics of Br···Br type II contact are 3.60 Å, 175.0° and 102.2°.

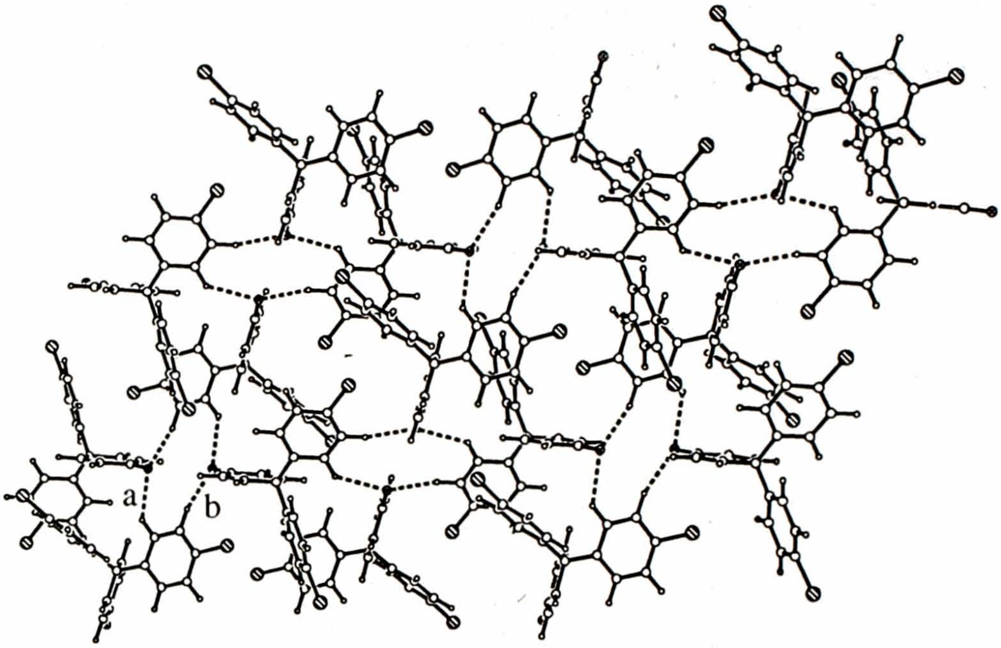


Figure 3. The crystal structure of 4,4-bis(*p*-bromophenyl)-2,5-cyclohexadienone **2**. Notice that compound **2** is isomorphous with **1**.

3.4 Crystal Structure of 4,4-bis(*p*-tolyl)-2,5-cyclohexadienone 3

The compound 4,4-bis(*p*-tolyl)-2,5-cyclohexadienone crystallizes in monoclinic space group $P2_1/c$. There are two symmetry independent molecules in the asymmetric unit. One molecule is forming a chain along [010] that connects 2_1 and *c*-glide related molecules through C–H···O interactions as shown in Figure 4a. The other molecule is connecting *c*-glide related molecules through C–H···π and C–H···O mediated chain along [001]. This is shown in Figure 4b. These two chains formed by symmetry independent molecules are connected further by an array of C–H···O interactions. The geometrical parameters of C–H···O and C–H···π interactions are given in Table 1. Chloro-methyl exchange was not observed in the family of cyclohexadienones because the interactions are weak and there is no robust synthon to direct the self-assembly. Further, the presence of more than one chlorine atom in the molecule and type II chlorine···chlorine contacts also cause departure from the chloro-methyl exchange rule.[16]

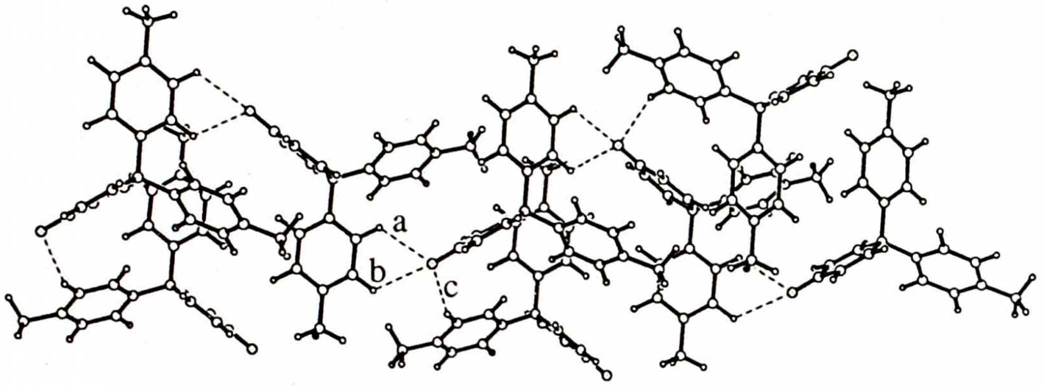


Figure 4a. The C–H···O mediated chain along [010] in the crystal structure of **3**

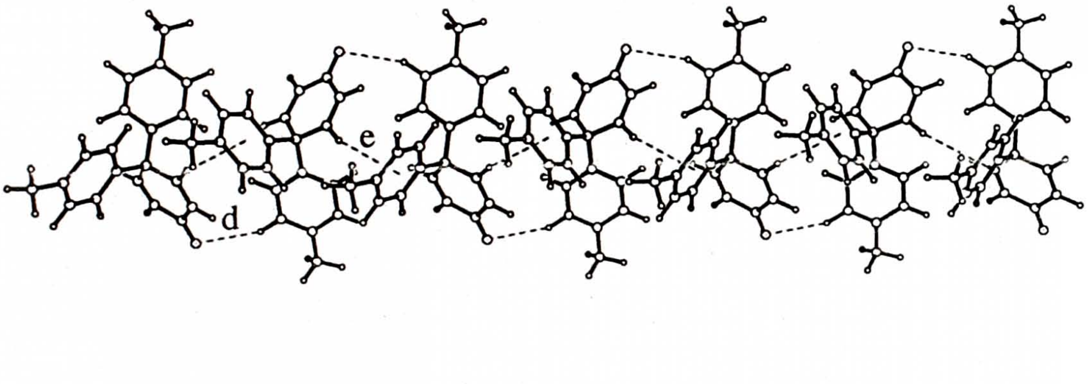


Figure 4b. The C–H···O and C–H···π mediated chain along [001] in the crystal structure of **3**

Table 1. Geometrical parameters of intermolecular interactions in **1**, **2** and **3**

Compound	Interaction[a]	d (Å)	D (Å)	θ (deg)
1	a) C–H···O	2.41	3.437(3)	156.0
	b) C–H···O	2.47	3.231(2)	126.0
	c) C–H···π[b]	2.83	3.761	165.6
	d) C–H···Cl	2.67	3.745(2)	170.9
2	a) C–H···O	2.58	3.608(7)	157.8
	b) C–H···O	2.50	3.250(7)	125.9
	c) C–H···π[b]	2.90	3.886	165.2
	d) C–H···Br	2.64	3.719(6)	169.1
3	a) C–H···O	2.60	3.328(2)	123.3
	b) C–H···O	2.63	3.343(2)	122.3
	c) C–H···O	2.62	3.606(2)	150.3
	d) C–H···O	2.72	3.721(2)	152.2
	e) C–H···π[b]	2.94	3.874	149.7

[a] All C–H distances are neutron normalized (1.083 Å). [b] π denotes the centroid of the phenyl ring.

3.5 4,4-bis(*p*-biphenylyl)-2,5-cyclohexadienone 4: A clay mimic host

The close packed structures of **1**, **2** and **3** suggested that the phenyl rings are small in size to form an open architecture and therefore the molecule **4** with linear biphenyl spacer was synthesized. Recrystallization of 4,4-bis(biphenylyl)-2,5-cyclohexadienone **4** from various solvents afforded diffraction quality crystals from 1,2-dimethoxyethane (DME). The X-ray structure of **4•**DME (2:1 stoichiometry, *C*2/*c* space group) contains the expected C–H···O hydrogen bond benzoquinone tape along [001] (H···O 2.66 Å, C–H···O 160.6°; C–H distance neutron-normalized to 1.083 Å). The second C–H···O bond of the tape is long (3.05 Å, 175.6°) but at the accepted distance limit.[17] The most significant feature from a crystal engineering objective is that the target benzoquinone tape synthon **I** has been obtained. This is shown in Figure 1. The biphenylyl groups form parallelepiped channels of 8 × 5 Å down the *c*-axis which are occupied by ordered DME guest species as shown in Figure 2. The channel direction is perpendicular to the benzoquinone tape direction.

Inversion related channels are connected through auxiliary (Ph) C–H···O hydrogen bonds (2.71 Å, 137.2°). C–H···O hydrogen bonds between host and guest (2.57 Å, 159.5°) further stabilize the ordered supramolecular architecture in **4**•DME.

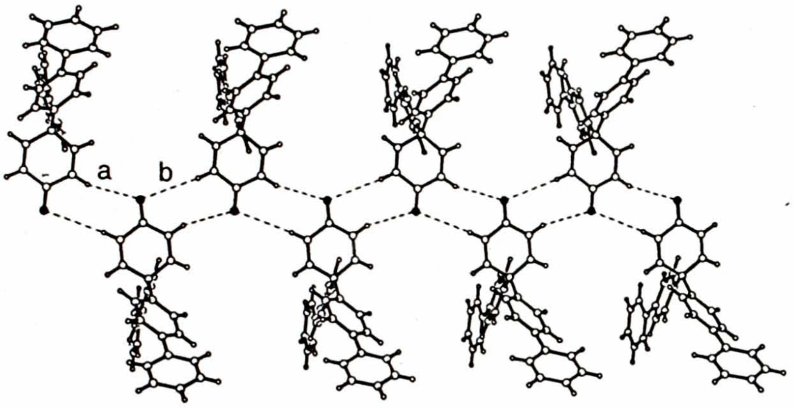


Figure 5.Crystal structure of **4**•DME in the *bc*-plane to show the benzoquinone tape synthon **I**. Guest molecules are not shown for clarity.

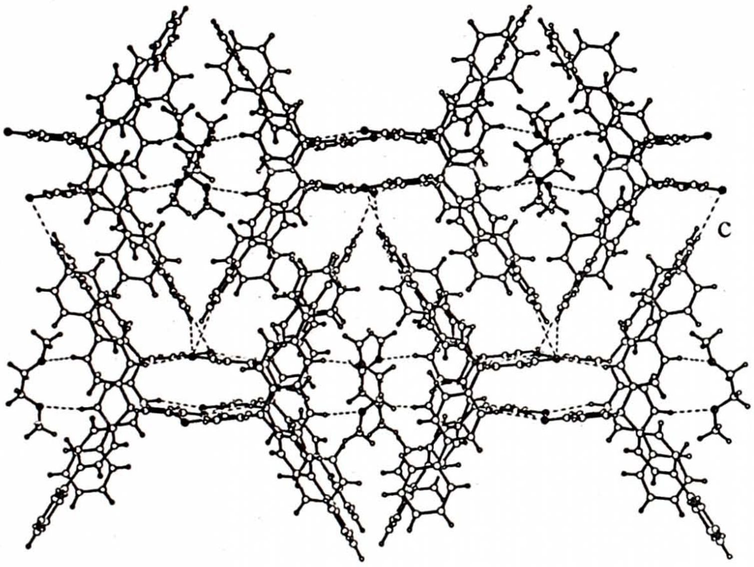


Figure 6.Crystal structure of **4**•DME down the *c*-axis. The network of host–host and host–guest C–H···O hydrogen bonds stabilize the ordered superstructure.

Continuing further, **4** was recrystallized from *n*-hexane, a solvent isosteric with DME but devoid of hydrogen bonding groups. The crystal structure of **4•*n*-**hexane (2:1) is isomorphous with identical arrangement of host atoms in the crystal. The metrics of quinone tape C–H···O bonds are 2.67, 161.9 and 2.99 Å, 175.1°; (Ph)C–H···O is 2.71 Å, 137.2°. In the channel, *n*-hexane is disordered over two conformations with 55% and 45% occupancy. This is the first example where *n*-hexane is isolated in two different conformations in the same crystal structure.

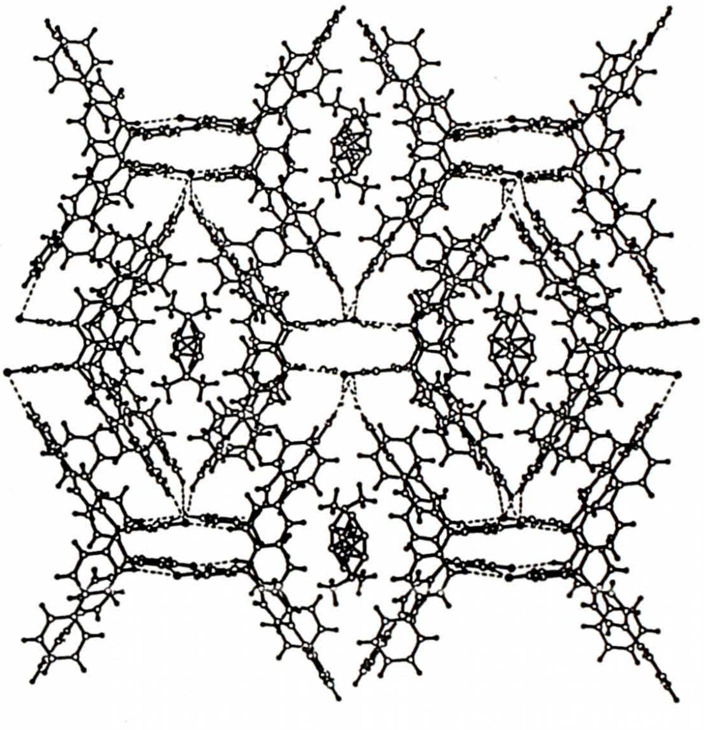


Figure 7. Crystal structure of **4•***n*-hexane down the *c*-axis.

A close examination of the crystal structures of the solvates of **4** shows that this host molecule can be classified as clay mimic organic host. If the lamellar 2D benzoquinone tape in **4** is considered as coordination bonds in naturally occurring clays, the biphenyl groups that separate the lamellar 2D patterns act as pillars in the crystal structure. Thus the crystal structure of **4** resembles the brick type alternating layer arrangement of organic clay mimics[5b] as shown in Figure 8. The utilization of O–H···O hydrogen bonding in the construction of similar clay mimic host material has been reported recently.[18] Further, the facile inclusion of guests in the open framework formed by **4** encouraged us to examine the recrystallization of host material **4** from other solvents. Host-guest 2:1 adducts were obtained with 1,4-dibromobutane (DBRB), 1,5-hexadiene(HDE) and 2,5-dimethylhexane (DMEH). C–H···Br interactions between host and guest molecule stabilize the structure in the case of dibromobutane solvate. When the host **4** was crystallized from perfluorohexane/EtOAc/EtOH in the expectation of getting perfluorohexane adduct, the host material crystallized with ethanol in 1:1 ratio. In the same manner, the host-guest adduct of **4** with 1,3-dimethylcyclohexane was obtained in a related experiment on the crystallization of **4** from cyclohexane. Instead of expected **4•**cyclohexane, **4** crystallized with 1,3-dimethylcyclohexane, which is an impurity present in cyclohexane. This host architecture provides a first example of including rare guest species such as 1,4-dibromobutane, 1,5-hexadiene, 2,5-dimethylhexane and 1,3-dimethylcyclohexane.

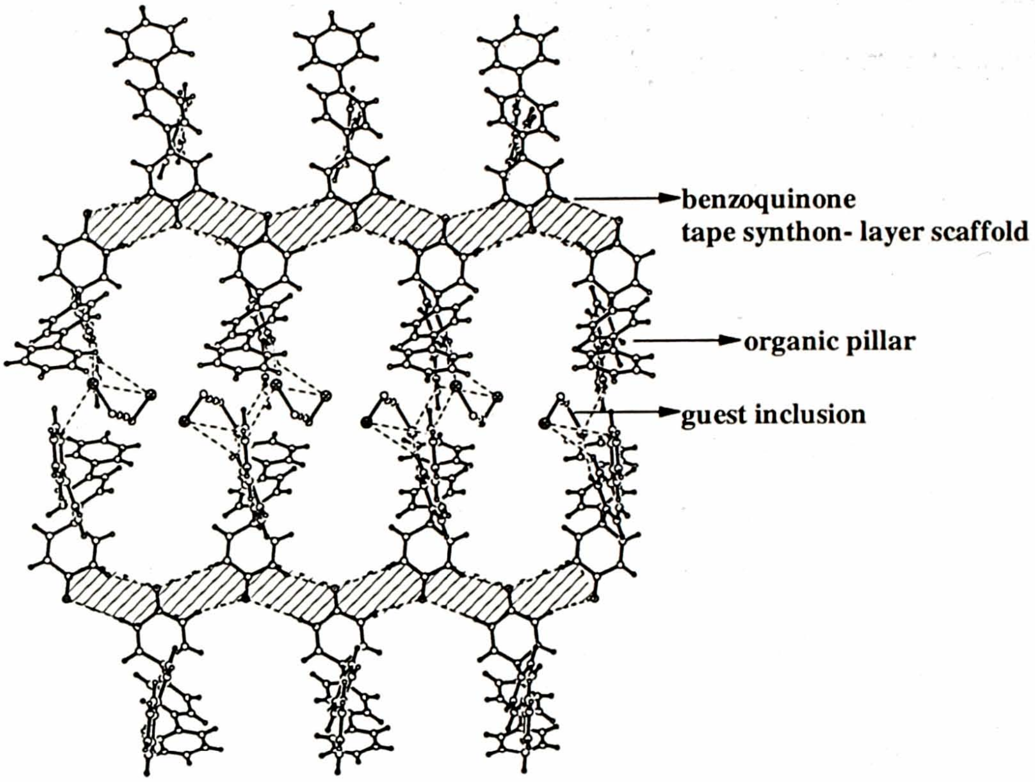


Figure 8. The clay mimic structure observed in **4**•DBRB and related structures.

In these isomorphous structures, the guest molecules are generally found in folded conformations. Except 1,2-dimethoxyethane, all other guests are disordered. Structure solution and refinement were routine and yielded converged models with good *R*-factors (0.05 to 0.06) for 1,2-dimethoxyethane, 1,3-dimethylcyclohexane, 1,4-dibromobutane and 1,5-hexadiene adducts. In the case of hexane and ethanol the *R*-factors are modest (0.067 and 0.08) and in the case of 2,5-dimethylhexane it is high (0.11) due to heavy twinning. In all structures, the guest molecule is occupying the inversion center in the cavity. EtOH resides on a general position. The geometrical parameters of C–H···O interactions are given in Table 2.

Table 2. Geometrical parameters of C–H···O interactions between the host molecules in the solvates of **4**

Compound	Interaction[a]	*d* (Å)	*D* (Å)	*θ* (deg)
4•DME	a) C–H···O	2.66	3.702(6)	160.6
	b) C–H···O	3.05	4.138(5)	175.6
	c) C–H···O	2.75	3.661(6)	138.2
4•hexane	a) C–H···O	2.67	3.713(5)	161.9
	b) C–H···O	2.99	4.069(5)	175.1
	c) C–H···O	2.71	3.586(5)	137.2
4•DBRB	a) C–H···O	2.66	3.698(6)	159.5
	b) C–H···O	3.06	4.147(7)	176.0
	c) C–H···O	2.82	3.686(7)	136.7
4•EtOH	a) C–H···O	2.70	3.751(5)	162.5
	b) C–H···O	3.01	4.096(5)	175.0
	c) C–H···O	2.92	3.743(5)	131.8
4•DMCY	a) C–H···O	2.66	3.707(4)	162.2
	b) C–H···O	2.99	4.078(4)	175.4
	c) C–H···O	2.75	3.622(4)	137.1

[a] All C–H distances are neutron normalized (1.083 Å).

3.5.1 Packing of phenyl groups in the crystal structures of 4

In general, the aromatic compounds that do not have any strong hydrogen-bond donor and acceptor groups tend to self-assemble via herringbone interactions, π···π interactions or with both. The biphenyl groups in **4** do not engage in the usual herringbone T-motif or π–π stacking interactions,[19] possibilities that would have resulted in a self-inclusion crystal. The isomorphous crystal structures of the pseudopolymorphs of **4** are extensively stabilized by numerous C–H···π interactions. The geminal biphenyl groups from inversion related molecules are connected by weak C–H···π interactions to form the channel. Aryl groups from such glide related channels are hydrogen bonded through a linear array of C–H···π interactions. The 2-fold related molecules of **4** are connected by auxiliary C–H···π interactions. All C–H···π interactions are in the distance-angle range 2.75-2.8

145-160°.

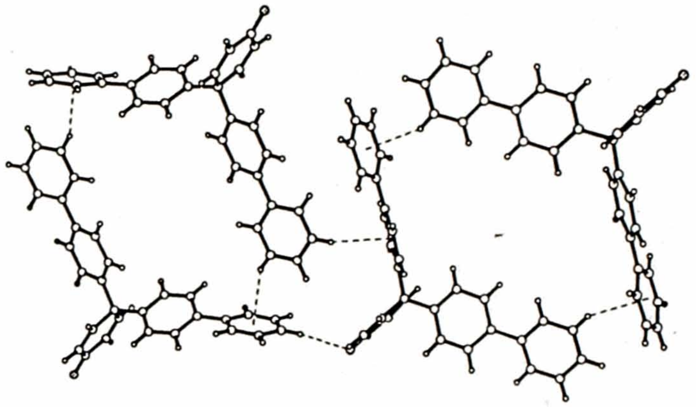


Figure 9. C–H···π interactions that connect the inversion related molecules within the channels and the glide related molecules from different channels formed by **4**.

3.5.2 Conformations of guests in the cavity of 4

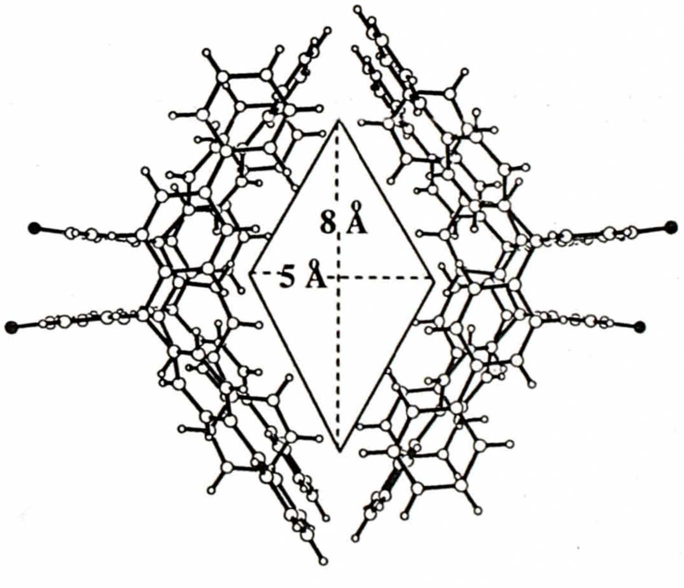


Figure 10. The microcavity (8 x 5 Å) of **4** directs inclusion of guest in folded conformation.

The guest molecules included in the cavity of **4** are generally found in the high energy folded conformations. Such results are relevant not only for host-guest complexes but also in computational chemistry for the comparison of calculated energies, conformations and geometries with experimental ones. In **4.**DME, 1,2-dimethoxyethane solvent is ordered and is present in a conformation that resembles the dimethoxyethane solvates in the CSD. In the *n*-hexane solvate of **4,** hexane is disordered over two conformations with 55% and 45% occupancies. The presence of hexane in folded conformation is unusual. The conformation of *n*-hexane has been studied computationally as an inclusion complex of Dianin's compound,[20] which has shown that *n*-hexane exists in the all-*trans zigzag* conformation, similar to that found in the crystal structure of pure hexane.[21] 1,4-Dibromobutane in **4.**DBRB is also disordered and is present in folded conformation. Ethanol occupies the general position and is highly disordered. A common feature in the conformations of the above mentioned guest molecules are that the end to end distance for the guest molecules included in the cavity of **4** is around 5.3-5.9 Å where as it is >6 Å for the solvents in *zigzag* conformation. This is because the dimensions of the host cavity (8 × 5 $Å^2$) forces the guest molecules to adopt a compact shape.[22] The host architectures built with strong hydrogen bonding such as O–H···O and N–H···O are rigid and robust whereas the host structures formed with weak non-conventional hydrogen bonding have flexibility. Thus open networks assembled with weak interactions have a degree of both stability and flexibility, a combination that results in adaptability and versatility towards guest inclusion.[23] Although the host cavity of **4** is assembled with weak C–H···O and C–H···π interactions, it is specific towards different guest molecules. This causes the change in the conformation for the various guest molecules when they are included. The cavity size remains the same (8 x 5 Å) for all the guest molecules. Toda and coworkers reported the trapping of guest molecules, 1,2-dichloroethane[24] and acrylic acid[25] in an unusual conformation in the rigid architecture of the host lattice. The conformations of the guests included in the host cavity of **4** are shown in Figure 11. The slightly elongated displacement ellipsoids for some atoms in the figure implies that there are other minor conformations that contribute to the disorder of guest molecules, but it is difficult to assign their exact position because of very low electron density.

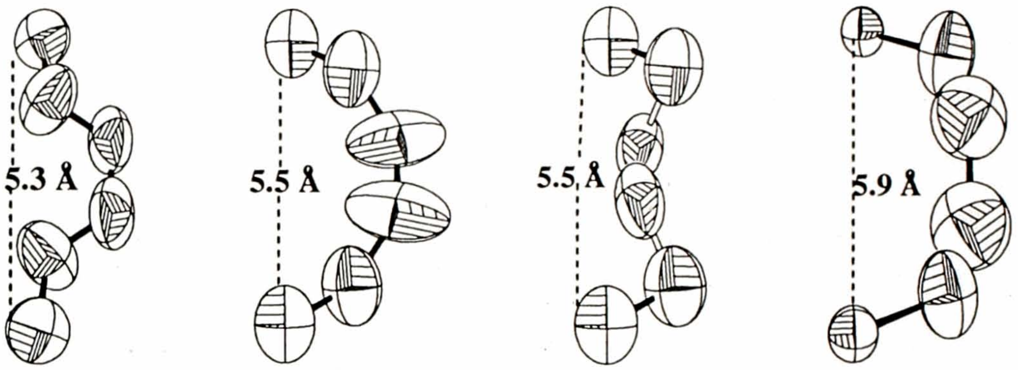


Figure 11. Displacement ellipsoids at 50% probability of the different guest molecules observed in the crystal structures of pseudopolymorphs of **4**. (a) 1,2-dimethoxyethane (b) *n*-hexane with 55% occupancy (c) *n*-hexane with 45% occupancy (d) 1,4-dibromobutane. End-to-end C···C distance is mentioned.

3.5.3 Isolation of 1,3-dimethylcyclohexane from cyclohexane

Host molecules may be classified into two main types: (i) hosts that form molecular complexes by fitting convex guest into the concave cavity (e.g. cyclodextrins, calixarenes and cyclophanes). (ii) hosts that form inclusion complexes by packing in such a manner as to leave cavities in the crystal structures in which various guests can reside. One of the most important uses of inclusion chemistry is the separation of a given guest from mixture by the formation of host-guest compounds. In this context, Weber has used 1,1'-binaphthyl-2,2'-dicarboxylic acid to separate a variety of guests such amides, carboxylic acids and nitriles.[26] 1,1-bis(4-hydroxyphenyl)cyclohexane has been utilized in the separation of isomers and aliphatic alcohols from mixtures.[27] The higher energy conformations of guest molecules included in the open structure of **4** prompted us to crystallize the host molecule **4** with cyclohexane in order to study the conformation included. Initial attempts to recrystallize **4** from cyclohexane yielded precipitate. Further attempts produced few crystals together with precipitate. The single crystal X-ray diffraction analysis established that instead of cyclohexane,[6] the host molecule **4** has included 1,3-dimethyl cyclohexane (DMCY) in its hydrophobic gallery. 1,3-dimethylcyclohexane is present as 10% impurity in the cyclohexane used for recrystallization. This was confirmed by gas chromatography mass spectroscopy. This adduct structure is a unique example of inclusion complex of 1,3-dimethylcyclohexane. This may be because the cyclohexane molecule is too small to fill the cavity. The crystal structure is isomorphous with other solvates of **4**. The guest molecule 1,3-dimethylcyclohexane occupies a special position. The guest 1,3-dimethylcyclohexane is disordered and in an unusual skew-boat conformation. This shown in Figure 12b.

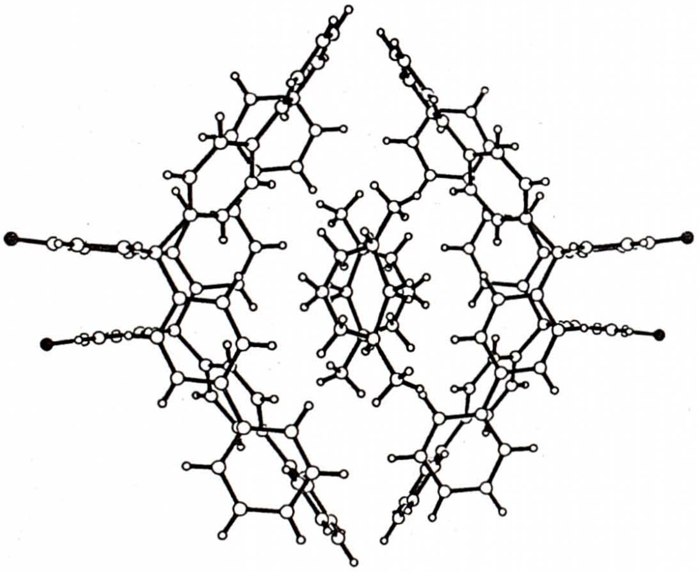


Figure 12a The Crystal structure of **4**•DMCY down c-axis.

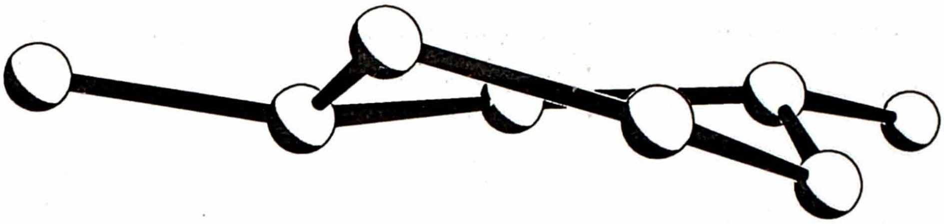


Figure 12b. The skew-boat conformation of disordered 1,3-dimethylcyclohexane included in the cavity of **4**.

3.6 Conclusion

The present study reveals that supramolecular synthesis can be carried out with weak C–H···O hydrogen bonds. While the structures of substituted phenyl benzoquinones **1**, **2** and **3** were found to have divergent structures, inclusion adducts of biphenyl analogue **4** are isostructural. Therefore replacement of geminal phenyl groups with biphenyl steers crystal packing towards a expected recurring benzoquinone tape motif **I** and yields a novel, organic host material with clay-like architectures. Compound **4** is a new host material, whose facile guest-inclusion property has been discovered by design rather than by chance. The host framework formed by **4** provides an opportunity to isolate the unusual high energy conformations of some guest molecules. A rare guest molecule, 1,3-dimethylcyclohexane has been extracted from cyclohexane in a pure state as an inclusion crystal with host **4**, leading to the utility of such materials in chemical purification. This study shows that new crystalline inclusion compounds can be designed using the principles of crystal engineering. This result has implications in inclusion chemistry, chemical separation and supramolecular synthesis.

3.7 Experimental section

The compounds **1**, **2**, **3** and **4** were synthesized from the corresponding benzophenones in four steps as given below.[13] To sodium hydride (192mg, 8 mmol), was added 4 ml of dry DMSO and the mixture was stirred for 30 minutes at 70° C under nitrogen atmosphere. Then the mixture was cooled to room temperature and 5 ml dry THF was added to that. The mixture was cooled to -5 ° C and benzophenone (2 mmol) in 5 ml THF was added. Then trimethylsulfonium iodide (3.2 mmol) in 6 ml DMSO was added slowly for a period of 10 minutes. The mixture was stirred at -5 ° C for 2 hr and at room temperature for 2 hr. Then the reaction mixture was added to ice cold water and the epoxide formed was extracted with CH_2Cl_2. The epoxide obtained in the first step was stirred with 0.5ml of BF_3Et_2O in dry CH_2Cl_2 for 30 minutes at 0 ° C. Then the reaction mixture was washed with water twice and the solvent was evaporated to obtain diaryl acetaldehyde. To the product of previous step and methylvinylketone in 30 ml dry ether, was added 0.5ml of 3N alc. KOH solution at 0 °C. The mixture was stirred at 0 °C for 2 hr and at room temperature for 2 hr. Then the reaction mixture was neutralized with 20% HCl solution and 5ml of benzene was added to dissolve the solid residue. The two phase mixture was extracted with EtOAc, washed with water twice, washed with brine solution, dried over sodium sulphate and the solvent was evaporated to obtain crude product. Purification of the crude material through column chromatography yielded pure 4,4-diaryl-2-cyclohexenone. To the cyclohexenone (1 mmol), in 1,4-dioxane was added DDQ (908 mg, 4 mmol) and catalytic amount of *p*-toluenesulfonic acid and the reaction mixture was refluxed for 72 hrs. Then the reaction mixture was filtered through celite and the filtrate was diluted with EtOAc, washed thrice with 30 ml of 10% NaOH solution, washed with water and brine, dried over sodium sulphate and solvent was evaporated under vacuum. The crude product was purified through column chromatography to obtain pure 4,4-diaryl-2,5-cyclohexadienone.

4,4-bis(*p*-chlorophenyl)-2,5-cyclohexadienone 1: m.p. 152–154 °C. ^{1}H NMR (δ, $CDCl_3$): 6.35-6.45 (d, 2H), 7.15-7.35 (m, 10H). IR (KBr): 3063, 1666, 1628, 1095, 1014, 821 cm^{-1}

4,4-bis(*p*-bromophenyl)-2,5-cyclohexadienone 2: m.p. 158–160 °C. ^{1}H NMR (δ, $CDCl_3$): 6.35-6.45 (d, 2H), 7.15-7.60 (m, 10H). IR: 3053, 1666, 1483, 1072, 1008, 821 cm^{-1}

4,4-bis(*p*-tolyl)-2,5-cyclohexadienone 3: m.p. 133–135 °C. ^{1}H NMR (δ, $CDCl_3$): 2.35 (s, 6H) 6.25-6.35 (d, 2H), 7.15-7.35 (m, 10H). IR (KBr): 3026, 1664, 1448, 856, 812 cm^{-1}

4,4-bis(*p*-biphenylyl)-2,5-cyclohexadienone 4: m.p. 126–128 °C. ^{1}H NMR (δ, $CDCl_3$): 6.45 (d, 2H), 7.25-7.50 (m, 12H), 7.50-7.65 (m, 8H). IR (KBr): 3057, 1668, 1624, 1449, 1446, 763 cm^{-1}

X-ray crystallography

The crystals of **1**, **2** and **3** were obtained on crystallization of the materials from EtOAc/hexane solvent system. The host-guest adducts of **4•**DME, **4•**DMH and **4•**HDE were crystallized by using the appropriate guests as solvents. Crystals of **4•***n*-hexane and **4•**DBRB and were obtained from 5% EtOAc/hexane and 2% 1,4-dibromobutane/CH_2Cl_2 mixture respectively. **4•**EtOH crystals were obtained from an experiment on recrystallization of **4** from a mixture of perfluorohexane, EtOAc and EtOH in the expectation of getting **4•**perfluorohexane crystals. In the same manner **4•**DMCY crystals were obtained from a related experiment on recrystallization of **4** from cyclohexane. Data on **1**, **2**, **3**, **4•**hexane, **4•**DBRB, **4•**DMH, **4•**HDE and **4•**DMCY were collected by Prof. W. T. Robinson at University of Canterbury, New Zealand and on **4•**EtOH was collected by Dr. R. K. R. Jetti and Prof. R. Boese at University of Essen, Germany on Bruker SMART diffractometer in the ω-2θ scan mode. Data on **4•DME** was collected on Enraf-Nonius MACH-3 diffractometer at University of Hyderabad. The incident radiation used for collecting the data is Mo-Kα X-ray (λ = 0.71073 Å). The structure solutions and refinements of the crystal structures were performed with SHELX97.[28] All the geometrical analysis was carried out with PLATON[29] on Silicon Graphics computer.

3.8 References and notes

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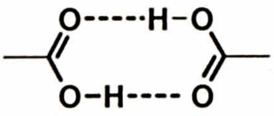
CHAPTER FOUR

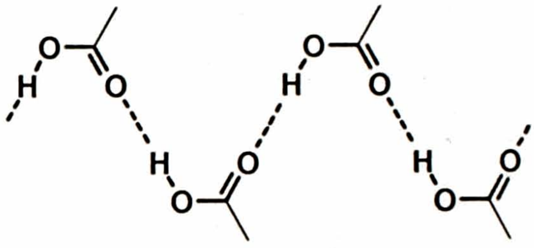
trans-1,4-DITHIANE-1,4-DIOXIDE: A NOVEL SPACER FOR CRYSTAL ENGINEERING

4.1 Introduction

The carboxylic acid group is the most studied hydrogen-bond functionality in crystal engineering.[1] O–H···O hydrogen bonds in carboxylic acids have featured significantly in the design and building of many supramolecular architectures.[2] Since it has a strong hydrogen bond donor as well as an acceptor, carboxylic acid group can readily form self-recognition hydrogen bonded patterns. The hydrogen bond formed by O–H donor group and C=O acceptor group of acid is strong and directional. Carboxylic acid functionalities are the second most common category of molecules archived in Cambridge Structural Database (CSD).[3] Robustness and repetivity of supramolecular synthon[4] make it a reliable design element in non-covalent synthesis.[5] In this context, the occurrence frequencies of 75 common ring motifs assembled with conventional hydrogen bonds in the CSD were classified by Allen *et. al.* recently.[6] Carboxylic acids form the centrosymmetric dimer **I** as the dominant aggregation pattern, but the occurrence frequency is modest, *ca.* 33% for all acids. When there is no competing functional group present, the probability increases to 96% in monocarboxylic acids. Open hydrogen bond catemer array **II** and single and double connected recognition motifs with alcohol and water molecules **III** and **IV** are also well known patterns of carboxylic acids.[7] Recognition of acid functional group with other complementary groups such as pyridine is more frequent.[8] This concept was invoked in the cocrystallization experiments of carboxylic acids with ketopiperazines.[9] A very recent CSD study[10] on the competition of different acceptor groups for the carboxylic acid donor showed that aggregations of O–H group of carboxylic acids with heteroatoms (N, S=O, P=O, N^+–O^-) are more preferable compared to dimer and catemer motifs with itself, e.g., acid-pyridine O–H···N hydrogen bond is found in 91% crystal structures that have both carboxylic acid and pyridine functional groups. This study highlights that the acid-acid aggregation does not generally form when a better acceptor is present in the system. Thus crystal design may be implemented by exploiting robust recognition in a heterosynthon.[11]



I



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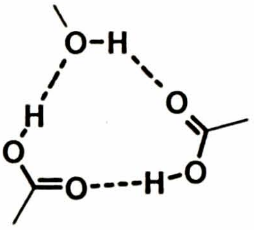
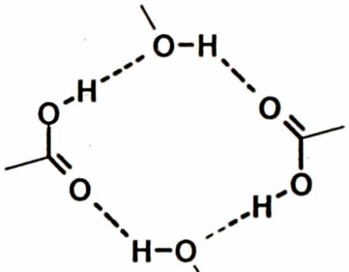


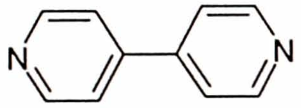
III



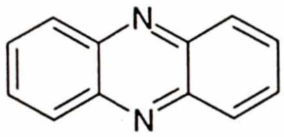
IV

4.2 Complementarity of carboxylic acid with other functional groups

The main goal in the design strategies is to identify reliable and robust supramolecular synthons. Many functional groups have been studied in a systematic way to identify reliable supramolecular synthons. Many of the best-known supramolecular synthons rely on the complementarity of two hydrogen-bonding groups. Such complementarity of two motifs has been utilized to synthesize many supramolecular architectures of acids. Many of the known systems exhibit bimolecular motifs with two strong hydrogen bonds or two weak hydrogen bonds. But the motifs with one strong hydrogen bond and one weak hydrogen bond are uncommon. In this context, 4,4'-bipyridine and its analogues, phenazine and 2-pyridone have emerged as spacer ligands. 4,4'-bipyridine **1**, and its analogues are utilized in the construction of many architectures *via* synthon **V**.[12] The robust heterodimer carboxylic acid-phenazine synthon **VI** was exploited in cocrystallization experiments of phenazine **2** with carboxylic acids, as phenazine is able to act as spacer between acid dimer.[13] Aakeröy[14] and Jones[15] used 2-pyridone **3** as a building block for binary cocrystallization with carboxylic acids as shown in synthons **VII** and **VIII**. A common feature observed in the molecular complexes formed by acids with the above mentioned ligands is that these ligands connect the acid molecules in a centrosymmetric manner and thus act as hydrophobic spacers in between acid dimers. In this context, our interest arose from the heterodimer **X** formed by acids with DMSO.



1



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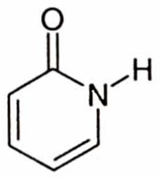

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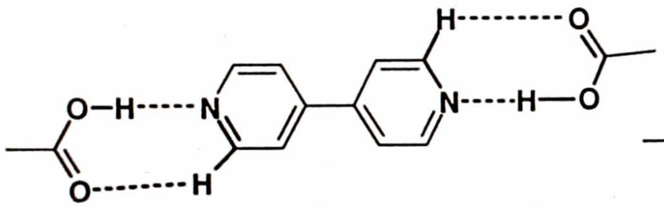

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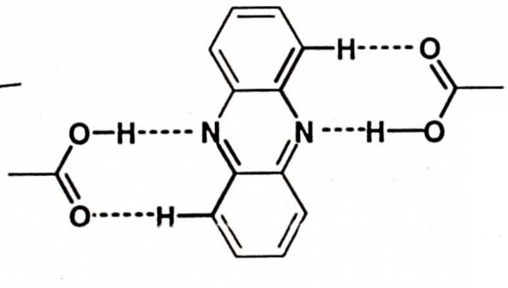
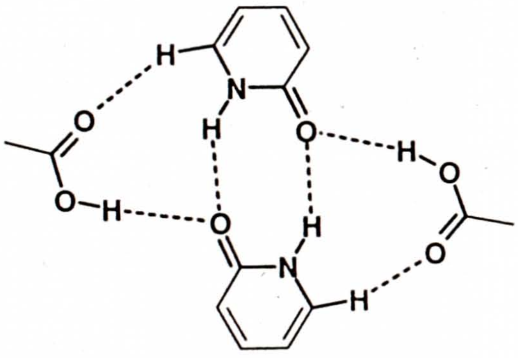
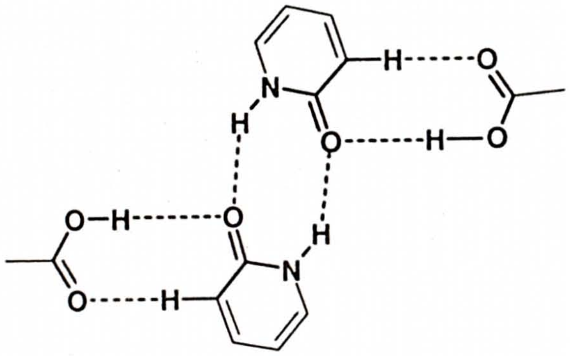


VI

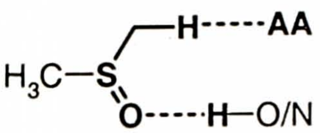


VII

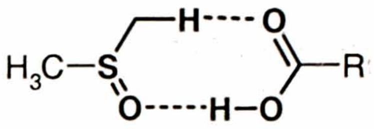


VIII

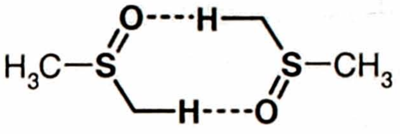
4.3 Recognition of carboxylic acids with DMSO



IX

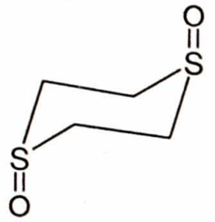


X



XI

Dimethylsulfoxide (DMSO) can act both as a potential donor (acidic C–H groups) and as a potential acceptor (S^+–O^-). DMSO has one of the highest tendencies among common solvents to be included in organic crystals. In a recent CSD study,[16] it was pointed out that DMSO has the second highest tendency for inclusion in crystals and this preference of DMSO for inclusion owes to its dual role in hydrogen bonding, acting as an efficient acceptor at the S=O group and as an effective C–H donor. Supramolecular synthons such as **IX**, **X** (a special case for carboxylic acids) and **XI** (self-association) were found to be particularly common in the crystal structures of DMSO solvates. The importance of synthon **X** was already mentioned by Weber *et. al.*,[17] many years ago in the study of DMSO solvates of some carboxylic acids. More recently, the role of DMSO in promoting crystallization of the gamboge pigment, guttiferic acid, has been described in terms of the persistence of synthons **X** and **XI.**[18] The CSD study of Steiner[10] also shows that acid-sulfoxide hydrogen bond O–H···O=S was found in 78% of crystal structures having the constituent moieties. New hydrogen bonded DMSO solvates of acids and other compounds continue to be reported regularly, with the special function of DMSO being highlighted.[19] To summarize, the ability of DMSO to form multi-point hydrogen bonded recognition patterns with the solute combined with its propensity for self-aggregation that result in its pronounced tendency to form solvates.



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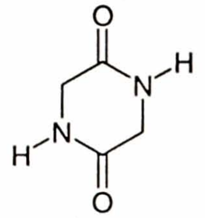

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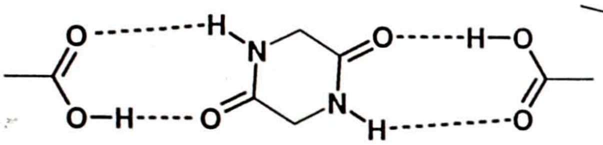
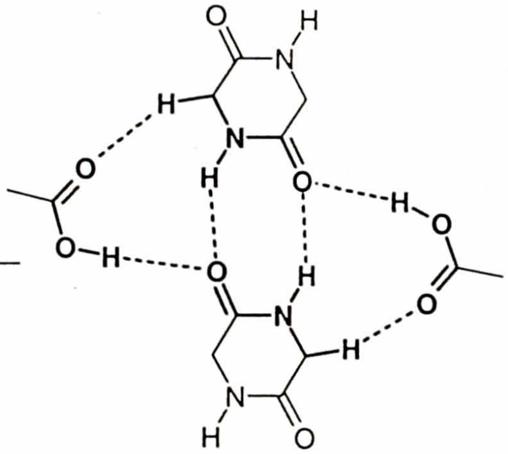
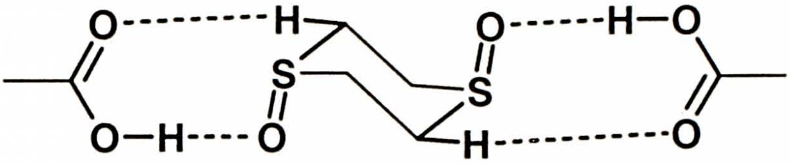


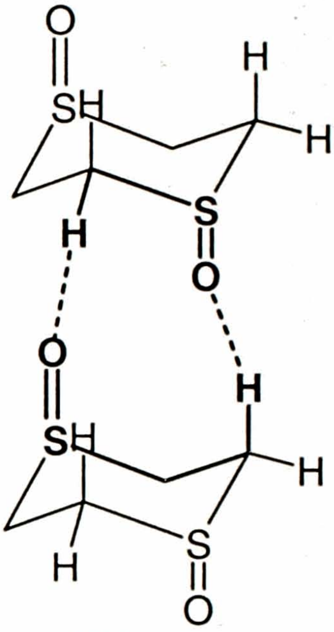


XII **XIII**

These observations prompted the present study of *trans*-1,4-dithiane-1,4-dioxide, **4**, a molecule that may be considered as a DMSO dimer equivalent. Further, disulfoxide **4** may be viewed as a C–H···O surrogate of 2,5-piperazinedione **5**, a diketone that has been used to prepare molecular complexes with salicylic acid[20] and formic acid.[21] It has been noted that diketopiperazine **5** aggregates with acids in two patterns. In one case the molecule itself is acting as a spacer by connecting the acid molecules. In the other case the self-assembled pattern acts as a spacer between acid moieties. The two patterns formed by **5** are shown as **XII** and **XIII**. The hydrogen bond forming abilities of **4** are expected to be nearly the same as DMSO (synthons **IX–XII**); the O-atoms of S=O are good hydrogen bond acceptors and the adjacent hydrogen atoms are activated C–H donors. Our interest in disulfoxide **4** accordingly arose from its potential as a hydrogen bond spacer in crystal engineering of carboxylic acids to extend the dimer pattern **I** to **XIV**.



XIV



XV

4.4 *trans*-1,4-Dithiane-1,4-dioxide as a novel spacer ligand

The crystal packing in complexes of **4** with 5-nitrosalicylic acid, **6**; succinic acid, **8**; 3,5-dinitrosalicylic acid, **7** and oxalic acid, **9** are described. The last molecular complex has been obtained as a hydrate. The C–H···O hydrogen bond forming ability of **4** is best appreciated by a study of its native crystal structure.[22] This structure was determined several years ago and is illustrated in Figure 1. Notably, synthon **XI** in DMSO is linearly extended to the 1-D tape pattern **XV**. It is significant to mention that cocrystallization of sulfoxide **4** was attempted with large number of mono, di and tricarboxylic acids (adipic acid, maleic acid, tartaric acid, trimesic acid, benzoic acid, bromoacetic acid and squaric acid), but cocrystals were obtained from the above mentioned four acids only. Cocrystals (**8**)•(**4**), (**7**)•(**4**) and (**9**)$_{0.5}$•(**4**)$_{0.5}$•(H_2O) were obtained from aqueous medium. The crystals of (**6**)•(**4**)$_{0.5}$ were obtained from a related experiment on cocrystallization of **7** with 1,4-dithiane in hot dioxane. Instead of expected (**7**)•(dithiane) cocrystals, (**6**)•(**4**)$_{0.5}$ crystallized from dioxane. This may be because the dithiane is oxidized to **4** and it crystallized *in situ* with **6**, which was present as an impurity in **7**. When cocrystallization of **4** with **6** was attempted in an independent experiment, no cocrystal was obtained. Although the exact reason why additive and impurities promote crystallization of elusive forms is not fully understood, examples are known in other systems also.[23]

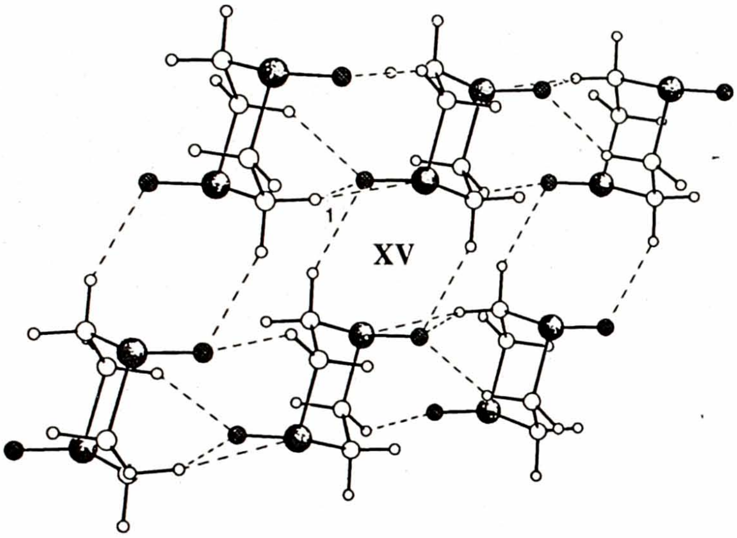


Figure 1. The crystal structure of *trans*-1,4-dithiane-1,4-dioxide **4**. Notice the synthon **XV**.

4.4.1 (5-Nitrosalicylic acid)•(*trans*-1,4-dithiane-1,4-dioxide), (6)•(4)$_{0.5}$

The crystal structure of **(6)•(4)**$_{0.5}$ in space group $P2_1/c$ is displayed in Figure 2. The most relevant pattern is based on synthon **XIV** with strong O–H···O (1.58 Å, 169.7°) and C–H···O (2.97 Å, 125.6°) hydrogen bonds between the carboxylic acid group and the disulfoxide. Disulfoxide **4** acts as a spacer between acid molecules, disrupting the usual carboxyl dimer synthon **I**. Synthon **XIV** may be viewed as a homologous dimeric extension of synthon **X**. An alternative mode of spacer action, exclusively *via* C–H···O hydrogen bonding is also seen as shown in Figure 2. The acidic C–H donor groups in disulfoxide **4** connects the inversion related acid molecules *via* C–H···O hydrogen bonds, shown as c and d in Figure 2 (Table 1).

Auxiliary C–H···O hydrogen bonds are formed to the nitro group. All in all, nearly all the hydrogen bonding sites in disulfoxide **4** are fully utilized. The phenolic O–H donor in **6** is intramolecularly hydrogen bonded to the carbonyl oxygen of acid group.

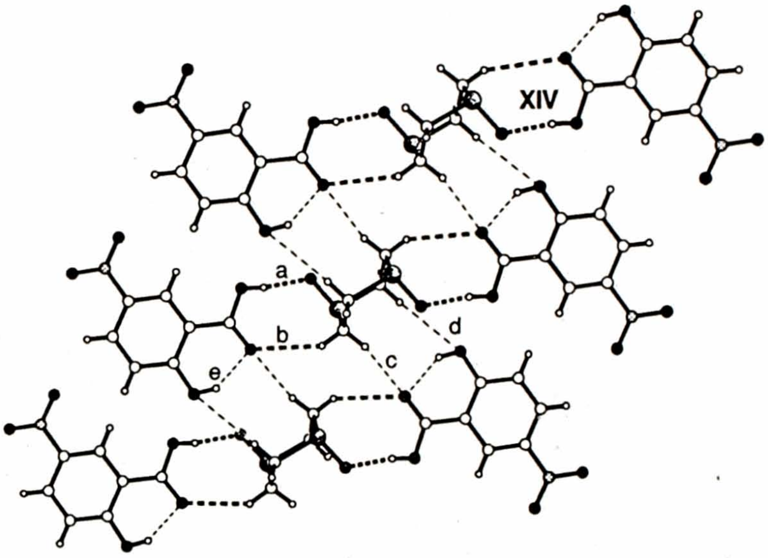


Figure 2. Crystal structure of (5-nitrosalicylic acid)•(*trans*-1,4-dithiane-1,4-dioxide)$_{0.5}$ (**6**)•(**4**)$_{0.5}$. Notice the role of synthon **XIV** in stabilizing the molecular complex.

4.4.2 (Succinic acid)•(*trans*-1,4-dithiane-1,4-dioxide), (8)•(4).

The structure is shown in Figure 3. The molecular complex crystallizes in triclinic space group $P\,\bar{1}$. The crystal structure contains an infinite 1-D pattern of disulfoxide and diacid molecules mediated by synthon **XIV**. Such tapes are in turn connected by C–H···O interactions (c), (d) and (e). Molecular complexation is presumably results from the fortuitous equivalence in the sizes of **4** and **8**. In effect, disulfoxide **4**, acts as a spacer in two-dimensions; along one dimension it is an O–H···O, C–H···O spacer and along the other it is a C–H···O, C–H···O spacer. The 1-D infinite pattern observed in this structure may be viewed as linear extension of synthon **X**. The formation of a unique structure through matching of critical molecular dimensions is also observed in a rare type of diamide packing, exemplified by succinamide, acetylenedicarboxamide and fumaramide.[24] The metrics of the intermolecular interactions are given in Table 1.

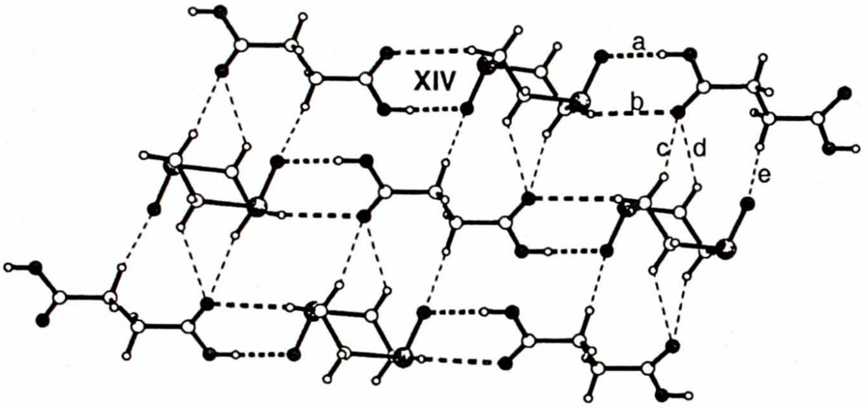


Figure 3. Crystal structure of (succinic acid)•(*trans*-1,4-dithiane-1,4-dioxide), (8)•(4). Notice the finite synthon **XIV** is extended to an infinite 1D tape.

4.4.3 (3,5-Dinitrosalicylic acid)•(*trans*-1,4-dithiane-1,4-dioxide), (7)•(4).

The molecular complex (*trans*-1,4-dithiane-1,4-dioxide)•(3,5-dinitrosalicylic acid), (7)•(4) adopts a centrosymmetric space group ($P2_1/n$). In this complex, self-association of inversion related molecules of disulfoxide **4** *via* C–H···O hydrogen bonding results in an infinite 1-D pattern **XV**. Such 1-D pattern is also observed in the crystal structure of **4.** The molecule **4** occupies a general position, and there are two inversion related tapes which are inturn, connected *via* C–H···O interactions. This entire pattern acts as a spacer between carboxylic acid molecules. The inversion related carboxylic acid molecules are connected to two inversion related molecules in the 1-D tape in such a way that the carboxylic acid is connected to two different molecules of **4** as shown in Figure 4. Once again, the carboxyl group is hydrogen bonded in an O–H···O and C–H···O fashion concurrently. The phenolic hydrogen is intramolecularly hydrogen bonded to the carbonyl oxygen (1.67 Å, 145.1°). Topologically similar synthons are also observed in the crystal structures of complexes of 2-pyridone with carboxylic acids[14,15] and diketopiperazine with formic acid.[21] The 1-D pattern constructed with synthon **XV** in this structure may be viewed as linear extension of synthon **XI**. The geometrical parameters of the intermolecular interactions are given in Table 1.

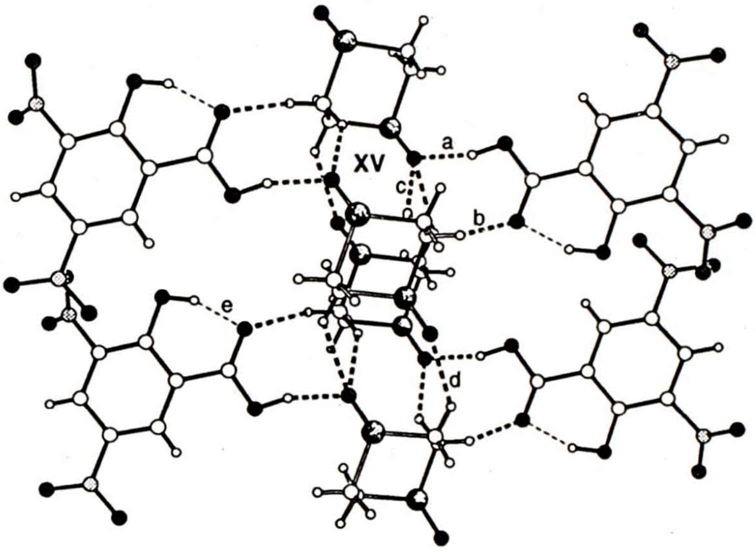


Figure 4. Crystal structure of (3,5-dinitrosalicylic acid)•(*trans*-1,4-dithiane-1,4-dioxide)$_{0.5}$ (**7**)•(**4**). Notice the self assembled pattern **XV** is acting as a spacer between acid molecules.

4.4.4 (Oxalic acid)•(*trans* 1,4-dithiane-1,4-dioxide)•(dihydrate), $(9)_{0.5}$•$(4)_{0.5}$•(H_2O).

The molecular complex of oxalic acid sulfoxide crystallizes in space group $P\bar{1}$ as a dihydrate. The inclusion of water in this ternary complex is not surprising, because oxalic acid crystallizes as a dihydrate in its native crystal structure.[25] The linear C–H···O mediated tape **XV** formed by sulfoxide molecules acts as a hydrophobic spacer between hydrated oxalic acid molecules and there is an elaborate network of O–H···O and C–H···O hydrogen bonds (Table 1). The acid group is connected to water molecules and the water molecules are inturn connected to sulfoxide molecule as shown in Figure 5b. Even more interestingly, if the oxalic acid dihydrate structure is divided into regions as shown in Figure 5a, it may be observed that disulfoxide **4** acts as a spacer between these regions in the structure of the ternary complex (Figure 5b). This produces a staircase-like pattern as shown in Figure 6. The oxalic acid molecules and water molecules constitute the flat step and the sulfoxide molecules give the height to the staircase. Such staircase networks were also identified recently in the crystal structures of pyrazine-2,3-dicarboxamide,[26] the molecular complex of benzene-1,2,4,5-tetracarboxylic acid and hexamethylenetetramine,[27] and in the inclusion compounds of tetrahalodiquinoline.[28]

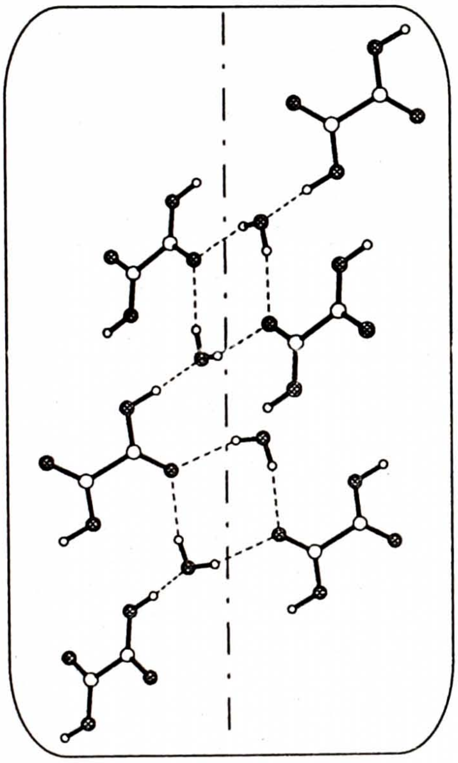


Figure 5a. The crystal structure of oxalic acid dihydrate.

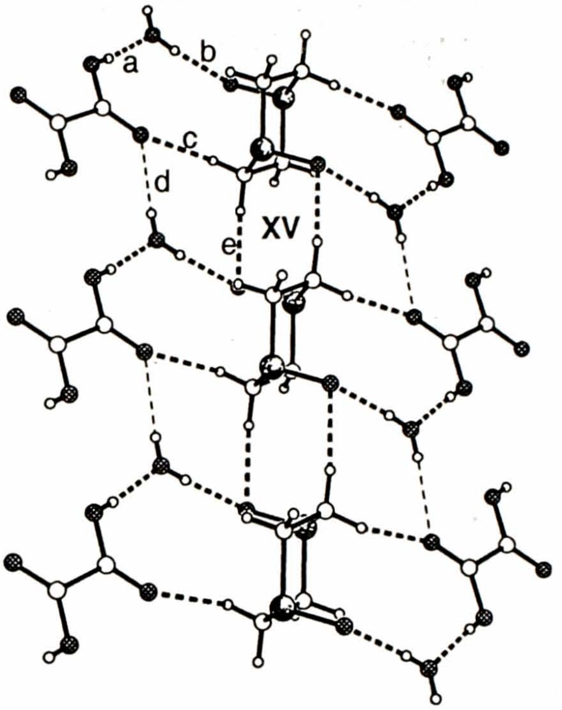


Figure 5b. Crystal structure of (oxalic acid)•(*trans*-1,4-dithiane-1,4-dioxide)•(dihydrate), $(\mathbf{9})_{0.5}$•$(\mathbf{4})_{0.5}$•(H_2O). Notice the interruption of acid-sulfoxide recognition by water molecule that connects the translation related oxalic acid molecules and sulfoxide molecules.

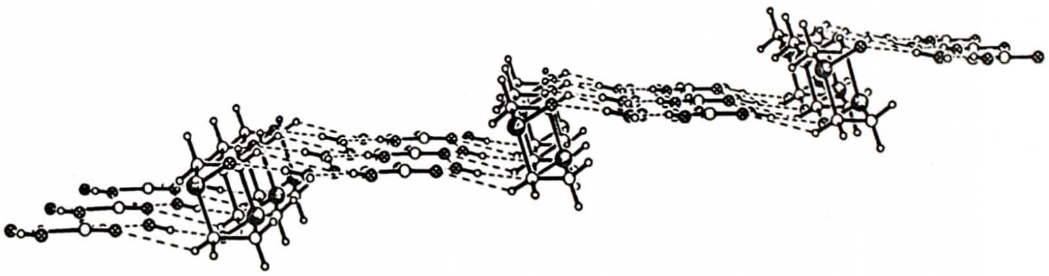


Figure 6. The staircase network formed by (oxalic acid)•(*trans*-1,4-dithiane-1,4-dioxide)•(dihydrate), $(\mathbf{9})_{0.5}$•$(\mathbf{4})_{0.5}$•(H_2O).

Table 1. Geometrical Parameters of Intermolecular Interactions

Complex	Interaction[a]	d (Å)	D (Å)	θ (deg)
(6)•**(4)**	a) O–H···O	1.58	2.554(3)	169.70
	b) C–H···O	2.97	3.752(3)	125.61
	c) C–H···O	2.46	3.479(3)	154.84
	d) C–H···O	2.77	3.833(3)	165.97
(7)•**(4)**	a) O–H···O	1.64	2.625(2)	176.54
	b) C–H···O	2.54	3.385(2)	133.97
	c) C–H···O	2.23	3.297(2)	166.28
	d) C–H···O	2.74	3.512(2)	127.89
	e) C–H···O	2.45	3.405(2)	146.06
(8)•**(4)**	a) O–H···O	1.59	2.542(3)	163.01
	b) C–H···O	2.40	3.346(4)	145.25
	c) C–H···O	2.40	3.276(4)	136.98
	d) C–H···O	2.58	3.466(3)	138.29
(9)•**(4)**(dihydrate)	a) O–H···O	1.57	2.544(2)	169.90
	b) O–H···O	1.74	2.716(2)	174.89
	c) C–H···O	2.82	3.494(2)	120.01
	d) O–H···O	1.94	2.918(2)	171.01
	e) C–H···O	2.28	3.268(3)	151.15

[a] O–H and C–H distances are neutron normalized (0.983 and 1.083 Å)

4.5 Database analysis

The occurrence of O–H···O and C–H···O hydrogen bonded synthon **X** between acid and sulfoxide groups was examined in the CSD (ConQuest 1.4, April 2002, 257, 162 entries). A sub-database of organic structures that contain CO$_2$H and CH$_2$S=O moieties with no disorder, 3D coordinates present, no errors, no ions, not polymeric, and with R factor <0.10 was created (48 hits, duplicate refcodes removed). A search of these 48 crystal structures was carried out for the occurrence of synthon **X** in the distance range: 1.5< O–H···O <2.2 Å, 140< ∠O–H···O <180° and 2.0< C–H···O < 3.0 Å, 120< ∠C–H···O <180° (O–H and C–H distances neutron normalized). Of the 20 hits retrieved, 11 structures are solvates of DMSO. The occurrence probability of synthon **X** when constituent functional groups are present, is roughly 42%. Acid-acid recognition was not observed when the sulfoxide moiety is present.

4.6 Energy calculation

The next exercise was to calculate the energy of centrosymmetric acid-acid dimer **I**, acid-sulfoxide synthon **X** and sulfoxide-sulfoxide synthon **XI** to rationalize why synthon **X** is preferred. This was implemented on acetic acid and dimethyl sulfoxide as models in RHF 6-31 G* basis set (Spartan Pro 1.0).[29] The computed minimum energies of synthons **I**, **X** and **XII** are -13.82, –15.54 and –7.41 kcal/mol, respectively. Thus formation of synthon **X** is energetically favored over synthons **I** and **XI** by 4.7 kcal/mol [(15.54 + 7.41) – (2 x 13.82) = –4.69]. A possible reason why crystal structures with combination of strong and weak hydrogen bond synthons are formed in preference to strong-strong and weak-weak hydrogen bonding is that propagation of crystal nuclei into larger aggregates and then to stable crystal is more likely in the former case. Crystal structures with isoenergetic combination of strong-strong and weak-weak hydrogen bonding motifs presumably dissociate at the weak-weak interface prior to reaching the final stages of crystallization.

4.7 Conclusion

trans-1,4-Dithiane-1,4-dioxide **4** is identified as a new spacer ligand for carboxylic acids. Crystal structures of **4** with four different carboxylic acids are described. The molecule is highly soluble in water and almost insoluble in organic solvents. Disulfoxide **4** is an unusual molecule with dense hydrogen bonding functionality. The S=O groups are excellent acceptors and the C–H groups, being activated, are good donors. The enthalpy of acid-sulfoxide recognition is also energetically favoured over acid-acid and sulfoxide-sulfoxide recognition. Four cocrystals were isolated among a large number of acids used in crystallization experiments. This could be because the hydrogen bonding requirements are so specific that complexation is difficult. It is also possible that the sulfoxide is strongly hydrogen bonded to water and so does not form complexes readily. Increasing the hydrophobicity of the sulfoxide molecule, e.g. adding alkyl groups, bigger ring size, is one way to overcome the solubility problem. In all four cases, elaborate O–H···O and C–H···O networks are formed. Strong O–H···O and weak C–H···O hydrogen bonding is shown to stabilize the association between carboxylic acid and sulfoxide **4** in the four molecular complexes studied. Molecule **4** is shown to act as a spacer between carboxylic acids in two ways: as a single molecule and as a C–H···O mediated tape. The common feature in the four crystal structures discussed above is the ability of the sulfoxide **4** to disrupt the acid-acid recognition pattern in the molecular complexes.

4.8 Experimental Section

trans-1,4-Dithiane-1,4-dioxide, 4.

trans-1,4-Dithiane-1,4-dioxide was synthesized using reported procedure[30]. To a solution of 1,4-dithiane (1.2 g, 10 mmol) in glacial acetic acid (20 ml) was added 30% hydrogen peroxide (2.4 ml, 20 mmol). The mixture was allowed to stand in the room temperature for 24 h. Removal of the acetic acid followed by successive crystallizations from 1:1 mixture of water and ethanol yielded pure *trans*-1,4-dithiane-1,4-dioxide. The compound decomposes at 252 °C. IR (KBr): 3485, 1618, 1400, 1014, 628 cm^{-1}.

3,5-Dinitrosalicylic acid, 6. [31]

A total of 22.5 g of conc. H_2SO_4 and 4.5 g of conc. HNO_3 were mixed and cooled in ice water. Salicylic acid (4.5 g, 32mmol) was added in small portions keeping the reaction mixture well cooled. After all the salicylic acid was added, the material was poured into ca. 250 ml of water, cooled in ice, and filtered off by suction. The crude material was dissolved by heating in dil. Na_2CO_3 solution, filtered, and salted out by adding excess of sat. Na_2CO_3 solution, dissolved in hot water, any insoluble impurities filtered off, and precipitated as the free acid by adding large excess of conc. HCl. Suction filtration of **6** and recrystallization from hot water gave the moist acid that was dried at 100 °C. m.p. 169-171 °C; IR (KBR): 1676, 1608, 1533, 1338 cm^{-1}.

(5-Nitrosalicylic acid)•(*trans*-1,4-dithiane-1,4-dioxide), (6)•(4).

A mixture of 3,5-dinitrosalicylic acid hydrate prepared above (61.5 mg, 0.25 mmol) and 1,4-dithiane (15 mg, 0.125 mmol) were dissolved in 5 ml of hot 1,4-dioxane with the idea of obtaining **(6)•(dithiane)** cocrystals. X-ray diffraction showed these crystals to have the composition **(6)•(4)**. Dithiane is oxidized to *trans*-1,4-dithiane-1,4-dioxide in air and it crystallized *insitu* with 5-nitrosalicylic acid, which was present in small amount in dinitrosalicylic acid. m.p. 231-234° C.

(Succinic acid)•(*trans*-1,4-dithiane-1,4-dioxide), (8)•(4)

A 1: 1 mixture of succinic acid (118 mg, 1 mmol) and *trans*-1,4-dithiane-1,4-dioxide (152 mg, 1 mmol) were dissolved in cold water. Plate like, colorless crystals were collected after two weeks. m.p. 198-200 °C; IR (KBr): 3414, 1705, 1402, 1309, 1190, 993 cm^{-1}.

(3,5-Dinitrosalicylic acid)•(*trans*-1,4-dithiane-1,4-dioxide),(7)•(4).

A powered mixture of 3,5-dinitrosalicylic acid (114 mg, 0.5 mmol) and *trans*-1,4-dithiane-1,4-dioxide (38 mg, 0.25 mmol) were dissolved in hot water and kept at 80 °C for 2 days to yield a pale yellow solid. Yellow color, plate like crystals of the complex were obtained when the solid was recrystallized from 1:1 water-EtOH. m.p. 199 – 204 °C; IR (KBr): 1678, 1601, 1529, 1338, 1261, 1016 cm^{-1}.

(Oxalic acid)•(*trans*-1,4-dithiane-1,4-dioxide)•(dihydrate), $(9)_{0.5}$•$(4)_{0.5}$•(H_2O)

Colorless, plate like crystals of the complex were obtained by crystallization of equimolar amounts of oxalic acid (90 mg, 1 mmol) and trans-1,4-dithaine-1,4-dioxide (152 mg, 1 mmol) from 5ml of water. The complex decomposes at 240° C. IR (KBr): 3489, 1697, 1217, 1018 cm^{-1}.

X-ray crystallography

Data on cocrystals **(6)•(4)**$_{0.5}$ and **(7)•(4)** were collected on Enraf-Nonius MACH-3 diffractometer at University of Hyderabad and on crystals **(8)•(4)** and **(9)•(4)**•(dihydrate) were collected on Nonius FAST area detector instrument by Dr. H. L. Carrell and A. K. Katz, Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia, U. S. A. The incident radiation is Mo-Kα X-RAY (λ = 0.71073) on both instruments. Data on cocrystals **(6)•(4)**$_{0.5}$ and **(7)•(4)** were collected at 293 K and crystals of **(8)•(4)** and **(9)•(4)** (dihydrate) were cooled to 120 K with the MSC liquid nitrogen system low temperature device attached to the diffractometer. The structure solutions and refinements of all crystal structures were performed with the SHELX97.[32] All the geometrical analysis were carried out with PLATON[33] on Silicon Graphics computer.

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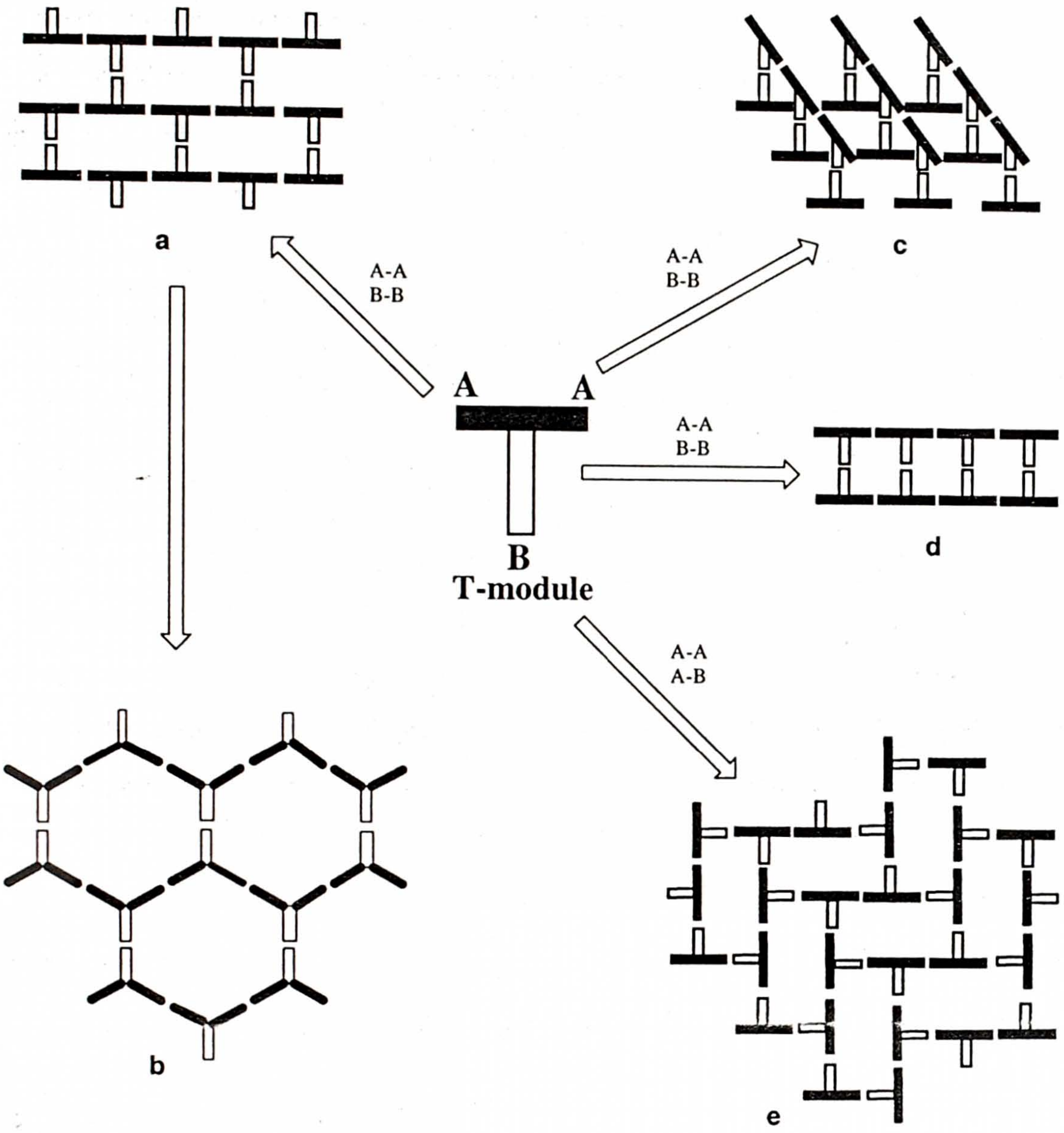
CHAPTER FIVE

BRICK WALL AND HEXAGONAL NETWORK STRUCTURES

5.1 Introduction

The design and synthesis of infinite two dimensional (2D) and three dimensional (3D) network structures using non-covalent soft bonds such as hydrogen bonds and strong metal-ligand coordination bonds is a current goal of crystal engineering.[1] Such network structures attract great attention due to their potential applications in materials science as functional solid materials[2] as well as fascinating structures.[3] One conceptual approach to building frameworks can be carried out by representing molecules as points or nodes and the intermolecular interactions connecting the molecules as node connectors.[4] A comprehensive catalogue of network structures of relevance to chemistry was compiled by Wells many years ago.[5] The network structures formed by coordination polymers have been studied extensively in recent years.[6] The recent review articles by Robson,[7] Zaworotko[8] and Yaghi[9] summarize many of the classical network structures. The topology of a given network is represented interms of the general symbol (*n*,*p*), where *n* is number of nodes in the smallest closed circuits in the net and *p* is the number of connections to neighboring nodes that radiate from any node. The network topology in coordination polymers can be usually designed by selecting the coordination geometry of metal and the chemical structure of organic ligands. A metal geometry of particular interest because of its potential range of network structures is simple and prototypal "T-shaped" module. Self-assembly of T-node molecules with three recognition sites produce ladder, brick wall, herringbone, or bilayer networks in crystal structures as shown in Scheme 1.[6] 2D brick wall and herringbone networks are topologically identical to the honeycomb grid because these are (6,3) nets. The conversion between topologically similar nets is controlled by supramolecular isomerism.[8] There are examples of supramolecular isomerism that are controlled by the conformation of the ligand[10] or by the nature of the solvent included.[11] Honeycomb architectures built from C_3 symmetric precursors, e.g. trisubstituted benzene, triazine and cyclohexane scaffold, are a popular target in organic structures.[12] Ladder, brick wall, bilayer and herringbone topologies are relatively common in coordination polymer systems,[6] i.e. crystal structures assembled with metal–ligand and hydrogen bonds. However, examples of organic structures in these network categories are fewer.[13] There is thus a need to develop strategies for the construction and modular control of ladder, brick wall and herringbone architectures using organic tectons. Tectons (Greek word tekton for "builder") are defined as "*molecules with sticky surface whose interactions are dominated by specific attractive forces that induce the assembly of aggregates with controlled geometries, and molecular tectonics is the art and science of supramolecular construction using tectonic subunits.*"[14] The exercise of generating network structures with organic molecules will expand the scope and diversity. In this chapter, the crystal structure of an organic T-shaped tecton, with a brick wall pattern is described. Further, the brick topology transforms to hexagonal and chair cyclohexane networks in its molecular complexes with spacer ligands 1,4-dioxane and *trans*-1,4-dithiane-1,4-dioxide.



Scheme 1. Various Network structures formed by T-shaped molecules a) brick wall b) hexagonal c) bilayer or tongue-and-groove d) ladder e) herringbone or parquet floor networks. Note the isomerism between topologically related brick wall and hexagonal networks.

5.2 T-Node coordination polymers: Recent literature

Coordination polymers illustrate how crystal engineering has formed a basis for the design of new network structures. In this context, the work of Wells is extensive and decisive and serves as a reference point.[5] Predictable self-organization of molecules into 2D, or 3D architectures requires an explicit knowledge of the controlling factors involved in the construction. The controlling factors that operate in the network structures of coordination polymers are metal coordination geometry, influence of counter anions or solvent molecule on the metal coordination sphere and its functionality and geometry of the ligand in addition to the metal/ligand ratio affecting the formation of coordination complexes. These factors are utilized appropriately to design coordination polymers by identifying recurring directional preferences of coordination bonds for transition metals in a series of complexes. The T-node coordination polymers that produce network structures with (6,3) topology may be obtained with a 1:1.5 ratio of metal ions to a linear spacer ligands (such as bipyridine, 4,4'-azopyridine, 1,2-dipyridyl ethane etc.). For example, the crystal of $[Co_2(azpy)_3(NO_3)_4]\bullet(Me_2CO\bullet 3H_2O)$ **1** has been obtained with 1:1.5 ratio of cobalt(II)nitrate to 4,4'-azopyridine (azpy) from acetone.[15] Self assembly of **1** produces a brick wall network as shown in Figure 1. The network includes acetone and water molecules as guests.

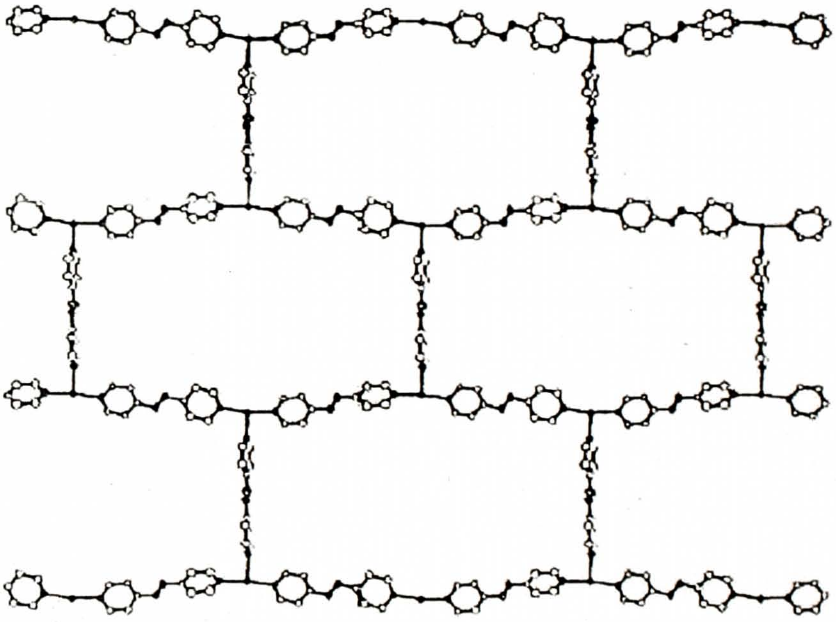


Figure 1. The brick wall network in the crystal structure of $[Co_2(azpy)_3(NO_3)_4]\bullet(Me_2CO\bullet 3H_2O)$ **1**. The nitrate anions and the guest molecules are omitted for clarity.

Two coordination polymers $[Cd(NO_3)_2(C_{12}\ H_{10}\ N_4)_{1.5}{\bullet}CH_2Cl_2]_n$, **2** and $[Co(NO_3)_2(C_{12}\ H_{10}\ N_4)_{1.5}{\bullet}CH_2Cl_2]_n$, **3** with T-node have been synthesized from the corresponding metal(II) nitarte hydrates and the bidentate donor ligand 1,4-bis(3-pyridyl)-2,3-diaza-1,3-butadiene and the structures were investigated.[16] The structures are isomorphous and both the crystals form noninterpenetrating (6,3) polycyclohexane network. CH_2Cl_2 molecules are incorporated in the network as guest molecules. The polycyclohexane network structure is shown in Figure 2.

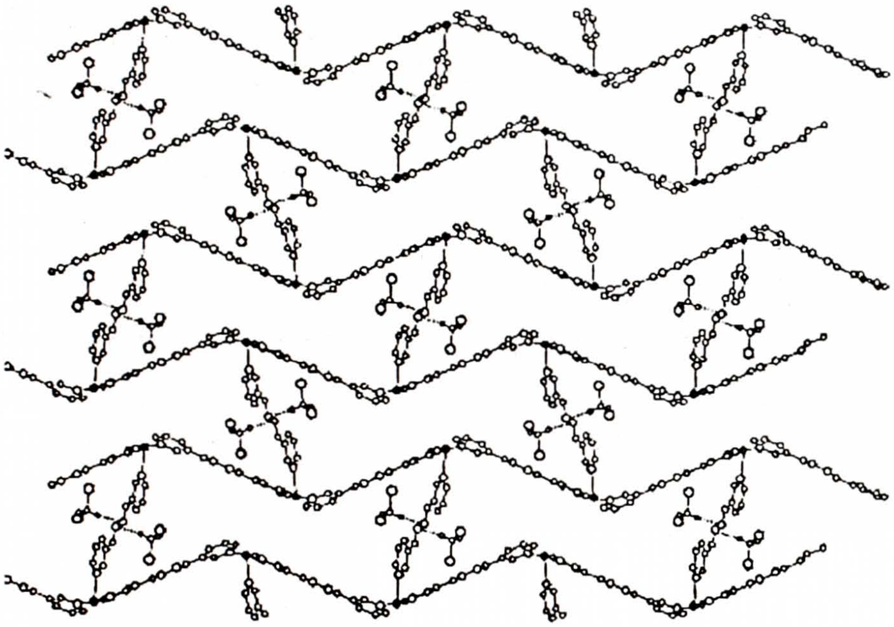
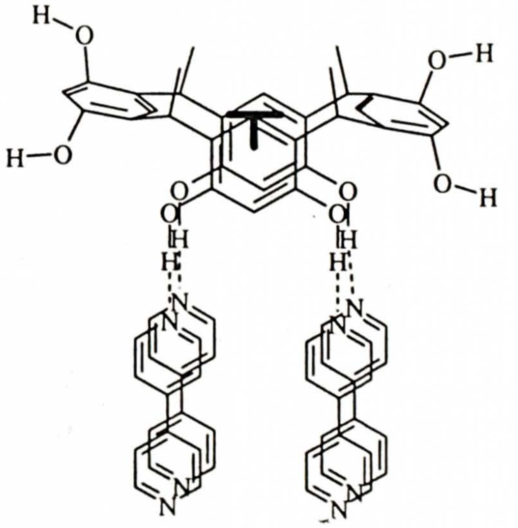


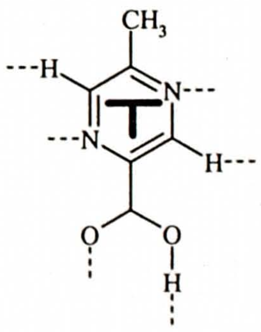
Figure 2. Polycyclohexane network observed in the structures of coordination polymers **2** and **3**.The metal centers are shown as black circles. CH_2Cl_2 guest molecules are included in the cyclohexane rings.

5.3 Organic T-modules

The factors that should be considered for the crystal engineering of organic networks with T-modules are: (i) a T-geometry at the metal center is easily achieved in square planar, octahedral and trigonal bipyramidal coordination with appropriate ligands, but it is difficult to design a T-shaped organic molecule given that the standard angles at carbon are 109°, 120° or 180°; (ii) in coordination polymer networks, the metal atom acts as the node and the ligands serve as the node connectors, whereas in organic networks the molecule is the node and hydrogen bonds and intermolecular interactions are the node connections; (iii) metal–ligand coordination bonds are strong and directional (30–60 kcal/mol), whereas hydrogen bonds (O–H···O, N–H···O, C–H···O; energy 2–10 kcal/mol)[17] exhibit moderate directionality in crystals. Because of (i) organic molecules generally do not adopt a T-node. The molecular complex of 4,4'-bipyridine with C-methylcalix[4]resorcinarene **4** adopts a T-module in its crystal structure results in the formation of a 2D brick framework,[13a,b] that possesses nanoscale cavities inwhich, aromatic guests are incorporated. But the T-module is supramolecular in nature. Very recently, in our research group 5-methylpyrazine-2-carboxylic acid **5** was identified as an organic T-node molecule,[13c] with T-node with three hydrogen bonding recognition sites on its molecular periphery. If the T-module is viewed as having two A and one B type hydrogen bond sites, then recognition via one A···A and two A···B interactions results in the herringbone network (Figure 3) in the crystal structure of **5**. Brick wall frameworks and hydrogen-bonded ladder networks are also obtained in the family of guanidinium–sulfonate lamellar architectures[18] and in some crystalline diols[19] respectively. These structures cannot be viewed as built from T-shaped building blocks.



4



5

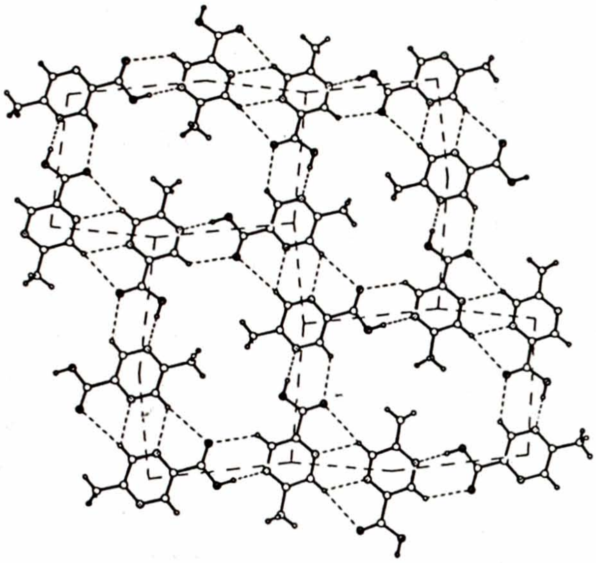
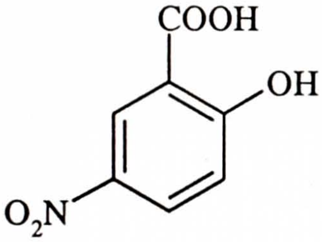


Figure 3. Herringbone network observed in **5**.

5.4 Brick wall network in 5-nitrosalicylic acid



6

As a part of an ongoing study on polymorphism and pseudopolymorphism,[20] the crystal structures of 5-nitrosalicylic acid **6** and its dioxane solvate were examined. A close examination of the structure of 5-nitrosalicylic acid shows the molecule as an organic analogue to T-node coordination polymer.

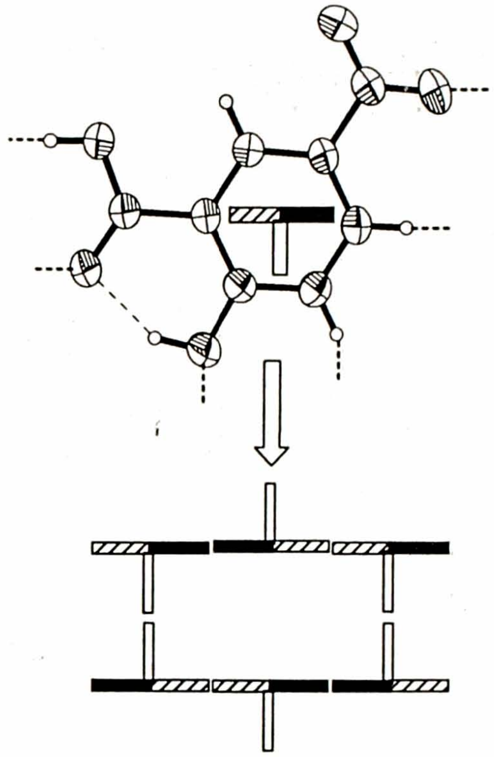
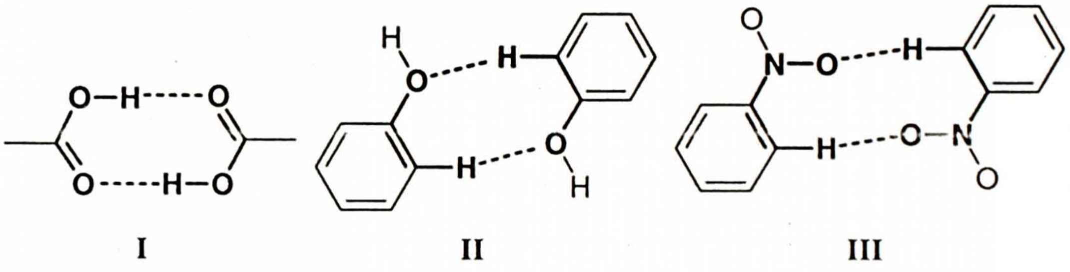


Figure 4. T-shaped molecule **6** with O–H···O, C–H···O and C–H···O hydrogen bond donors that furnish T-shape to the molecule.



Scheme 2

Compound **6** crystallize in triclinic space group $P\,\bar{1}$. The dominant hydrogen bond pattern is the centrosymmetric dimer formed by the carboxylic acid group. Acid **6** has three different types of hydrogen bond groups as shown in Scheme 2 for bidentate recognition on its densely functionalized molecular periphery: COOH group as O–H donor and C=O acceptor, (Ph)C–H donor and OH acceptor, (Ph)C–H donor and (nitro)O-acceptor. The three recognition sites furnish a T-shape to the molecule as shown in Figure 4. Each molecule in the crystal structure is hydrogen bonded to three of its inversion related partners *via* centrosymmetric synthons **I**, **II** and **III**. The COOH group forms the expected dimer synthon **I** with O–H···O hydrogen bond (d, θ: 1.70 Å, 178.7°). The other two node connections of the T-molecule extend via C–H···O dimers **II** and **III** involving activated C–H donors and phenolic and nitro O-acceptors (2.36 Å, 174.1°; 2.45 Å, 137.2°). The OH group is intramolecular hydrogen bonded to the carbonyl oxygen of COOH group (1.75 Å, 147.3°). If the T-module is viewed as having two A and one B type hydrogen bond sites, then recognition *via* two A···A and one B···B interactions results in the brick wall architecture as shown in Figure 5. If the molecules are reduced to nodes and the intermolecular interactions are considered as node connectors, then the result is seen in Figure 6.

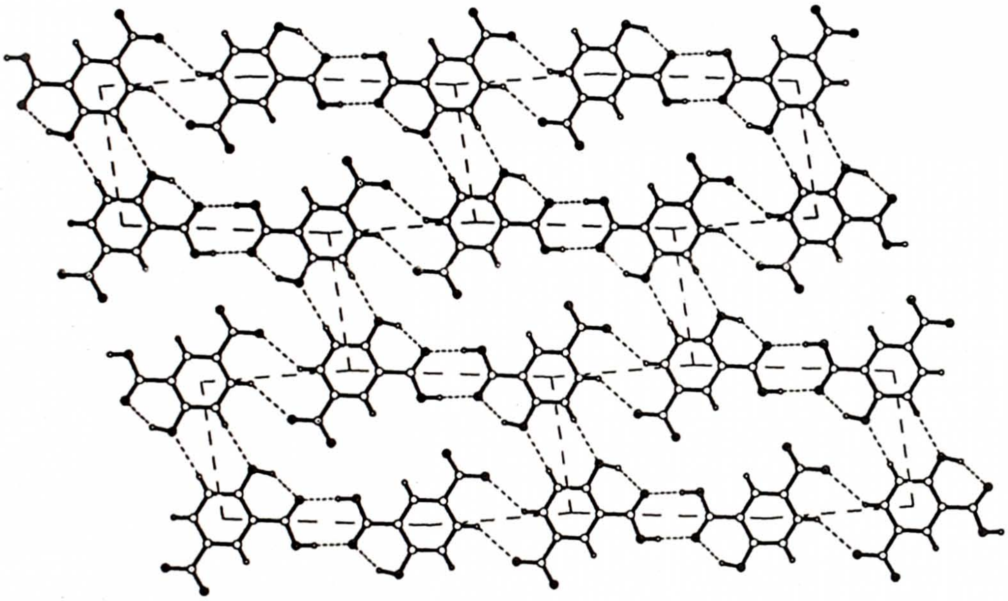


Figure 5. Crystal structure of **6** to show the brick wall network. Note the self-assembly of T-module *via* like recognition, A···A and B···B, to produce the brick wall architecture.

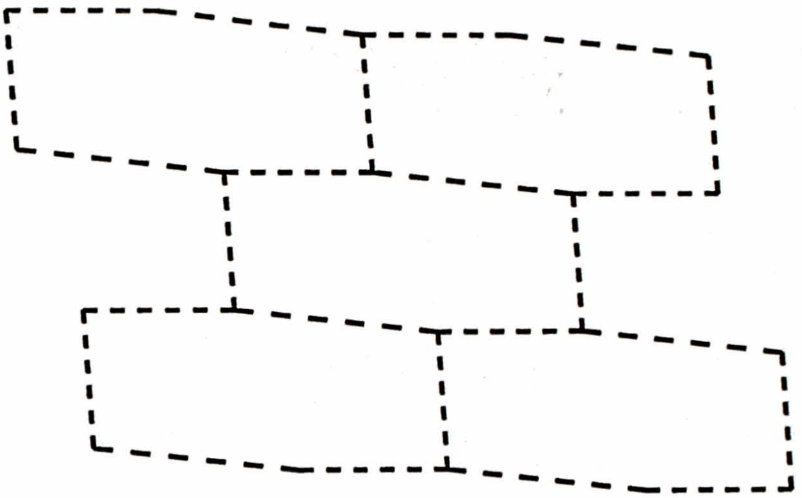
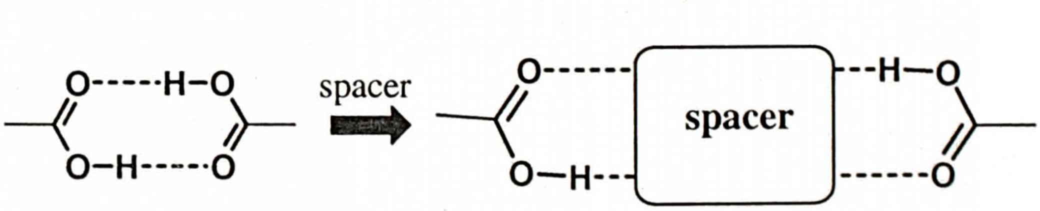


Figure 6. Supramolecular brick wall network in **6**. Molecules are reduced to nodes and the node connectors are the intermolecular interactions.

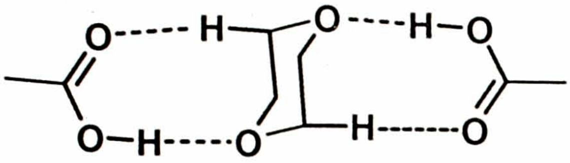
5.5 Honeycomb and cyclohexane networks

The next task was to expand the brick wall network of **6** in a modular fashion using the robust and reliable recognition of carboxylic acid with spacer ligands, e.g. 4,4'-bipyridine, phenazine, pyrazine, and 2-pyridone as shown in Scheme 3. Crystallization of **6** with 4,4'-bipyridine gave salt formation while no co-crystals were obtained with phenazine and pyrazine, presumably because of solubility mismatch. Continuing further, the compound **6** was crystallized from 1,4-dioxane, as it is known to extend the acid dimer pattern linearly in the case of 3,5-dinitrosalicylic acid *via* synthon **IV**.[20] In the same manner, the crystal structure of the molecular complex of **6** with *trans*-1,4-dithiane-1,4-dioxide (**DTDO**) was analysed.[21]



Scheme 3

5.5.1 Brick wall to pseudo honeycomb network



IV

Single crystals of the 2:1 complex, **6•dioxane** were obtained at ambient temperature and it crystallizes in monoclinic space group $P2_1/c$. In the crystal structure, dioxane molecule acts as spacer between acid molecules. The expected synthon **IV**, acid–dioxane–acid (O–H···O: 1.64 Å, 168.6°), further fortified by a (dioxane)C–H···O(carbonyl) hydrogen bond (2.74 Å, 127.7°) aggregates molecules along one direction. The ortho-C–H groups of **6** donate hydrogen bonds to the nitro and carboxyl O-acceptors of a *c*-glide related molecule, and further this molecule accepts C–H···O bonds from another *c*-glide related molecule (3.07 Å, 176.3°; 2.26 Å, 162.4°). To complete the structure, a C–H···O hydrogen bond connects **6** and dioxane (2.43 Å, 128.1°). The phenolic OH group forms an intramolecular O–H···O bond (1.78 Å, 143.1°) with carbonyl oxygen. In effect, the T-shaped molecular node in the parent crystal structure adopts a Y-geometry (Figure 7) because the same donor and acceptor groups of **6** now engage in different hydrogen bond motifs. As a result, the brick wall pattern of **6** transforms to a pseudo-honeycomb topology in **6•dioxane**. The pseudo-honeycomb pattern is shown in Figure 8.

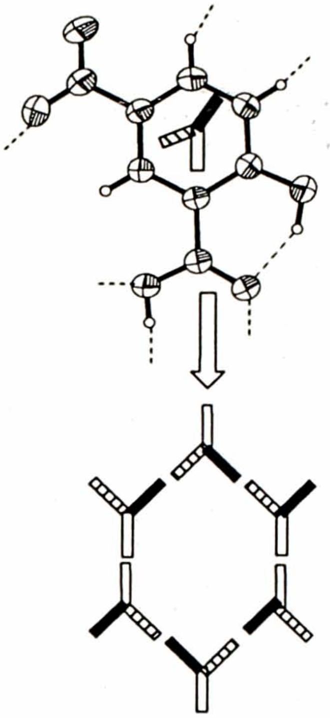


Figure 7. Y-shaped molecule **6** in **6•dioxane** solvate.

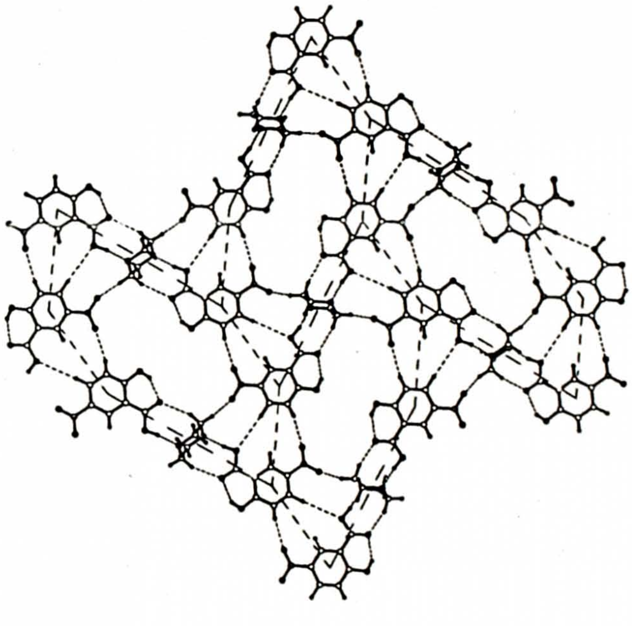


Figure 8. Pseudo-honeycomb structure of **6•dioxane** to show the linearly expanded synthon **IV** and C–H···O interactions with nitro and carboxyl O-atoms in the other two directions.

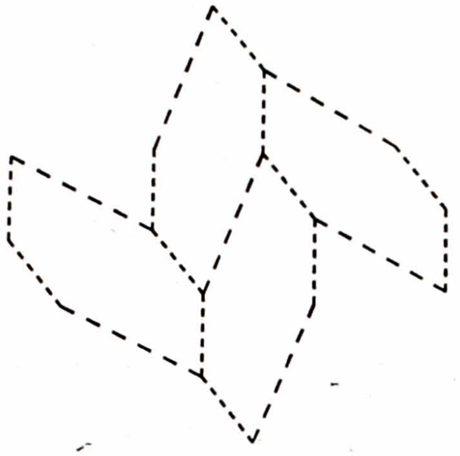


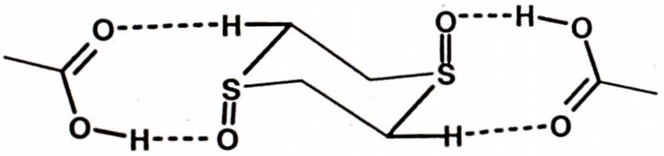
Figure 9. Supramolecular pseudo-honeycomb network in **6•dioxane**.

Table 1. Geometrical Parameters of Intermolecular Interactions

	Interaction[a]	*d* (Å)	*D* (Å)	θ (deg)
6	a) O–H···O	1.70	2.685(2)	178.7
	b) C–H···O	2.45	3.323(2)	137.2
	c) C–H···O	2.36	3.442(2)	174.1
	d) O–H···O	1.75	2.640(2)	147.3
6•dioxane	a) O–H···O	1.64	2.610(2)	168.6
	b) C–H···O	2.74	3.435(2)	127.7
	c) C–H···O	2.26	3.308(2)	162.4
	d) C–H···O	3.07	4.167(2)	176.3
	e) C–H···O	2.43	3.222(2)	128.1
	f) O–H···O	1.78	2.593(2)	143.1

[a] O–H and C–H distances are neutron normalized (0.983 and 1.083 Å)

5.5.2 Supramolecular polycyclohexane network



V

The crystal structure of the molecular complex of **6** with *trans*-1,4-dithiane-1,4-dioxide (**DTDO**), discussed in Chapter 4 is isomorphous with that of the 1,4-

dioxane solvate. The brick wall network in the crystal structure of **6** transforms to a supramolecular cyclohexane network in crystal structure of the molecular complex **6•DTDO**. The carboxylic acid dimer synthon **I** in the brick wall network is linearly extended to synthon **V** *via* O–H···O (1.58 Å, 169.7°) and C–H···O (2.97 Å, 125.6°). hydrogen bonds. The *ortho* hydrogens in the phenyl ring connects the carboxylic oxygen and the S=O group of the *glide* related neighbour *via* C–H···O (2.46 Å, 154.8°) hydrogen bonds. This molecular complex exhibits a chair poly cyclohexane type network as shown in Figure 10. Supramolecular chair cyclohexane structures have been observed in the crystal structures of ethynylferrocene[22] and in the molecular complex of 1,3,5-trihydroxybenzene with 4-methylpyridine[23]. These networks are not assembled from T-modules. Supramolecular cyclohexane motif has also been assembled from T-modules in coordination polymers.[18] The supramolecular chair polycyclohexane pattern is shown in Figure 11.

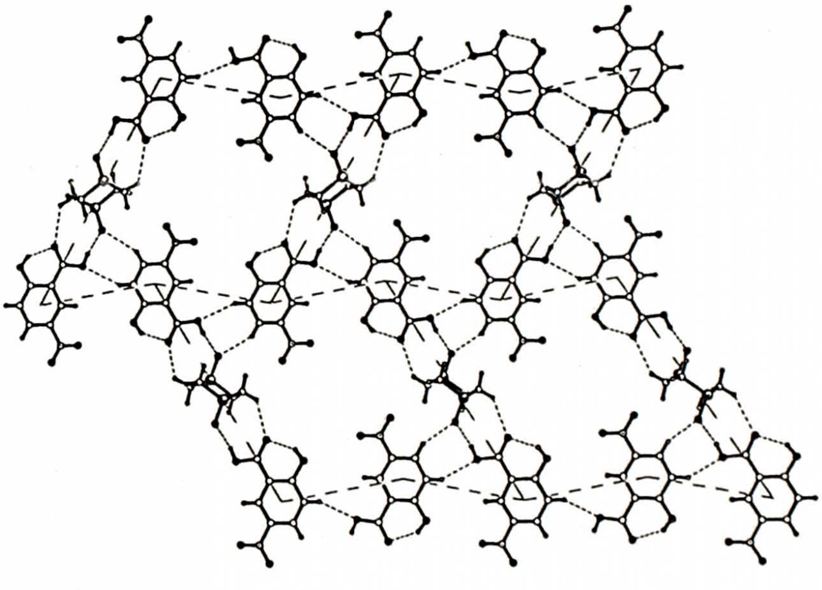


Figure 10. Crystal structure of the molecular complex of **6•DTDO** to show the polycyclohexane network.

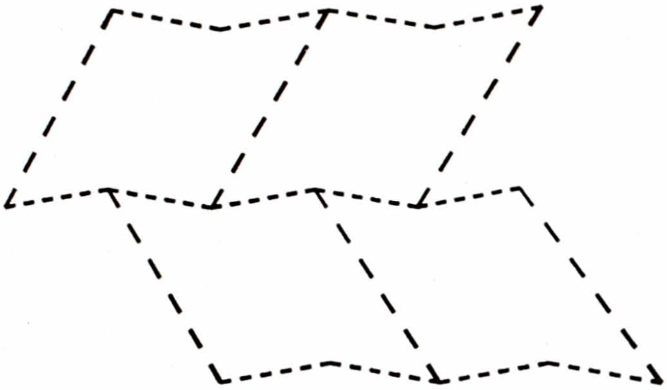


Figure 11. Supramolecular polycyclohexane network formed by **6•DTDO**.

5.6 Conclusion

A comparison of organic and coordination polymer networks lead to novel strategies for the design of organic crystal structures, opening up new directions for crystal engineering. The brick wall network structure formed by an organic T-shaped molecule is described. Further, the brick network transforms to pseudo honeycomb and supramolecular chair cyclohexane networks in its dioxane solvate and its molecular complex with *trans*-1,4-dithiane-1,4-dioxide. This study highlights the complementary role of strong and weak hydrogen bond synthons in self-assembly. The strong O–H···O carboxylic acid dimer in the brick wall network transforms to linearly extended motifs **IV** and **V** in the complexes with spacer ligands dioxane and **DTDO** and thus result in topologically identical networks. The weak C–H···O interactions in the networks have variable geometries in crystals, resulting in transformation from brick wall to honeycomb and chair cyclohexane networks. The strong hydrogen-bonded synthons **I**,**IV** and **V** impart robustness to the design strategy while the weak C–H···O interactions give a degree of flexibility that causes transformation from one architecture to another. Thus, networks may be built and modularly expanded with organic tectons.

5.7 Experimental section

X-ray crystallography

The compound 5-nitrosalicylic acid was purchased from Lancaster. Pale yellow coloured, X-ray quality crystals were obtained upon recrystallization from EtOH. The 1,4-dioxane solvate **6•dioxane** was obtained when 5-nitrosalicylic acid was crystallized from 1,4-dioxane at ambient temperature. Data on **6** was collected on Bruker SMART diffractometer by Prof. R. Boese and M. T. Kirchner at University of Essen, Germany and on **6•dioxane** was collected on Enraf-Nonius MACH-3 diffractometer at University of Hyderabad. The incident radiation is Mo-Kα X-RAY ($\lambda = 0.71073$) on both instruments. The data were collected in the ω-2θ scan mode. The structure solutions and refinements of the crystal structures were performed with SHELX97.[24] All the geometrical analysis was carried out with PLATON[25] on Silicon Graphics computer.

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Appendix-I

List of 422 reference codes for the families of dimorphic compounds found in the CSD search

ABIKEB
ABUNIU
ACBNZA
ACEMID
ACPRET
ACRDIN
AHPAZP
AMYTAL
ATCPEN
AZELAC
AZIBYR
BANGOM
BAQBEA
BASVUM
BAZYAC
BAMWEV
BDOTHY
BEBCIU
BEGLAA
BENCLN
BENZIL
BERPAP
BEYZIO
BIBKUS
BIDLOP
BIPCOS
BIPDEJ
BISMEV
BOCPRO
BOKCEJ
BOKVOM
BPHENO
BPNECH
BPROMA
BUJBEN
BZINDA
BZYACO
CAPLEK
CAWDUZ
CAXMOD
CAZFUE
CBENPH
CBFBZF
CEBKEZ
CEJHUU
CEMQOA
CERBEG
CEWGAM
CHIPTH
CHXAMH
CIMETD
CITRIG
CIVCEP
CIVTUW
CIYRIL
CLACAM
CLACET
CLBZAM
CLPHOL
CMPIXZ
CORDCP
COXDHN
CRESOL
CRETAL
CTVHVH
CUHNEY
CUKCAM
CUVSIV
CUYQUI
CYACAC
CYVTPA
DAHMIL
DAMLIM
DANGAL
DASPAO
DAVVUR
DAVWAY
DAWBEI
DAWHOY
DAZABZ
DBNTHR
DBPHEN
DCHEXC
DCHXYK
DCLNAP
DEFDUN
DEHREN
DETSUQ
DICNIM
DIUREA
DIXTEN
DLMETA
DLMSUC
DMBZAC
DMNPYO
DMURAC
DOLJET
DOLLOW
DOQNAY
DOZYAS
DPENAM
DPHSAM
DPIPDS
DPPETH
DTBPTR
DUDZIL
DUGKAR
EBIGUR
EDAXEM
ENVFUR
EPOPDO
FABRAB
FABRIJ
FAJTIT
FAYGAN
FBPAZD
FEHKOS
FEVNAV
FIBKUW
FIFFAB
FIKFIO
FLYITU
FOBSOE
FOJMOG
FUGJUM
FUGYAH
FUMAAC
FURGAA
FUWSOF
FUYJAK
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GAMBUT
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GICTIV
GIMBUZ
GLUCIT
GLURAC
GLYGLY
GOBYAX
GOLLUO
GORBOE
GOTGOV
GOXJOS
GOXWAR
GUGJAP
HADKIG
HADNOP
HAXBUD
HAXHET
HDXMOR
HIHKUE
HIHROF
HIJFIP
HIRPAZ
HISRUW
HIWJIG
HNIABZ
HOFNOF
HOHRIF
HOKPUS
HORTAJ
HORXOB
HPTSIO
HXDYNB
HXOPEN
IBULLA
IMDIAC
IMPTHA
INDIGO
ISXZCB
JARXUV
JATFUF
JIMVUW
JOYHEK
JUBFOB
JUVJAL
KAHLEK
KAJQOB
KASSOM
KAXXAI
KETYAJ
KOGSEE
KENVEU
KOKQUW

BOWWOZ
KUXJUI
LABHAX
LABJON
LAGWOH
LAURAC
LCYSTI
LCYSTN
LEBCIE
LEDQEQ
LEPRON
LEZJAB
LELUAC
LHISTD
LICMIT
LIGXUU
LIKBOW
LILJUL
LOCVOO
LOQLAE
LORVAP
LOTZEZ
MAKDEH
MALEHY
MANPIM
MATDEQ
MBABIQ
MBPHOL
MBZANQ
MCHTEP
MELVEE
MELXEG
MEPHCB
MNBZAC
MNPHOL
MPTRZS

COYMOS
MSFURY
MSTEAR
MUROXA
NAFZUP
NAPYMA
NAQRIG
NAYQEJ
NMBYAN
NBZOAC
NDOCLH
NETKOM
NITPOL
NITRIR
NIVPAJ
NMZNON
NOGUNA
NOSWAT
NUNHUZ
NXENAM
OLENAN
OPOXAZ
OXALAC
OXYTET
PABHAB
PACBOK
PACFOO
PACPAK
PAHRIZ
PANQUO
PBBTAZ
PCBZAM
PCHSAN
PCPZOL
PDHTEZ
PEHZUX

DMANTL
PELCIS
PENCEN
PERLEN
PERYTN
PEWXAQ
PHENOL
PHTGLY
PHTRPL
PIDFEN
PINPAD
PLENAC
POCPUS
POFHUN
POKJEE
POMDAW
POPGEG
POXHYN
PROGST
PTCDEC
PTZTCQ
PUCMIJ
PULNUF
PUMVIC
PYRENE
QAXSUD
QEKBEN
QEKDIT
QIDVII
QIJTOS
QIXFUY
QIYFEJ
QNACRD
QNGHSU
QOCNAX
QODTAE

FOVYOE
QOGREJ
QOYNOH
QUIDON
QUKVUN
QUPHEN
RAKWIG
REKBUE
RESORA
RIFQAY
RIGHUK
RORNIV
SAFPIY
SAXJEG
SAXPOW
SEBTAU
SEJWUZ
SESHUT
SESPEL
SICXIL
SIHVOU
SIKLIH
SILTOW
SILTUC
SILXUG
SINZIY
SIRXOG
SICVAB
SIWDEH
SLFNMB
SOMKOU
SOVWIG
STPYAZ
SUCNOT
SUQFIT
SUQVOP

HIMWIJ
SUWMIG
TALJIZ
TASVIS
TBTYAC
TCYETY
TBDOCP
TEBGAT
TECCAF
TEHKOG
TELKUQ
TEMBES
TEPHTH
TETBEZ
TETNIP
TEYJEM
TFMETH
THALID
THIOUR
TICNOI
TIJZIV
TINJAB
TIWYIH
TMETTS
TOBRUX
TOCPIM
TORSEM
TORTEZ
TOXGLU
TOZKOI
TPHPOR
TPPOSS
TRDMPP
TSCARB
TTHCTD
TUDROZ

KUVWON
TUMPOG
TUQCOX
UCUVAP
UDAYUT
VAPKIG
VEQNEK
VESMOV
VEXJEN
VISSOF
VITTAC
VOBNAB
VOHNOV
VOSQUP
VUCFUU
VUSFIY
VUSZEO
VUTZIT
WEBSIF
WEDLEW
WEXWOL
WIMBAV
WIRXAW
WOGRIT
WOTZAG
XAYBOO
XEHHEX
XELLEF
XELLOP
XEPXOF
XEWMER
XEWMOB
YACREZ
YAWPER
YAXDUW
YEJLII

YEJNAC
YEJRUA
YEPHAC
YERRUT
YEJNAC
YIDLEC
ZECZIQ
ZEDPIH
ZENQDX
YIDLEC
ZEPFAB
ZILHOR
ZILNOX
ZIWVIK
ZEPFAB
ZODJEH
ZOGQAN
ZOSLAU
ZOWSUZ
ZODJEH
ZOYMOP
ZZZJIQ
ZZZMUC
ZZZNQS
ZOYMOP

List of 42 reference codes of trimorphic systems

ADIPAC
AMBACO
AMNTPY
BIXGIY
BZCHOL
CENRIW
DBEZLM
DCLBEN
DETBAA
DHNAPH
DMFUSC
DPGUAN
DPYRAM
ESTRON
FEGWAP
GLYCIN
HPTHEL
HXACAN
HYQUIN
MABZNA
MALNAC
MBYINO
NIMFOE
NITPOL
NOETNA
NOJHEZ
OCHTET
PBBTAZ
PHTHCY
PTRPHE
PUBMUU
PUPBAD
REPFOH
SAMPYM
SIFLOI
SOBPEE
STARAC
SUCACB
SULAMD
TIZWAA
YUYHIJ
ZZZVTY

Reference codes of three tetramorphic systems

BEWKUJ
PYRZIN
PIMELA

Reference code of a pentamorphic system

SUTHAZ

Reference code of a hexamorphic system

QAXMEH

Appendix-II

Table 1. Crystallographic data for the compounds in this study

	Chapter 2			
	A	**B**	**C**	**D**
Empirical formula	$C_{18}H_{14}O$	$C_{18}H_{14}O$	$C_{18}H_{14}O$	$C_{18}H_{14}O$
Crystal system	monoclinic	triclinic	triclinic	orthorhombic
Space group	$P2_1$	$P\bar{1}$	$P\bar{1}$	*Pbca*
a [Å]	7.9170(6)	10.0939(2)	18.3788(4)	10.7921(6)
b [Å]	8.4455(6)	16.2592(3)	19.9701(4)	17.4749(12)
c [Å]	10.3086(9)	16.2921(4)	24.4423(5)	27.9344(19)
α [deg]	90	88.2570(10)	95.0080(10)	90
β [deg]	105.758(2)	85.3380(10)	111.6880(10)	90
γ [deg]	90	83.6450(10)	105.2180(10)	90
Volume [Å^3]	663.36(9)	2648.00(10)	7871.8(3)	5268.2(6)
Z	2	8	24	16
D_{calc} [g/cm^3]	1.233	1.236	1.247	1.242
T, K	160(2)	150(2)	140(2)	100 (2)
F (000)	260	1040	3120	2080
$2\theta_{max.}$	50.8	52.76	56.8	56.56
Range h	-8 to 9	-12 to 10	-9 to 9	-13 to 14
Range k	-2 to 9	-11 to 20	-18 to 26	-16 to 23
Range l	-11 to 11	-20 to 15	-14 to 32	-37 to 37
N-total	2010	14324	23729	37963
N-independent	1010	9875	16805	6538
N-observed	860	8926	13088	4820
parameters	184	686	2222	371
R_1 [$I>2\sigma(I)$] [a]	0.0508	0.0682	0.1121	0.0589
WR_2	0.1337	0.1688	0.1783	0.1243
GOF	1.135	1.224	1.238	1.061

Table 1. *Continued...*

Chapter 3				
1	**2**	**3**	**4•DME**	**4•hexane**
$C_{18}H_{12}OCl_2$	$C_{18}H_{12}OBr_2$	$C_{20}H_{18}O$	$(C_{30}H_{22}O)$ $(C_4H_{10}O_2)_{0.5}$	$(C_{30}H_{22}O)$ $(C_6H_{14})_{0.5}$
monoclinic	monoclinic	monoclinic	monoclinic	monoclinic
C2/c	*C2/c*	$P2_1/c$	*C2/c*	*C2/c*
17.6945(7)	17.552(11)	17.520(3)	25.464(5)	25.052(5)
10.3941(7)	10.529(6)	14.954(3)	19.751(4)	20.185(4)
17.0239(8)	17.219(9)	12.1712(19)	9.770(2)	9.722(2)
90	90	90	90	90
109.223(1)	107.813(2)	108.658(2)	97.720(3)	98.274(2)
90	90	90	90	90
2956.4(3)	3030.1(3)	3021.2(9)	4868.9(2)	4865.4(2)
8	8	8	8	8
1.416	1.772	1.206	1.210	1.200
168(2)	171(2)	158(2)	293(2)	168(2)
			1880	1864
52.74	53.74	52.78	56.06	52.8
-21 to 21	-19 to 22	-21 to 20	-33 to 32	-30 to 31
-12 to 12	-13 to 12	-18 to 18	-26 to 26	-25 to 24
-21 to 20	-14 to 21	-4 to 15	0 to 12	-4 to 12
11544	6590	23357	11573	16786
2833	2954	6112	5886	4736
2309	2270	4286	1352	2282
190	190	416	308	317
0.0509	0.0452	0.0440	0.0522	0.0675
0.1124	0.1082	0.1198	0.1077	0.1716
0.834	1.039	1.024	1.001	0.890

Table 1. *Continued..*

Chapter 3			*Chapter 4*	
4•DBRB	**4•DMCY**	**4•EtOH**	**(6)•(4)**	**(8)•(4)**
$(C_{30}H_{22}O)$	$(C_{30}H_{22}O)$	$(C_{30}H_{22}O)$	$(C_7H_5NO_5)$	$(C_4H_6O_4)$
$(C_4H_8Br_2)_{0.5}$	$(C_8H_{16})_{0.5}$	(C_2H_5OH)	$(C_4H_8O_2S_2)_{0.5}$	$(C_4H_8O_2S_2)$
monoclinic	monoclinic	monoclinic	monoclinic	triclinic
*C*2/*c*	*C*2/*c*	*C*2/*c*	$P2_1/c$	$P\bar{1}$
25.227(2)	25.05292)	24.747(5)	6.5864(13)	6.2210(12)
20.229(8)	20.280(4)	20.772(4)	23.353(5)	6.5660(13)
9.788(3)	9.718(2)	9.759(2)	7.0345(14)	7.6850(15)
90	90	90	90	89.78(3)
97.621(7)	98.11(3)	98.01(3)	96.07(3)	79.36(3)
90	90	90	90	64.55(3)
4951.0(3)	4887.8(17)	4967.8(17)	1075.9(4)	277.56(9)
8	8	8	4	1
1.359	1.175	1.213	1.600	1.617
168(2)	293(2)	293(2)	293	293
2088	1808	1912	536	142
53.06	52.88	56.8	55.92	56.52
-31 to 30	-31 to 31	-32 to 32	0 to 8	0 to 8
-22 to 24	-23 to 25	-23 to 27	0 to 30	-7 to 8
-12 to 12	-12 to 5	-12 to 12	-9 to 9	-10 to 10
16339	19400	21688	2781	1335
5049	4986	6193	2577	1335
2611	2879	1902	1264	1278
312	317	322	182	94
0.0498	0.0561	0.0800	0.0448	0.0364
0.1261	0.1528	0.1949	0.0998	0.0967
0.784	1.005	1.041	1.094	1.116

Table 1. *Continued..*

Chapter 4		*Chapter 5*	
(7)•**(4)**	**(9)**•**(4)**dihydrate	**6**	**6**•dioxane
$(C_7H_4N_2O_7)$ $(C_4H_8O_2S_2)$	$(C_2H_2O_4)_{0.5}$ $(C_4H_8O_2S_2)_{0.5}(H_2O)$	$C_7H_5NO_5$	$(C_7H_5NO_5)$ $(C_4H_8O_2)_{0.5}$
monoclinic	triclinic	triclinic	monoclinic
$P2_1/n$	$P\bar{1}$	$P\bar{1}$	$P2_1/c$
13.766(3)	6.2640(13)	5.2010(7)	5.3656(11)
6.2818(13)	6.6570(13)	8.8753(13)	22.995(5)
18.675(4)	7.6130(15)	9.2841(13)	7.9984(16)
90	100.12(3)	62.449(2)	90
111.53(3)	97.09(3)	75.388(2)	90.79(3)
90	114.20(3)	81.657(3)	90
1502.3(5)	278.22(10)	367.47(9)	986.8(3)
4	2	2	4
1.682	1.661	1.655	1.248
293	293	298(2)	293(2)
784	146	188	390
54.94	56.54	56.4	56.0
0 to 17	0 to 8	-6 to 6	0 to 7
0 to 8	-8 to 8	-11 to 11	0 to 30
-24 to 22	-10 to 9	-12 to 12	-10 to 10
3578	1340	4525	2602
3438	1340	1791	2371
2691	1305	1565	1359
253	97	118	158
0.0450	0.0383	0.0583	0.0343
0.1199	0.1001	0.1693	0.0856
1.041	1.105	1.077	1.080

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