# STRUCTURAL STUDIES OF SOME *GEM*-ALKYNOLS

A Thesis
Submitted for the Degree of
Doctor of Philosophy

By
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to

Amma and Nannagaru

## STATEMENT

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

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

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## CERTIFICATE

Certified that the work **'Structural Studies of Some *gem*-Alkynols'** has been carried out by **N.N. Laxmi Madhavi** under our supervision and that the same has not been submitted elsewhere for a degree.

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My sincere apologies to all those whose names I would like to very much mention here but am unable to do so because of lack of space. I wish to convince one and all that the contribution made by those whose names I am unable to mention is as valuable and significant as the ones I did, if not more.

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Yours gratefully

N.N.Laxmi Madhavi

## PREFACE

Crystal engineering deals with the rationalisation and design of crystal structures. Studies in crystal engineering have explored strong and weak hydrogen bonds and various other intermolecular interactions. However, the interplay between strong and weak interactions has not been generally explored in a deliberate manner so far. The thesis is an attempt to understand the interplay between strong and weak hydrogen bonds formed by the *gem*-alkynol group. General principles of crystal engineering are discussed in Chapter one and the *gem*-alkynol functionality is introduced.

Polymorphism denotes the ability of a compound to crystallise in more than one distinct crystal structure. Many terms regarding polymorphism have appeared in literature. The crystal structures discussed in Chapter two offer a test of the existing terminology and definitions of polymorphs. The implications of identifying these polymorphs with one or the other term are discussed.

Importance of interaction orthogonality in establishing the structural repetitivity is described in Chapter three. Synthon repetitivity has been demonstrated in a pair of *gem*-alkynols, despite the high degree of interaction interference typical of *gem*-alkynol family.

The crystal structures studied in Chapter four were analysed to explore the crystal packing of the *gem*-alkynol group in the presence of halogen atoms. The difference in these structures are discussed based on the different crystal packing demands of F, Cl and Br atoms. It is shown that the packing features of F-atom are different from Cl and Br, while the behaviour of Cl is midway between F and Br.

Aromatic hydrogen bonds are discussed in Chapter five. Topological similarity between the synthons formed by the hydroxy and ethynyl groups is highlighted when these groups are hydrogen bonded to phenyl rings. A new facet of supramolecular similarity between hydroxy and ethynyl groups is revealed from this study.

Evidence for the characterisation of C–H···$\pi$ interaction as a weak hydrogen bond is discussed in the appendix at the end of the thesis. Also the general experimental procedure with spectroscopic data of the compounds and salient

crystallographic details of the crystal structures discussed in this thesis have been given in appendix. A full list of atomic coordinates has been deposited with the University of Hyderabad and can be obtained from Dr. Ashwini Nangia (ansc@uohyd.ernet.in) or Prof. Gautam R. Desiraju (grdch@uohyd.ernet.in), School of Chemistry, University of Hyderabad.

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CHAPTER ONE

# INTRODUCTION

## Crystal engineering

Chemistry has progressed from the molecular to the supramolecular paradigm. Research in the molecular regime is concerned with the mastering of the covalent bond. Supramolecular chemistry is the chemistry of the non-covalent bond and deals with the rules governing molecular association and the structures and properties of collective molecular species.[1] The chemical and geometrical complementarity of the interacting molecules leads to their association. Billions of molecules associate to form crystals. Crystal engineering has evolved to a mature field of research[2] and deals with molecular aggregation in the solid state. Crystal engineering is defined as 'the understanding of intermolecular interactions in the context of crystal packing and in the utilisation of such understanding in the design of new solids with desired physical and chemical properties'.[3] Analysis and design are the two principal components of crystal engineering. Today, the field of crystal engineering has an enormous impetus because of its applications[4] in nonlinear optics, catalysis, microporous materials, piezoelectricity and solid state reactivity.

The identification of a crystal as a supermolecule *par excellence*[5] has further heightened interest in crystal engineering and has brought the subject into the mainstream of supramolecular chemistry. Indeed, crystals constitute one end of the supramolecular continuum and may be regarded as hard supermolecules in contrast to the softer supramolecular aggregates which exist in solution. The realisation that a crystal is one of the best examples of a supermolecule led to the recognition of crystal engineering as a supramolecular equivalent of organic synthesis.[6] Such a likening of these two distinct fields bridges the gap between them. In fact this provides a means of profitably applying the vast knowledge and experience associated with the mature field of organic synthesis to the developing subject of crystal engineering. Many parallels between these two fields may be

drawn and the traditional knowledge about synthesis may be extended to the supramolecular regime.

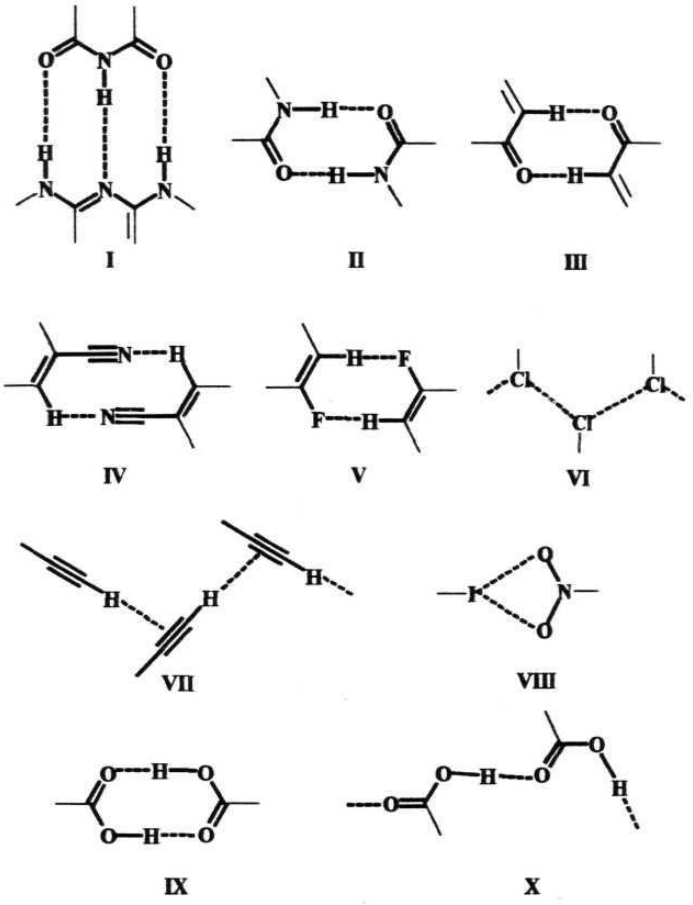
**Supramolecular synthons**

In the light of this comparison between organic synthesis and crystal engineering, supramolecular synthons have been identified and are defined as 'structural units within supermolecules which can be formed and/or assembled by known or conceivable synthetic operations involving intermolecular interactions'.[6] It should be noted that synthons are designed combinations of interactions and need not be identical to the interactions. They depict the various ways in which complementary portions of molecules approach each another. Accordingly, supramolecular synthons consist of chemical and geometrical information necessary for molecular recognition and for the generation of supermolecules. Many synthons can be identified within a crystal structure. But the most significant synthons are those in which maximum of structural information is stored in a unit of economical size. Supramolecular synthons allow structural simplification without losing important chemical information. Some applications of the supramolecular synthon concept in crystal engineering are discussed in this thesis.

**Analysis and synthesis**

The analytical co ıponent of crystal engineering involves the identification of intermolecular interactions and their robust patterns, the supramolecular synthons; also involved is the comparison of crystal structures in terms of supramolecular synthons. Once an understanding is gained about synthons, the design of crystal structures may be undertaken. It is important to note that while an understanding of crystal structures in terms of the known repertoire of supramolecular synthons is helpful, new synthons continue to be identified during analysis. In other words, the analytical and synthetic components of crystal engineering work in synergy and practising any one of these requires expertise in the other. Since the primary

concern of this thesis is about analysis, the following sections focus on the principles and results of rationalisation of crystal structures.




**Scheme 1**. Supramolecular synthons discussed in this chapter.

**Intermolecular interactions in crystals**

At the heart of crystal engineering and supramolecular chemistry lies the exploitation of intermolecular interactions. With the ever increasing ease in the determination of crystal structures and with the widespread use of the Cambridge Structural Database (CSD)[7], analysis of various kinds of intermolecular interactions has become very convenient. Organic crystals typically include two

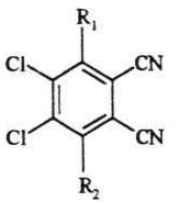
kinds of interactions: medium-range isotropic forces and long-range anisotropic forces. Isotropic forces include C···C, C···H and H···H interactions and lack directionality. Hydrogen bonds of the stronger (O–H···O, O–H···N, N–H···O and N–H···N) and weaker (C–H···O, C–H···N, O–H···π, N–H···π, C–H···π, C–H···halogen) type, and also interactions between hetero atoms X···X (X = O, N, S, P and halogen) constitute the anisotropic forces.

The nature and properties of the hydrogen bond have been extensively studied and much is known about the stronger varieties such as O–H···O and N–H···O. The archetype of the weak hydrogen bond is the C–H···O interaction and its classification as a hydrogen bond went through some controversy in the initial years.[8] After several studies, C–H···O and C–H···N interactions are well accepted as weak hydrogen bonds.[9] Spectroscopic, gas-phase, quantum chemical and statistical methods have unequivocally proved the hydrogen bond character of C–H···O and C–H···N interactions. The choice and emphasis of the work described in this thesis is on the weak intermolecular interactions.

Interactions of the weaker variety are easily deformed by other forces in the crystal. This makes their study different and difficult. Structural and statistical analysis[10] assume much significance. The range of geometries observed for weak interactions is rather large. The weaker the interaction the more it is easily deformed and therefore the larger the range of geometries observed. A large body of data is therefore required to make any significant assessment of a weak interaction. The CSD with approximately 200 000 crystal structures has evolved to become an indispensable tool for the study of weak interactions. When a sufficiently large amount of data are examined, the deforming effects of other interactions stand effectively cancelled. Thus statistical methods provide an invaluable tool to assess and infer the nature of weak intermolecular interactions. For example, the directionality and electrostatic nature of C–H···O hydrogen bond have been shown to be similar to those of strong hydrogen bonds.[11]

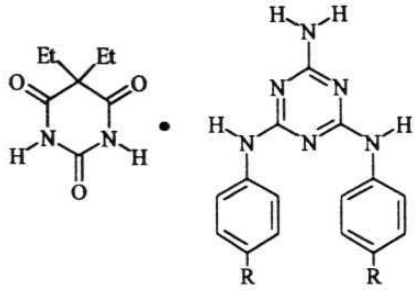
**Hierarchy of intermolecular interactions**

Once the basic features of the interactions are known, the next step in crystal engineering is to unravel the effects of the individual interactions in the crystal structures of related compounds and, if possible, to rank the interactions in terms of their efficacy in crystal packing. This is generally a non-trivial exercise.




**1a** $R_1 = R_2 = H$
**b** $R_1 = R_2 = OMe$
**c** $R_1 = R_2 = OEt$
**d** $R_1 = R_2 = OPr$
**e** $R_1 = R_2 = OBu$
**f** $R_1 = OH$, $R_2 = n\text{-}Oc$
**g** $R_1 = R_2 = n\text{-}Oc$
**h** $R_1 = R_2 = OH$

For instance, consider the eight crystal structures in a series of 1,4-disubstituted 2,3-dicyano-5,6-dichlorobenzene, **1a-1h**.[12] The dicyano-dichlorobenzene consists of molecular tapes that are linked by dimers of C≡N···Cl interactions. The same pattern is observed when the methoxy groups are in 1,4 positions. However, as the bulk of the alkoxy groups is increased, the C≡N···Cl interactions become distorted to the point that hydrophobic interactions of the alkoxy chains are the major determinants of the structure. In the case of the dihydroxy derivative, the O–H···N interactions are dominant. From the analysis of these structures it is understood that the presence of a hydroxy group dominates the C≡N···Cl interactions thus stabilising the structure with O–H···N bonds. In the absence of long aliphatic chains and other strong donor/acceptor groups, C≡N···Cl interactions dominate the crystal packing while hydrophobic interactions control the packing when the size of alkoxy group is increased. This study reveals that specific interactions become dominant or supportive in the totality of the structure depending on the rest of the interactions present. However, in some cases the weaker interactions do change the patterns of the stronger ones.

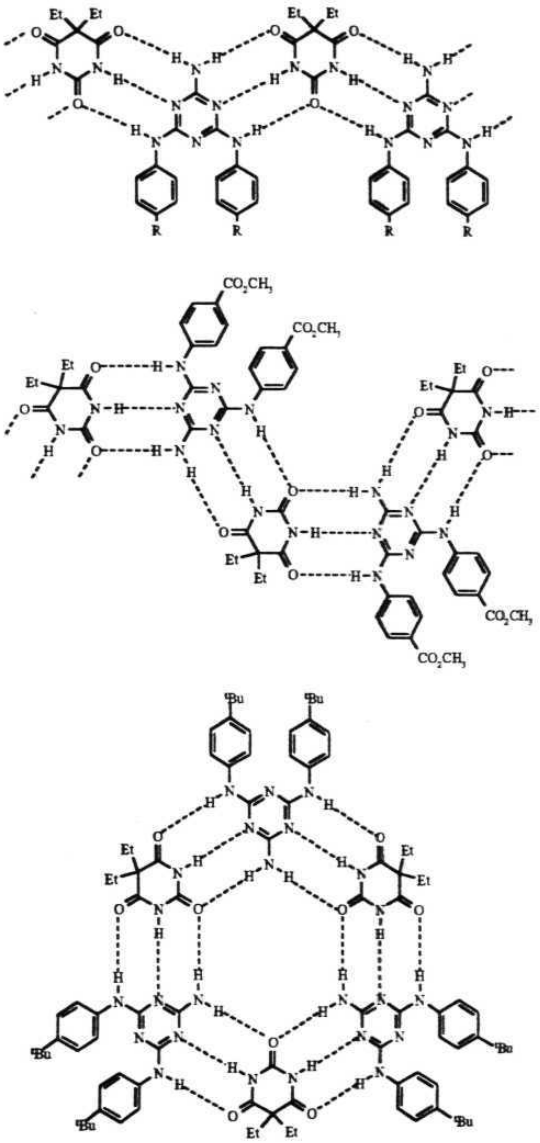


**2a** R = $CH_3$
**b** R = F
**c** R = Cl
**d** R = Br
**e** R = I
**f** R = $CO_2CH_3$
**g** R = $^t$Bu

In another study, a series of complexes of substituted melamines and barbituric acid have been analysed **2a-2g**.[13] The complementarity of these two compounds led to the formation of hydrogen bonded tapes in these complexes. As the size of the substituent is increased variations in the topologies of the tapes are observed (Scheme 2). When the substituent is small (R = $CH_3$, F, Cl, Br, I) linear tapes are formed. Formation of crinkled tape (R = $COOCH_3$) and a cyclic hexamer (R = $^t$Bu) are observed when the size of the substituent is further increased. In all these cases, the primary structure (the hydrogen bonded synthon **I**) is invariant unlike the previous example. The differences in these structures are rationalised in terms of the interactions of the substituent groups on the adjacent melamine molecules. This study reveals that while the triply hydrogen bonded synthon **I** governs the primary structure, the substituent groups play a critical role in determining the secondary and tertiary structure.

**Strong and weak hydrogen bonds – comparison through individual interactions**

Strong and weak hydrogen bonds have many similar attributes, properties and structural effects.[14] This can be judged from the following two examples where C–H···O hydrogen bonds effectively replace N–H···O and O–H···O hydrogen bonds without losing the structural integrity and geometrical relationships. The two crystalline complexes of $\beta$-cyclodextrin-diethanolamine **3** and $\beta$-cyclodextrin-pentane-1,5-diol **4** are isostructural.[15] In these host-guest complexes the N–H···O



**Scheme 2.** Hydrogen bonded tapes in complexes of substituted melamines and barbituric acid. Linear tapes (top), crinkled tapes (middle) and cyclic hexamer (bottom). Notice the variation in motifs with the change in size of substituent on melamine.

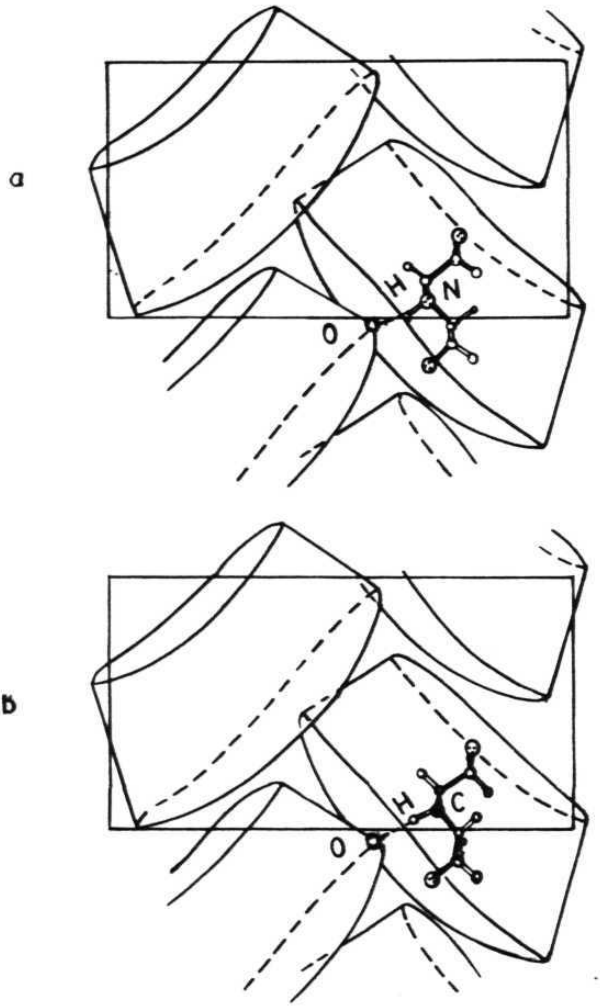
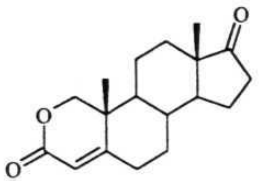


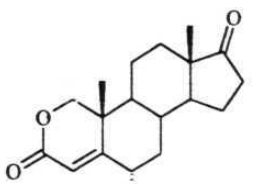

**Figure 1**. Isostructural compounds **3** and **4** illustrating the similarities of strong and weak hydrogen bonds. The N–H···O hydrogen bond in **3** (a) is replaced with C–H···O hydrogen bond in **4** (b). Cyclodextrin molecules are drawn schematically for clarity. Only the oxygen atom that is involved in hydrogen bonding is shown.

hydrogen bond between the constituent species in the former is replaced by a C–H···O hydrogen bond in the latter (Figure 1). The importance of the C–H···O hydrogen bond contributing to the stability and to the very existence of the latter

complex would have been difficult to understand in the absence of the former complex. Structural comparison of very closely related systems is therefore a rewarding exercise in studies of weak hydrogen bonds. It has been shown in a recent study that the formation of a solid-solution of 2-oxa-4-androstene-3,17-dione **5** and its 6$\alpha$-hydroxy analogue **6** is due to the similar properties of O–H···O and C–H···O hydrogen bonds.[16] The above two examples show the structural similarities between strong and weak hydrogen bonds through individual interactions.



**5**

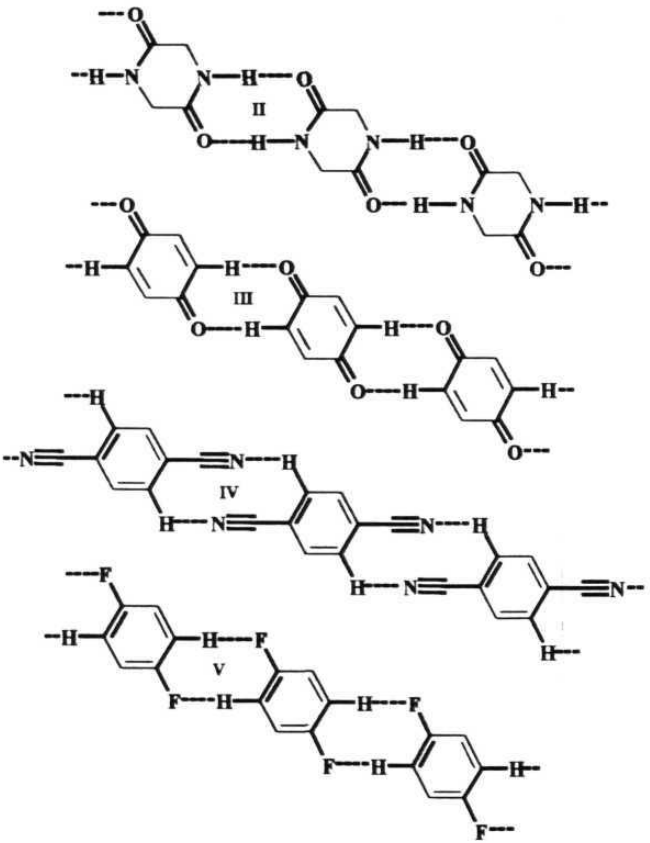


**6**

**Strong and weak hydrogen bonds – comparison through supramolecular synthons**

Crystal structures can be analysed in terms of supramolecular synthons and in the following examples it is shown that synthons help in comparing seemingly different crystal structures. Scheme 3 displays the linear tape structures in piperazine-2,5-dione **7**, 1,4-benzoquinone **8**, 1,4-dicyanobenzene **9** and 1,4-difluorobenzene **10**. All these structures are topologically similar but are generated from different synthons **II**, **III**, **IV** and **V**. While synthon **II** is based on strong N–H···O bonds, the three others are generated from weak C–H···O, C–H···N and C–H···F hydrogen bonds. These structures illustrate that similarities between strong and weak hydrogen bonds are manifested in terms of topologically equivalent synthons. Unlike the individual interactions observed in **3-6**, the patterns observed in **7-10** appear in several structures. Their presence in different structures and in different crystalline environments suggests that they are robust. Such robustness and repetitivity is an important criterion which distinguishes supramolecular

synthons from mere patterns. An advantage of identifying synthons of this kind is their further use in the synthesis of new and desired structures. The synthon concept shows parallels between structures which are otherwise unrelated. The utility of this concept may thus be also appreciated in these terms.




**Scheme 3**. Linear tape structures in **7**, **8**, **9** and **10**. The topology of the four synthons is the same though they are formed with strong (**II**) and weak (**III**, **IV** and **V**) hydrogen bonds.

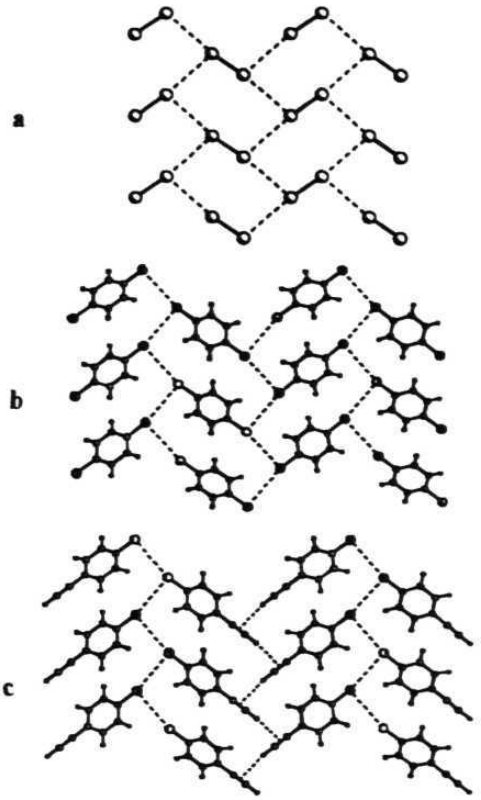



**Figure 2**. Layered structures in **11** (a), **12** (b) and **13** (c) showing the transferability of synthon between different structures.

### Synthon transferability

The crystal structures of solid $Cl_2$ **11**, monoclinic 1,4-dichlorobenzene **12**, and 4-chloroethynylbenzene **13** are shown in Figure 2. All these molecules contain Cl-atoms. In addition, **13** contains ethynyl groups. All the three structures are similar to one another. While **11** and **12** are stabilised by Cl···Cl chain synthon **VI**, **13** is stabilised by the alternating synthons **VI** and **VII**. The structures of **11** and **12** are virtually identical with the aromatic rings in **12** acting as spacers. A comparison of the three structures suggests that synthon **VI** can be transferred from one structure to another. This concept of synthon transferability is described in Chapter three.

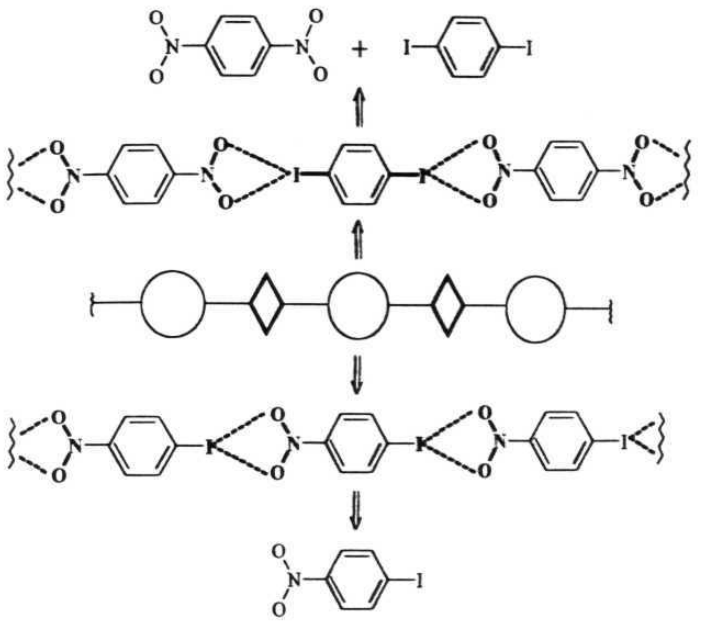
Additionally the topological similarity between synthons **VI** and **VII** may be noted.

**Supramolecular synthesis**

Supramolecular synthons play a crucial role in the synthetic component of crystal engineering. A suitable example to illustrate this is the I···$NO_2$ synthon **VIII**. It has been found that the I-atom forms close contacts with two O-atoms of an $NO_2$ group. The polarisation-induced attraction between the heteroatoms in this pattern is immediately obvious and the CSD has been searched for its occurrence.[17] Symmetrical and unsymmetrical variations of synthon **VIII** have been observed and confirms the robustness and transferability of this synthon. Synthon **VIII** can be used in the synthesis of a target crystal structure.

Crystal structures are conveniently depicted as networks with molecules acting as nodes and supramolecular synthons as node connectors. Implicit here is the simplification of complex structures through nodes and node connectors. Taking advantage of such a simplification, targets in crystal engineering may then be defined in terms of networks with various topologies *viz.* ribbons, layers and a variety of two and three dimensional networks. The synthetic exercise therefore takes the network as the starting point and the molecule as the end point — a supramolecular retrosynthesis.

The general supramolecular retrosynthetic plan may be described as networks (crystal structures) ⇒ supramolecular synthons ⇒ cons.ituents (molecules). Scheme 4 illustrates the supramolecular retrosynthesis of a linear ribbon structure.[18] Synthons **VIII** are taken as the node connectors with phenyl ring as the molecular nodes. The polar nature of the synthon **VIII** leads to two possibilities resulting in a molecular compound or a molecular complex. Following this work, a very similar strategy has been used with the C≡C–H···$NO_2$ synthon to generate similar one-dimensional structures.[19] Retrosynthetic analysis has also been extended to two- and three-dimensional networks resulting in functionalised solids.



**Scheme 4**. Retrosynthetic analysis of a linear ribbon structure through I···$O_2N$ synthon.

**Interaction interference**

Intermolecular interactions that are directional possess specific geometries. These geometries vary from a narrow (stronger interactions) to a broader (weaker interactions) range depending on the strength of the interaction. Crystal structures are a result of balance between various intermolecular interactions. When the geometrical requirements of two interactions can be met in isolated regions of a structure, these two interactions are said to be structurally insulated. If the geometric demands of two interactions come into conflict, optimisation of one interaction changes the normal pattern of the other and this phenomenon is termed as interaction interference. Similar arguments can be extended to supramolecular synthons and one finds structural insulation or interference between synthons.

In the following examples, some unusual geometries of strong hydrogen bond patterns are observed because of interaction interference. In all the cases it is

found that the optimisation of weak interactions, in these cases of C–H···O hydrogen bonds, becomes important and a change in the normal pattern of stronger bonds is imposed. In essence the weaker interactions interfere with the stronger ones in forming and stabilising the structure. The COOH groups are well-known to form dimeric synthons **IX** around an inversion centre. In 3,5-dinitrocinnamic acid however, the COOH group forms the dimer synthon **IX** around a two-fold axis.[20] This occurs because of the dominance of C–H···O bonds.

In a family of 4-substituted-1-cubane carboxylic acids studied recently, the COOH group has been found to form repeatedly a rare O–H···O catemer **X** rather than the normal centrosymmetric dimer synthon **IX**.[21] The hydrogen bonding pattern is a catemer with symmetry independent *syn*- and *anti*-conformations of COOH group. The unusual catemer arises in these compounds due to the stabilisation by auxiliary C–H···O hydrogen bonds which are formed by acidic cubyl C–H groups and the carboxyl O-acceptor atoms. A very similar situation is seen in 4-chloro- and 4-bromophenylpropiolic acids where a *syn-anti* O–H···O catemer **X** is formed and the aromatic C–H groups participate in the auxiliary C–H···O hydrogen bonds.[22]

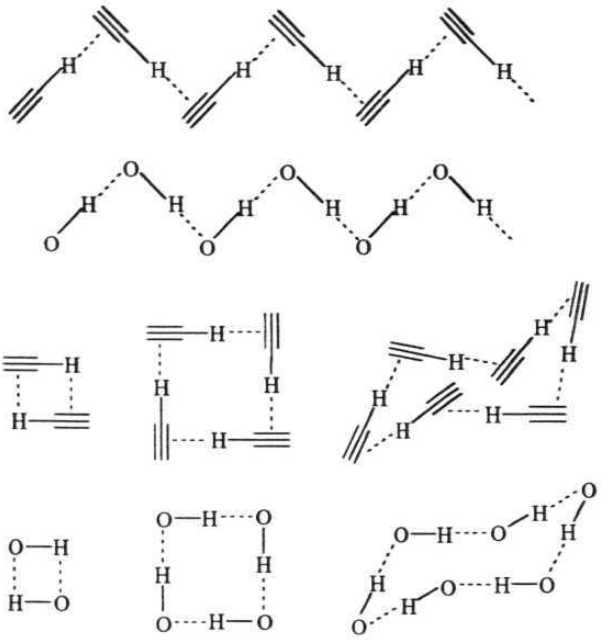
In all the above cases the weak interactions interfere with stronger ones and result in structural anomalies. In general, it is difficult to perceive when such interaction interference would occur and in what kind of systems. Interaction interference is a useful phenomenon, especially for weak interactions, because it provides a medium to understand the nature of weak interactions which is otherwise unrevealed. The work described in this thesis is a deliberate attempt to probe such interference between interactions and synthons formed by hydroxy (OH) and ethynyl (C≡C–H) groups. Before getting into further details, a description of the normal interaction trends of hydroxy and ethynyl groups will be presented.

**Similarity between hydroxy and ethynyl groups**

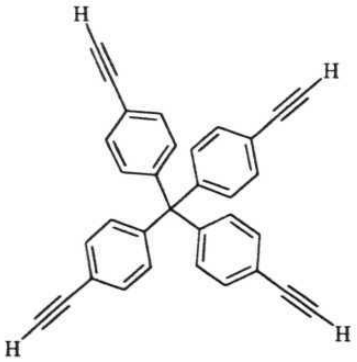
The hydroxy group is well studied in structural chemistry. It can act as a hydrogen bond donor and acceptor simultaneously. This dual capacity of the hydroxy group enables it to form chain and ring patterns of various sizes some of which are shown in Scheme 5.[23] All these synthons are cooperative: due to mutual polarization of the involved groups, the two hydrogen bonds enhance the strength of each other, and the total hydrogen bond energy is larger than the sum of two isolated hydrogen bonds.

The terminal alkyne, or ethynyl group is of current interest with regard to its hydrogen bonding properties. It serves as a model to explore weak hydrogen bonding effects because of the acidity of the hydrogen atom, its ability to act as hydrogen bond donor and acceptor simultaneously and its suitability for infra-red spectroscopic experiments.[24] The ethynyl group forms hydrogen bonds with other acceptors that are as strong as P=O[25] and as weak as aromatic moieties.[26] With the associated π-electrons it also accepts hydrogen bonds from strong and weak donors. The ability to act as a donor and an acceptor simultaneously enables the terminal alkyne group to participate in cooperative hydrogen bond networks very similar to the hydroxy group.

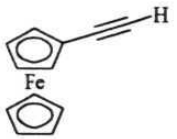
Some networks formed by the ethynyl group are shown in Scheme 5. A cooperative chain pattern is observed frequently in the structures containing ethynyl group.[27] Acetylene forms ≡C–H···C≡C tetramers. Recently, this tetramer was also identified in the crystal structure of tetrakis(4-ethynylphenyl)methane **14**.[28] Incidentally, this is the first crystal structure reported to form diamondoid network sustained by weak hydrogen bonds. A hexamer of ≡C–H···C≡C formed by three symmetry independent molecules is observed in the crystal structure of ethynylferrocene **15**.[29] The long range nature of ≡C–H···C≡C interactions is shown from this crystal structure by IR spectroscopic studies.



**Scheme 5**. Cooperative patterns formed by hydroxy and ethynyl groups. Notice the topological similarities between corresponding patterns.



**14**




**15**

Topologically, the synthons formed by the ethynyl group are similar to those formed by the hydroxy group. Though the ideal geometries of the kinds of interactions involved in these synthons are somewhat different (roughly tetrahedral in O–H···O and roughly orthogonal in ≡C–H···C≡C) they do form almost

equivalent synthons. Such similarity immediately suggests the possibility of forming similar crystal structures. An interesting comparison between these two functionalities is furnished by γ-hydroquinone **16** and 1,4-diethynylbenzene **17**, and is shown in Figure 3. A layer structure is formed in both cases with O–H···O chains present in the former and ≡C–H···C≡C chains in the latter. In essence, one may say that the ethynyl group plays the same role as the hydroxy group in the crystal structures because of the great similarities in the donor-acceptor capabilities of the two groups.

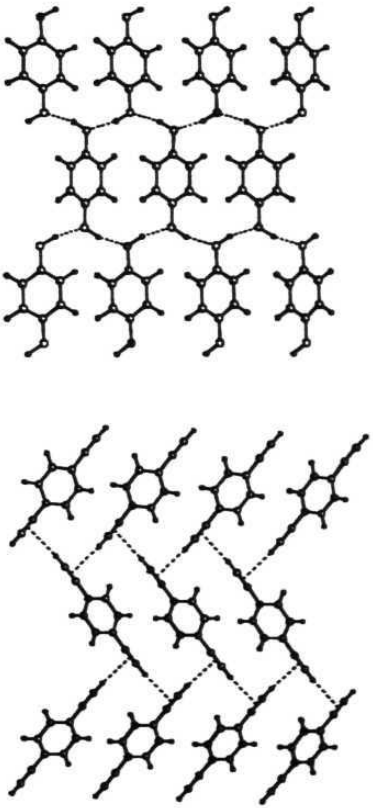
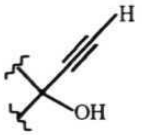


**Figure 3**. O–H···O chains in γ-hydroquinone **16** (top) and ≡C–H···C≡C chains in diethynylbenzene **17** (bottom). Notice the topological similarity between the two synthons.

**The *gem*-alkynol functionality**




*gem*-alkynol

It is noted that when the hydroxy and ethynyl groups are taken independently they form synthons specific to them. What happens when these functionalities are taken together in the *gem*-alkynols? In addition to O–H···O, ≡C–H···C≡C two other interactions become possible: ≡C–H···O and O–H···C≡C. The objective of the present work arose from a previous study in this laboratory on the neutron diffraction analysis of 2-ethynyl-2-adamantanol **18**.[30] The structure of **18** is characterised by O–H···O, O–H···C≡C and ≡C–H···O interactions. A very short ≡C–H···O hydrogen bond is observed in this structure due to a cooperative interaction pattern. There are two molecules in the asymmetric unit. Both the molecules form a cooperative hydrogen bond cycle as shown in Figure 4. The H atom of the hydroxy group which is not involved in the cooperative hydrogen bond pattern forms a O–H···C≡C hydrogen bond while the second ethynyl group is passive.

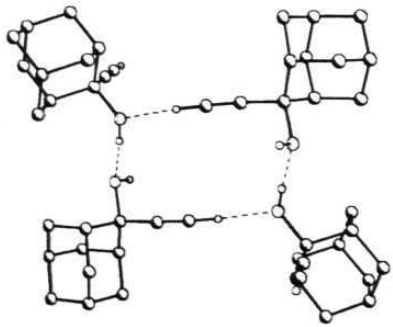


**Figure 4**. Cyclic hydrogen bond pattern formed by the hydroxy and ethynyl groups in the crystal structure of **18**.

The involvement of hydroxy and ethynyl groups in O–H···C≡C and ≡C–H···O interactions clearly indicates the interaction interference in this compound and so our interest turned to the *gem*-alkynol functionality.

**CSD studies on *gem*-alkynol**

The CSD was searched for the *gem*-alkynol group and its interaction patterns analysed.[31] However, these studies did not yield much information to understand the crystal packing behaviour of the *gem*-alkynol group because:

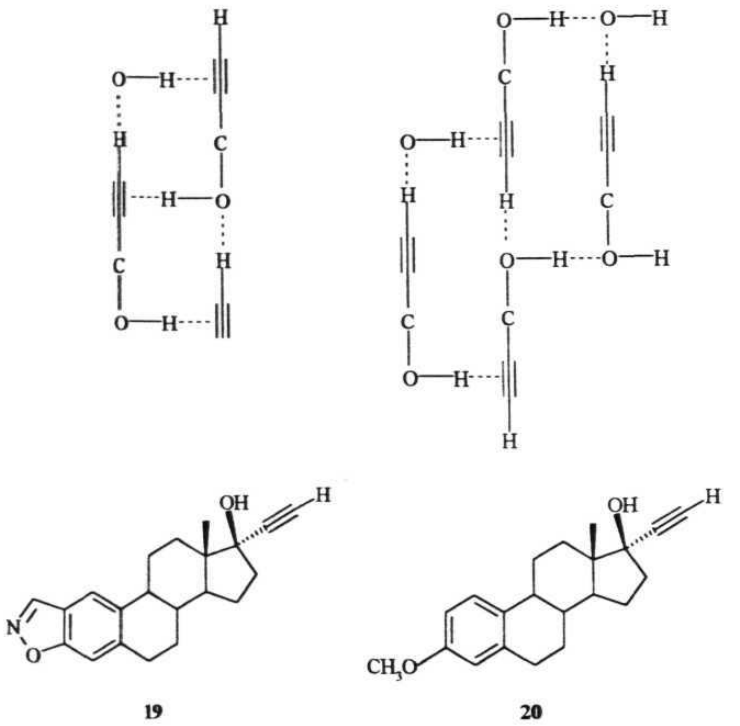
a) The number of structures reported is small. There were only 76 compounds when this project was started. The October 1998 release of CSD (version 5.16) contains 94 compounds with a *gem*-alkynol group.

b) About 65% of the reported structures are steroids. The crystal packings of these compounds are generally governed by packing requirements of the big, rigid steroidal framework and the role of the *gem*-alkynol at the 17-position is minor at best. Even so, some interesting cooperative hydrogen bonding patterns involving the *gem*-alkynol group were observed in this sub-family. These patterns are observed in the steroids donazole **19**[32] and mestranol **20**[33] and are shown in Scheme 6.

c) Many a times, the *gem*-alkynol group is associated with other competing functionalities capable of forming strong interactions. About half the compounds in the retrieved structures contain carbonyl, hydroxy (apart from the hydroxy of *gem*-alkynol) and other groups. These groups are involved in the hydrogen bonded patterns along with the *gem*-alkynol functionality.

d) No homogeneity of structures was found so that information could be extracted in a systematic way.

e) All possible interactions for the *gem*-alkynol functionality ranging from very strong (O–H···O) to very weak (C–H···C≡C) hydrogen bonds are observed, but with unexpected frequencies. Analysis of these 94 structures for the interactions involving the *gem*-alkynol moiety exclusively showed 16 O–H···O, 6 O–H···C≡C, 28 ≡C–H···O and 14 ≡C–H···C≡C contacts.



**19** **20**

**Scheme 6**. Cooperative hydrogen bond patterns formed by *gem*-alkynol functionality in **19** and **20**.

f) No repetition of a major pattern of hydrogen bonds is seen. Apart from the O–H···O and ≡C–H···C≡C chains there are many diverse extended patterns formed from these interactions a~ is shown in **18**, **19** and **20**. No robust synthons could be extracted from the strucuures in the CSD. Such robustness is essential for further synthetic strategies of crystal engineering.

Therefore, the present work involves the analysis of crystal structures containing a *gem*-alkynol functionality. The strategy used has been to place two *gem*-alkynol groups in a symmetrical fashion on relatively simple molecular frames with some systematic variations. These variations include: (a) placing the *gem*-alkynol groups on a flexible framework (Chapter two), (b) placing the *gem*-alkynol groups on a rigid framework (Chapter three). (c) In the above two

variations, the *gem*-alkynol groups are placed on hydrocarbon frameworks to minimise the interference with other interactions. At the next level the *gem*-alkynol groups are placed on a rigid framework that also contain other heteroatoms to see possible structural changes (Chapter four) (d) Additionally some mono *gem*-alkynolated systems are studied (Chapter five). In the following chapters the rich structural chemistry of the *gem*-alkynol functionality is described.

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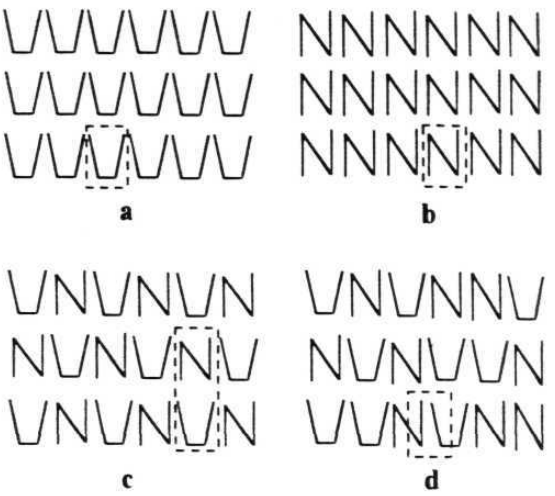
CHAPTER TWO

# HELICAL TRIMERIC O–H···O SYNTHON IN THE POLYMORPHS OF *TRANS*-1,4-DIETHYNYLCYCLOHEXANE-1,4-DIOL

## Polymorphism

Polymorphism is defined as the ability of a compound to crystallise in more than one distinct crystal structure.[1] Polymorphism has received immense academic and industrial interest because of its implications in the understanding of intermolecular interactions in varied solid state environments and structure-property relationships.[2] The routine occurrence of polymorphism in special classes of compounds such as polyfunctional systems or conformationally flexible systems has been noted. Though polymorphism appears to be a problematic phenomenon for crystal engineering, polymorphic structures provide a special case to understand the supramolecular features of a given molecule in different crystalline environments.

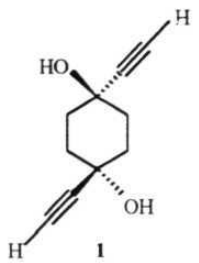
It is recognised that the simple definition of the polymorphism given above does not fully encompass the diverse structures that have appeared in the literature. In this direction, several additional terms have appeared. The usage of the word polymorphism is subjective and the term supramolecular isomerism[3] is also used for polymorphism. There is no clear consensus on the exact definition of polymorphism. In general, polymorphism denotes different arrangements of rigid molecules in the solid state. This simple view does not hold when molecules could exist as tautomers, zwitterions or different conformers. Tautomeric polymorphism[4] has been invoked but has been very rarely reported. Pseudopolymorphism[5] denotes the crystal structures of the same chemical substance that differ in the nature or stoichiometry of included solvent molecules. Pseudopolymorphism is not a polymorphism in real sense, because it involves different chemical species.



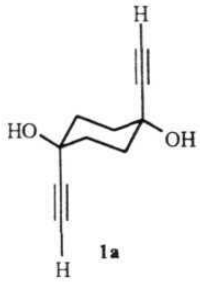

**Scheme 1**. Schematic representation of some possible arrangements of a molecule with two conformations. The rectangle defined by the broken line represents one possible choice of the unit cell. (a) and (b), conformational polymorphs; (c) conformational isomorphism; (d) conformational synmorphism.

The terms conformational polymorphism, conformational isomorphism and conformational synmorphism[6] are related to conformationally flexible systems. Scheme 1 displays these situations schematically. Conformational polymorphism is the existence of different conformers of the same molecule in different polymorphic modifications (Scheme 1a-b). Conformational isomorphism is the existence of different conformers of a molecule in the same crystal structure. This results in more than one molecule per crystallographic asymmetric unit. Thus, each crystallographic site in the unit cell is always occupied by the same conformer and the ratio of conformers is defined by whole numbers as in Scheme 1c. Conformational synmorphism describes the situation in which different conformers of a molecule are distributed randomly throughout the crystal lattice. Such a situation usually exists when two or more conformers have similar overall molecular shapes. Thus, at any particular molecular site a number of conformations may be adopted, the relative population being determined by the relative intra- and intermolecular energies involved as shown in Scheme 1d. The

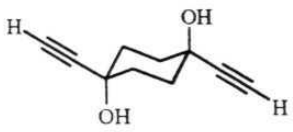
crystal structures examined in the following sections offer a test of the existing terminology and definitions of various polymorphs and the implications of identifying them with one or other term are described in this chapter.




**1**




**1a**



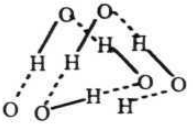

**1b**

**Three polymorphic forms of *trans*-1,4-diethynylcyclohexane-1,4-diol**

**Structural description of forms A and B**

Following the strategy discussed in Chapter one, *trans*-1,4-diethynylcyclohexane-1,4-diol **1** was identified as the starting point in the *gem*-alkynol structural series. Dialkynol **1** with a hydrophobic molecular core has been chosen to minimise any possible competitive intermolecular interaction effects. It was hoped that the intrinsic hydrogen bond preferences of the alkynol functionality could be discerned in a more clear fashion. Dialkynol **1** was synthesised from 1,4-cyclohexanedione. The reaction product contains both the *cis*- and *trans*-isomers. The pure *trans*-isomer, **1** was separated from the amorphous *cis*-isomer by repeated recrystallisations from ethyl acetate. In principle, **1** can exist in two conformations **1a** and **1b**. While the two hydroxy groups are diequatorial in **1a**, they are diaxial in **1b**. Further recrystallisation of pure **1** yielded crystals of two modifications, **A** and **B**, in the same flask. Both forms crystallise in the space group $P\bar{1}$ with Z = 3, both structures have three symmetry independent half molecules occupying distinct inversion centers, and both structures assemble around a spine of helical, cooperatively assisted, trimeric motif **2** formed *via* O–H···O hydrogen bonds (Table 1, Figure 1a, 1b). However, form **A** contains two

molecules of conformer **1a**, while the third molecule is in **1b** conformation. The reverse is true in form **B**: two molecules have diaxial hydroxy groups **1b** and the third has the diequatorial hydroxy conformation **1a**. It is interesting to note that form **B** is about 3% more efficiently packed than form **A** ($C_k^* = 66.7$ *vs* 68.5 in form **B**) which is compensated for by the better O–H···O hydrogen bonds in form A (mean $d = 1.715$ Å *vs* 1.745 Å in form **B**).



**2**

**Scheme 2**. Helical trimeric O–H···O synthon observed in the crystal structures of forms **A**, **B**, **C** and diol **3**.

**Table 1**. O–H···O geometries in the structures of polymorphs **A**[a], **B**[a] and **C**[b].

| | $D$ (Å) | $d$ (Å) | $\theta$ (°) |
|---|---|---|---|
| **A** | 2.682 | 1.704 | 172.87 |
| | 2.691 | 1.709 | 176.15 |
| | 2.691 | 1.733 | 163.70 |
| **B** | 2.733 | 1.752 | 176.45 |
| | 2.705 | 1.724 | 175.77 |
| | 2.740 | 1.759 | 175.54 |
| **C** | 2.633 | 1.641 | 176.81 |
| | 2.777 | 1.803 | 163.86 |
| | 2.756 | 1.798 | 170.09 |
| | 2.889 | 1.910 | 174.20 |

[a] All O–H bond lengths are neutron normalised (0.983 Å). [b] Neutron diffraction data.

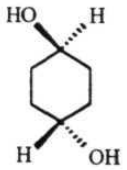
**Form C**

A third crystalline form was also isolated which was characterised by both low-temperature X-ray and neutron diffraction. Form **C** ($P2_1/c$, $Z = 4$) is a 1:1 hydrate of the diequatorial hydroxy conformer **1a**, and the O–H···O helical trimer, **2** is maintained in the crystal structure *via* the assembly of two symmetry-

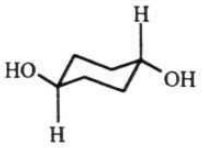
independent half-molecules of **1a** and one O-H donor from a water molecule (Figure 2a, Table 1). The second O-H donor of the water molecule interlinks inversion-related trimers ($d$ = 1.91 Å, $\theta$ = 174°). In effect, the water molecule replaces the axial hydroxy group in form **A** so that the trimeric O–H···O hydrogen bonded helical spine is the dominant recurring pattern in the three crystalline forms of **1**.

**Similarity with *trans*-cyclohexane-1,4-diol**

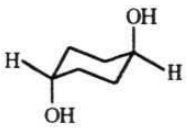
From the observation of the three forms of **1** it would appear that the presence of both the conformers is required for the formation of the robust helical trimeric synthon in the unsolvated polymorphs, a supposition that is reinforced by the crystal structure of *trans*-cyclohexane-1,4-diol **3**.[7] The diol **3** also contains the helical O–H···O trimer, **2** and crystallises in space group $P2_1/n$ with 1.5 molecules per asymmetric unit. The molecule sitting in the general position has diequatorial hydroxy groups, **3a**, while the molecule on an inversion centre has diaxial hydroxy groups, **3b**. The O–H···O trimer is then formed by two diequatorial and one diaxial conformer, as in form **A** of **1**. The packing diagram for **3** is shown in Figure 2b.




**3**




**3a**




**3b**

**Discussion**

In all the three structures **A**, **B** and **C**, the dominant cooperative hydrogen bond pattern is formed by the hydroxy group of the *gem*-alkynol moiety whereas the ethynyl group is almost passive. The formation of trimeric helix with different asymmetric independent molecules seems to suggest that they behave like

alcohols.[8] Why is it that both conformers are required for trimer formation in forms **A** and **B** of **1**, and in diol **3**? It may be that the simultaneous presence of inversion centres (arising from the molecular structures of **1** and **3**), and the 3- or $3_1$-axes that could arise if the trimer formed from three identical conformers of **1** or **3**, would impose significant constraints on the crystal packing efficiency. It appears that these constraints are alleviated by the presence of both conformers in

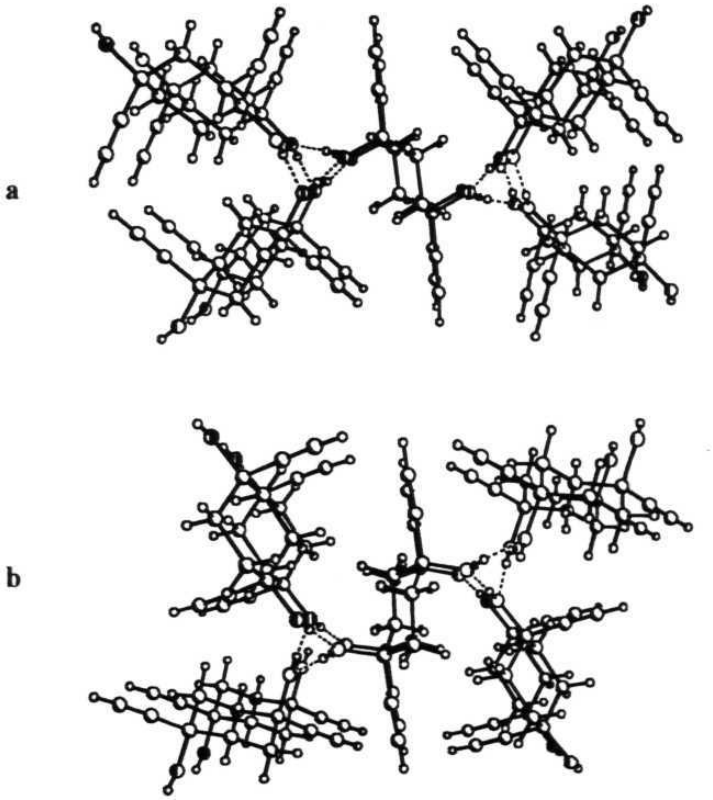



**Figure 1**. Perspective view of the crystal structures. (a) form **A** of **1**, (b) form **B** of **1**, to show the common helical O–H···O trimeric synthon and the conformations adopted by **1**.

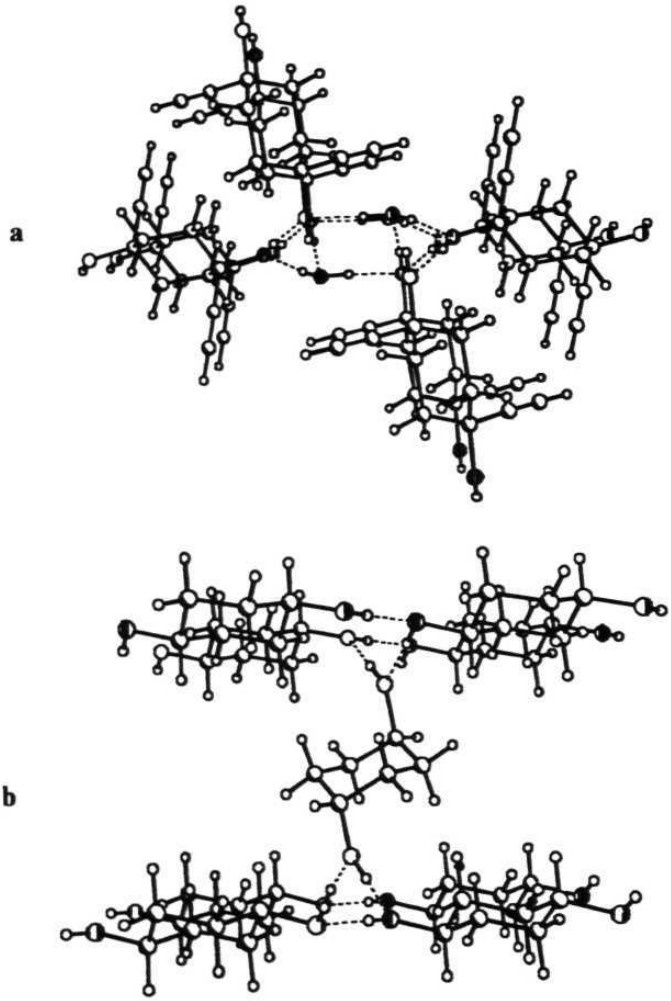



**Figure 2**. Perspective view of (a) monohydrated form **C** of **1**, (b) helical synthon **2** in diol **3**. Water molecule substitutes the role of one of the conformers in form **C**.

forming the trimeric hydrogen bonded synthon. There are no clear or simple ways of supporting or refuting this conjecture. Nevertheless, it is noted that the Cambridge Structural Database (CSD)[9] contains no examples of single-conformation cyclohexane-1,4-diols that form O–H···O trimers,[10] but that single-

conformation alicyclic diols do form such trimers (around $3_1$-axes), but only where the molecules do not have additional inversion symmetry.[11] These arguments provide a rationale for the ready incorporation of water in form **C** as a replacement for the other conformer of **1**.

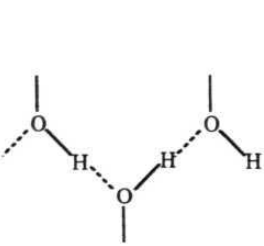
The structures described above have a number of important implications.

(a) The two forms **A** and **B** reveal-a new and unforeseen facet of polymorphism thereby calling for a reevaluation of existing definitions or a unified, general formalism. Specifically, **A** or **B** when taken individually exhibit conformational isomorphism. What would one term the phenomenon when the two forms are taken together?

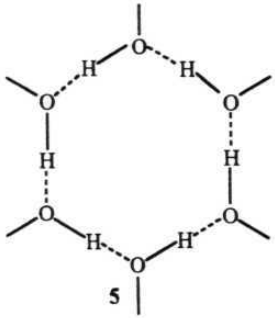
(b) The definition of forms **A** and **B** of **1** as polymorphs and form **C** as a pseudopolymorph is quite subjective. If **1a** and **1b** are considered as rapidly equilibrating conformers of **1**; then the definitions hold. However, if **1a** and **1b** are viewed as distinct molecular species, then forms **A** and **B** are simply binary crystals of 2:1 and 1:2 stoichiometry, and form **C** is a hydrate of **1a**.

(c) The isolation of three concomitant crystalline modifications[1b] of **1** suggest that the energy differences between them are small (1-2 kcal $mol^{-1}$) and that crystal forces influence the molecular conformation. It is unlikely that the polymorphs are kinetically controlled crystals because the three forms are stable over time.

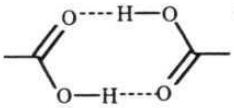
(d) The recurrence of the O–H···O helical trimer in structures of **1** and **3** confirms that this is a robust supramolecular synthon which is insensitive to a change in substitution from ethynyl (in **1**) to the much smaller H-atom (in **3**). The extent to which a molecular structure can be perturbed without changing the structure-determining synthons in its crystal structure is a contemporary theme in crystal engineering.



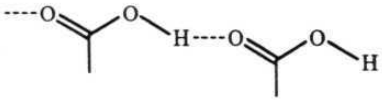
**4**



**5**



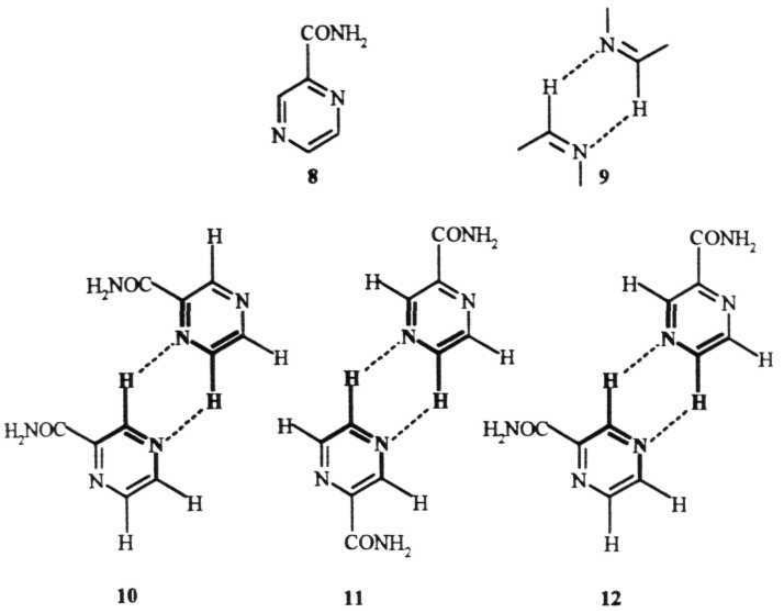
**6**



**7**

**Supramolecular synthons and polymorphism**

The occurrence of polymorphism can be explained in terms of supramolecular synthons. If a functional group can form more than one synthon this would lead to the possibility of polymorphism. A well known example is hydroquinone which exists in three polymorphic modifications $\alpha$, $\beta$ and $\gamma$. Each of these forms is characterised by a distinct synthon of O–H···O hydrogen bonds: chain synthon **4** in the $\gamma$-form, hexamer synthon **5** in the $\beta$-form and the combination of **4** and **5** in the $\alpha$-form. Similarly the dimer and catemer synthons (**6** and **7**) of carboxylic acid groups lead to two polymorphic crystal structures of oxalic acid.[12] Another way the synthons could manifest themselves in polymorphs is revealed by the modifications of pyrazine-2-carboxamide, **8**.[2a] In this compound, the same C–H···N dimer synthon, **9** is formed from chemically distinct locations of the molecule which finally leads to polymorphism (Scheme 3). In this light it is interesting to note that the three modifications of **1** include the same supramolecular synthon, **3**. However, this synthon is formed from a varied combination of different conformers of **1** and thus leads to polymorphism.



**Scheme 3**. The C–H···N hydrogen-bonded supramolecular synthon **9** is optimized in the polymorphs of pyrazine carboxamide **8** in alternative arrangements **10** through **12**.

The structures of the three forms of **1** resemble structures of simple diols much more closely than they resemble the structures of other *gem*-alkynols reported in the CSD, wherein one finds considerable interaction interference between the stronger O–H···O hydrogen bonds and weaker interactions (C–H···O, O–H···π and C-H···π) that involve the alkyne C-H and π-cloud, i.e., the role of the ethynyl group is minimal and amounts to close packing of hydrophobic groups. In further attempts at exploring the structural chemistry of the *gem*-alkynol functionality, the flexible molecular skeleton in **1** (cyclohexane ring) was replaced by a more rigid skeleton and these structures are discussed in the next chapter.

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10. The CSD (Version 5.16, October 1998, 190 307 entries) was culled for the O–H···O helical trimers formed by the cyclohexane-1,4-diol moieties (only

error-free, ordered organic compounds for which 3D co-ordinates field is present and $R \leq 0.01$ are taken). The hits with the fused ring systems were removed. One hit (VAVPOX) was obtained. Only one conformer of the molecule is present in the crystal structure and the helical trimer is formed by the three hydroxy groups present in the molecule.

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CHAPTER THREE

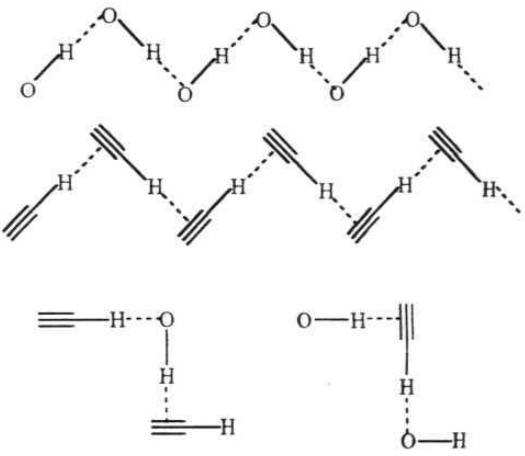
# SYNTHON TRANSFERABILITY AND STRUCTURAL REPETITIVITY IN *GEM*-ALKYNOLS

## Introduction

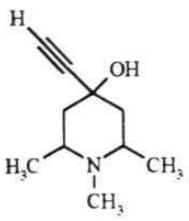
Crystal engineering requires the identification of common patterns in a series of crystal structures, so as to understand them in terms of mutual interplay between particular intermolecular interactions.[1,2] Since interactions arise from molecular functionalities one of the important aims of crystal engineering is, in effect, to establish correspondences between molecular and crystal structures.[3] Even though a complete and general connection between molecular and crystal structure has proved to be elusive, it is seen that certain patterns may be associated with specific functional groups. Carboxyl groups tend to form dimers, alcohols form rings or chains, aromatic rings form herringbone patterns,[4] and so on. However, no specific pattern is found for *gem*-alkynol in the family of compounds containing this functionality.[1,5,6] The CSD (Version 5.16, October 1998, 190 307 entries)[7] contains 94 crystal structures with a *gem*-alkynol functionality (only organic compounds without charged residues and for which 3D-coordinates field is present were taken and duplicate hits were removed manually). Analysis of these structures showed 16 O–H···O, 28 ≡C–H···O, 6 O–H···C≡C and 14 ≡C–H···C≡C contacts where all donor and acceptor atoms originate exclusively from *gem*-alkynol. The diversity of more extended patterns formed with these interactions is shown in Scheme 1 by the synthons that occur more or less frequently in this group.

These 94 *gem*-alkynols are a diverse lot though a majority of them (61) are steroids with *gem*-alkynol moiety at the C-17 position. The list also contains other quite different compounds, such as phenyl-rich molecules (4) and molecular complexes (6), which have been investigated with considerations other than crystal engineering in mind. The lack of structural repetitivity among these compounds may arise from the close juxtaposition of two hydrogen bond donors and two

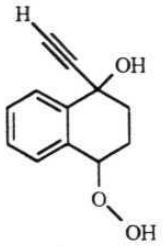
acceptors. In this sterically hindered situation, and also with their incorporation into cooperative networks, the four possible interactions, O–H···O, ≡C–H···O, O–H···C≡C and ≡C–H···C≡C become competitive. The packing adopted by any particular compound then becomes extremely sensitive to other molecular features. As has been described in Chapter one, the *gem*-alkynol functionality forms various interaction patterns. The presence of functional groups that are capable of acting as strong hydrogen bond donors and acceptors (there are 45 such compounds among the 94 retrieved from the CSD) interfere with *gem*-alkynol moiety and make the patterns even more diverse. For example, the crystal structures of two compounds **1** (BABFIT)[8] and **2** (VUYXES)[9] that contain strong hydrogen bond donor and/or acceptor in addition to *gem*-alkynol functionality may be considered (Figure 1).



**Scheme 1**. Some common supramolecular synthons in the crystal structures of *gem*-alkynols.



**1**



**2**

Compound **1** has an additional acceptor in the form of an N-atom. The hydroxy group of the *gem*-alkynol moiety in **1** forms an O–H···N hydrogen bond and the ethynyl group forms a ≡C–H···O bond. In **2**, the *gem*-alkynol hydroxy group forms O–H···O hydrogen bonded tetramers with the peroxy hydroxy group. The ethynyl group forms a ≡C–H···Ph interaction. These representative examples illustrate that the packing adopted by any particular compound in *gem*-alkynol family is extremely sensitive to molecular features. In essence, the unusually high level of interaction interference of *gem*-alkynol generates several quite different interaction patterns, so that it is not at all easy to establish the crucial molecule-supermolecule correspondences[3] that are so important in crystal engineering.

As shown in Figure 1, the presence of other functional groups that are capable of acting as strong hydrogen bond donors and acceptors leads to unnecessary complications in the crystal packing. The fact that 72 of the crystal structures contain single enantiomers is a further complication in that simpler centrosymmetrical packing patterns are precluded in these cases. Accordingly, *trans*-1,4-diethynyl-1,4-dihydroxy-2,5-cyclohexadiene, **3** was identified as a starting point in the crystal engineering exercise.[10] The symmetry of the molecule was expected to extend to a centrosymmetric packing, while the small size, and the absence of functional groups other than the alkynol fragment, was expected to result in further simplification leading to a packing that could be rationalised and subsequently repeated in another derivative.

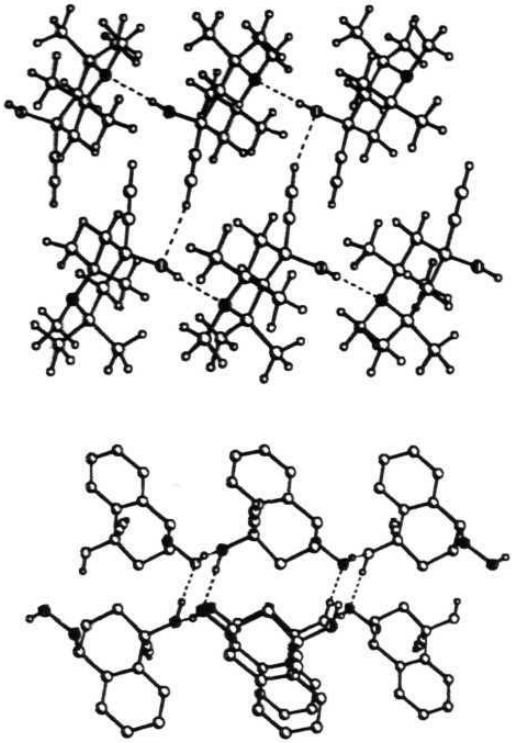
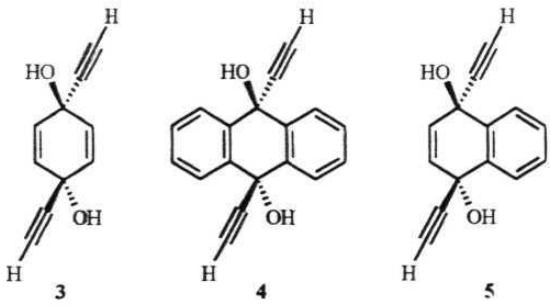


**Figure 1**. Crystal structure of **1** (top) and **2** (bottom, hydrogen atoms are removed for clarity) to illustrate the diverse patterns formed by *gem*-alkynols.



**Alkynol 3 – a structure with non-replaceable functionalities**

*Trans*-1,4-diethynyl-1,4-dihydroxy-2,5-cyclohexadiene, **3** crystallises in the space group *Pbca* ($Z' = 0.5$). The molecules are located on inversion centres. Glide related molecules form O–H···O hydrogen bonds (Table 1) which extend to cooperative O–H···O–H··· chains parallel to [010]. In each chain, any hydroxy group participates in two hydrogen bonds, one as a donor and the other as an acceptor. This is a common pattern in the crystal structures of phenols.[11] Adjacent chains associate to form layers parallel to (001) (Figure 2). The ethynyl group forms ≡C–H···O hydrogen bonds with the $2_1$- related molecules while the translation related molecules along the *b*-axis form C–H···C≡C bonds (Figure 3). Figure 3 shows that each of the C($sp^2$)–H groups is important in the densely packed layer parallel to (100). The structure of **3** is yet another example of heavy structural interference, in the typical family of *gem*-alkynols. The various functional groups (hydroxy, ethynyl, alkenic) are intimately involved with one another and they also interact with the hydrocarbon residues. Disturbing any of these will result in a total change in the structure, so that substitutional manipulation at any of the alkenic positions would destroy the structure. Attention shifted therefore to the *trans*-dibenzoalkynol **4**.

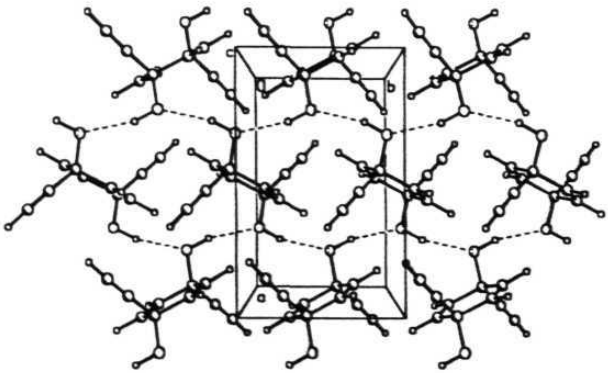



**Figure 2**. Crystal structure of **3**. Note the infinite cooperative O–H···O–H··· chains formed between *b*-glide related molecules.

**Table 1**. Hydrogen bonding interactions in the crystal structures of **3-5**.[a]

| | Interaction | $D$ (Å) | $d$ (Å) | $\theta$ (°) |
|---|---|---|---|---|
| **3** | O–H···O | 3.074 | 2.120 | 163.10 |
| | ≡C–H···O | 3.304 | 2.385 | 141.74 |
| | C–H···O | 3.459 | 2.678 | 128.59 |
| | C–H···M[b] | 3.653 | 2.903 | 126.57 |
| **4** | O–H···O | 2.845 | 1.903 | 159.54 |
| | ≡C–H···O | 3.120 | 2.069 | 162.70 |
| | O–H···M | 3.372 | 2.421 | 162.65 |
| | ≡C–H···M | 3.863 | 2.843 | 156.98 |
| **5** | O–H···O | 2.836 | 1.882 | 162.83 |
| | O–H···O | 2.831 | 1.894 | 158.46 |
| | ≡C–H···O | 3.129 | 2.101 | 157.39 |
| | ≡C–H···O | 3.141 | 2.069 | 169.56 |
| | O–H···M | 3.389 | 2.470 | 155.52 |
| | O–H···M | 3.486 | 2.608 | 148.67 |
| | ≡C–H···M | 3.762 | 2.738 | 157.57 |
| | ≡C–H···M | 3.804 | 2.774 | 158.91 |

[a] All O–H, C–H bond lengths are neutron-normalised (0.983, 1.083 Å respectively). [b] M is the midpoint of C≡C bond.

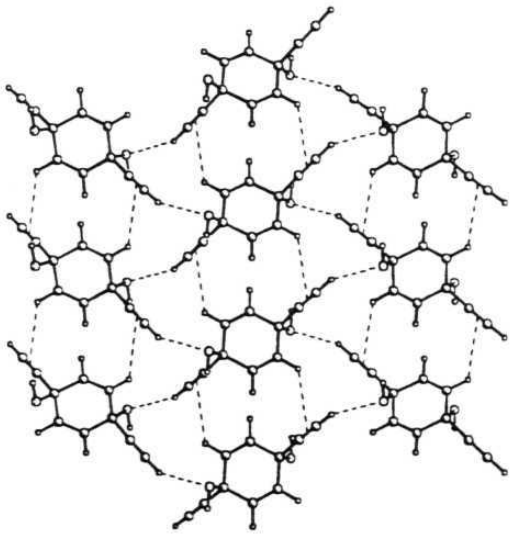
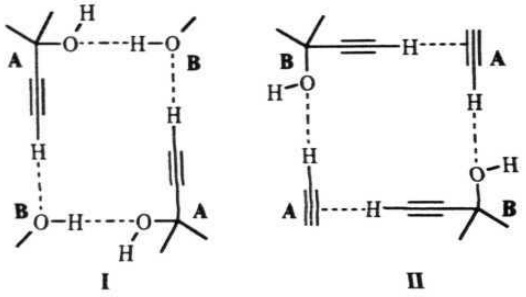


**Figure 3**. Densely packed layer parallel to (100) in the structure of **3**. Notice the ≡C–H···O and C–H···C≡C hydrogen bonds. Replacement of any of the alkenic H-atoms with a substituent is expected to change the structure.




**A** and **B** refer to symmetry independent molecules

**Orthogonal arrangement of hydrogen bonds and phenyl···phenyl interactions in 4**

The crystal structure of symmetrical *trans*-dibenzoalkynol **4** was determined. The compound crystallises in the space group $P\bar{1}$ with two half molecules in the asymmetric unit. The alkynol groups from these two sets of molecules constitute the centrosymmetric cooperative synthons **I** and **II**. Both these overlapping synthons involve both of the symmetry-independent molecules (**A** and **B**), but while **I** is built with O–H···O and ≡C–H···O hydrogen bonds (Table 1), **II** is built with ≡C–H···O and ≡C–H···C≡C bonds. All these hydrogen bonds lie within $(1\,\bar{1}\,0)$ and form a sheet structure (Figure 4). The fused phenyl rings protrude from either side of the hydrogen-bonded sheet and interdigitate with the corresponding rings in the adjacent sheets as shown in Figure 5. The hydrogen bonded and close-packed domains of this structure are structurally orthogonal, and clearly the interaction interference between the hydrogen bonding groups and the fused ring hydrocarbon portions of alkynol **4**, is minimal. Transferability of synthons between different structures is possible when interaction interference is minimal. Thus, orthogonal arrangement in **4** led to the structure determination of unsymmetrical alkynol **5** anticipating a similar hydrogen bonding pattern as in **4**.

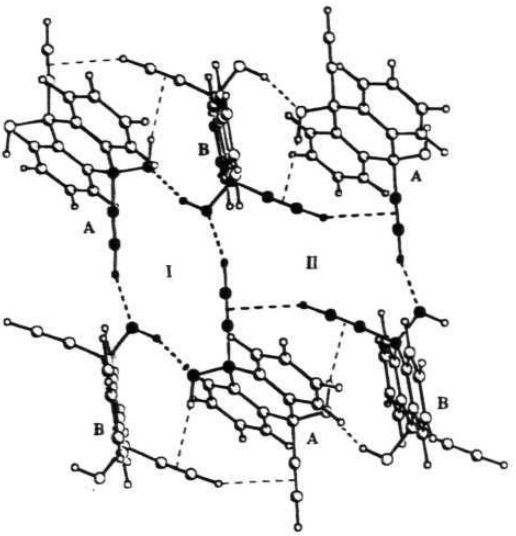



**Figure 4**. Crystal structure of **4** in $(1\,\bar{1}\,0)$ to show the cyclic synthons **I** and **II**. Notice the elaborate cooperative network of strong and weak hydrogen bonds.

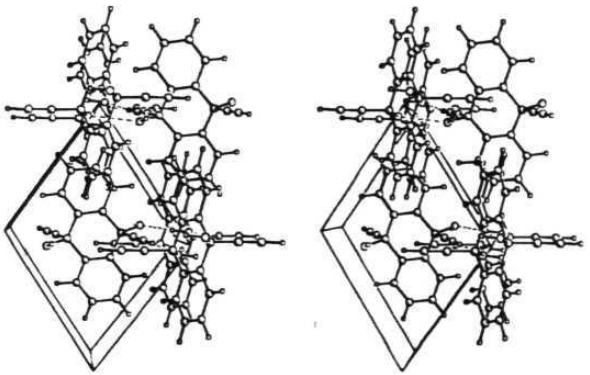


**Figure 5**. Stereoview of the crystal structure of **4** down [001] to show the interdigitation of the anthryl residues. The view is perpendicular to that shown in Figure 3.

**Structural prediction of 5**

Alkynol **5** has one less fused phenyl ring than **4**. The compound crystallises in the space group $P2_1/c$ ($Z' = 2$). The extended hydrogen bonded sheet with overlapping synthons **I** and **II** observed in **4** is retained intact in this structure as anticipated (Figure 6) i.e., synthon transfer has taken place. It is noteworthy that the crystal structures of alkynols **4** and **5** are very closely related, with only a minor difference in the disposition of the fused benzo rings. In **5**, the rings are situated on the same side of the hydrogen bonded sheets so that aromatic-aromatic interdigitation alternates with sheet-sheet close-packing (Figure 7). In **4**, the molecules lie on inversion centres so that interdigitation occurs on both sides of the molecular plane. These alternative modes of interdigitation may be compared by examining Figures 5 and 7.

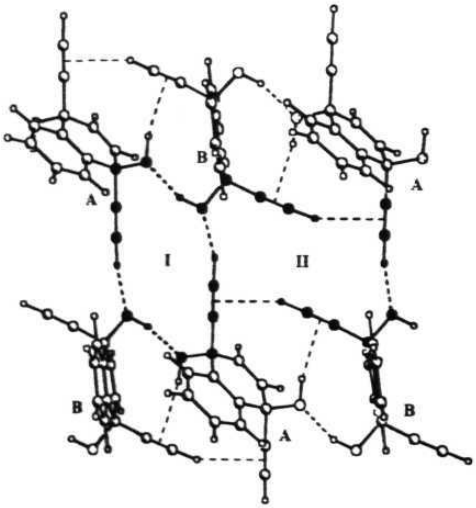



**Figure 6**. Crystal structure of **5**. Notice the near identity to Figure 3.

The manner of interdigitation of benzo rings in **4** and **5** is very similar. In general, one may expect that the substituted benzo rings in compounds **6** and **7** (R = simple substituent groups) might also interdigitate in the same way.

Accordingly, it can be predicted that other members of this family are likely to adopt similar crystal structures, thereby leading to structural repetitivity.

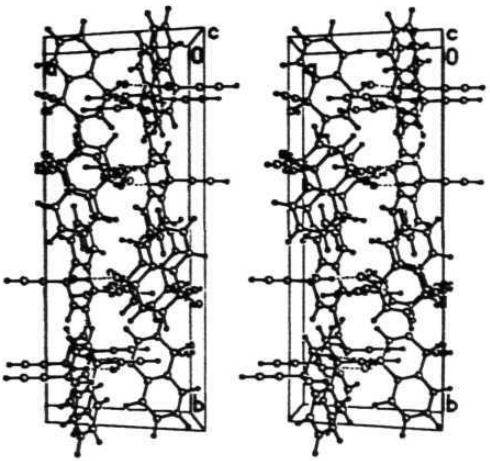
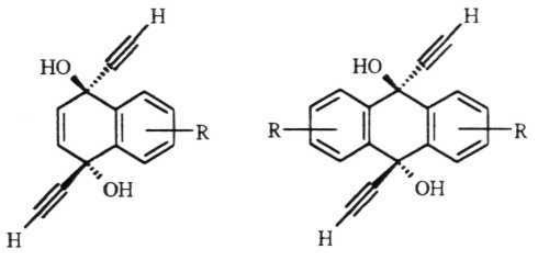



**Figure 7**. Interdigitation of naphthyl residues in the crystal structure of **5**. Compare this with Figure 5.




**6** **7**

## Conclusions

The interesting feature in **4** and **5** is synthon **I** which has been noted in the crystal structure of 2-ethynyladamantan-2-ol[12] (the original initiation of this project), where it is also formed from portions of two symmetry-independent molecules. This is the first instance of structural repetitivity of a major synthon

(formed by two groups of *gem*-alkynol) in this family between compounds with widely different substituent groups. The repetitivity of a synthon is an indication of its robustness.

Further it is of note that a fairly abstruse hydrogen bonded network is repeated in alkynols **4** and **5**. Anticipation of the structure of **5** was possible because of the orthogonal and non-interfering arrangement of hydrogen bonding and phenyl-phenyl interactions in **4**. This situation is similar to the crystal structure of 4-aminophenol[3a] in which the OH···$NH_2$ and phenyl···phenyl interactions are insulated from each other and in contrast to the structures of 2- and 3-aminophenol[3b] which show a high degree of interaction interference. Interaction orthogonality is of key importance in establishing the beginnings of structural repetitivity in systems where severe structural interference is likely.

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CHAPTER FOUR

# HALOGEN ATOM INTERACTIONS IN TETRAHALO-1,4-DIETHYNYL-CYCLOHEXA-2,5-DIENE-1,4-DIOLS

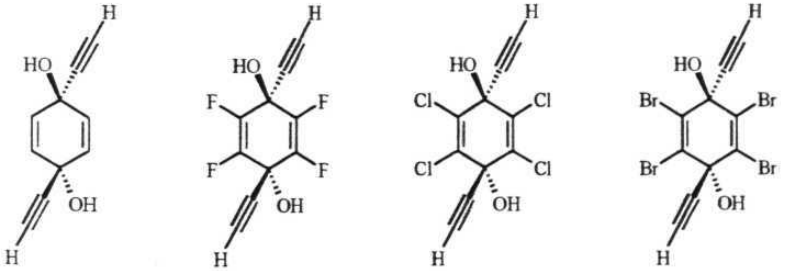
## Introduction

Interactions between halogen atoms in crystals is a matter of long-standing interest.[1] These interactions form the basis of the so-called '4Å chloro rule' from which the phrase 'crystal engineering' originated and therefore are of special signficance in this field. Though halogen atom interactions are known for a long time they have not been studied as extensively as other weak intermolecular interactions, such as C–H···O hydrogen bonds.[2] Statistical studies with the help of CSD revealed that halogen···halogen (from here on X···X, X = Cl, Br, I) interactions occur in two predominant geometries in crystals.[3] These are termed type I and type II interactions (Scheme 1). The two angles at the X atoms in an interaction C–X···X–C are defined as $\theta_1$ and $\theta_2$. While the type I geometry is identified by two equal or nearly equal angles ($\theta_1 \cong \theta_2$), the type II geometry is associated with two rather unequal angles with one angle ($\theta_1$) close to 180° and the other ($\theta_2$) close to 90°. The predominance of these two geometries has been attributed to close packing around an inversion centre in the type I case and to a polarisation-induced attraction[1g,4] in the type II case. In support of these arguments it has been found that wl le easily polarisable I-atoms are almost exclusively involved in I···I interactions with type II geometry, Cl···Cl contacts occur with type I and type II geometries almost to the same extent.

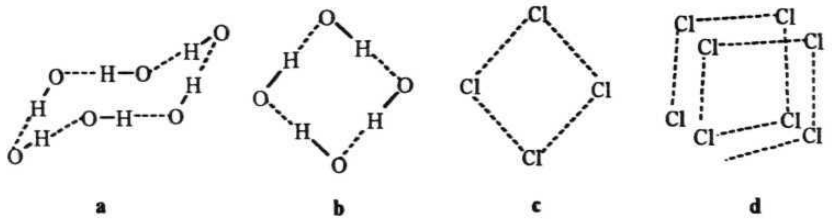

Type I ($\theta_1 \approx \theta_2$) Type II ($\theta_1 \approx 180, \theta_2 \approx 90°$)

**Scheme 1**. Preferred geometries of halogen···halogen interactions.

However, other studies showed the possibility that close packing of elliptically shaped halogen atoms[1h,5] will also lead to a type II geometry and argued in favour of reduced repulsion rather than increased attraction. Revised statistical analyses have been performed on a larger body of data and also with hetero X···X interactions (with two different halogen atoms).[6] These studies showed that in hetero X···X interactions, the type II geometry becomes important with a polarisable heavier halogen atom and polarising lighter halogen atom (the smaller of the two angles is associated with lighter halogen atom). The discussion of X···X interactions that follows in this chapter is applicable only to Cl, Br and I atoms. Fluorine being hardly polarisable is not expected to be involved in such interactions. Continuing with this line of thought, the Cl atom lies between F and Br atoms, and shows a behaviour half-way between them. These conclusions are implicit in the recent statistical studies but lack proper experimental support.




Diethynylated derivatives (**1-4**) of benzoquinone, fluoranil, chloranil and bromanil were synthesised and their crystal structures analysed to explore the structural chemistry of *gem*-alkynol functionality. The crystal structure of **1** is detailed in the previous chapter. The tetrahalo-1,4-diethynyl-cyclohexa-2,5-diene-1,4-diols (**2-4**) reveal interesting features of halogen atom interactions that are useful in the context of halogen atom interactions in particular and to crystal engineering in general. The geometrical parameters for O–H···O hydrogen bonds are given in Table 1. The other interactions are included in Table 2.



**Scheme 2**. Supramolecular synthons in structures **2-4**.

**Hexameric O–H···O synthons and ≡C–H···F interactions in 2**

The fluoro derivative **2** crystallises in the space group $P\bar{1}$ ($Z' = 3 \times 0.5$). Three symmetry independent molecules occupy distinct inversion centres at 0 ½ 0, ½ 0 ½ and ½ ½ ½. All the hydroxy groups participate in O–H···O hydrogen bonding and extend to a six membered ring with a chair conformation, a supramolecular chair as shown in Scheme 2a. This O–H···O hexamer synthon is also located on an inversion centre (at 0 ½ ½). Three independent molecules contribute to the hexamer synthon and each independent pair of molecules is located at 1,4 positions in an anti-parallel disposition (Figure 1). Each hexamer synthon is thus connected to six others through molecular spacers and extend to a three-dimensional network (Scheme 3a). This three-dimensional network has octahedral supramolecular nodes (the O–H···O hexamer synthons) and linear ditopic spacers (molecular core). In essence, this network defines the connectivity in three-dimensions through similar (independent) molecular spacers (which is reflected in almost equal unit cell dimensions) (Table 3).

**Table 1**. O–H···O hydrogen bond geometries in the crystal structures of **2-4**.[a]

| | *D* (Å) | *d* (Å) | *θ* (°) |
|---|---|---|---|
| **2** | 2.756 | 1.778 | 173.45 |
| | 2.718 | 1.735 | 178.76 |
| | 2.733 | 1.785 | 160.94 |
| **3** | 2.652 | 1.713 | 158.52 |
| **4** | 2.724 | 1.829 | 149.81 |
| | 2.688 | 1.854 | 140.65 |
| | 2.724 | 1.774 | 161.61 |
| | 2.739 | 1.809 | 156.61 |

[a] All O–H bond lengths are neutron-normalised (0.983 Å).

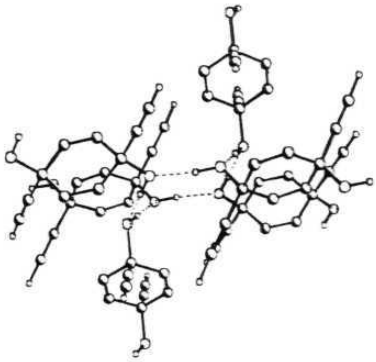


**Figure 1**. Supramolecular chair formed by O-H···O hydrogen bonds in **2**. The F atoms are removed for clarity.

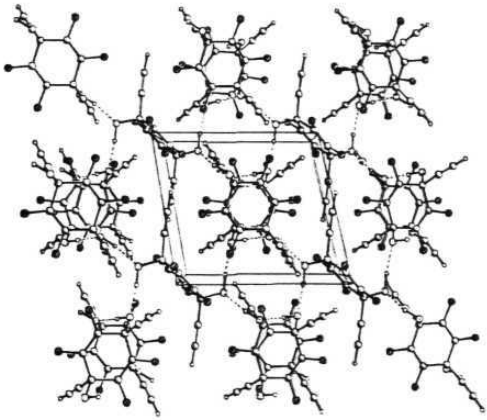
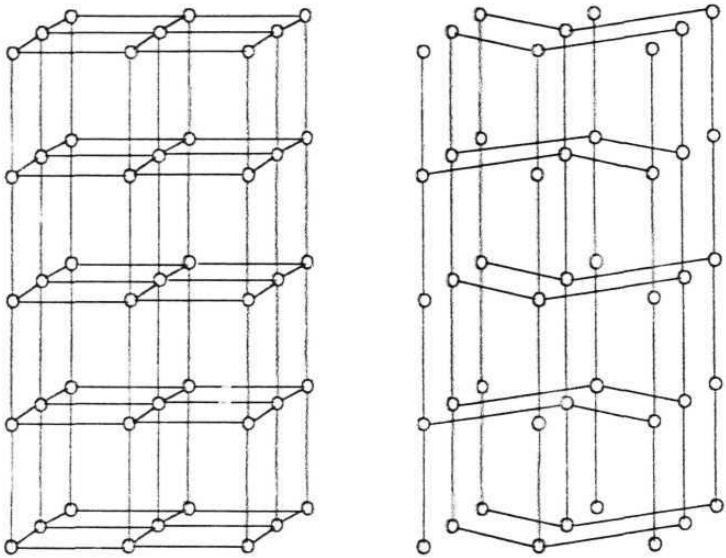


**Figure 2**. Crystal structure of **2** viewed down [010]. Notice the O-H···O hexamers and the three-dimensional interlinking of these hexamers.

The three-dimensional packing of **2** is shown in Figure 2. Two of the three independent ethynyl groups form three C–H···F (Table 2) interactions.[7] One of these C–H···F interactions ($d$ = 2.608 Å) forms a dimeric motif between $a$-translation related molecules. The dimer and the O–H···O hexamer alternate along the $b$-axis. Other C–H···F interactions link translation related molecules along the $b$-axis. It is noteworthy that a short C–H···F interaction ($d$ = 2.335 Å, $\theta$ = 171°) is

observed. Only two out of the six independent F atoms form an F···F contact with a distance less than the van der Waals sum (Table 2).




**Scheme 3**. Schematic representation of the three-dimensional networks in **2** (a), and **3** and **4** (b). The open circles represent O–H···O hexamers in (a) and O–H···O tetramers in (b). The lines connecting the circles represent molecular spacers. Notice the octahedral and tetragonal connectivities in (a) and (b) respectively. Notice that in both cases the network depiction consists of supramolecular nodes and molecular node-connectors.

**Symmetrical tetramer synthons of O–H···O and Cl···Cl interactions in 3**

The chloro derivative **3** crystallises in the high symmetry tetragonal space group $I4_1\,a$ (Z=8) with molecules located on inversion centres. Here too the hydroxy groups are involved in O–H···O hydrogen bonds but this time the interactions extend to a tetramer synthon around a $\bar{4}$ axis (Scheme 2b). Again, each molecule with its two hydroxy groups connects two tetramer synthons. In other words, each tetramer synthon is connected to four others through molecular spacers and extend to a three-dimensional network depicted in Scheme 3b.

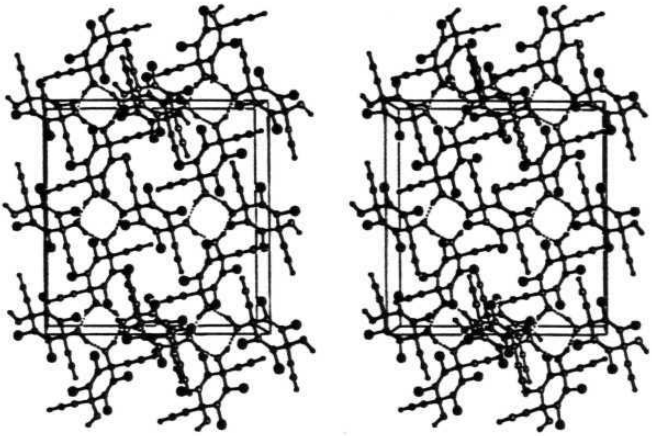


**Figure 3**. Stereoview of **3** viewed down tetragonal axis showing O–H···O synthons and network. The O–H···O tetramers are formed around $\bar{4}$ axis.

**Table 2**. C–H···X and X···X geometries in the crystal structures of **2-4**.[a]

| | | *D* (Å) | *d* (Å) | $\theta$ (°) |
|---|---|---|---|---|
| **2** | C–H···F | 3.409 | 2.335 | 171.07 |
| | | 3.348 | 2.536 | 130.95 |
| | | 3.630 | 2.607 | 157.27 |
| | F···F[b] | 2.865 | | 173.72/90.59 |
| **3** | C–H···Cl | 3.696 | 3.025 | 120.58 |
| | Cl···Cl[b] | 3.605 | | 161.86/78.48 |
| | | 3.731 | | 166.00/127.76 |
| **4** | C–H···Br | 3.900 | 3.071 | 133.74 |
| | | 3.750 | 2.979 | 128.47 |
| | | 3.720 | 2.952 | 128.16 |
| | C–H···C≡C | 3.507 | 2.821 | 121.27 |
| | Br···Br[b] | 3.421 | | 163.03/116.10 |
| | | 3.661 | | 157.83/75.45 |
| | | 3.515 | | 172.95/110.85 |
| | | 3.680 | | 167.16/120.57 |
| | | 3.882 | | 166.76/68.05 |
| | | 3.839 | | 152.30/116.60 |

[a] All C–H bond lengths in the structures are neutron-normalised (1.083 Å). [b] For X···X interactions *D* is the distance between interacting halogen atoms, $\theta$ values are as defined in the introduction.

The three-dimensional architecture of O–H···O hydrogen bonds is supported by other weak interactions in the crystal (Figure 3). Both the symmetry independent Cl atoms are involved in type II Cl···Cl interactions. Each independent atom is linked to a symmetry related atom and therefore two symmetry independent Cl···Cl interactions (that is four interactions per molecule) are found in the structure (Table 2). One of these interactions ($d$ = 3.731 Å) extend to a closed Cl···Cl tetramer synthon (Scheme 2c) around the $\bar{4}$ axis. The other interaction ($d$ = 3.605 Å) forms a Cl···Cl helical tetramer (Scheme 2d) around a $4_1$-axis. The O–H···O and Cl···Cl tetramer synthons alternate along the $\bar{4}$ axis. A long C–H···Cl contact is formed by the ethynyl group.

**Polarisation-induced type II Br···Br interactions in 4**

The bromo analogue **4** crystallises in the space group $P\bar{1}$ ($Z$ = 4). Each of the four symmetry-independent molecules is located on a distinct inversion centre. All the hydroxy groups are involved in O–H···O hydrogen bonds and the extended pattern is again a tetramer synthon (Scheme 2b). Each independent molecule contributes one hydroxy group to the tetramer and also connects adjacent tetramers. The three-dimensional network of O–H···O tetramers is similar to that in the chloro analogue (Scheme 3b). Thus the chloro and bromo derivatives form topologically similar networks in their crystal structures.

Figure 4 displays the three-dimensional packing of **4**. The four symmetry-independent molecules are cross-linked by Br···Br interactions. On an average, each molecule forms three Br···Br interactions (Table 2). Three of four independent ethynyl groups form C–H···Br contacts while the fourth one forms a ≡C–H···C≡C contact. While the O–H···O network topology in **4** is the same as that found in **3** no tetrameric Br···Br synthons (in closed or helical variation) are observed. However the Br···Br interactions in **4** are effectively shorter than the Cl···Cl interactions in **3** as revealed from the percent reduction in their contact distances when compared to their respective van der Waals sum. The Cl···Cl and

Br···Br contact distances in **3** ($d$ = 3.605-3.731 Å) and **4** ($d$ = 3.421-3.882 Å) are in the ranges 103.0-106.6% and 92.5-104.9% of their respective van der Waals sum (3.50 and 3.70 Å for Cl···Cl and Br···Br).

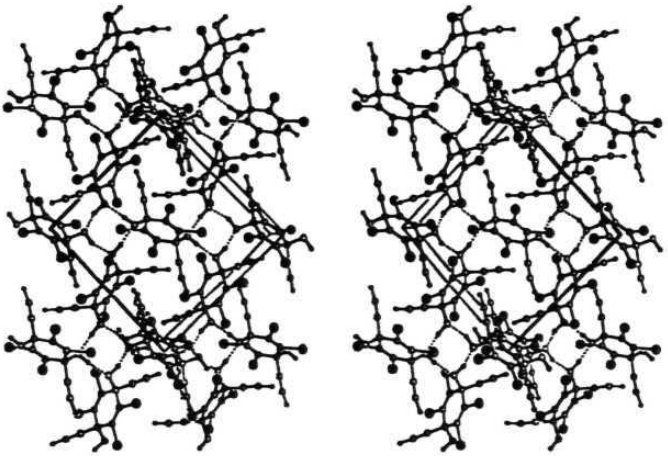
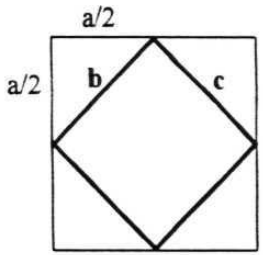


**Figure 4**. Stereoview of **4** to show O–H···O hydrogen bonds down the *a*-axis. The O–H···O tetramer synthons are formed by four symmetry-independent molecules. Notice the similarity to Figure 3.




**Scheme 4**. The relationship between the unit cells of **3** (thin lines) and **4** (thick lines).

The similarity of the network topologies in **3** and **4** leads to a pseudo-tetragonal symmetry in **4**. Scheme 4 shows how the unit cell of **4** can be derived from that of **3**. The lengths of the *a*-axis in **4** and *c*-axis in **3** are similar, that is *a*-axis is the

pseudo-tetragonal axis in **4**. Therefore the *a*- and *b*-axes in **3** are related to *b*- and *c*-axes in **4**. This relation has been found to be: *b* (or *c*) of **4** ≅ $a/\sqrt{2}$ of **3**.

**Table 3**. Cell parameters for the crystal structures **2-4**.

| | **2** | **3** | **4** |
|---|---|---|---|
| Space group | $P\bar{1}$ | $I4_1/a$ | $P\bar{1}$ |
| *a* (Å) | 8.9002(18) | 16.758(2) | 8.9147(3) |
| *b* (Å) | 9.2388(18) | 16.758(2) | 12.6402(5) |
| *c* (Å) | 9.6721(19) | 8.865(2) | 12.6547(5) |
| $\alpha$ (°) | 93.73(3) | 90 | 85.7380(10) |
| $\beta$ (°) | 98.73(3) | 90 | 69.6250(10) |
| $\gamma$ (°) | 114.46(3) | 90 | 72.72 |

**Structural comparison of 1-4**

A comparison of the halogen derivatives **2-4** along with the parent compound **1** (described in Chapter three) is in order. In all the above structures, the *gem*-alkynol group is involved in intermolecular interactions. While the hydroxy group forms O–H···O hydrogen bonds, the ethynyl group forms ≡C–H···halogen interactions. The dominant interactions in all these structures are the O–H···O hydrogen bonds. In the parent compound these interactions extend to a chain pattern but they form cyclic patterns in the halogen derivatives **2-4**. These O–H···O synthons are interlinked by molecular spacers in all the cases. In **1**, the glide related chains form a two-dimensional network through such interlinking. In **2**, each O–H···O hexamer synthon is connected to six others to produce a three-dimensional network. In **3** and **4** the O–H···O tetramer synthons are cross-linked in a three-dimensional fashion. The hydroxy groups are equally saturated with respect to their hydrogen bond potential in all variations of O–H···O synthons: chain, hexamer, tetramer. Thus the variation in the kind of synthon formed (which in turn causes the variation in the kind of network generated) may be attributed to the varying demands of different substituents, be they isotropic or directional.

At a gross level, the explanation offered with regard to O–H···O patterns in mono alcohols[8] could answer questions about the variation in the kind of O–H···O

synthons seen in **1-4**. This study reveals that as the bulk of the molecular core increases, the O–H···O patterns form translation related chain, $2_1$- or glide-related chain and cyclic patterns or multiple molecules in the asymmetric unit. Accordingly, the transition from a glide related chain to cyclic patterns (or multiple molecules in the asymmetric unit) from **1** to **4** may be attributed to the increase in substituent size from H to Br. However, this is a very rough approximation of the kind of pattern obtained (*e.g.*, a chain or a cyclic pattern) but does not explain the intricate details in the structure. For example it is not clear why the networks in **3** and **4** are very closely related yet different, or why **2** adopts a hexamer pattern and not say the helical trimer pattern seen in the flexible alkynols described in Chapter two. A more detailed and in-depth analysis will become necessary after more structural data are available.

It is important to record here some details of a recent study on the crystal structures of $\gamma$-hydroquinone and tetrahalogenated hydroquinones.[9] All these structures consist of identical O–H···O synthons ($2_1$-chain patterns) and identical O–H···O networks. The differences between the structures occur in the mutual arrangement of O–H···O networks and it is identified that these differences are characteristic of the substituent groups H, F, Cl or Br. In the present context, it is of paramount importance to note that the O–H···O synthons in all these structures are *identical*. Such similarity between the O–H···O synthons is observed because the synthons of other functional groups are effectively insulated from the O–H···O synthons.[10] The similarity of these compounds at a molecular level to the ones studied in this work may be noted. That different O–H···O synthons are observed in **1-4** therefore clearly indicates a high degree of synthon interference in these structures. In the following sections, such interference is analysed and the distinct crystal packing demands of halogen atoms are revealed.

**Nature of halogen atom interactions**

As discussed in Chapter three the replacement of $sp^2$ C–H groups in **1** by other groups would destroy the structure. Replacement of H atoms by F atoms in fact

reverses the polarity at that site and the newly substituted F atoms are forced to be in a repulsive proximity of O atoms. The structure type observed for **1** is therefore not realistic for **2**. Thus **2** seeks to adopt a structure in which its hydrogen bonding and/or electrostatic requirements are met with. No O–H···F interactions are found. This is in accordance with recent database and computational studies.[11] The hard nature of F makes it least approachable by hydrogen bond donors despite its high electronegativity. Strong hydrogen bond donor groups such as O–H and N–H inevitably include strong acceptors[12] (O and N) and therefore O–H···O or N–H···N hydrogen bond formation is a more realistic possibility. Weak hydrogen bond donors such as C–H groups avoid the automatic introduction of other acceptors and recent statistical and experimental studies on compounds containing the elements C, H and F only,[7] have shown that F atoms indeed participate in C–H···F hydrogen bonding. In this connection the structure of **2** is revealing in that it contains strong and weak hydrogen bond donors in the same molecule and illustrates the two features described above by forming short ≡C–H···F hydrogen bonds. The general reluctance of F atoms in forming halogen···halogen interactions is also identifed.

The structure type observed for **2** does not support the halogen···halogen interactions and is not suitable for **3**. The chloro derivative **3** therefore adopts a different structure with O–H···O tetramers. The symmetry of these tetramers extend to the macroscopic level and **3** crystallises in the tetragonal space group $I4_1/a$. Within these high symmetry networks the neighbouring Cl atoms interact with one another in type II geometries. Two kinds of Cl···Cl synthons, closed and open variations of tetrameric Cl···Cl interactions, are observed. The high symmetry of the O–H···O synthons and networks impose similar symmetry restrictions on these Cl···Cl interactions and the Cl···Cl contact distances are somewhat longer than van der Waals distances.

The easily polarisable nature of Br-atoms makes the bromo derivative **4** adopt a structure similar to that of **3**. Thus O–H···O tetramers are again formed and a similarly symmetrical network is generated. A high symmetry packing pattern as

in **3** would lead to long contact distances for Br···Br interactions. The overall symmetry of the network in **4** is reduced to triclinic with four independent molecules in the crystal and short type II Br···Br interactions are observed. Thus the Br atoms prefer to form short polarisation-induced type II interactions which interfere with robust O–H···O synthons and networks. Such interference leads to destruction of symmetry of O–H···O patterns in **4**. A comparison of the structure of **2** on one hand and those of **3** and **4** on the other reveals that F prefers to form hydrogen bond type C–H···F interactions and Cl and Br prefer to form polarisation-induced type II halogen···halogen interactions. A close inspection of **3** and **4** uncovers the small differences between Cl and Br atoms. The polarisability of Cl and Br atoms drives the O–H···O networks into a tetragonal symmetry. While the Cl···Cl interactions are inherently weak and therefore adjust to the symmetry of O–H···O synthons with longer contact distances, the strength of Br···Br interactions coupled with the requirement for short contact distances distort the symmetry of O–H···O synthons. Polarisation-induced interactions become increasingly important with increasing size of the halogen atoms.

## Conclusions

Alkenic C–H, C–F, C–Cl and C–Br are the functionalities that discriminate between alkynols **1-4**. The hydroxy groups in all these structures form O–H···O hydrogen bonds and the ethynyl groups involve in C–H···X interactions (X = O in **1**, F in **2**, Cl in **3** and Br or π(≡) in **4**). Different O–H···O synthons, chains in **1**, hexamers in **2** and tetramers in **3** and **4** are observed. These variations in the synthons of stronger hydrogen bonds occur to satisfy the interaction demands of the variable functional groups in the molecules. That is, alkenic C–H groups in **1** form C–H···C≡C, the C–F groups in **2** form ≡C–H···F and the C–Cl and C–Br groups in **3** and **4** form type II halogen···halogen interactions. A comparison of **2** with **1** as well as with **3** and **4** suggests that interactions of F-atom are not comparable with those of H-atom or of Cl- and Br-type. Because of its hard nature, the F-atom is not involved in polarisation-induced interactions as are the

heavier halogen atoms (Cl, Br and I). Alkynols **3** and **4** reveal a subtle difference between interactions of Cl- and Br-atoms. The polarisability of Cl-atoms is less than those of Br-atoms and type II Cl···Cl interactions are weaker than type II Br···Br interactions. Such inherent weakness of Cl···Cl interactions leads to formation of Cl···Cl synthons which fit into the overall symmetrical network of O–H···O hydrogen bonds. The high polarisability of Br-atoms demands the formation of short type II Br···Br interactions which destroy the symmetry of O–H···O synthons. In effect, while Br-atom interactions interfere with O–H···O synthons because of their strength, Cl-atom interactions attune to the symmetry of O–H···O synthons. These structures demonstrate that polarisation-induced interactions become realistic and more important with increasing size of the halogen atoms.

**References and Notes**

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CHAPTER FIVE

# AROMATIC HYDROGEN BONDS IN SOME *GEM*-ALKYNOLS

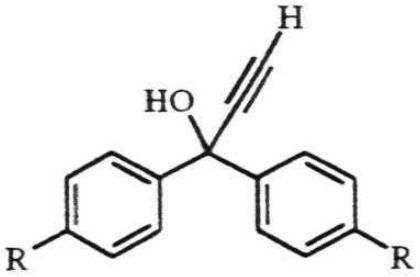
## Introduction

Conventionally, electronegative atoms such as O and N are regarded as hydrogen bonding elements and O–H···O, O–H···N and N–H···O are known as strong hydrogen bonds. These interactions form part of many significant supramolecular synthons and have been extensively studied in crystal engineering. With the development of the subject, weakly acidic C–H groups have also been found to be involved in intermolecular interactions with O and N acceptors. Such C–H···O and C–H···N interactions have been shown to exhibit hydrogen bonding characteristics in every respect. However, these C–H hydrogen bonds are weaker than conventional hydrogen bonds. Since the C–H acidity varies over a wide range depending on the nature of its environment, the strength of C–H···O hydrogen bonds varies equally and in some cases the C–H groups form interactions as strong as weak O–H···O hydrogen bonds.

The essential character of O and N atoms which makes them hydrogen bond acceptors is their ability to extend electron density to electron deficient H-atoms. In this light, it seems reasonable to think that phenyl rings with their π-electron density can also act as hydrogen bond acceptors. Indeed several instances have been found where π electrons of aromatic rings, triple bonds (C≡C) and double bonds (C=C) are directed at electron deficient H-atoms. Interactions involving π-electrons have attracted much interest and in a recent book a detailed account of X–H···π (X = O, N, C and Cl) interactions has been discussed.[1] Another recent book deals exclusively with C–H···π interaction.[2] IR spectroscopic studies provide evidence for the hydrogen bond character of O–H···π interaction with red shift in O–H stretching frequency.[3] Similar shifts are also observed for C–H···π interactions.[3b,4] The O–H···π and C–H···π interactions involving aromatic acceptors are therefore called aromatic hydrogen bonds. Further, X–H···π

interactions have also been found in gaseous state[5] and their existence is also proved by quantum-chemical calculations.

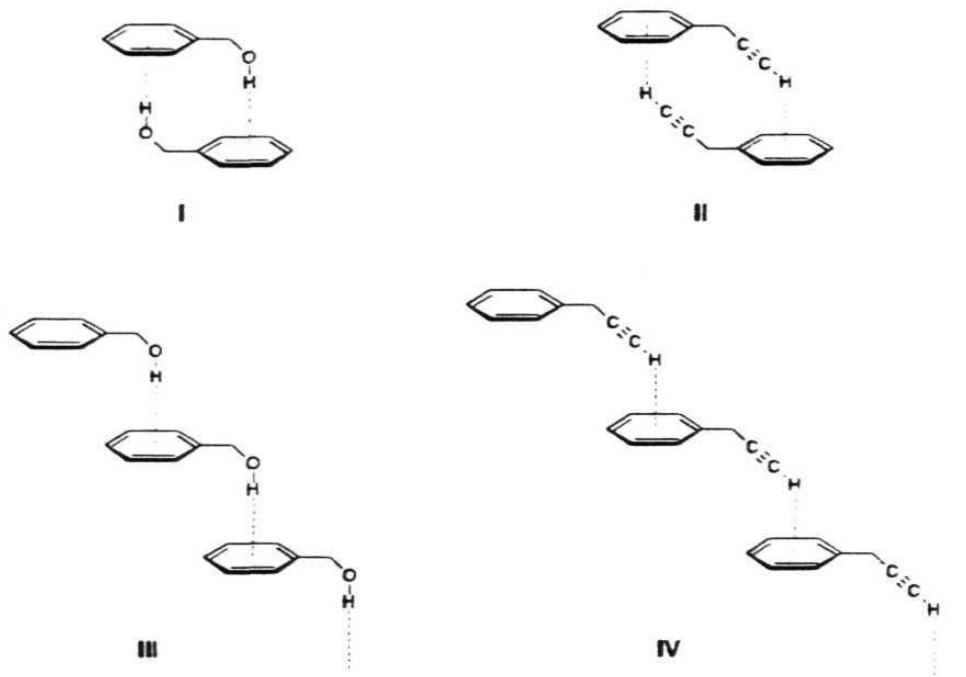
Spectroscopic identification of X–H···π interactions as aromatic hydrogen bonds provides a confident lead to their further characterisation through a structural approach. Such structural studies can be dealt with either by statistical methods or through a detailed study of a series of similar structures. Statistical approaches furnish details that are otherwise not obtainable. For example, the long range character of C–H···O interactions has been revealed with CSD studies that explains the electrostatic nature of these interactions as opposed to isotropic van der Waals interactions.[6] However, the reliability of the results obtained from statistical studies largely depend on the quantity and quality of the available data. An analysis of ≡C–H···C≡C interaction had to be performed on 32 observations in 25 crystal structures due to the lack of data.[7] Nevertheless, this analysis showed a distribution of H···π distances that is characteristic of bona fide hydrogen bonds. In the absence of enough data on *gem*-alkynols we have taken the approach of studying a series of structures in detail.




**1** R = H
**2** R = Me
**3** R = Cl
**4** R = Br
**5** R = Ph

In view of our interest in *gem*-alkynol functionality and with the above background, we identified the structure of diphenylethynylmethanol, **1**[8] to be interesting as it contains O–H···Ph and ≡C–H···C≡C interactions. In the present study, *gem*-alkynols **2-5** have been synthesised and their structures determined by single crystal X-ray diffraction. Additionally, the crystal structure of the chloro derivative **3** has also been determined by single crystal neutron diffraction techniques. All the structures show the involvement of hydroxy and ethynyl group

interactions with aromatic rings. These O–H···Ph and ≡C–H···Ph interactions extend to closed and extended supramolecular synthons **I-IV** shown in Scheme 1. The importance of these synthons in structural architecture will become clear in the following sections. The geometrical parameters for these and various other interactions observed in structures **1-5** are given in Table 1.




**Scheme 1**. Dimer (**I** and **II**) and chain (**III** and **IV**) synthons generated by O–H···Ph and ≡C–H···Ph interactions. Notice the topological similarity between **I** and **II**, and between **III** and **IV**.

**O–H···Ph and ≡C–H···C≡C hydrogen bonds in alkynol 1**

The mono *gem*-alkynol **1** crystallises in the space group $P2_1/n$ ($Z$ = 4). While the hydroxy groups participate in intermolecular O–H···Ph bonds, the ethynyl groups form ≡C–H···C≡C interactions. Inversion related molecules are connected with O–H···Ph hydrogen bonds and form dimeric molecular units through synthon **I** (Figure 1a). Herringbone interactions between aromatic rings mediate the close packing of these dimers parallel to $(1\bar{1}0)$ and extend to a two-dimensional packing. The ethynyl groups project outwards from this two-dimensional packing and form cooperative chains of ≡C–H···C≡C interactions along the *b*-axis (Figure 1b). In essence, **1** represents a structure stabilised exclusively by weak

interactions. No strong O–H···O interactions which could in principle occur are actually found.

**Table 1**. Geometrical parameters for various interactions found in the crystal structures of **1-5**.[a]

| | Interaction | *D* (Å) | *d* (Å) | *θ* (°) |
|---|---|---|---|---|
| **1** | O–H···X1[b] | 3.474 | 2.499 | 171.37 |
| | ≡C–H···M[b] | 3.655 | 2.594 | 166.06 |
| | C–H···X1 | 3.966 | 2.985 | 150.81 |
| | C–H···X1 | 3.937 | 3.061 | 138.35 |
| **2** | O–H···X1 | 3.324 | 2.358 | 167.20 |
| | ≡C–H···X1 | 3.987 | 3.026 | 148.18 |
| | ≡C–H···X2[b] | 3.715 | 2.696 | 156.54 |
| | C–H···O | 3.412 | 2.647 | 127.20 |
| | C–H···O | 3.705 | 2.831 | 137.77 |
| | C–H··· C≡C | 3.795 | 2.924 | 137.63 |
| | C–H···X1 | 3.525 | 2.661 | 136.38 |
| **3**[c] | O–H···X1 | 3.463/3.471 | 2.544/2.569 | 155.52/158.43 |
| | O–H···X2 | 3.329/3.331 | 2.386/2.409 | 160.34/163.05 |
| | ≡C–H···X1 | 3.472/3.481 | 2.608/2.637 | 136.20/137.74 |
| | ≡C–H···X2 | 3.597/3.604 | 2.548/2.591 | 162.72/163.81 |
| | C–H···O | 3.330/3.341 | 2.340/2.360 | 151.13/150.24 |
| | C–H···M | 3.776/3.782 | 2.757/2.759 | 156.73/157.13 |
| | C–H···M | 3.594/3.606 | 2.768/2.783 | 132.84/133.25 |
| | Cl···Cl[d] | 3.376/3.394 | | 173.96/93.54 |
| | | | | 172.98/93.85 |
| | Cl···Cl | 3.724/3.736 | | 148.43/75.89 |
| | | | | 148.40/76.31 |
| **4** | O–H···X1 | 3.560 | 2.633 | 157.47 |
| | O–H···X2 | 3.379 | 2.429 | 162.28 |
| | ≡C–H···X1 | 3.483 | 2.532 | 145.90 |
| | C–H···O | 3.378 | 2.367 | 154.65 |
| | C–H···M | 3.596 | 2.780 | 131.99 |
| | C–H···M | 3.841 | 2.833 | 154.71 |
| | Br···Br[d] | 3.502 | | 173.79/93.42 |
| | Br···Br | 3.829 | | 150.96/77.46 |
| **5** | O–H···X1 | 3.450 | 2.541 | 153.74 |
| | ≡C–H···X1 | 3.450 | 2.471 | 149.74 |
| | C–H···O | 3.311 | 2.595 | 122.95 |
| | C–H···M | 3.756 | 2.975 | 129.35 |

[a] All O–H and C–H bond lengths in the structures determined by X-ray diffraction are neutron-normalised (0.983 and 1.083 Å respectively). [b] X1 and X2 are ring centroid and midpoint of bond in phenyl acceptor. M is the midpoint of ethynyl bond. [c] Both X-ray and neutron values are given for **3**. [d] For Cl···Cl and Br···Br interactions *D* is the distance between interacting halogen atoms, *θ* values are as defined in Chapter four.

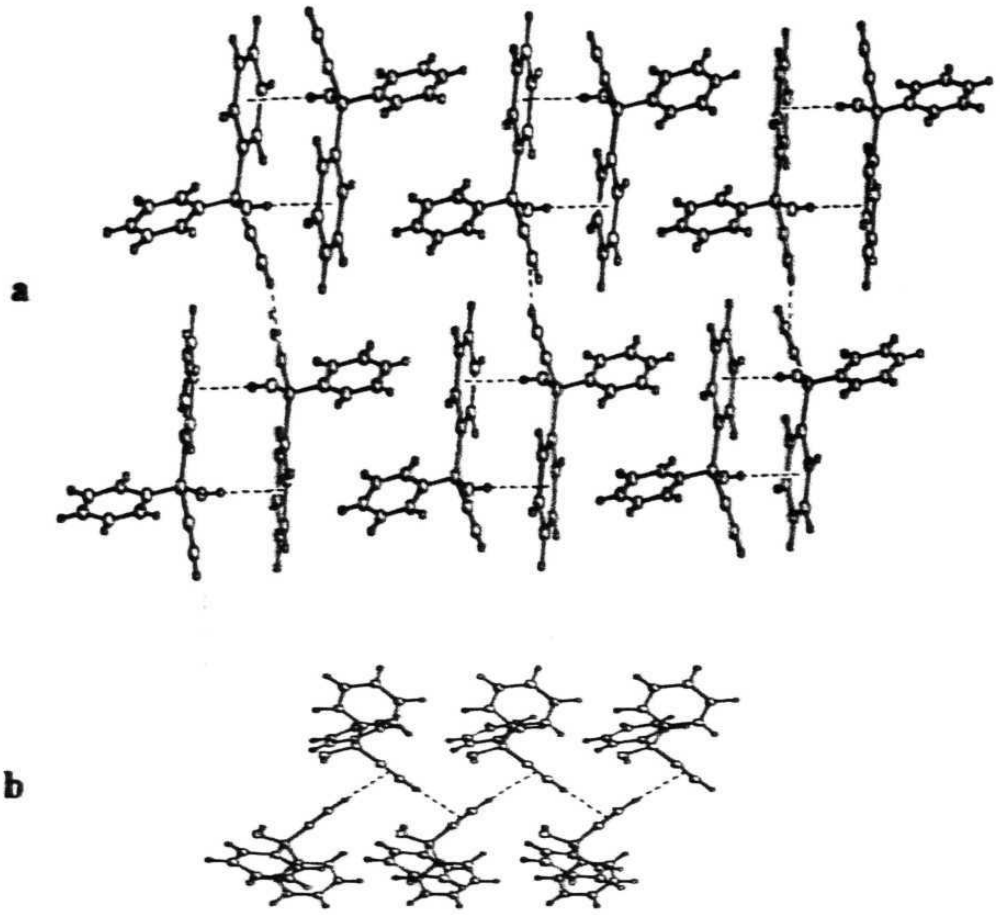



**Figure 1.** Crystal structure of **1**. (a) View down *b*-axis showing O–H···Ph dimer synthons **I**. Notice the outward projection of ethynyl groups. (b) Cooperative ≡C–H···C≡C chain along the *b*-axis.

**O–H···Ph and ≡C–H···Ph aromatic hydrogen bonds in alkynol 2**

Compound **2**, the tolyl derivative of **1**, crystallises in the space group $P\bar{1}$ ($Z$ =2). One of the H-atoms of a methyl group is disordered over two positions. As in **1**, inversion related molecules are connected with O–H···Ph hydrogen bonds *via* synthon **I** (Figure 2a). However, the mutual arrangement of O–H···Ph dimers in **2** is different from that observed in **1** (compare Figures 1a and 2a). A two-dimensional packing of O–H···Ph dimers may again be traced in the structure of **2** (Figure 2a) which is maintained by stacking and weak C–H···Ph, C–H···C≡C and C–H···O interactions involving methyl C–H groups. The ethynyl groups are projected outward from this two-dimensional packing and involve in ≡C–H···Ph interactions which link *b*-translation related molecules through synthon **IV** (Figure 2b).

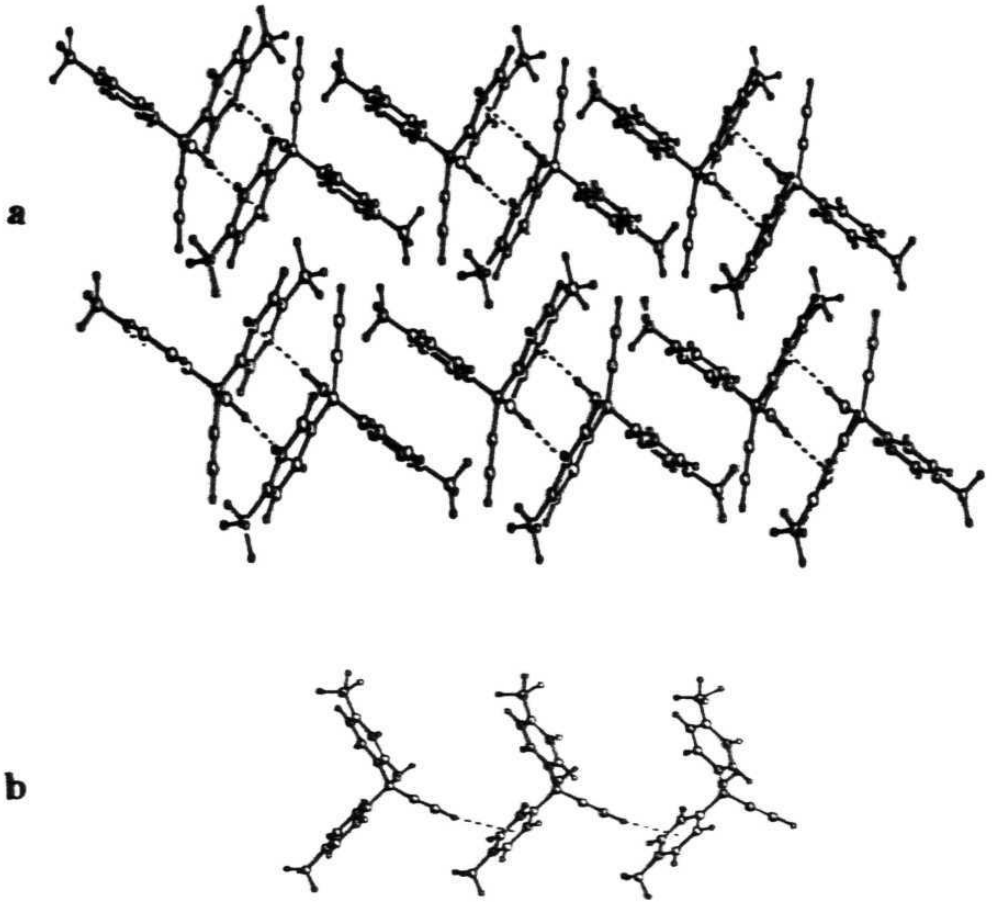



**Figure 2**. Crystal structure of **2**. (a) View down the *a*-axis showing a two-dimensional packing parallel to $(2\,\bar{2}\,2)$ with O–H···π(Ph) dimer synthons **I**. Notice the outward projection of ethynyl groups. Notice that the mutual arrangement of synthons is different from that in compound **1**. (b) The ≡C–H···Ph interactions extend to form synthon **IV** along the *b*-axis.

It may be noted that the hydroxy groups form the same synthon **I** in both structures **1** and **2**[9] whereas the ethynyl groups form different synthons. The ethynyl group in **1** interacts with itself and in **2** it interacts with a phenyl ring forming synthon **IV**. This difference may be attributed to interaction demands and bulk of the methyl group which cannot fit into the structure of **1**. In any case, both the groups in *gem*-alkynol functionality participate in non-conventional hydrogen bonds in both the structures.

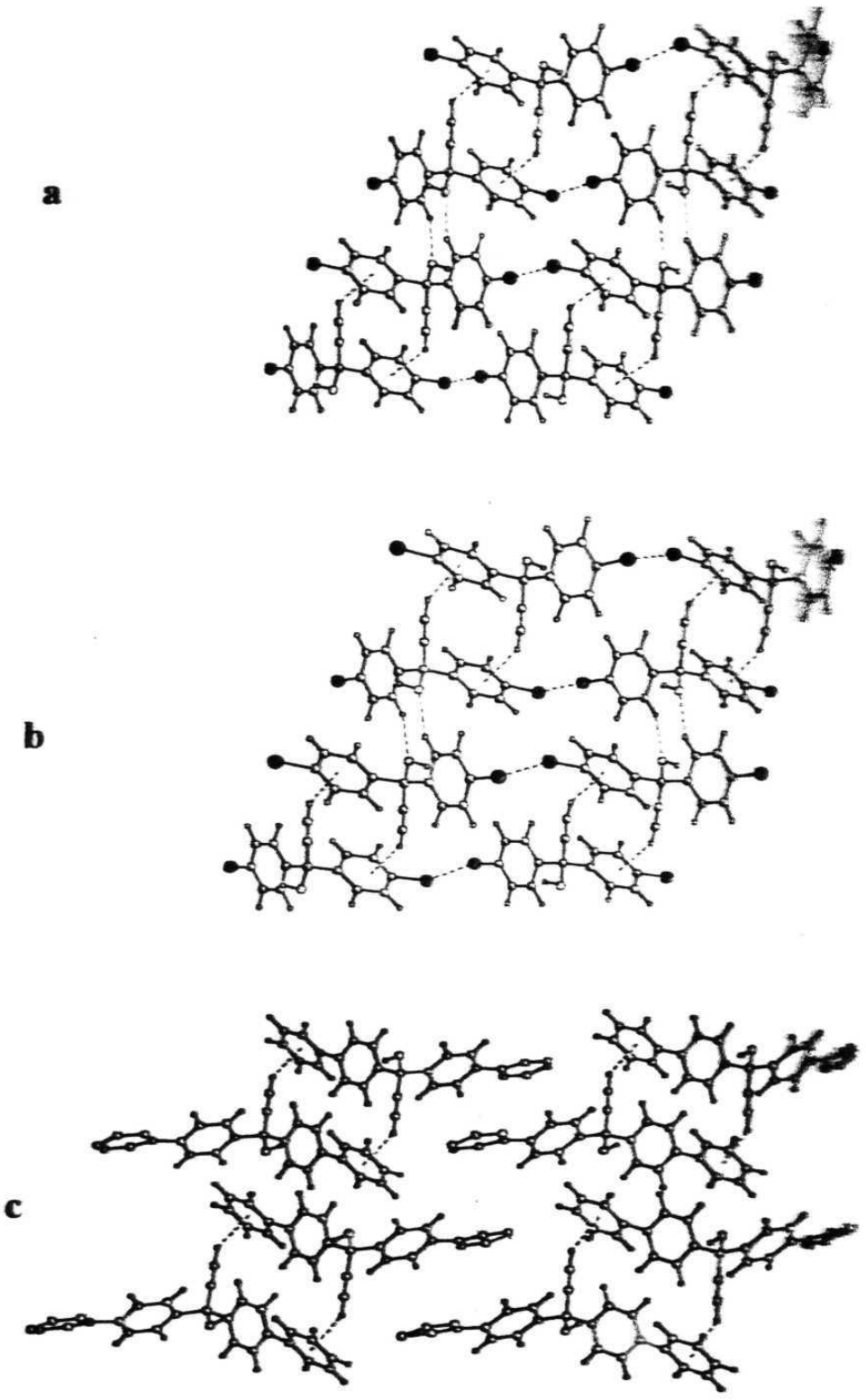



**Figure 3**. Crystal structures of **3** (a), **4** (b) and **5** (c) viewed down the *a*-axis. Notice synthon II in **3** and **4** and its extended variation in **5**. Notice the isostructural relationship between **3** and **4**. Only one orientation of the disordered phenyl group is shown. Notice the overall similarity between the structures.

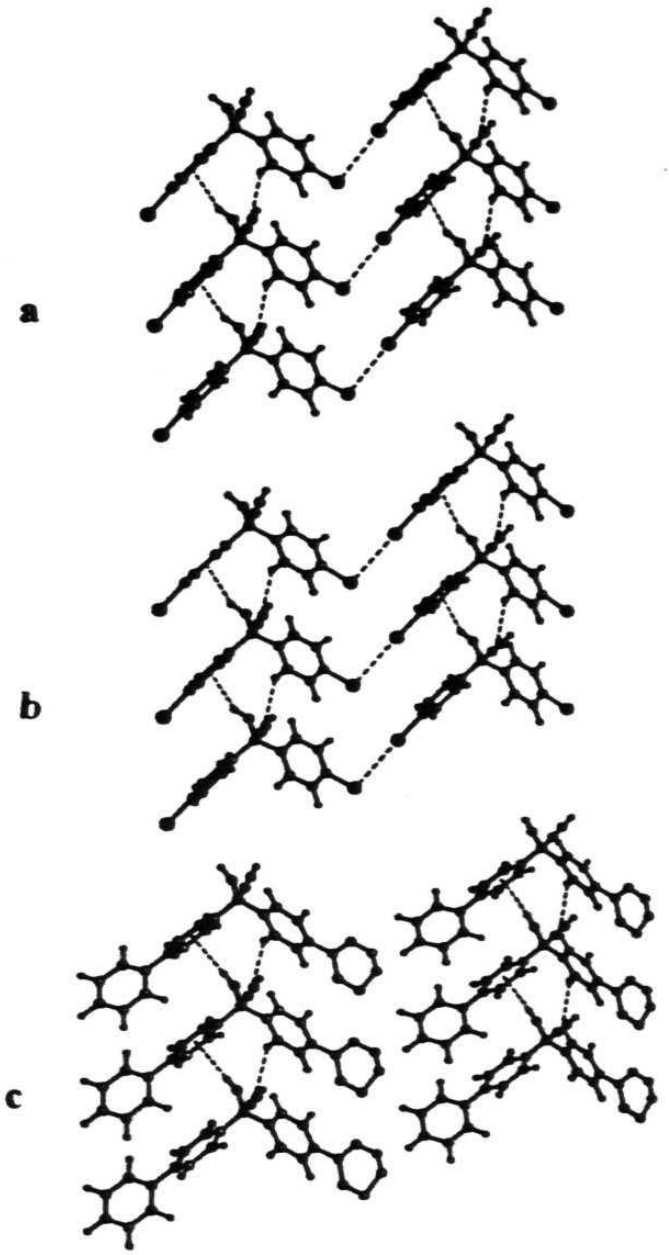



**Figure 4**. Crystal structures of **3** (a), **4** (b) and **5** (c) from a different view illustrating synthon **III**. Notice the topological similarity between the type II halogen···halogen interactions in **3** and **4**, and the herringbone interactions between substituted phenyl rings in **5**.

**Isostructural dichloro- and dibromo-alkynols 3 and 4**

The structures of **3** and **4** are discussed together because they are isostructural. Both compounds crystallise in the space group $P\bar{1}$ ($Z = 2$). Unlike in **1** and **2**, inversion related molecules in **3** are related by ≡C–H···Ph interactions and form dimeric species through synthon **II** (Figure 3a). These dimers are linked through

phenyl C–H···O dimers along the *b*-axis. Translation related molecules are connected with type II Cl···Cl interactions ($d$ = 3.39 Å, $\theta$ = 173/94°) along the *c*-axis. All these interactions may be said to form a two-dimensional packing from which the hydroxy groups project outwards (as depicted in Figure 3a). The hydroxy groups link the *a*-translation related molecules through O–H···Ph interactions and extend to synthon **III** (Figure 4a). Synthon **III** is further assisted by phenyl C–H···C≡C interactions.

Figures 3b and 4b display the structure of the dibromo derivative **4** which is sustained by synthons **II** and **IV** along with C–H···O dimers and type II Br···Br interactions ($D$ = 3.50 Å and $\theta_1/\theta_2$ = 174/93°). The isostructural relationship to **3** may be noted which is in accordance with the chloro-bromo exchange rule.[10]

**Non-interchangeable chloro and methyl groups in alkynols 2 and 3**

It may be noted that while dimethyl- and dichloro-alkynols **2** and **3** resemble each another in forming O–H···Ph and ≡C–H···Ph aromatic hydrogen bonds, their overall structures are different. While the methyl groups in **2** are involved in C–H···π and C–H···O interactions the chloro groups in **3** are involved in type II Cl···Cl interactions. There is a general belief that when methyl or chloro groups play mere space-filling roles in a structure they can be interchanged without altering the overall crystal structure. This is the so-called chloro-methyl exchange rule.[11] In the present case, however, the structures of methyl and chloro groups are distinct and involve interactions specific to these groups. Perhaps such differing demands of methyl and chloro groups lead to the formation of different O–H···Ph and ≡C–H···Ph synthons in **2** and **3** (**I** and **IV** in the former and **II** and **III** in the latter). The fact that chloro-methyl exchange rule is not applicable to **2** and **3** accentuates the significance of type II Cl···Cl interactions in **3** which is further corroborated by the observation that the dibromo derivative **4** is isostructural with type II Br···Br interactions.

**Near similarity of 5 to 3 and 4**

The structure of **5** ($P\bar{1}$, $Z = 2$) is very similar to those of **3** and **4**. One of the substituted phenyl rings is disordered over three positions. Two of the three phenyl rings share one carbon atom. Inversion related molecules are connected with a pair of ≡C–H···Ph bonds (Figure 3c). These interactions are accepted by one of the substituted phenyl rings (which is ordered) leading to an extended variation of synthon **II** with an intervening phenyl ring. It appears that such an extended synthon formation facilitates close packing of the substituted phenyl rings. Translation related molecules along the *a*-axis are connected with O–H···Ph bonds and extend to synthon **III** (Figure 4c). This is exactly similar to that observed in **3** and **4** leading to similar dimensions for the *a*-axes in **3**, **4** and **5** (5.7082, 5.7906, 5.6413 Å respectively). The disordered phenyl ring is involved in herringbone interactions with the ordered one along the *c*-axis. These herringbone interactions substitute the type II halogen···halogen interactions in **3** and **4**. This may be appreciated from the fact herringbone interactions between phenyl rings and type II interactions between halogen atoms have roughly similar topology (T and L respectively). It is for this reason that the structure of **5** bears a close resemblance with those of **3** and **4**. It is of note that one of the substituted phenyl rings which is involved in ≡C–H···Ph interactions is ordered while the other which is involved in herringbone motif is not. This points to the cumulative effect of weak ≡C–H···Ph hydrogen bonds in holding molecules together and their possible structural role in crystal engineering.

**Neutron diffraction analysis of alkynol 3**

In a conventional hydrogen bond of the type O–H···O, the hydrogen bond is accepted to exist when the two interacting O-atoms are at a proximity of 2.8 Å or closer. The exact location of H-atoms is non-critical for the identification of a conventional hydrogen bond. This is not the case for non-conventional hydrogen bonds of the type O–H···π, C–H···O, C–H···π etc. Since these interactions are

relatively weak, their identification as hydrogen bonds requires the exact location of H-atoms. Because H-atoms diffract X-rays very poorly, reliable detection of their positions is difficult by X-ray diffraction methods. In the case of aromatic or alkyne C–H groups, the H-atom positions could be discerned from the geometry, but the O–H group is an especially problematic with the H-atom having full conformational freedom. Further, the H-atom vibrational amplitude increases with the decreasing strength of the interaction and in this sense it is even more difficult to find the positions of H-atoms in weaker interactions. Neutron diffraction methods offer reliable locations of H-atoms and a study of weak hydrogen bonds such as O–H···π and C–H···π is greatly strengthened and properly assessed by neutron data.

In structures **1-5** the H-atoms participating in aromatic hydrogen bonds point towards ring centroids in some cases or to one of the bond centres in other cases (Table 1). Similar situations are found for ethynyl acceptors: sometimes the H-atoms is directed to the bond midpoint or to one of the C-atoms. To evaluate these unusual geometries and in view of assessing weak hydrogen bonds, single crystal neutron diffraction analysis of alkynol **3** has been performed.[12] The interaction geometries for the neutron data are also given in Table 1. A comparison of X-ray and neutron values suggest that the latter experiments in essence verify the former ones and reveal the quality of high precision low temperature X-ray data reported here.

**Off-centred X–H···π hydrogen bonds**

There is a view that the aromatic hydrogen bond X–H···Ph requires the X atom to lie above the phenyl ring and that the X–H vector should point towards the ring centroid. According to this view, when the geometry is off-centred these interactions should not be called as aromatic hydrogen bonds. However, a combination of neutron diffraction and IR spectroscopic studies have shown that off-centred O–H···Ph interactions indeed exhibit hydrogen bond characteristics.[4a,13] Also, gas-phase studies [5a] have shown that the acceptor directionality of aromatic

moieties is extremely soft and allows for considerably different hydrogen bond geometries with not much of a difference in bond energy. This means that X–H···Ph interactions can be easily and freely adjusted within the framework of other crystal forces. As may be noted from Table 1 some of the X–H···Ph (and also some of the X–H···C≡C) interactions exhibit off-centred geometry. These interactions not only include hydroxy groups but also ethynyl groups, and in this sense off-centred ≡C–H···Ph interactions may be considered as aromatic hydrogen bonds too. What is of interest with regard to crystal engineering is the following: the intrinsic weakness of these hydrogen bonds allow them to be adjusted within the crystal lattice and at the same time they are strong enough to form robust supramolecular synthons which govern the crystal packing as such.

**Structural comparison of alkynols 1-5**

Strong O–H···O hydrogen bonds are not observed in structures **1-5**. Instead, weak hydrogen bonds involving π acceptors are found in all the structures. Both hydroxy and ethynyl groups participate in these weak hydrogen bonds in donor as well as acceptor situations (Table 1) and generate synthons **I-IV**. These structures represent a high degree of interaction interference. When the *gem*-alkynol group is involved in aromatic hydrogen bonds two different phenyl rings act as acceptors for hydroxy and ethynyl groups. A comparison of the structures reveals a smooth variation from **1** to **5**. In the parent compound **1** while the hydroxy groups participate in synthon **I** the ethynyl groups form part of cooperative ≡C–H···C≡C chain synthon. Replacement of *para*-H atoms with methyl groups changes the structure type in **2**, yet retaining the synthon **I**. The ethynyl groups now generate synthon **IV**. In **3-5** the *gem*-alkynol functionality participates in synthons **II** and **III** (in **5**, **II** occurs in an extended variation). It appears that within this family of structures synthons **I-IV** occur in mutually exclusive combinations [**I** and **IV** (or ≡C–H···C≡C chain synthon) in **1** and **2**, **II** and **III** in **3-5**]. The formation of different synthons in different structures may have to do with the interaction

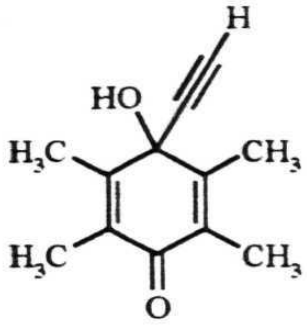
requirements of the substituents. In **2** the methyl groups form C–H···Ph dimers (Figures 2a), in **3** and **4** the halogen atoms are involved in type II halogen···halogen interactions (Figures 4a and 4b) and in **5** the substituted phenyl rings participate in herringbone interactions (Figure 4c). The structure type observed in **2** is a kind of bridge between structures in **1** and **3-5** because it (**2**) resembles **1** in forming O–H···Ph dimer synthons **I**, and with **3-5** because of its hydroxy and ethynyl groups forming aromatic hydrogen bonds.

**Supramolecular similarity between hydroxy and ethynyl groups**

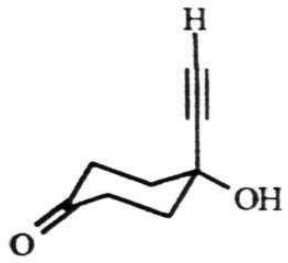
It was mentioned in Chapter one that the hydroxy and ethynyl groups, when hydrogen bonded to themselves, are capable of forming equivalent supramolecular synthons. These synthons (chain or ring patterns) include O–H···O or ≡C–H···C≡C interactions. In this work it is found that the hydroxy and ethynyl groups participate in aromatic hydrogen bonding, that is they do not self-associate, and form synthons **I-IV**. The topological similarity between synthons formed by hydroxy groups (**I** and **III**) and those formed by ethynyl groups (**II** and **IV**) may be easily noted.[14] Thus hydroxy and ethynyl-groups form topologically similar supramolecular synthons not only when they hydrogen bond to themselves, but also when they are involved in hydrogen bonding with other acceptors as weak as phenyl rings. A new facet of supramolecular similarity between hydroxy and ethynyl groups is revealed from this study. Such a similarity combined with their robustness points to their use in further studies of crystal engineering.

**Carbonyl group in presence of *gem*-alkynol**

The compounds 4-ethynyl-4-hydroxy-2,3,4,5-tetramethyl-cyclohexa-2,5-diene-1-one, **6** and 4-ethynyl-4-hydroxy-cyclohexanone, **7** were obtained as by-products during the synthesis of the diethynyldiols and their crystal structures were determined to see the effect of the carbonyl group in the presence of *gem*-alkynols.




**6**




**7**

**6** crystallises in the space group $P2_1/c$ with two molecules in the asymmetric unit. Each symmetry-independent molecule forms a dimer around an inversion centre with O–H···O=C (Table 2) hydrogen bonds. These dimers are connected with ≡C–H···O=C hydrogen bonds forming layers. Figure 5 shows a layer formed by one of the symmetry independent molecules. Alternating symmetry independent layers are in the (200) planes. Each layer is linked to the adjacent layers by methyl C–H···O–H interactions.

**Table 2**. Intermolecular interactions in the crystal structures of **6** and **7**.[a]

| | Interaction | $D$ (Å) | $d$ (Å) | $\theta$ (°) |
|---|---|---|---|---|
| **6** | O–H···O | 2.786 | 1.803 | 178.46 |
| | O–H···O | 2.826 | 1.849 | 171.82 |
| | ≡C–H···O | 3.271 | 2.307 | 147.26 |
| | ≡C–H···O | 3.151 | 2.085 | 167.40 |
| | C–H···O | 3.593 | 2.514 | 174.08 |
| | C–H···O | 3.634 | 2.561 | 170.80 |
| | C–H···O | 3.619 | 2.559 | 165.88 |
| | C–H···O | 3.447 | 2.441 | 153.95 |
| **7** | O–H···O | 2.820 | 1.840 | 175.04 |
| | ≡C–H···O | 3.373 | 2.577 | 129.67 |
| | C–H···O | 3.482 | 2.402 | 175.17 |
| | C–H···O | 3.507 | 2.619 | 138.77 |

[a] All O–H and C–H distances are neutron-normalised (0.983 and 1.083 Å respectively).

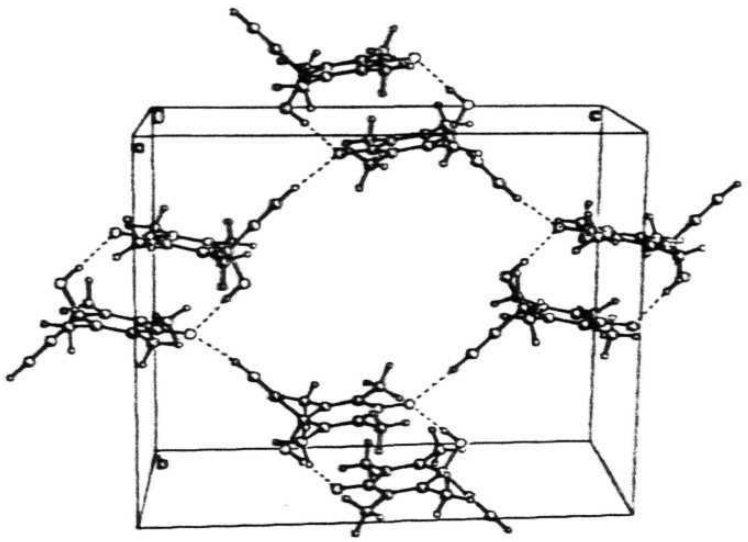


**Figure 5**. Hydrogen bonded layer of **6** in (200). The second symmetry independent molecule also forms a very similar layer.

**7** crystallises in the monoclinic space group $P2_1/c$ with one molecule in the asymmetric unit. Here too, layers are formed in the planes parallel to (010) by translation related molecules through O–H···O=C (Table 2) and ≡C–H···O=C hydrogen bonds (Figure 6). The layers are in turn connected by hydrophobic interactions on one side and by methylene C–H···O–H interactions on the other side.

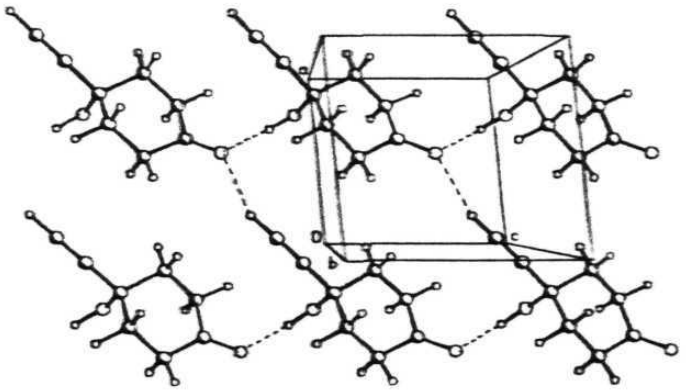


**Figure 6**. Hydrogen bonded layer of **7** in (010).

In both structures, **6** and **7**, the hydrogen bond is constituted with a strong donor and a strong acceptor. The CSD[15] (Cambridge Structural Database, Version 5.16, October 1998, 190 307 entries) contains 94 *gem*-alkynols of which 39

contain one or more carbonyl groups. In 34 of these cases, the hydroxy group is hydrogen bonded to a C=O group. In two cases, Z' = 2; while one of the carbonyl groups accepts an O–H···O=C bond, the other forms a C–H···O=C bond. In the recently reported structure of 1-ethynyl-2-(2'-carbethoxy-1'-vinyl)-2,3-dimethyl-6-isopropyl-cyclohexan-1-ol,[16] not included in the latest version of the CSD, the C=O group accepts a hydrogen bond from the ethynyl group rather than from the hydroxy group.

In essence, therefore, if a carbonyl group is present in an ethynyl alcohol it nearly always tends to accept a hydrogen bond from the hydroxy group. In other words, such a carbonyl group is a much better hydrogen bond acceptor than either of the acceptors in the *gem*-alkynol moiety.

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# SUMMARY AND OUTLOOK

Several *gem*-alkynol compounds have been synthesised and their structural chemistry has been explored. Systematic analysis of crystal structures is an essential theme of crystal engineering which uncovers the subtleties in the interaction patterns of various functional groups in the solid state. The *gem*-alkynol group is a potentially useful functionality in structural supramolecular chemistry with its unique capability to form four types of intermolecular interactions with varying degrees of strength and directionality. All the four possible interactions (O–H···O, O–H···C≡C, C–H···O and ≡C–H···C≡C) have been found in the structures studied in this work.

This work began with a background of a few reported crystal structures consisting of the *gem*-alkynol group. With a limited knowledge on the supramolecular behaviour of this functional group, the approach of the work has been to investigate the structures of series of simple compounds with slight variations at the molecular level. Other functional groups capable of donating or accepting strong hydrogen bonds are generally avoided.

The three polymorphic structures described in Chapter two are based on a flexible cyclohexyl molecular frame. All the three structures are sustained by trimeric helical O–H···O synthon. Comparison with another related structure revealed that two different molecular conformations associate invariably with the O–H···O pattern, provided the hydroxy groups are placed on the 1,4-positions of a cyclohexyl moiety. An interesting feature exhibited by the three polymorphs is the non-participation of the ethynyl groups in any kind of significant intermolecular interactions.

Moving to a rigid hydrocarbon framework as in the benzoquinone derivative described in Chapter three, resulted in a structure in which all the functional groups are involved in the supramolecular construction in an effective way. Robust supramolecular synthons involving the interactions of hydroxy and ethynyl groups (O–H···O, O–H···C≡C etc) extend to similar two-dimensional

architecture in the structures of 9,10-anthraquinone and 1,4-napthoquinone derivatives. The importance of structural orthogonality in establishing structural repetitivity is demonstrated here despite the high degree of interaction interference typical of *gem*-alkynol family.

Chapter four describes the structures of halogenated *gem*-alkynol compounds. Fluoro, chloro and bromo derivatives have been analysed. Cyclic O–H···O synthons are formed by the hydroxy groups and the ethynyl groups participate in C–H···X interactions. Depending on the packing requirements of a particular halogen atom, hexameric or tetrameric O–H···O synthons have been found. The variation in the structure type is ascribed to the varied nature of halogen atoms. Polarisation-induced halogen···halogen interactions become more realistic with increasing size of the halogen atom. While the F-atoms are hardly polarisable and form C–H···F interactions, easily polarisable Br-atoms participate in type II Br···Br interactions. The supramolecular behaviour of Cl-atoms is midway between the lower and higher analogues.

The hydroxy and ethynyl groups form aromatic hydrogen bonds in the *gem*-alkynol structures presented in Chapter five. Through these aromatic hydrogen bonds both the hydroxy and ethynyl groups generate topologically similar supramolecular synthons unveiling the supramolecular similarity between them in a new perspective. Also it is shown that a carbonyl group is a better hydrogen bond acceptor than either of the acceptors in the *gem*-alkynol functionality.

In classical views, hydrogen bond formation follows laws of hierarchy: strong hydrogen bond donor forms a bond with the strong hydrogen acceptor, the second strong donor forms a bond with the second strong acceptor and so on. The hydrogen bond arrangements found in the crystal structures of *gem*-alkynols do not generally follow such a hierarchy. Ideally, the *gem*-alkynol functionality is capable of forming four directional intermolecular interactions. The positioning of the hydroxy and ethynyl groups on the same carbon atom causes some geometrical complications. Consequently, it is not always possible to account for all the four

interactions of the *gem*-alkynol functionality. In general, the hydroxy group dominates and steers the crystal packing (as in the structures described in Chapter two). This is not always true. At times, interaction interference of the hydroxy and ethynyl groups is inevitable and the structures described in Chapter five clearly illustrate this effect. In such cases the ethynyl group contributes significantly to the crystal cohesion. The answer to the more difficult question — when does an ethynyl group of *gem*-alkynol functionality participate in hydrogen bonding? — is still unclear. More data is required before any confident answer can be arrived at such a question.

The work described in this thesis attempts to understand the interaction patterns formed by the *gem*-alkynol functionality. Analysis and synthesis are the two important features of crystal engineering and practising any one of these, requires expertise in the other. The analytical component of crystal engineering with regard to the structural properties of *gem*-alkynol functionality is highlighted in this work. There is significant structural interference in the patterns formed by *gem*-alkynol functionality and reliable crystal design with this functionality is still a distant goal.

# EVIDENCE FOR THE CHARACTERISATION OF THE C–H···π INTERACTION AS A WEAK HYDROGEN BOND: TOLUENE AND CHLOROBENZENE SOLVATES OF 2,3,7,8-TETRAPHENYL-1,9,10-ANTHYRIDINE

## Introduction

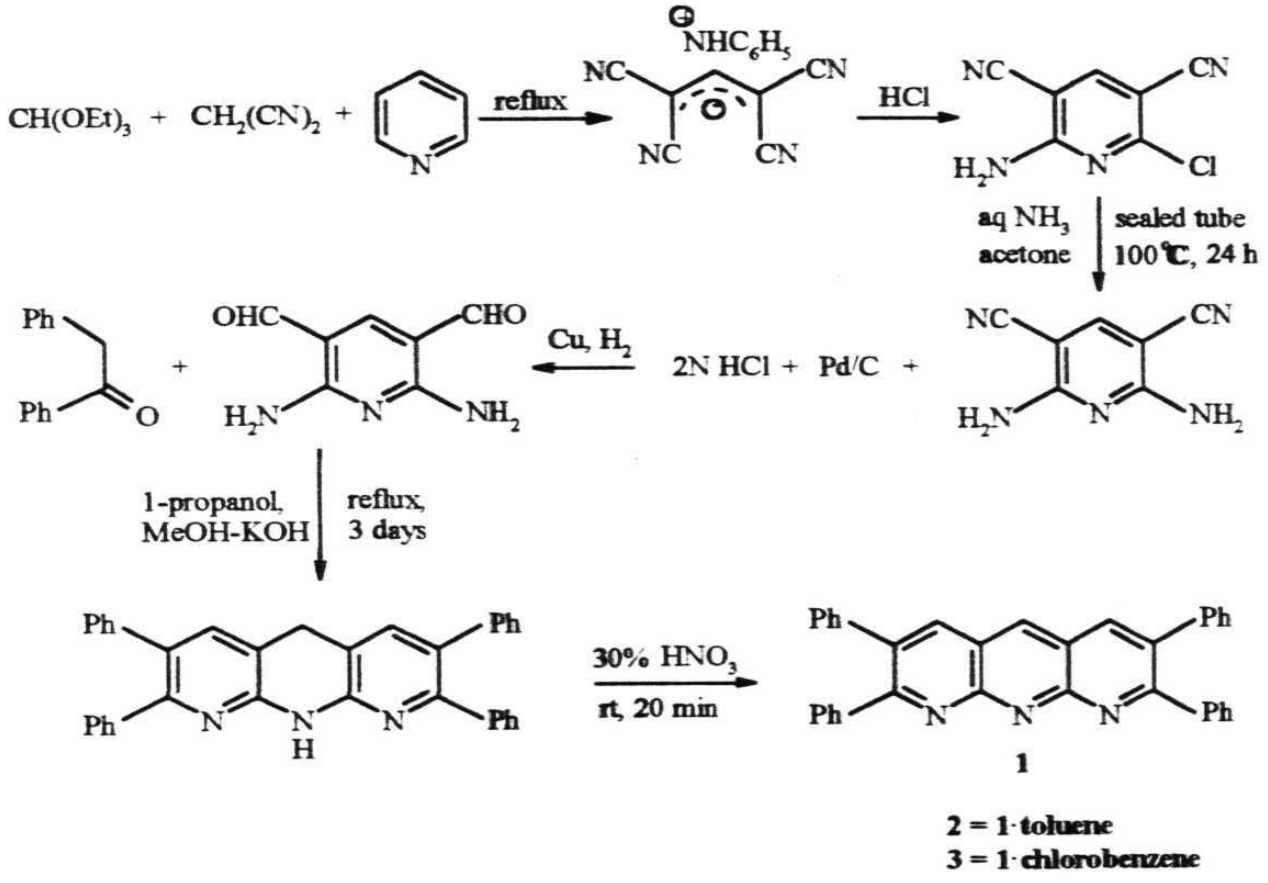
The study of C–H···Ph (in general, C–H···π) interactions is of great importance in structural chemistry and in structural biology.[1] Many studies are being carried out to understand the nature of these interactions. The donor strengths of C–H groups have a very wide range that spans the scale from zero to the strengths of weaker types of O–H groups. In a recent CSD study, mean distances of different C–H groups (Table 1) to the faces of the phenyl groups have been determined.[2] This study showed that the distances follow the same trend as for conventional O, N, $Cl^-$ acceptors i.e., the donor strengths are ranked as $CHCl_3$ > C≡C–H > $CH_2Cl_2$ > $ClCCH_2$. This means that the influence of C–H donor acidity parallels that for conventional acceptors, and suggests that C–H···O and C–H···Ph interactions are of a related nature. It is well known that C–H···O interaction is a hydrogen bond. The C–H···Ph interactions formed by strong acidic C–H donors like terminal alkynes are established as hydrogen bonds through IR spectroscopy.[3] With falling C–H acidity, the hydrogen bond nature of these C–H···Ph interactions falls and blurs into the van der Waals region and it is unclear whether to call these interactions as hydrogen bonds or not. In this work, evidence for the characterisation of a C–H···Ph interaction as a hydrogen bond is shown where the interaction is formed by the C–H group of a phenyl ring.

The compound 2,3,7,8-tetraphenyl-1,9,10-anthyridine **1** has been synthesised[4] as shown in Scheme 1 in continuation of a project in our laboratory. Compound **1** failed to crystallise in several organic solvents such as $CHCl_3$, EtOAc, benzene, mesitylene, xylene, nitrobenzene, fluorobenzene, bromobenzene, pyridine. Bright yellow crystals were obtained from toluene and chlorobenzene and elemental

analysis showed that they correspond to the 1:1 solvate **2** and **3**. The fact that **1** forms only two solvates prompted the X-ray study of these structures.

**Table 1**. C–H···Ph contact distances for different types of C–H groups. The distance *d* is the normal distance of the H atom to the Ph plane (cut-off: 2.9 Å).

| Donor | n contacts | *d* (Å) |
|---|---|---|
| $Cl_3CH$ | 14 | 2.38 ± 0.16 |
| C≡C–H | 26 | 2.63 ± 0.14 |
| $Cl_2CH_2$ | 52 | 2.65 ± 0.15 |
| $ClCCH_2$ | 43 | 2.73 ± 0.14 |
| $C_2CH_2$ | 5518 | 2.74 ± 0.74 |
| $CCH_3$ | 6772 | 2.75 ± 0.10 |




**Scheme 1**

## Opposed solvent positioning in 2 and 3

The crystal structures of **2** and **3** were determined at low temperature by X-ray diffraction. Both of them crystallise in the space group $P2_1/c$ with nearly

identical unit cell dimensions. The gross packing features of the heterocyclic molecule **1** is identical in both structures. This is shown in the NIPMAT (Non-bonded Interaction Pattern MATrix) plots (Figure 1 and 2).[5] The two crystal structures are shown in Figures 3 and 4. The two solvent molecules toluene and chlorobenzene are situated in a pocket formed by three molecules of **1**. However, the Me and Cl substituents point in almost opposite directions in the two structures indicating that the chloro-methyl exchange[6] is not applicable to **2** and **3**. In other words, electronic factors are involved in the stabilisation of solvent molecules in one or both structures.

The interactions involving the toluene and chlorobenzene molecules are given in Table 2. A very short C–H···Ph interaction (contact **a** in Figure 3) which is of H···ring centroid type[3] is found in **2**. Another somewhat longer C–H···Ph interaction **b** is also observed such that the toluene molecule is positioned at unequal distances from adjacent glide related molecules. The corresponding two contacts **g** and **h** in **3** (Figure 4) are longer than **a** which are formed by C–H groups that are chemically equivalent. Unlike the toluene molecule in **2**, the chlorobenzene molecule in **3** may be considered as being disposed at nearly equal distances to the adjacent molecules of **1**.

**Table 2**. Interaction geometries of the toluene and chlorobenzene molecules in the crystal structures of **2** and **3**.

| Interaction | *D* (Å) | *d* (Å) | $\theta$ (°) |
|---|---|---|---|
| **a** C–H···X1 | 3.521 | 2.536 | 150.82 |
| **b** C–H···X1 | 3.737 | 3.003 | 125.43 |
| **c** C–H···X | 3.785 | 2.895 | 139.49 |
| **d** C–H···X | 3.893 | 3.005 | 139.53 |
| **e** C–H···N | 3.703 | 2.755 | 146.40 |
| **f** C–H···N | 3.863 | 2.827 | 160.82 |
| **g** C–H···X1 | 3.528 | 2.607 | 142.47 |
| **h** C–H···X1 | 3.573 | 2.618 | 146.81 |
| **i** C–H···N | 3.748 | 2.863 | 138.94 |

X and X1 are the centroids of the phenyl rings of **1** and solvent molecules respectively. All C–H bond lengths are neutron-normalised (1.083 Å).

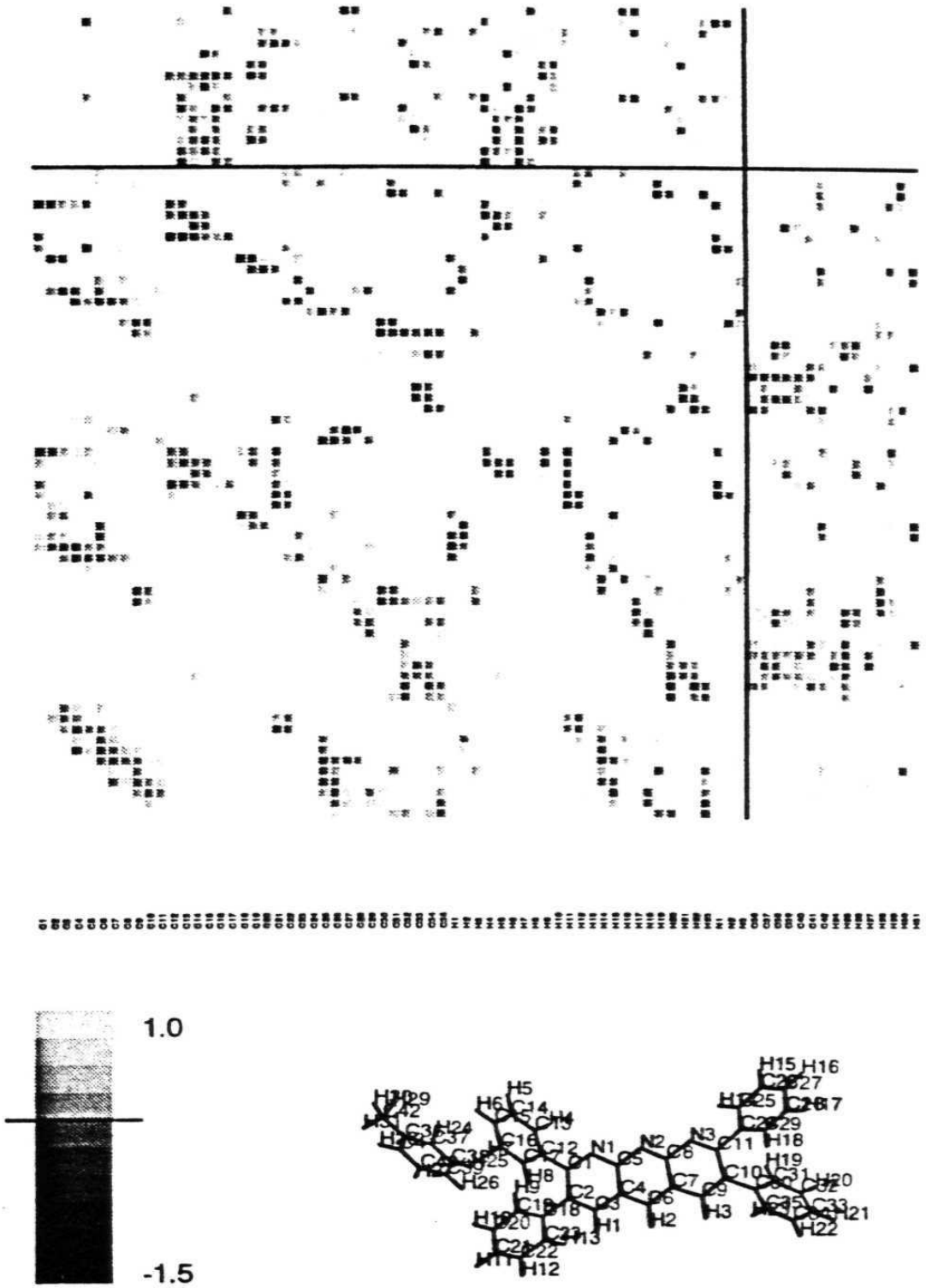
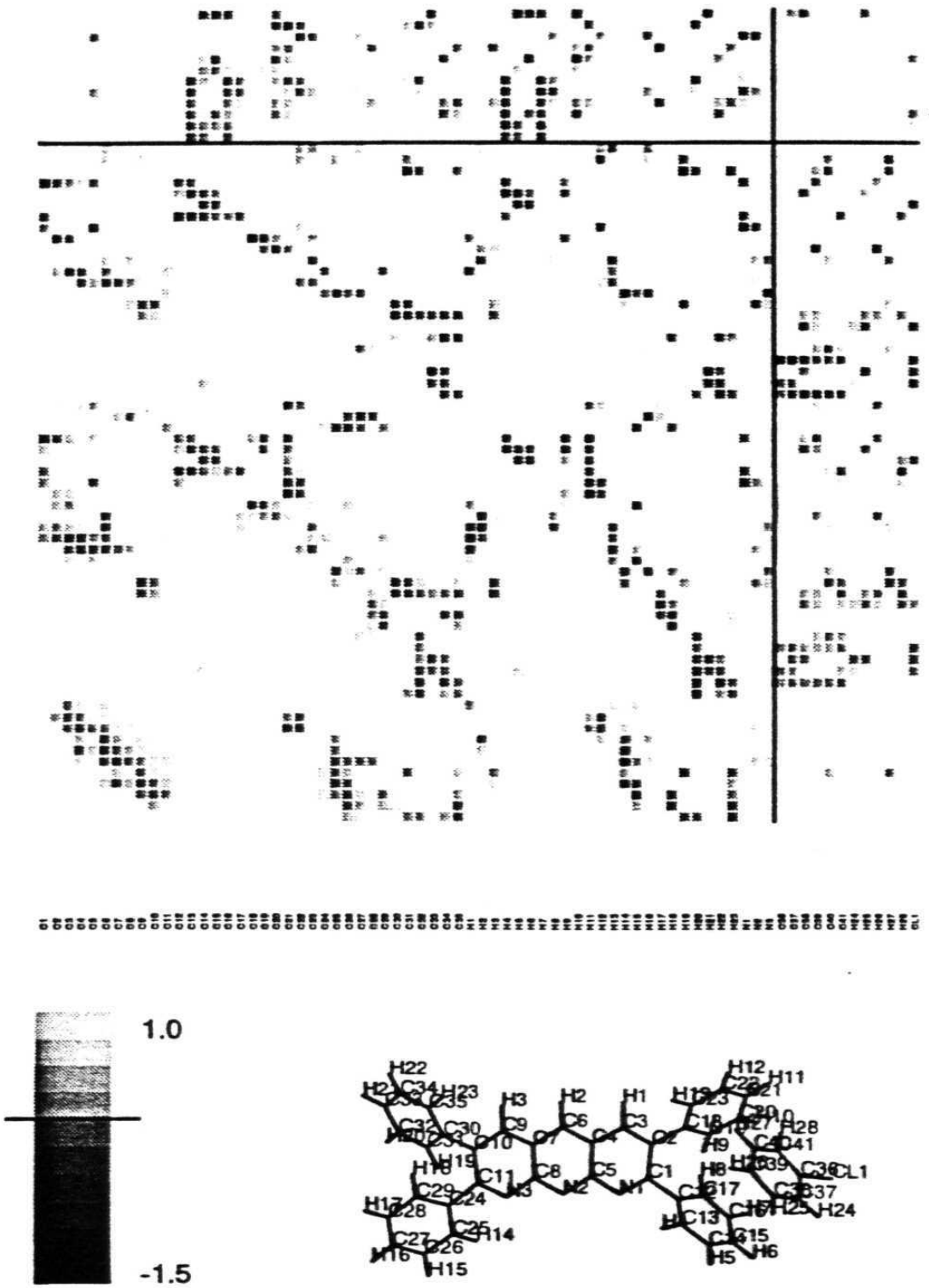



**Figure 1**. NIPMAT plot of **2**.




**Figures 2**. NIPMAT plot of **3**. Notice the similarities in the interactions of **1** in **2** and **3** by comparing with Figure 1.

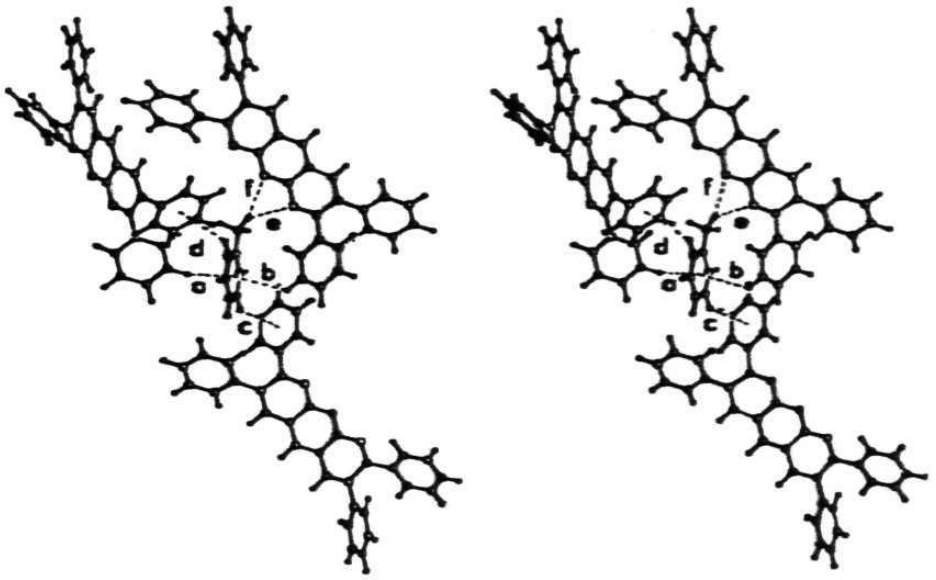



**Figure 3**. Stereoview of the crystal structure of solvate **2** approximately down [010], showing the binding of the toluene molecule. The anthyridine molecules are inversion- and glide-related. Interactions **a-f** are indicated. Notice the cooperative scheme of C–H···Ph hydrogen bonds and the positioning of the methyl H-atom between the two heterocyclic N-atoms. Interaction **a** is short.

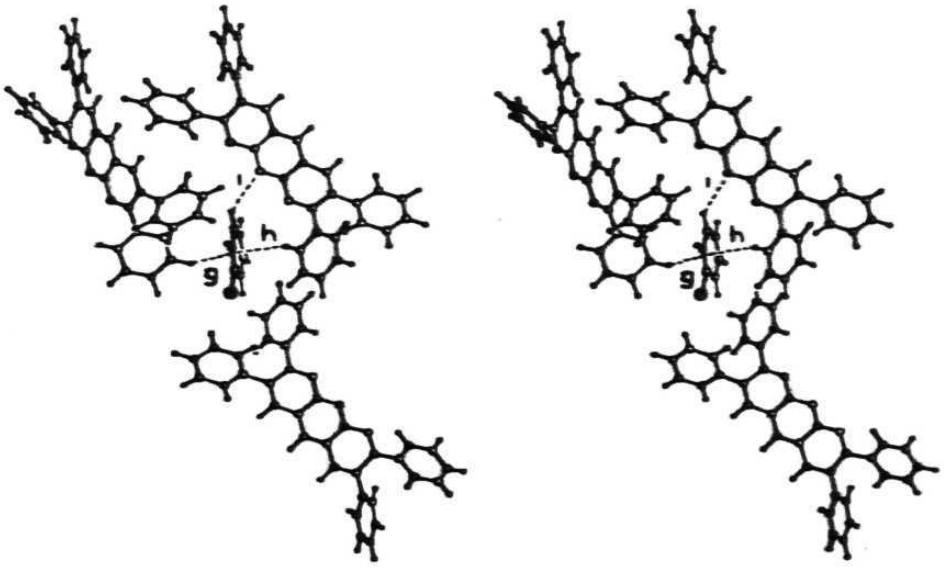



**Figure 4**. Stereoview of the crystal structure of solvate **3** showing the binding of the chlorobenzene molecule. Interactions **g-i** are indicated. Contrast this with Figure 3. Notice that the Cl-atom is not involved in any specific intermolecular contact.

**Evidence for C–H···Ph interaction as a hydrogen bond**

In general, short intermolecular distances such as **a** in **2** are taken as evidence of crystal stabilisation but it should be noted that shortness alone does not constitute proof of an attractive interaction. It is always possible that a short contact is repulsive and that it arises from the overall balance of interactions in a crystal structure.[7] However, in this case, the shortness of **a** with respect to **g** and **h** also correlates with the electron-rich character of the aromatic ring in toluene *vis-a-vis* chlorobenzene, and also given that there would be little steric problem were the toluene molecule to be placed symmetrically between the two approaching C–H groups, one may state with confidence that the C–H···Ph interaction **a** is stabilised by the electron rich aromatic ring in toluene. Hydrogen bonds of all types are fortified by increasing acidities and basicities of donor and acceptor groups respectively.[8,9] The observations here adduce evidence that the C–H···Ph interaction has structural properties of weak hydrogen bonds, similar to O–H···π and N–H···π interactions.[10] Because of its weakness, however, it is difficult in general to obtain clear evidence for the existence of this type of hydrogen bond. It is possible to do so in this case because structures **2** and **3** are similar in just about every respect except the interaction of interest.

**Cooperativity of C–H···Ph interactions**

Hydrogen bonds formed by carbon acids and π-bases are soft and this in turn can lead to the cooperative patterns of interactions.[11] The structure of **2** is revealing in this context. It would seem that the weak hydrogen bond **a** is able to activate the C–H groups in the toluene molecule at least to the extent that the long contacts **c-f** are possible. Interactions **c** and **d** formed by the aromatic C–H groups are of the C–H···Ph type while interactions **e** and **f** formed by the methyl C–H groups are of the C–H···N type. Though long, these contacts are within the accepted distance ranges.[5,12] In contrast, there is just one extra interaction of the C–H···N type in the unactivated structure **3** (contact **i**). All these interactions may make only small contributions to the crystal binding energy but they help in

defining the structures of the solvates. For example, it is possible that these secondary interactions are the causes for the opposite orientations of the toluene and chlorobenzene molecules referred to above. Although the binding of chlorobenzene in the anthyridine pocket is poorer than that of toluene, it is still not just shape-controlled; compound **1** failed to form diffraction-quality crystals with either fluorobenzene or bromobenzene. In this regard, the formation of solvates **2** and **3** is reminiscent of guest-induced host crystallisation of the type encountered in the benzene solvate of the mono-enol form of cyclohexane-1,3-dione.[13]

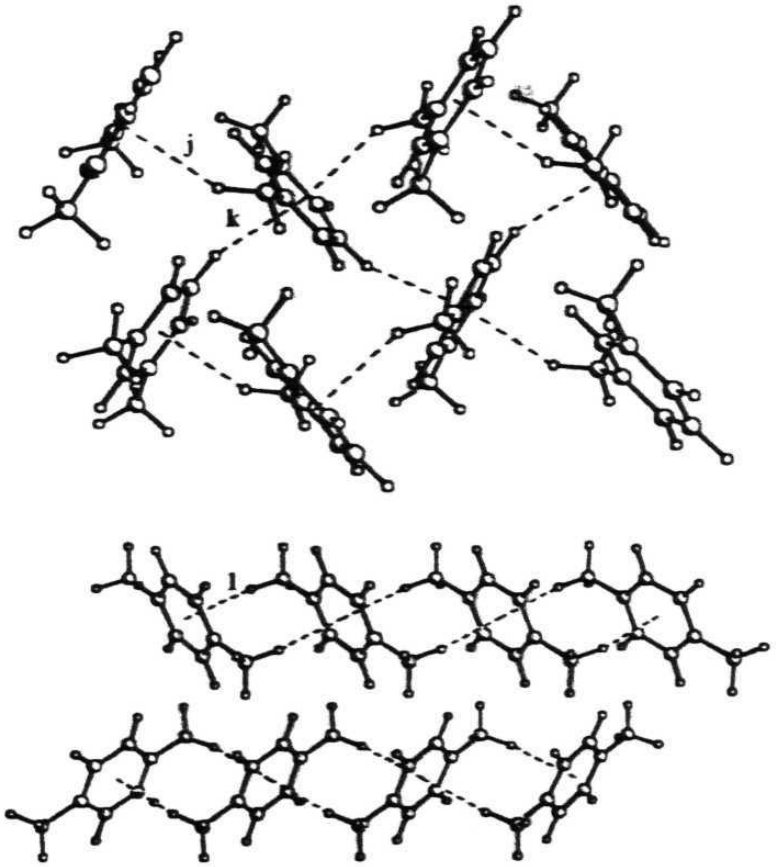



**Figure 5**. Crystal structures of *m*-xylene (top) and *p*-xylene (bottom) showing the cooperative C–H···Ph hydrogen bonds.

It is interesting to note here a similar example where methyl groups are activated due to cooperativity and form short contacts.[14] In the crystal structures of *m*- and *p*-xylenes cooperative chains of C–H···Ph interactions are found (Figure 5). The values for the interactions **j** ($d$ = 2.626 Å, $\theta$ = 150.5°), **k** ($d$ = 2.714 Å, $\theta$

= 137.8°) and **I** ($d$ = 2.589 Å, $\theta$ = 160.7°) are obtained from the neutron powder diffraction data of perdeuterated *m*- and *p*-xylenes.

## Conclusions

Much work has been done in the area of C–H···π interaction since the postulation of its existence.[15] With the current interest in crystal engineeing and supramolecular chemistry, there is a new appreciation for this form of intermolecular association. The hydrogen bond is an attractive, directional interaction which, though predominantly electrostatic, also has polarisation and charge transfer characterstics. While it has always been recognised that C–H···π interactions in highly activated systems such as terminal alkynes are of the hydrogen bond type, the present work shows that even moderately activated systems such as tolyl rings participate in interactions that may be considered to be weak hydrogen bonds formed by soft acids and soft bases.

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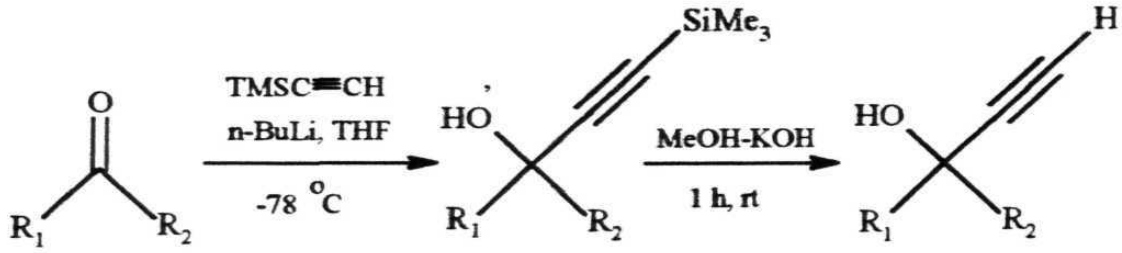
## EXPERIMENTAL

The compounds studied in this thesis were synthesised and crystallised by the candidate in Hyderabad. X-ray data were collected by Ms. C. Bilton at the University of Durham. Neutron diffraction experiments were conducted at the pulse neutron source, ISIS, Oxford, on the Laue time-of-flight diffractometer, by Ms. C. Bilton and Dr. C.C. Wilson. Both the X-ray and neutron data were collected under the supervision of Prof. J.A.K. Howard.

The compounds were synthesised in two steps by the following scheme. All operations were performed in an atmosphere of dry nitrogen using standard syringe-septum techniques. Solvents were dried by standard methods and distilled prior to use. The general experimental procedure is given for one equivalent of ketone.

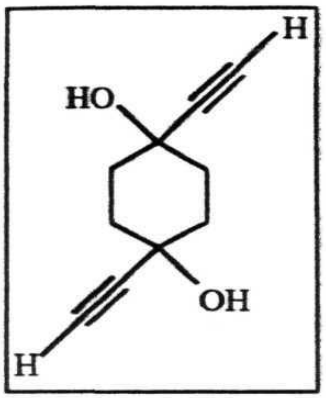



a). A solution of trimethylsilylacetylene (4.4 mmol) in 15 mL of THF was treated with n-butyllithium (4.2 mmol) at -78 °C. After stirring for 15 min, a solution of ketone (4 mmol) in THF was added dropwise and the stirring continued at low temperature for 30 min and at room temperature for 1 h. Brine was added to the reaction mixture and was extracted with diethyl ether. The organic phase was dried over magnesium sulphate and filtered and the ether removed. The solid obtained was taken to the next step without purification.

b). The solid was dissolved in methanol and a solution of methanolic KOH was added slowly and stirred for 1 h at room temperature. Water was added to the reaction mixture and was extracted with ethylacetate. It was then dried over

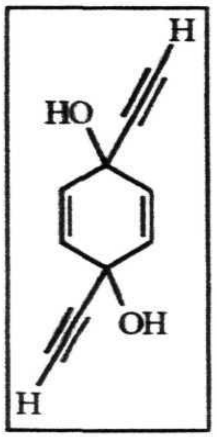
magnesium sulphate and solvent removed. Crystals were obtained by the purification of the crude material on column chromatography followed by recrystallisation.

**Spectroscopic data**




**$^1$H NMR**: δ 2.48 (s, 2H), 1.97 (s, 8 H).

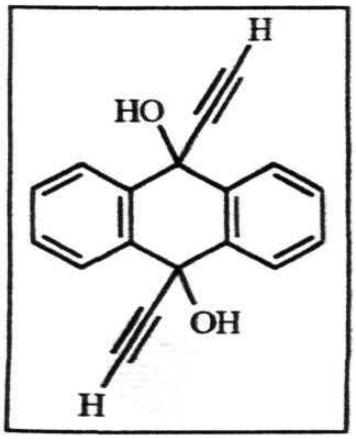
**IR**: cm$^{-1}$ 3297, 2957, 2861, 2105, 1455, 1350, 1279, 1258, 1082, 999, 949, 741, 664, 552, 507.




**$^1$H NMR**: δ 6.10 (s, 4H), 2.55 (s, 2H), 1.70 (br s, 2H).

**IR**: cm$^{-1}$ 3468, 3267, 2924, 2102, 1413, 1367, 1221, 1086, 1041, 1003, 916, 787, 686.

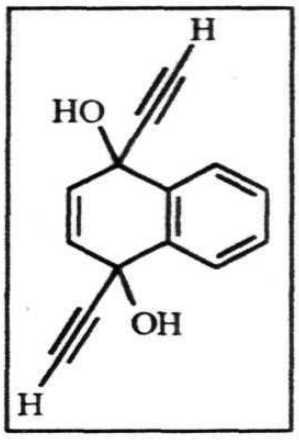
**mp**: 179-180 °C (sublimes).




**$^1$H NMR**: δ 8.10 (dd, J 8, 3 Hz, 4H), 7.41 (dd, J 8, 3 Hz, 4H), 2.90 (s, 2H), 2.80 (s, 2H).

**IR**: cm$^{-1}$ 3516, 3408, 3273, 3207, 2110, 1483, 1446, 1381, 1329, 1244, 1020, 974, 916, 763, 736, 646.

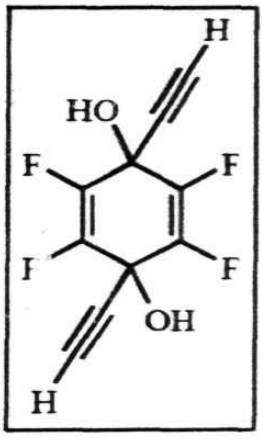
**mp**: 206-207 °C.




**$^1$H NMR**: δ 7.85 (d, J 8 Hz, 2H), 7.46 (d, J 8 Hz, 2H), 6.22 (s, 2H), 2.65 (s, 2H), 2.60 (s, 2H).

**IR**: cm$^{-1}$ 3342, 3312, 3283, 3273, 3146, 3050, 2957, 2114, 1635, 1487, 1452, 1394, 1313, 1161, 1128, 989, 945, 763, 655.

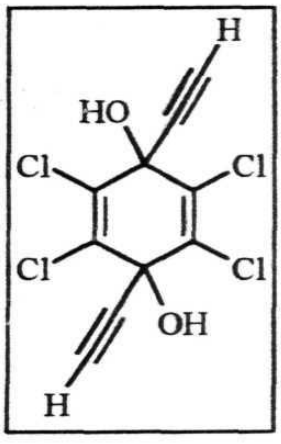
**mp**: 134 °C.




**$^1$H NMR**: δ 2.80.

**IR**: cm$^{-1}$ 3312, 2137, 1730, 1385.

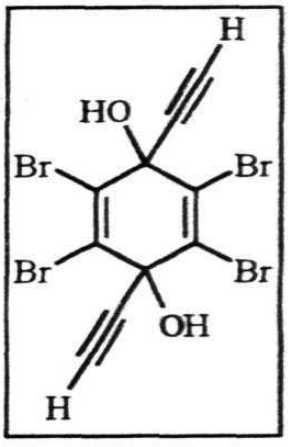
**mp**: 132-133 °C.




**$^1$H NMR**: δ 2.80.

**IR**: cm$^{-1}$ 3301, 2118, 1640, 1375, 1312, 1125, 1071, 1038, 787, 735, 683, 602.

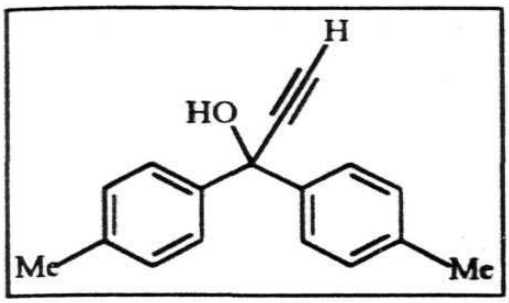
**mp**: 205-206 °C (sublimes).




**$^1$H NMR**: δ 2.84.

**IR**: cm$^{-1}$ 3586, 3495, 3279, 2128, 1608, 1383, 1102, 1032, 837, 750, 675, 632, 577.

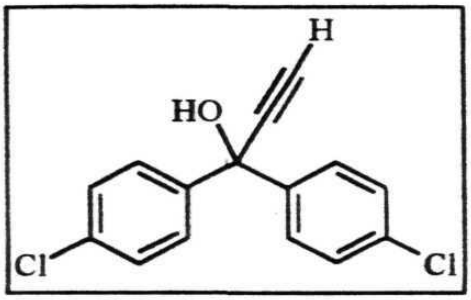
**mp**: 220 °C (decomposes).




**$^1$H NMR**: δ 7.47 (d, J 6 Hz, 4H), 7.10 (d, J 6 Hz, 4H), 2.82 (s, 1H), 2.70 (s, 1H), 2.32 (s, 6H).

**IR**: cm$^{-1}$ 3534, 3285, 3023, 2921, 2110, 1904, 1507, 1406, 1324, 1194, 1067, 897, 725, 662, 538.

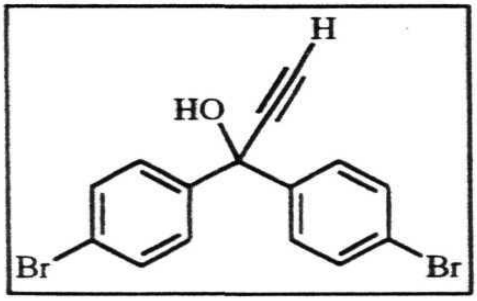
**mp**: 95-96 °C.




**$^1$H NMR**: δ .7.50 (d, J 8 Hz, 4H), 7.34 (d, J 8 Hz, 4H), 2.92 (s, 1H), 2.85 (s, 1H).

**IR**: cm$^{-1}$ 3559, 3283, 1590, 1483, 1399, 1285, 1194, 1156, 1090, 1069, 1013, 988, 820, 727, 644, 542.

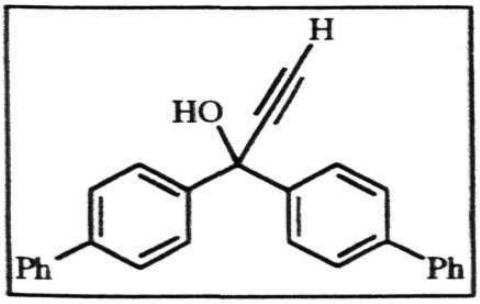
**mp**: 72-73 °C.




**$^1$H NMR**: δ 7.46 (s, 8H), 3.02 (s, 1H), 2.92 (s, 1H).

**IR**: cm$^{-1}$ 3557, 3283, 2112, 1912, 1655, 1583, 1395, 1280, 1194, 1155, 1066, 987, 818, 723, 679, 642, 540.

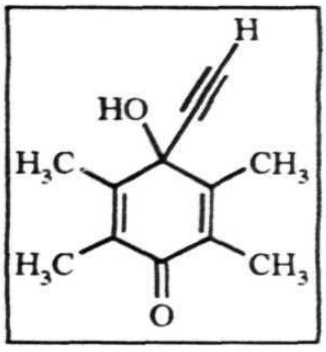
**mp**: 97 °C.




**$^1$H NMR**: δ 7.77-7.36 (m, 18H), 2.96 (s, 1H), 2.94 (s, 1H).

**IR**: cm$^{-1}$ 3559, 3277, 3030, 1597, 1483, 1398, 1159, 1067, 984, 901, 839, 768, 737, 696, 652, 567.

**mp**: 157 °C.




**$^1$H NMR**: δ 2.70 (br s, 1H), 2.40 (s, 1H), 2.15 (s, 6H), 1.85 (s, 6H).

**IR**: $cm^{-1}$ 3412, 3277, 3259, 2930, 2718, 2116, 1669, 1611, 1377, 1165, 999, 862, 723, 690, 596, 551.

**mp**: 148 °C.

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

| | *Chapter 2* | | |
|---|---|---|---|
| | **A** | **B** | **C (neutron data)** |
| Emp. formula | $C_{10}H_{12}O_2$ | $C_{10}H_{12}O_2$ | $C_{10}H_{14}O_3$ |
| Formula wt. | 164.20 | 164.20 | 182.00 |
| $T$ (K) | 150 | 150 | 150 |
| Crystal system | Triclinic | Triclinic | Monoclinic |
| Space group | $P\bar{1}$ | $P\bar{1}$ | $P2_1/c$ |
| $a$ (Å) | 6.2074(3) | 6.4140(2) | 9.925(3) |
| $b$ (Å) | 10.0187(5) | 9.6367(3) | 6.1343(12) |
| $c$ (Å) | 11.5666(5) | 11.7852(4) | 16.725(3) |
| $\alpha$ (°) | 103.005(2) | 105.689(2) | 90 |
| $\beta$ (°) | 93.424(2) | 101.838(1) | 104.12(3) |
| $\gamma$ (°) | 94.572(2) | 94.736(1) | 90 |
| $Z$ | 3 | 3 | 4 |
| $V$ (Å$^3$) | 696.41(6) | 678.98(4) | 987.5(3) |
| $D_{calc}$ (Mg/m$^3$) | 1.175 | 1.205 | 1.224 |
| $F$ (000) | 264 | 264 | 126 |
| $\theta$ range | 1.81-30.33 | 1.85-27.49 | 1.74-23.54 |
| Index ranges | $-8 \le h \le 8$ | $-7 \le h \le 8$ | $0 \le h \le 22$ |
| | $-11 \le k \le 13$ | $-10 \le k \le 12$ | $0 \le k \le 19$ |
| | $-16 \le l \le 15$ | $-12 \le l \le 15$ | $-34 \le l \le 33$ |
| $R1$ | 0.0409 | 0.0461 | 0.0888 |
| $wR2$ | 0.1026 | 0.0966 | 0.1270 |
| Gof | 1.046 | 1.145 | 3.792 |
| N-total | 3618 | 3061 | 2661 |
| N-observed | 3027 | 2554 | 2659 |
| Variables | 235 | 235 | 244 |

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

| *Chapter 3* | | | *Chapter 4* |
|---|---|---|---|
| **3** | **4** | **5** | **2** |
| $C_{10}H_8O_2$ | $C_{18}H_{12}O_2$ | $C_{14}H_{10}O_2$ | $C_{10}H_4F_4O_2$ |
| 160.16 | 260.28 | 210.22 | 232.13 |
| 150 | 150 | 150 | 150 |
| Orthorhombic | Triclinic | Monoclinic | Triclinic |
| *Pbca* | $P\bar{1}$ | $P2_1/c$ | $P\bar{1}$ |
| 8.8316(2) | 8.7684(18) | 10.8247(3) | 8.9002(18) |
| 5.90030(10) | 8.9558(18) | 22.6384(8) | 9.2388(18) |
| 15.6123(4) | 10.315(2) | 10.4783(3) | 9.6721(19) |
| 90 | 113.78(3) | 90 | 93.73(3) |
| 90 | 102.06(3) | 118.1850(10) | 98.73(3) |
| 90 | 102.59(3) | 90 | 114.46(3) |
| 4 | 2 | 8 | 3 |
| 813.54(3) | 682.2(2) | 2263.28(12) | 708.3(2) |
| 1.308 | 1.267 | 1.234 | 1.633 |
| 336 | 272 | 880 | 348 |
| 2.61-27.45 | 2.29-30.38 | 1.80-30.33 | 2.15-29.88 |
| $-11 \le h \le 9$ | $-11 \le h \le 12$ | $-15 \le h \le 14$ | $-12 \le h \le 12$ |
| $-7 \le k \le 7$ | $-12 \le k \le 12$ | $-30 \le k \le 19$ | $-12 \le k \le 12$ |
| $-18 \le l \le 20$ | $-14 \le l \le 13$ | $-14 \le l \le 13$ | $-13 \le l \le 13$ |
| 0.0358 | 0.0540 | 0.0596 | 0.0336 |
| 0.0880 | 0.1084 | 0.1401 | 0.0895 |
| 1.097 | 1.050 | 0.983 | 1.031 |
| 934 | 3623 | 6159 | 3722 |
| 837 | 2404 | 3713 | 3376 |
| 71 | 229 | 369 | 242 |

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

| *Chapter 4* | | *Chapter 5* | |
|---|---|---|---|
| **3** | **4** | **2** | **3** |
| $C_{10}H_4Cl_4O_2$ | $C_{10}H_4Br_4O_2$ | $C_{17}H_{16}O$ | $C_{15}H_{10}Cl_2O$ |
| 297.93 | 475.77 | 236.30 | 277.13 |
| 150 | 150 | 150 | 150 |
| Tetragonal | Triclinic | Triclinic | Triclinic |
| $I4_1/a$ | $P\bar{1}$ | $P\bar{1}$ | $P\bar{1}$ |
| 16.758(2) | 8.9147(3) | 6.8286(14) | 5.7082(1) |
| 16.758(2) | 12.6402(5) | 8.2407(16) | 11.3645(2) |
| 8.865(2) | 12.6547(5) | 12.658(3) | 11.5167(1) |
| 90 | 85.7380(10) | 106.73(3) | 117.268(1) |
| 90 | 69.6250(10) | 98.71(3) | 99.257(1) |
| 90 | 72.72 | 101.39(3) | 96.726(1) |
| 8 | 4 | 2 | 2 |
| 2489.6(7) | 1275.76(8) | 652.0(2) | 639.734(17) |
| 1.590 | 2.477 | 1.204 | 1.439 |
| 1184 | 880 | 252 | 284 |
| 2.43-27.39 | 1.69-27.48 | 1.72-27.48 | 2.05-27.31 |
| $-21 \le h \le 20$ | $-11 \le h \le 11$ | $-8 \le h \le 8$ | $-6 \le h \le 7$ |
| $-21 \le k \le 19$ | $-16 \le k \le 16$ | $-10 \le k \le 7$ | $-11 \le k \le 14$ |
| $-9 \le l \le 11$ | $-16 \le l \le 16$ | $-14 \le l \le 16$ | $-14 \le l \le 12$ |
| 0.0489 | 0.0336 | 0.0478 | 0.0378 |
| 0.1160 | 0.0730 | 0.1199 | 0.0987 |
| 1.091 | 1.148 | 1.033 | 1.110 |
| 1421 | 5818 | 2964 | 2826 |
| 1202 | 4966 | 2362 | 2617 |
| 82 | 321 | 231 | 203 |

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

| *Chapter 5* | | | |
|---|---|---|---|
| **3** (neutron data) | **4** | **5** | **6** |
| $C_{15}H_{10}Cl_2O$ | $C_{15}H_{10}Br_2O$ | $C_{27}H_{20}O$ | $C_{12}H_{14}O_2$ |
| 277.13 | 366.05 | 360.43 | 190.23 |
| 150 | 150 | 150 | 150 |
| Triclinic | Triclinic | Triclinic | Monoclinic |
| $P\bar{1}$ | $P\bar{1}$ | $P\bar{1}$ | $P2_1/c$ |
| 5.7280(1) | 5.7906(12) | 5.6413(3) | 9.0200(18) |
| 11.3620(2) | 11.325(2) | 10.2599(5) | 14.010(3) |
| 11.5210(1) | 11.907(2) | 17.3238(9) | 16.612(3) |
| 117.240(1) | 115.67(3) | 100.450(2) | 90 |
| 99.250(1) | 99.43(3) | 97.790(2) | 93.56(3) |
| 96.860(1) | 97.91(3) | 95.477(2) | 90 |
| 2 | 2 | 2 | 8 |
| 641.865(17) | 674.8(2) | 969.51(9) | 2095.2(7) |
| 1.433 | 1.801 | 1.235 | 1.206 |
| 284 | 356 | 380 | 816 |
| 1.25-16.16 | 1.96-30.16 | 1.21-30.45 | 1.90-27.49 |
| $0 \le h \le 12$ | $-6 \le h \le 8$ | $-7 \le h \le 7$ | $-11 \le h \le 11$ |
| $-20 \le k \le 21$ | $-15 \le k \le 12$ | $-14 \le k \le 13$ | $-18 \le k \le 17$ |
| $-19 \le l \le 10$ | $-15 \le l \le 16$ | $-21 \le l \le 23$ | $-21 \le l \le 21$ |
| 0.0668 | 0.0276 | 0.0759 | 0.0515 |
| 0.1281 | 0.0691 | 0.2025 | 0.1244 |
| 5.444 | 1.071 | 1.038 | 1.006 |
| 2929 | 3456 | 5270 | 4796 |
| 2928 | 2879 | 3419 | 3037 |
| 253 | 203 | 322 | 329 |

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

| *Chapter 5* | *Appendix* | |
|---|---|---|
| **7** | **2** | **3** |
| $C_8H_{10}O_2$ | $C_{42}H_{31}N_3$ | $C_{41}H_{28}ClN_3$ |
| 138.16 | 577.70 | 598.11 |
| 150 | 120(2) | 120(2) |
| Monoclinic | Monoclinic | Monoclinic |
| $P2_1/c$ | $P2_1/c$ | $P2_1/c$ |
| 6.5503(13) | 17.543(5) | 17.646(4) |
| 16.931(3) | 9.308(4) | 9.319(3) |
| 6.4930(13) | 18.972(4) | 18.807(2) |
| 90 | 90 | 90 |
| 95.42(3) | 98.580(10) | 100.480(10) |
| 90 | 90 | 90 |
| 4 | 4 | 4 |
| 716.9(2) | 3063(2) | 3041.1(12) |
| 1.280 | 1.253 | 1.306 |
| 296 | 1216 | 1248 |
| 2.41-27.49 | 2.64-27.48 | 2.45-27.49 |
| $-8 \le h \le 8$ | $0 \le h \le 22$ | $0 \le h \le 22$ |
| $-21 \le k \le 16$ | $0 \le k \le 11$ | $0 \le k \le 12$ |
| $-8 \le l \le 8$ | $-24 \le l \le 24$ | $-23 \le l \le 22$ |
| 0.0549 | 0.0497 | 0.0463 |
| 0.1037 | 0.1300 | 0.1125 |
| 1.067 | 1.090 | 0.702 |
| *1657* | *6891* | *6802* |
| 1074 | 6891 | 6296 |
| 131 | 530 | 518 |

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   A. Anthony, G.R. Desiraju, R.K.R. Jetti, S.S. Kuduva,
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9. Halogen atom interactions in tetrahalo-1,4-diethynyl-cyclohexa-2,5-diene-1,4-diols
   Manuscript under preparation.