Acc. Chem. Res. **2002,** *35,* 565−573

Hydrogen Bridges in Crystal Engineering: Interactions without Borders

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Received July 26, 2001

ABSTRACT
A hydrogen bond, X−H···A, is an interaction wherein a hydrogen atom is attracted to two atoms, X and A, rather than just one and so acts like a bridge between them. This attraction always increases with increasing electronegativity of X and A, and in the classical view all hydrogen bonds are highly electrostatic and sometimes even partly covalent. Gradually, the concept of a hydrogen bond became more relaxed to include weaker interactions, provided some electrostatic character remains. In the limit, these weak hydrogen bonds have considerable dispersive−repulsive character and merge into van der Waals interactions. A great variety of hydrogen bonds are observed in the solid state and the aim of this article is to highlight some features common to all these bonds and further to suggest that the term *hydrogen bridge* is perhaps a better descriptor for them. Such a description recognizes an interaction without borders and one that admits of much variation in its relative covalent, electrostatic, and van der Waals content.

Introduction

Hydrogen bonds are so widespread in chemistry and biology and have so many structural and mechanistic consequences that concerns as to what they are have been rapidly outpaced by observations about what they can do.[1,2] The only rigorous answers to questions that probe the nature of the hydrogen bond can originate from theory.[3] However, theoretical treatments of intermolecular interactions are especially challenging, and the hydrogen bond is no exception. Our own work in the areas of crystal engineering[4] and recent developments in solid-state supramolecular chemistry[5] have led us to hydrogen bonding, especially to the domain of the weak hydrogen bond.[6] During the last 15 or so years we have made several observations on hydrogen bonds both in the laboratory (crystallography) and through statistical analysis (database research).[7−9] Through these observations, it has been possible to draw several conclusions about the nature of the hydrogen bond phenomenon. This paper, in which results of the last 5 years are highlighted, is an account of our approach toward a problem of fundamental interest and importance. In particular, the extension of the hydrogen bond concept to weaker interactions provides many insights that more clearly—and fully—define its nature and scope.

Hydrogen bonds in crystals are of great chemical variety and span energies between 0.25 and 40 kcal mol^{-1}.[10] Even so, all hydrogen bonds have some features in common. The aim of this article is to highlight these common characteristics and thereby to suggest that the term *hydrogen bridge* (in use till the 1930s) might perhaps be a better descriptor for this interaction, if only in a linguistic context. In a chemical context too the term *bridge* may be more appropriate, at least to those for whom the term *bond* carries with it implications and attributes that are clearly not enjoyed by what many supramolecular and structural chemists have identified as this interaction type. In any case, there is a broad consensus that a *hydrogen bond* is a distinctive interaction. If this distinct identity were more clearly appreciated with a distinct name, then the term *hydrogen bridge* would be a possibility. This having been said, the term *hydrogen bond* is used consistently in this article, until the final section, wherein a justification is given for the alternative term *hydrogen bridge*.

Definitions and Criteria of Hydrogen Bonding

A hydrogen bond, X−H···A, is an interaction wherein a hydrogen atom is attracted to two atoms, X and A, rather than just one and so acts like a bridge between them. It was recognized from early times that this attraction always increases with the increasing electronegativity of X and A,[11] and the electrostatic nature of all hydrogen bonds is accepted without question. It is important to note that the term "electrostatic" is used here to refer to interactions that have an r^{-1} to r^{-3} energy/distance dependence or thereabouts, so that dipole−dipole interactions are included. According to textbooks, all forces between molecules are of electrostatic nature. In this article, however, the term "electrostatic" is defined somewhat arbitrarily (for example, octupole related terms are not included) so that a distinction may be made between electrostatic and van der Waals interactions. The term "van der Waals" is used to describe interactions between dipoles and/or induced dipoles, which have an r^{-6} dependency.

Hydrogen bonds are electrostatic interactions but the proportion of electrostatic character can vary—some hydrogen bonds also have charge-transfer character so that the H···A link is partly covalent. With these additional connotations of covalency, the concept of the hydrogen *bond* became deeply entrenched in the imagination of chemists. It is little wonder then that when weak hydrogen bonds were first proposed, these suggestions were largely met with scepticism. After all, interactions such as C−H···O and O−H···π are hardly covalent if only marginally elec-

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10.1021/ar010054t CCC: $22.00

trostatic. However, the concept of a hydrogen bond gradually became more relaxed with the realization that while X−H···A interactions may span a wide energy range, they still retain many similar characteristics.

Even so, some operational definition of a hydrogen bond is needed, for otherwise any approach of any X−H group toward any species A will have to be considered a hydrogen bond, and the term itself will lose all meaning and value. Various criteria have been used to classify an interaction as a hydrogen bond. These criteria are geometrical, energetic, spectroscopic, or functional. None of these criteria is all encompassing and exceptions are known everywhere. However, each of them is accurate and useful in the particular context in which it was proposed. From the viewpoint of crystal engineering and supramolecular chemistry, we have preferred to rely on a functional criterion—the more long range an interaction, the more specific will be its orienting effect during crystallization and self-assembly. So, we have proposed that any interaction X−H···A with an r^{-4} or shallower energy/distance dependence should be termed a hydrogen bond.[6] According to such a definition, all O−H···π interactions are hydrogen bonds as is the C−H···π interaction in acetylene, but the C−H···π interaction in benzene is not. Such a definition concentrates on the borderline between a hydrogen bond and a van der Waals interaction. However, the reader will note that in the end this and any other criterion of hydrogen bonding is simplistic and subjective, some would say even arbitrary.

The hydrogen bond is not a simple interaction but a complex conglomerate of at least four component interaction types: electrostatics (acid/base), polarization (hard/soft), van der Waals (dispersion/repulsion), and covalency (charge transfer). The partitioning into these components has been well-studied.[12] In this article, hydrogen bonds are treated in terms of their electrostatic, van der Waals, and covalent components. The polarization component is not completely independent of these three components. Generally, the more electrostatic an interaction, the harder it is. Softness increases with covalent character and also with van der Waals character. Much of our own research deals with C−H···O and other weak hydrogen bonds. In these cases, there is a changing trade off between electrostatic and van der Waals character. Polarization is discussed specifically in the case of C−H···F−C hydrogen bonds. Charge transfer involves transfer of electrons from an occupied orbital of one molecule to the unoccupied orbitals of the other and is therefore conceptually similar to covalency. Very strong hydrogen bonds have a quasi-covalent nature with a large charge-transfer contribution.

The Classical View: Covalency and Electrostatics

Pronounced covalent character in a hydrogen bond is found only occasionally and that too in very strong bonds (energy range 20−40 kcal mol^{-1}). The donors and/or acceptors should be unusually activated, as, for example, when they are related as acid and conjugate base, typically in an intramolecular arrangement. Additionally or alternatively, charge, resonance or cooperative assistance renders covalent character to a hydrogen bond.[13−15] Because of the covalent character, the H···A distance is greatly shortened (2.2−2.5 Å for the O···O distance in an O−H···O hydrogen bond) and the X−H···A angle is close to 180°.

The notion of the hydrogen bond as an electrostatic interaction goes way back to Pauling, who assumed that only if the atoms X and A are very electronegative (F, O, Cl, N, Br) would the deshielding of the H atom and in turn the electrostatic attraction between H and A be sufficiently high to term the interaction a bond.[11] Indeed, electrostatic character is dominant in the ubiquitous N−H···O, O−H···O, and O−H···N bonds. Even while a more open definition of a hydrogen bond by Pimentel and McClellan recognized that donors such as C−H and acceptors such as a π system can participate in this interaction[16] and while some spectroscopic evidence had already appeared in this regard,[17,18] the classical dogma was in favor of a strongly electrostatic interaction. As it happens, the nonbonded distance X···A (or H···A) in all highly electrostatic X−H···A interactions is considerably shorter than the corresponding sums of van der Waals radii of the respective elements. Somewhere along the line, this consequence of electrostatics became a criterion for establishing an interaction as a hydrogen bond. With such a cyclic argument, it is not surprising that only strongly electrostatic interactions could be defined as hydrogen bonds.

Evidence of the structural consequences of C−H···O and other kinds of weak hydrogen bonds led, however, to a gradual reconsideration of the above line of thinking. The work of Sutor,[19] Leiserowitz,[20] and Kennard,[21] among others, during the period 1960−1982, and of Desiraju and Steiner,[6] among others, from around 1985 has been reviewed elsewhere. Suffice it to say that this entire body of work shows the existence of interactions, which while not as strong (and as electrostatic) as N−H···O, O−H···O, and O−H···N, display many of the geometrical, structural, and spectroscopic characteristics of their stronger cousins, if perhaps not to the same degree.

These continued encounters with weak hydrogen bonds mandated a resolution of conflicts between existing definitions and newer experimental work. Remnants of older arguments surfaced briefly, advocated by Donohue[22] in 1968 and by Cotton[23] in 1997. These authors recommended the use of very conservative distance criteria (3.25 Å for C···O in a C−H···O geometry; 2.41 Å for H···N in C−H···N) in order to classify an interaction as a hydrogen bond. Longer separations would be termed van der Waals interactions. These arguments can be questioned on two counts: (1) the proposed cutoffs are unnecessarily restrictive. Mascal[24] showed that many contacts shorter than the van der Waals separation but longer than what would be accepted by Cotton’s criterion are “genuine” hydrogen bonds; (2) the use of a van der Waals criterion is itself incorrect. This is a more serious matter. The use of a van der Waals distance cutoff criterion for an interaction that

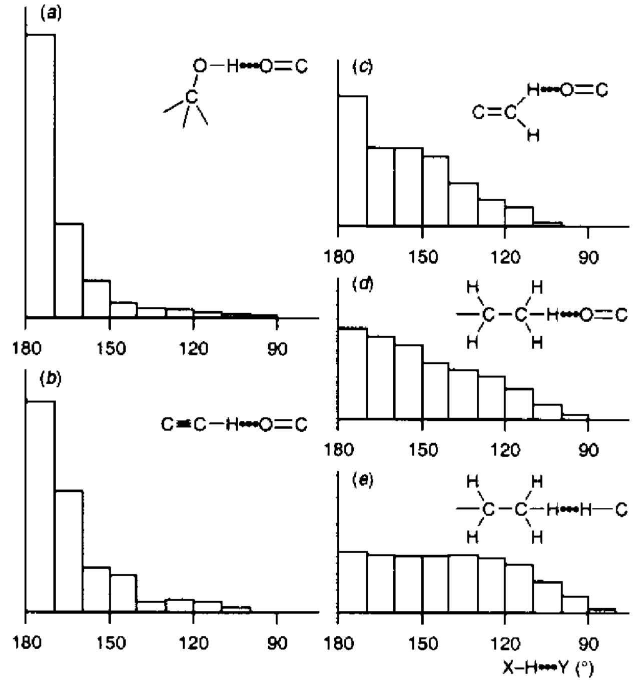


FIGURE 1. Histograms b, c, and d show the directionality of C–H⋯O hydrogen bonds formed by C–H groups of varying acidity. The distributions are cone-corrected. Compare these with histograms a and e which represent strong hydrogen bonds and van der Waals interactions.

is admittedly of electrostatic character is without basis. Sensibly, it is not reasonable to expect that an interaction can be electrostatic (roughly r^{-1} dependence) until a certain distance and then switch suddenly to a van der Waals contact (roughly r^{-6} dependence). It is more chemically intuitive to expect that the change between N–H⋯O and O–H⋯O contacts on one hand and C–H⋯O and C–H⋯N contacts on the other is a matter of gradually decreasing electrostatic character and increasing dispersive character.

This indeed is what is revealed in a Cambridge Structural Database (CSD)[25] study of the angular preferences of the hydrogen bond angle, θ, for a variety of X–H⋯A geometries (Figure 1).[26] For O–H⋯O contacts, there is a sharp falloff in angle from a linear geometry (mean θ 154°). This is as expected. Interestingly, there is a nearly similar distribution for C(sp)–H⋯O (mean θ 152°) with hardly any contacts having $\theta < 140°$. For the less activated vinyl donors, the mean angle falls to 143° and the distribution widens. For the even weaker methyl donor of the ethyl group the mean is reduced further to 137°. Even so, directional behavior persists through all these categories with linear geometries being favored. These distributions are in contrast to the plateau obtained for the C–H⋯H angle in C–H⋯H–C contacts of methyl groups. This isotropic distribution is as would be expected for a true van der Waals contact. The sequence of histograms shows that there is a smooth progression from O–H⋯O through C–H⋯O interactions of decreasing donor acidity but *that there is no transition to nondirectional behavior*. This is good confirmation of at least some electrostatic character in the weakest of hydrogen bonds. This is not to say that these bonds are of no energetic consequence. Computational studies by Dixon and others on C–H⋯O hydrogen bonds formed by the (admittedly activated) C^{α}–H bond in proteins provide a lower limit of -2.1 kcal mol^{-1} stabilization per bond,[27] while Stoddart, Houk, and coworkers address similar issues in supramolecular assemblies leading to catenane and rotaxane structures in solution.[28,29]

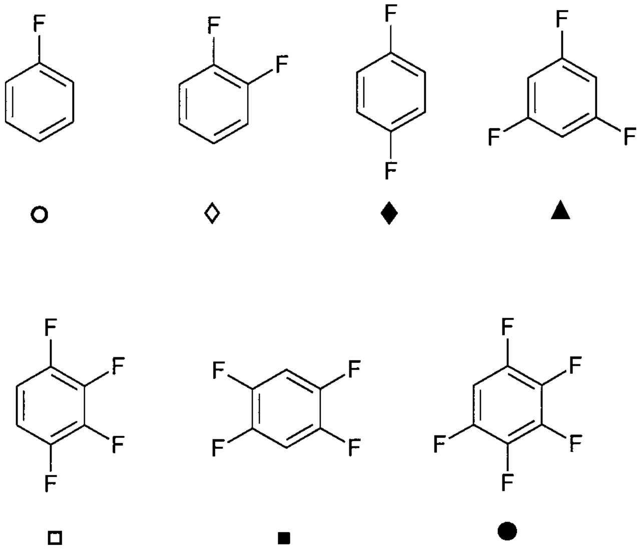
The Weak Hydrogen Bond

The weak hydrogen bond has been defined as an interaction X–H⋯A, wherein a hydrogen atom forms a bond between two structural moieties X and A, of which one or even both are only of moderate to low electronegativity.[6] The oldest and certainly the prototype interaction is the C–H⋯O, but one would also include others such as P–H⋯O, C–H⋯N, and M–H⋯O (M = metal) wherein a weak donor associates with a strong acceptor. The alternative situation wherein a strong donor associates with a weak acceptor is exemplified by O–H⋯π, N–H⋯π, O–H⋯M, and O–H⋯S. Finally, and at the limit of the phenomenon, one needs to consider the association of a weak donor with a weak acceptor. In this category, the most controversial members are the C–H⋯F–C and C–H⋯Cl–C varieties. In all these cases, the lower acid/base strengths lead to lower electrostatic stabilization of the interaction that is compensated for partly by a dispersive stabilization.

Fluorine acceptors are a special case. The ability of the so-called organic fluorine, an uncharged F–C group, to accept a hydrogen bond has been debated.[30,31] Despite its electronegativity, organic fluorine accepts a hydrogen bond only with great difficulty because of its hardness, that is, lack of polarizability. The C–H⋯F–C hydrogen bond is unique in that it is very weak but of the soft donor–hard acceptor variety. To test the acceptor ability of organic fluorine, we undertook a crystallographic study of a series of fluorobenzenes.[32] The compounds studied are given in Scheme 1 and were selected for the following reasons: (1) they do not contain other acceptors, stronger than fluorine, that would surely compete better for the donors; (2) they contain only one type of donor; (3) with increasing fluorine content, the C–H acidity increases.

The crystal structures were determined and the C–H⋯F geometries noted. Generally, shorter H⋯F distances were observed with increasing fluorine content. This is as might be expected if C–H bond activation influences the C–H⋯F geometry. Figure 2 is a scatter plot of H⋯F distances d against the C–H⋯F angles θ (H atom positions normalized) for (a) all interactions between C(sp^2)–H and C(sp^2)–F groups in the CSD and (b) interactions in the fluorobenzenes selected in our study. The difference between these scatter plots is unmistakable. In Figure 2a, there is some kind of inverse correlation between d and θ, but there are too many points in the top right-hand corner corresponding to crystallographic noise. Figure 2b, in contrast, shows a definite negative correlation that is very characteristic of hydrogen bonding. The top right-hand

Scheme 1. Fluorobenzenes for Which C−H···F−C Interactions Are Shown in Figure 2b. The Symbols Shown below Each Compound Also Refers to Figure 2b



corner is completely empty and suggests that a C−H···F contact in these fluorobenzenes is there for a chemical reason rather than merely contributing to overall (isotropic) crystal packing. Last, these scatter plots show that only when carbon acidity is enhanced and only in the absence of competing acceptors is the hydrogen bond accepting ability of organic fluorine even revealed. Similar C−H activation is possible in fluorophenyl carboranes, leading to characteristic C−H···F interactions.[33] The situation with organic chlorine is comparable. Work from several authors shows that while the C−H···Cl−C is hardly a hydrogen bond, activation of the acceptor via anion formation or metal coordination results in interactions of the hydrogen bond type,[34−37] leading in optimal cases to predesigned supramolecular architectures.[38]

The scope of weak hydrogen bonding has been extended considerably by inclusion of organometallic examples. This topic has been reviewed in detail elsewhere by Braga, Brammer, and others.[6,39−41] Suffice it to say that with the advantages of polarizable donors and acceptors and of cooperativity effects it is possible to have metal-atom-containing species as donors and acceptors in hydrogen bonding situations. In the end, it appears that even with minimum residual electrostatic character, an interaction X−H···A shows many hydrogen bond-like properties. The difficulty in understanding interactions formed by the association of weak donors with weak acceptors is that the major stabilization arises from dispersion. The transition from a hydrogen bond to a van der Waals interaction is gradual and several situations may be found in the gray area that lies between these regions.

The C−H···π Hydrogen Bond: Dispersion−Repulsion

The C−H···π geometry is very common but the interaction is of variable character because of the wide range of C−H group acidity and π-basicity. The interaction has also been called by different names; organic chemists have termed it a "CH/π interaction",[42] structural biologists prefer the term "phenyl interactions",[43] and in the crystal engineering literature they are referred to as "herringbone" interactions[4] or "hybrid" interactions.[44] Or are these geometries the outcome of straightforward close packing?

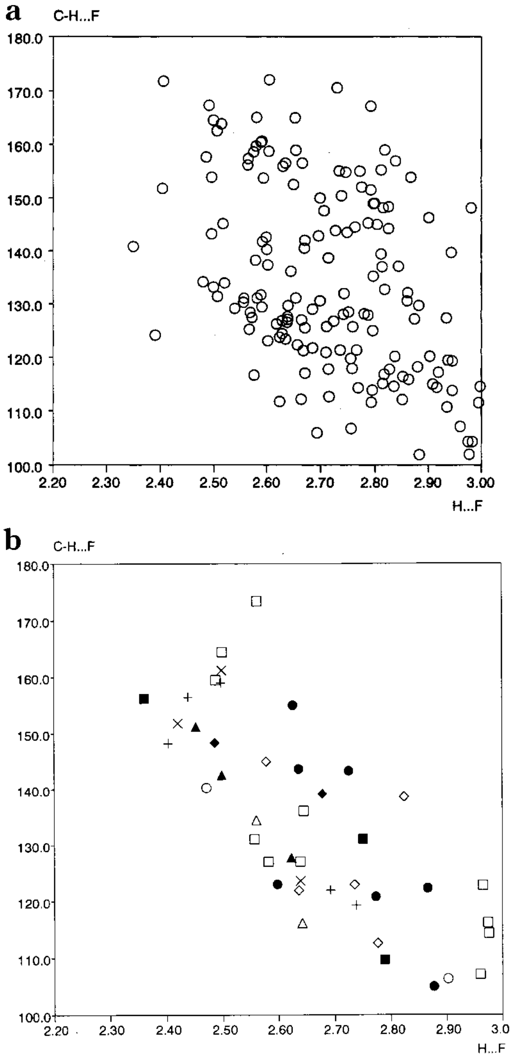


FIGURE 2. Scatter plots of normalized distances *d* against angles θ in C−H···F interactions: (a) All interactions of the type C(sp^2)−H···F−C(sp^2); (b) All C−H···F interactions in the fluorobenzenes in Scheme 1. The contacts from each compound are indicated according to the code in Scheme 1.

A distinctive feature of π-acceptors is that they are of the multiatom type. While C−H···π interactions to phenyl rings have been often identified, there is still limited consensus concerning their directional properties. Some authors have held that the donor group interacts with the centroid of the aromatic ring. Others have stated that the C−H group interacts with one or more of the individual ring carbon atoms. During our studies of this phenomenon, we realized that frequency distributions of these interactions must be corrected for the fact that the acceptor, being of a multiatom type, has a finite area.[45] This area correction, which takes the form *N*/*r*, is analogous to the cone correction *N*/sin θ that is used for hydrogen bond angle[46] because both of them attempt to

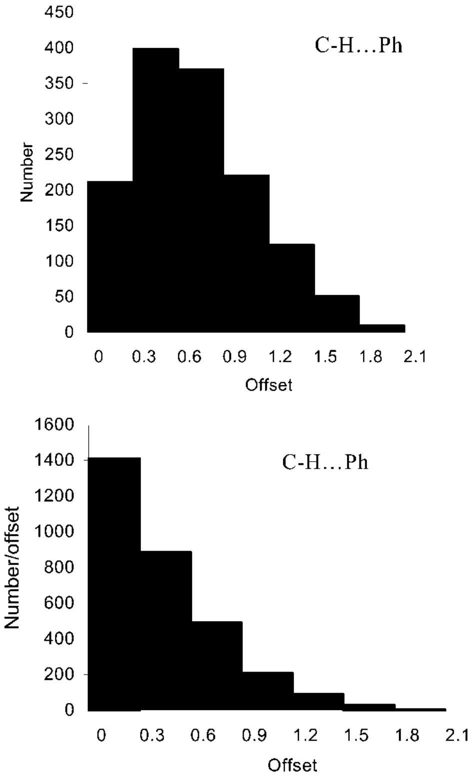


FIGURE 3. Observed (above) and area-corrected (below) histograms of $C-H\cdots Ph$ hydrogen bonds. The correction is with respect to the center of the phenyl ring. Notice the tendency for hydrogen bond formation toward the ring center.

separate out chemical and geometrical factors affecting hydrogen bond trajectories. Figure 3 shows uncorrected and corrected histograms of offsets *r* for $C-H\cdots\pi$ hydrogen bonds. The corrected histogram shows convincingly that these interactions are directed toward the centroids of the respective phenyl rings. This preference may arise from either or both steric and electronic reasons. These reasons and many consequences of $C-H\cdots\pi$ hydrogen bonds, both in the solid state and in solution, have been discussed by Nishio.[42]

Despite the extreme weakness and very feeble electrostatic character of $C-H\cdots\pi$ interactions, their structural effects are surprisingly noticeable. In a pair of nearly isostructural toluene and chlorobenzene solvates of 2,3,7,8-tetraphenyl-1,9,10-anthyridine, it was noticed that a $C-H\cdots\pi$ interaction of 2.61(2) Å from a C−H group in the heterocycle to the π-cloud of chlorobenzene is shortened to 2.54(2) Å in the corresponding toluene solvate, reflecting the better acceptor character of the latter.[47] Even methyl groups seem to be able to function as hydrogen bond donors. In 2,4,6-tris(4-methylphenoxy)-1,3,5-triazine, a noncentrosymmetric packing is adopted because the methyl group can form $C-H\cdots\pi$ interactions (D, 3.60 Å; d, 2.77 Å; θ, 133°) with an orientation that sustains three-dimensional chirality.[48] Figure 4 shows the two-dimensional trigonal network that is obtained with the $C-H\cdots\pi$ interactions extending into the third dimension around 3_1 and 3_2 axes. Related motifs appear regularly in the crystal engineering literature. Zaworotko, for example, has described a novel supramolecular “chair form cyclohexane” constituted with such $C-H\cdots\pi$ interactions.[49]

Surely significant is the fact that activation of either the donor or the acceptor component of the $C-H\cdots\pi$

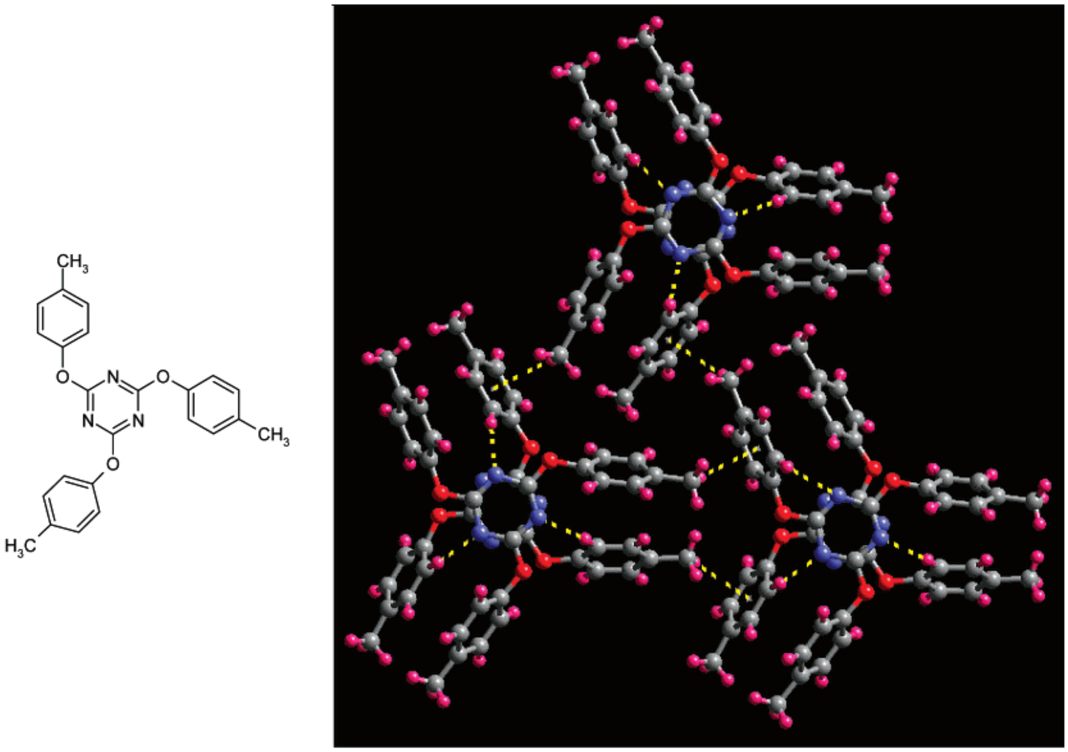


FIGURE 4. $C-H\cdots\pi$ hydrogen bonds from methyl groups to phenyl rings orient molecules of 2,4,6-tris(4-methylphenoxy)-1,3,5-triazine in a polar packing in space group *R*3*c*, leading to bulk octupolar NLO.

interaction leads to its strengthening. This is good evidence of its hydrogen bond nature. Unusually short distances are observed when the C−H group in a phenyl ring has an ortho diazonium substituent[50] or when a C−H group donates to a cyclopentadienyl anion.[51] If the C−H···π interaction is of a purely van der Waals type, such donor or acceptor activation should not result in bond shortening. As in the case of the C−H···F interaction, the presence of even a little electrostatic character confers on the C−H···π interaction many of the attributes of stronger hydrogen bonds. Repeated observation of such experimental facts leads to the idea that the concept of the hydrogen bond is a very broad one without definite borders. This concept tolerates much variation in the covalent, electrostatic, and van der Waals content of the interaction without altering its important properties. In the crystal engineering context, the most important common property that is seen across a wide range of hydrogen bond types is the ability of these interactions to steer and control crystal packing.

Crystal Engineering and Interaction Hierarchy

Crystal structures are the result of intermolecular interactions, and given any particular crystal structure it is generally possible to rationalize it in terms of the interactions in it. However, the reverse operation, namely, deducing a crystal structure, given the molecular structure of a compound is decidedly nontrivial. This is so because a crystal structure is often not the result of hierarchic interaction preferences that follow from molecular functionality. Rather, the packing is determined by a convolution of a large number of strong and weak interactions, each of which affects the other intimately. Small changes in the molecular structure can therefore result in large changes in the crystal structure. In crystal engineering, however, one attempts to remedy this state of affairs and design systems wherein the system of interactions *is* hierarchic. In this way, one tries to obtain crystal structures that are related in more obvious ways to molecular structures—and more nearly approach the ultimate goal of crystal structure prediction. In summary, weak hydrogen bonds need to be considered carefully in crystal engineering because they can affect crystal packing in unpredictable ways.

Hydrogen bonding is the most important interaction type in crystal engineering because it combines strength with directionality. However, potential for the formation of both strong and weak hydrogen bonds can blur interaction hierarchy and thereby make the engineering exercise more difficult. In the family of cubanecarboxylic acids, the usual carboxy dimer O−H···O synthon that is characteristic of carboxylic acids is consistently replaced by the rare syn-anti catemer synthon shown in Figure 5.[52,53] This surprising result is obtained because of a phenomenon known as *interaction interference*. The cubyl group contains C−H groups that are particularly activated with respect to the formation of C−H···O hydrogen bonds. These bonds stabilize in turn the catemer structure vis-à-vis the dimer. Both dimer and catemer contain the same number of O−H···O hydrogen bonds and normally one might predict that the vastly more common dimer pattern would be preferred. In the cubane series, however, the weaker C−H···O bonds act as discriminators and alter the O−H···O topology.

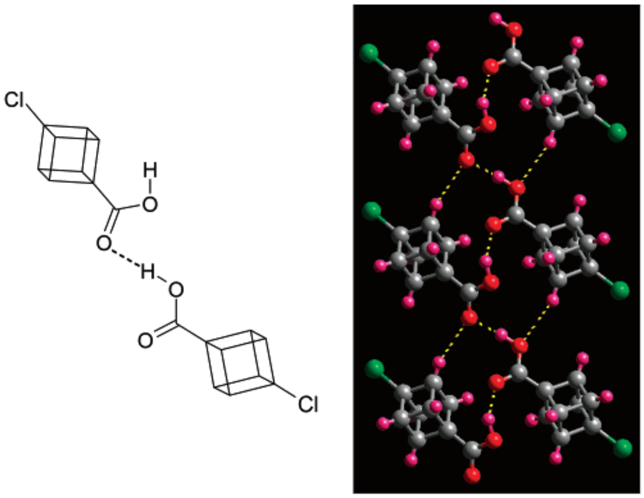


FIGURE 5. 4-Chlorocubanecarboxylic acid to show the O−H···O with C−H···O mediated syn-anti catemer. It is presumed that in the absence of the activated cubyl C−H group, the preferred hydrogen bond pattern would be the common carboxylic acid dimer.

Finally, let us take the case of tetrakis(4-nitrophenyl)-methane, a new host molecule with considerable structural adaptability over a range of solvents with which it forms host−guest inclusion compounds.[54] Figure 6 shows how molecules of the host assemble with C−H···O interactions to generate tetrahedral scaffolding leading in turn to a 2-fold interpenetrated diamondoid network. Such networks are well-known, but the present case is unprecedented in that the network connections are made exclusively with weak interactions, C−H···O and π−π. The network is stable enough in that included solvents such as dioxane, THF, and anisole may be exchanged with one another and weak enough that the solvates obtained can reversibly transform to an alternative rhombohedral host topology with removal of solvent and/or change in temperature. Such structural modulation is unusual in host−guest chemistry; generally a host network is robust and withstands any kind of removal or introduction of guest molecules or is so fragile that it collapses completely upon removal of guest. The partly stable and partly flexible nature of the host framework may perhaps be attributed to the intermediate weakness of the connecting C−H···O hydrogen bonds. Weakness, rather than strength, leads to increased structural adaptability and, with it, to ease of crystal engineering.

The Hydrogen Bridge: Wasserstoffbrücke

The above discussion shows that hydrogen bonds of differing strengths have broadly similar if graded effects in the building up of crystals from molecules. For weaker interactions, more of them are needed for any particular

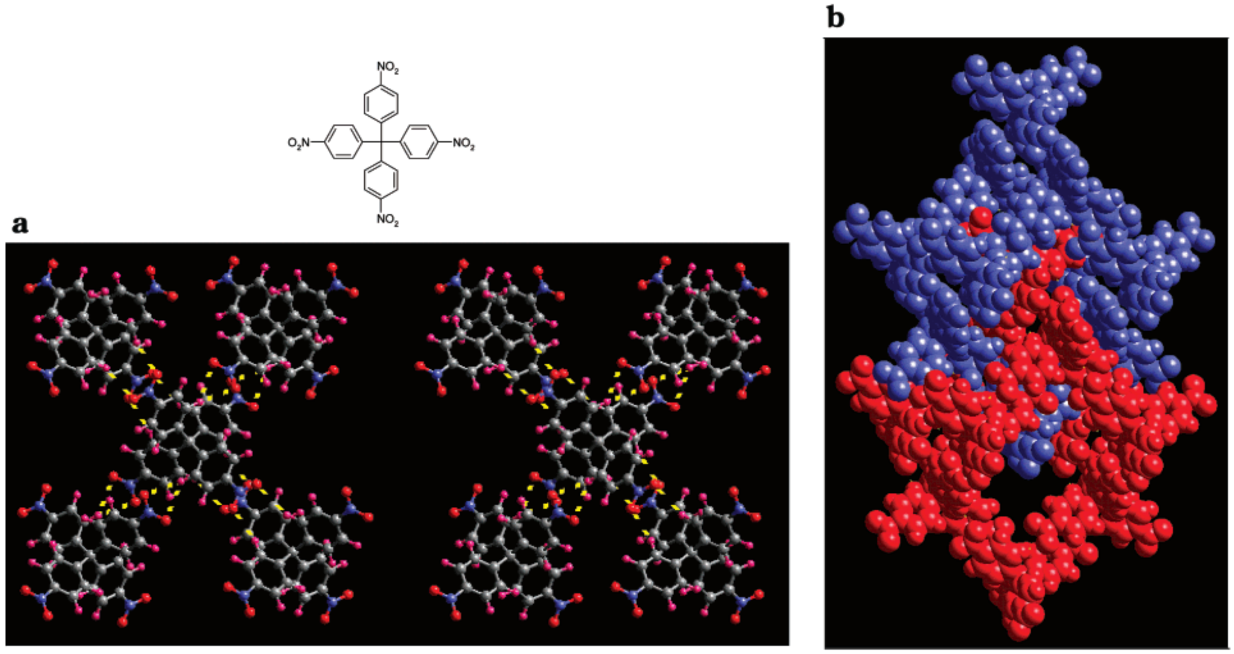


FIGURE 6. (a) Stereoview to show how C—H···O hydrogen bonds form molecular connectors in the diamondoid network structure of tetrakis-(4-nitrophenyl)methane. (b) Interpenetration of the networks. There is still enough empty space for guest inclusion in the vertical channels. This is the first example of a diamondoid network held together by weak hydrogen bonds.

energy based requirement, but other than this, there is a broad phenomenological similarity across a wide range of X—H···A varieties. Indeed it is at the functional level rather than at a geometrical, energetic, or spectroscopic level that all hydrogen bonds are similar, and it is little surprise that it is in the fields of crystal engineering and supramolecular chemistry that the hydrogen bond is most clearly identified as an interaction type without internal borders. The hydrogen bond, it must be emphasized, is a complex and a composite interaction. It is complex because it is made up of all the atoms within the interacting system; in its simplest, nonbifurcated form it consists of three atoms X, A, and the all-important bridging H. It is of a composite nature because it has three main and independent ingredients: covalency, electrostatics, and van der Waals character. The proportions of these three components depend on the nature of X and A.

The solid state is an extraordinary medium in which to observe and study the phenomenon of hydrogen bonding.[10] The weaker and more dispersive hydrogen bonds may be observed only in crystals; strong to very strong hydrogen bonds may be observed anywhere, but the degree of quantitative understanding that is possible in crystals remains unparalleled.[13,15] Further, the availability of a tool such as the CSD[25] means that very weak interactions may be examined and assessed with reliability. A number of hydrogen bonds studied by us and by others in the recent literature are collected in Figure 7. This is a schematic diagram that shows the interplay of effects in many different variations of the interaction. The figure shows the hydrogen bridge as a borderless interaction that lies between the extremes of a half-covalent bond (with much electrostatic character), a pure electrostatic interaction, and a pure van der Waals interaction. There are, in effect, three axes in this figure radiating out from the centroid of the boomerang and showing the extent of these three main characteristics. It may be noted that the sketch excludes the physically impossible combination of covalency and van der Waals character. The sketch shows all hydrogen bonds as being electrostatic, with variations toward covalency among the so-called very strong hydrogen bonds and toward van der Waals character in the domain of the weak hydrogen bond. If these are the extremities of the boomerang, the central region corresponds to the classical or conventional hydrogen bond. The exact positions of some of the interactions, especially in the weak hydrogen bond region, are debatable. However, what is clear is the continuum that is characteristic of the interaction as a whole.

It is interesting to study the transition between these three component types. "Normal" hydrogen bonds such as N—H···O and O—H···O are electrostatic. The transition to covalency occurs smoothly and the limiting situation is provided by the fully symmetric X—H—X bond with two equal X—H distances. It is more difficult to evaluate the transition to a purely electrostatic interaction. Such an interaction would be nondirectional and can occur if the partners carry large charges but only small dipole or quadrupole moments. The transition to a pure van der Waals interaction is even more difficult to assess and involves many of the situations detailed in this Account. The CH_4···Ar is probably a pure dispersive interaction but not so the recently described blue-shifted C—H···F—C hydrogen bond,[55] which clearly fits into an expanded definition of a hydrogen bond with C—H bond shortening following from the dominance of dispersion over electrostatics.

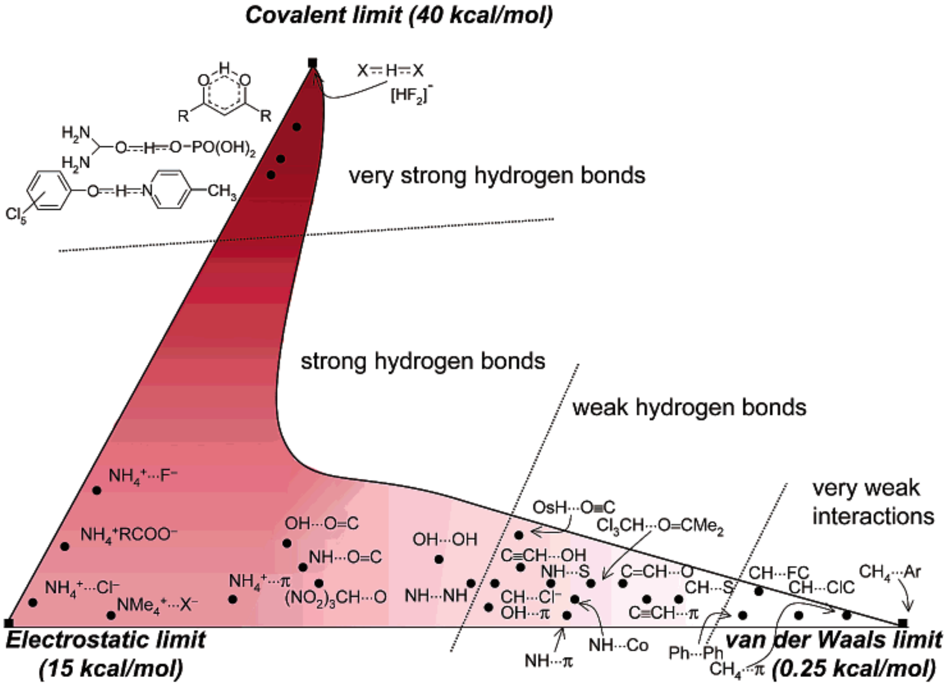


FIGURE 7. The hydrogen bridge. The composite nature of the interaction is highlighted by the three extreme situations of widely differing energies. The sketch is not strictly quantitative but the coloring attempts to provide a visual scale of energies. The figure serves as a rough guide to the balance of electrostatics, van der Waals nature, and covalency in any X−H⋯A interaction. For the weak interactions, the covalent character is very small and may be interpreted as charge transfer. A van der Waals interaction is considered to have dispersive and repulsive components.

Studies of the weak hydrogen bond have often prompted inquiries as to whether these interactions are hydrogen bonds or not.[56−58] This has led sometimes to heated discussions as to what constitutes a “hydrogen bond” and in the end even a “bond”. Such issues are, by their very nature, more semantic than chemical. By definition, a definition cannot be correct or incorrect. It can, however, be useful or have outlived its usefulness. It should never, in any case, hinder study of a phenomenon because of linguistic limitations and psychological difficulties. The term *hydrogen bond* has served the scientific community well for about 70 years.[11] With the ever-increasing relevance of this interaction and its applicability across a wide range of chemical and biological situations, there is much to be said for renewing the older descriptor *hydrogen bridge*. The term originated in the 1930s[59] and continues to be used today in written and spoken communication by German-speaking scientists. Jeffrey and Saenger have indeed commented that this term is perhaps more appropriate.[2] If the term “bond” has other hallowed connotations in chemistry, it might be far preferable to refer to hydrogen bonds as hydrogen bridges, for so different are they from covalent bonds. A bridge is a more user-friendly descriptor for an interaction that brings together many different atoms in many different ways and is a more apt representation of the openness and the absence of borders that is characteristic of modern supramolecular chemistry.[60] The terminology of a *hydrogen bridge* does not carry with it the unnecessary and incorrect implication that a hydrogen bond is like a covalent bond but only much weaker. Above all, the concept of the hydrogen bridge recognizes that exact definitions are all but impossible in the study of complex phenomena.

It is a pleasure to thank the many students who have contributed to this work and whose names are included in the references. Discussions and joint work with Roland Boese, Dario Braga, Judith Howard, and Ashwini Nangia form an integral part of this study. Above all, I acknowledge the collaboration of Thomas Steiner, my coauthor in our book on the weak hydrogen bond. Continuing support for our research from the Department of Science and Technology, Government of India, is gratefully acknowledged.

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AR010054T