

A Bond by Any Other Name

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bond theory · hydrogen bonds · solid-state structures ·
spectroscopy · structure elucidation

1. The Hydrogen Bond

Why are chemists and biologists still interested in hydrogen bonding?^[1] The hydrogen bond $X-H\cdots Y-Z$ is an attractive interaction in which an electropositive H atom intercedes between two electronegative species X and Y and brings them closer together. The fundamental importance of the interaction follows from this particular role in molecular association. The hydrogen bond is strong enough to hold molecules such as XH and YZ together at normal temperatures and directional enough so that this association is orientationally specific. However, and depending on the nature of X and Y, it can also become weak enough to allow these molecules to come apart and directionless enough to permit loss of orientational specificity in the association of XH and YZ, more like a hydrophobic interaction. This chameleon-like nature of the interaction continues to baffle and excite the researcher.^[2] Accordingly, the hydrogen bond plays a crucial role both in stabilizing static structures and in mediating dynamic processes. This is what accounts for its importance as a structure-defining element in supramolecular chemistry and as a major facilitator of biological reactions.^[3] Depending on the nature of X, Y, and Z, the energy of a hydrogen bond lies in the range 0.5 to 40 kcal mol⁻¹. The strongest hydrogen bonds are stronger than the weakest of covalent bonds, while the weakest hydrogen bonds are practically indistinguishable, in energy terms, from van der Waals interactions. It is the intermediate energy range of many hydrogen bonds that makes them able to both associate and dissociate quickly at ambient temperatures—and it is this attribute that accounts for the importance of the hydrogen bond in mechanistic biology. All in all, it comes as no surprise that roughly one new paper on hydrogen bonding gets indexed in SciFinder every hour.

The hydrogen bond is a complex interaction that has at least four chemical characteristics: electrostatics (acid/base); polarization (hard/soft); van der Waals (dispersion/repulsion); and covalency (charge transfer).^[2k] It generally contains a minimum of four atoms, X, H, Y, and Z (or groups of atoms because a group of atoms can also constitute a valid acceptor fragment). The entire species $X-H\cdots Y-Z$ is properly consid-

ered as the *hydrogen bond* because each part ($X-H$, $H\cdots Y$, and $Y-Z$) affects the other parts and is likewise affected by them. It is misleading to think that only the $H\cdots Y$ part constitutes the hydrogen bond. In a typical example that illustrates the interdependence of X, H, Y, and Z, a metal hydride $M-H$ is polarized sufficiently in the presence of an electronegative atom like oxygen in an $O=C$ fragment so that the H atom becomes protic and a hydrogen bond of the type $M^{\delta-}-H^{\delta+}\cdots O^{\delta-}$ is formed.^[4a] It is a characteristic of complex systems that, in their totality, they are more than the sum of their constituents.^[4b] Accordingly, they are hard to define. In truth, exact definitions are all but impossible in studies of complex phenomena. A hydrogen bond is not a very weak covalent bond. It is also not a very strong van der Waals interaction. It is not even a particularly strong type of directional dipole–dipole interaction.

2. What's in a Name?

Chemists seem to be particularly intrigued by names and nomenclature. The history of chemistry is strewn with names that were once hotly contested and disputed by various protagonists. The great Emil Fischer is reported to have complained that the organic chemists of his time did not even accord the status of an “organic” compound to urea. Pauling and Ingold quarreled about the terms *resonance* and *mesomerism*. Resonance won the day but now, after many decades have elapsed, can one say that it really mattered? An aromatic compound originally had a pleasant if rather gripping smell. The word *aromatic* continues to be in chemical use today but no one will even try to associate it with smell. Certainly, an antiaromatic compound is not one with no smell! What have we chemists done with the word *aromatic*? Essentially, we have taken it out of the English language and have absorbed it into the language of chemistry. It has become a trivial name. Chemists are famous for using trivial names for compounds and for phenomena. *Ethanoic acid* means something, or at least the name leads logically to the chemical structure of the compound. Does *acetic acid* inherently mean anything? But how many of us will call the compound *ethanoic acid*?

I will move to the present and to my own field of crystal engineering and solid-state supramolecular chemistry. What was originally a *coordination compound* became a *coordination polymer* and was then transformed into a *metal–organic framework compound*.^[5] No one knows if all coordination

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polymers are metal–organic framework compounds or vice versa. Does anyone care? A *binary crystal* became a *molecular complex* which then became a *co-crystal* (also *cocrystal*, on the other side of the Atlantic, with much discussion on both sides about whether or not the hyphen should be used), which in turn appears as if it might well metamorphose into a *multicomponent molecular crystal*.^[6] Terms like *mixed crystal* and *solid solution* have also persisted tenaciously for the same or similar phenomena, and there is not always complete exclusivity between these terms. Why do chemists fight about names so much?

A possible reason for all this disputation about nomenclature is that chemistry still remains a gloriously qualitative subject.^[7] All scientists will strive for both accuracy and generality in a name but there will be fuzzy areas in which one or the other of these most desirable attributes will just have to give. In largely qualitative disciplines, say certain areas of biology or ecology, a name is just that, a name. In a more quantitative subject like physics, many names have a clear scientific meaning and implication. A subject like chemistry, which is sometimes qualitative and sometimes quantitative, runs into problems. Chemists want their names to have a scientific meaning but the exceptions become uncomfortably large because of the qualitative nature of the subject. It is here that chemists resort to the trick of the trivial name. This trick is all too seductive. The general idea is that a term is acceptable if the largest numbers of chemists are in a maximum degree of agreement about what it means. A trivial name is the victory of such a consensus. In the case of *acetic acid*, there is no disagreement about what the term signifies. For the term *aromatic*, there is a very substantial degree of agreement so that detractors may be dismissed as being somewhat eccentric. But problems arise with the all-important word *bond*, especially when these bonds become weak. And whether one likes it or not, this word *bond* occurs in the term *hydrogen bond*. And some hydrogen bonds are weak.^[8]

3. The Name Is Bond

The bond is the central concept in chemistry, and the delineation of the properties of the chemical bond and the idea of electron sharing, in the early part of the 20th century, is what demarcated chemistry from physics in general, and quantum chemistry from quantum mechanics in particular.^[1a] It is little wonder that the word *bond* has an almost religious connotation for chemists. It is this word that confers on us an identity that distinguishes us from all other scientists. Every chemist has his or her own idea as to what constitutes a bond. In large measure, these perceptions are practically identical for strong bonds and there is no big problem. We have covalent bonds, ionic bonds, metallic bonds, and hydrogen bonds. What common feature unites all these bonds? A *bond brings together atoms, molecules, or ions in chemically acceptable and meaningful ways*. This is my linguistic definition, but it is a reasonable one. To elaborate, a bond is something that draws chemical species together in ways that can be detected, experimentally or computationally. This definition (like many others in science) depends on the possibility of detection of a

phenomenon and on the reliability of the measurement technique that underlies such detection. The stronger the bond, the more unambiguous its detection and measurement. Because the definition depends on the detection of some species, it could also be temperature dependent.

The nomenclature of hydrogen bonds did not pose special problems in the era of Pauling, who was clear and unambiguous in the use of the word *bond* when he stated that “*under certain conditions an atom of hydrogen is attracted by rather strong forces to two atoms, instead of only one, so that it may be considered to be acting as a bond between them*”.^[1a] The H atom is the seat of bonding in say $X-H\cdots Y-Z$ because it is the key ingredient that brings atoms X and Y together. The bridging H atom is crucial to this entire enterprise,^[1d] and hence the phenomenon is called *hydrogen bonding* and not just any other kind of bonding. Given such an interpretation, the use of the word *bridge* (which was used prior to Pauling and which is still extant in the German-speaking territories) is hardly objectionable. I have myself suggested that if a chemist finds the term *bond* to be objectionable for some of the weaker varieties (although just why this should be the case is not easily apparent to me), then one could just as well call it a *hydrogen bridge*.^[2k] But, in any event, hydrogen bonds of the Pauling variety (typically $N-H\cdots O$, $O-H\cdots O$, $O-H\cdots X^-$, $F-H\cdots F^-$) do not pose problems. They are short, they are linear, their formation is energetically very favorable, and they can be identified spectroscopically. They are easily detected because they are strong: this strength follows from the electronegativities of the elements X and Y.

The entire problem with hydrogen bond nomenclature arose after it was realized that the domain of hydrogen bonding could be extended to interactions $X-H\cdots Y-Z$ in which the electronegativities of the elements X and Y are moderate to weak. Typical of these “new” hydrogen bonds are the $C-H\cdots O$, $C-H\cdots N$, $O-H\cdots \pi$, $N-H\cdots \pi$, and $C-H\cdots \pi$ interactions.^[2d,g-j,9] Because of the weakness of these interactions, their analysis in terms of crystallographic, spectroscopic, and computational data was just that much more subtle and implicit, so that reasonable doubt began to arise in the mind of chemists as to whether these new interactions could indeed be called hydrogen bonds. The jugular approach to addressing these ambiguities was to simply maintain that Pauling’s definition was infallible for all time and to banish these new interactions from the domain of hydrogen bonding.^[10] This approach was largely followed until the late 1960s (and sometimes much later) despite the spectroscopic and crystallographic work that had appeared by then. And yet there were new stirrings in chemical thought: most valuable was the definition provided by Pimentel and McClellan who, in 1960, defined hydrogen bonds as being “*said to exist when 1) there is evidence of a bond, and 2) there is evidence that this bond specifically involves a hydrogen atom already bonded to another atom*”.^[1b] It is important to realize that the Pimentel and McClellan definition makes no assumptions about the nature of X and Y and that it enables an evaluation of the hydrogen-bonding potential of groups like C–H, P–H, and As–H among others, and of π acceptors. Because its single electron is involved in the covalent bond X–H, the H atom is always deshielded in the forward (polar) direction. This

deshielding occurs irrespective of the nature of the X atom. Does this mean then that an X–H group is always a potential hydrogen-bond donor, even if there is no significant accumulation of electron density on the X atom? Many years later, Jeffrey and Saenger posed the question: “Should the $C-H\cdots O=C$ interaction be referred to as a hydrogen bond, even though there is every reason to suspect that the carbon atom is not electronegative and may even carry a net positive charge? By Pauling’s definition, the answer is no. By Pimentel and McClellan’s definition, the answer is yes.”^[1e] Refinement of the latter definition led to a quantification by Steiner and Saenger who, in 1993, considered a hydrogen bond as “any cohesive interaction $X-H\cdots Y$ where H carries a positive and Y a negative (partial or full) charge and the charge on X is more negative than on H .”^[11]

Note now that a positive charge on the atom X is not precluded.

4. A Bond for All Seasons

But I am moving too quickly. The International Union of Pure and Applied Chemistry (IUPAC) had defined the hydrogen bond, and this IUPAC definition is given in its Compendium of Chemical Terminology, popularly referred to as the Gold Book. The definition says that a hydrogen bond is

“... a form of association between an electronegative atom and a hydrogen atom attached to a second, relatively electronegative atom. It is best considered as an electrostatic interaction, heightened by the small size of hydrogen, which permits proximity of the interacting dipoles or charges. Both electronegative atoms are usually (but not necessarily) from the first row of the Periodic Table, i.e., N, O or F. Hydrogen bonds may be intermolecular or intramolecular. With a few exceptions, usually involving fluorine, the associated energies are less than $20\text{--}25\text{ kJ mol}^{-1}$ ($5\text{--}6\text{ kcal mol}^{-1}$) ...”^[12] Amazingly, this over-conservative definition appeared as late as 1997. The objective reader will recognize that it is limited to the perceptions of the Pauling era, in other words it reflects the scientific thinking that prevailed forty years prior to its appearance. Other parts of the definition may also be termed superfluous, too narrow, or arguably even erroneous. In this background, the IUPAC set up, in 2005, another task force, consisting of 14 crystallographers, spectroscopists, and theoreticians, to examine the existing Gold Book definition and to recommend changes, if any. A subset of the task force, a core group of five scientists, was directly responsible for its activities; these core group members were in constant communication with one another.^[13]

The entire group, and some extra invitees, met in Pisa, Italy in 2005 (Figure 1), while the core group members met again in late 2006 in Bangalore and Coorg, India. Inevitably,



Figure 1. Top: Members of the IUPAC Task Group and others who assembled in Pisa in September 2005 for a discussion meeting on hydrogen bonding: the prelude to formulating an updated definition of the phenomenon. The photograph was taken by Roger Klein, task group and core group member. Bottom: Participants in photograph: 1) Verma Chandra, 2) Ibon Alkorta, 3) Mark Zottola, 4) Enrique Espinosa, 5) Isabel Rozas, 6) Pavel Hobza, 7) Walther Caminati, 8) David Capelletti, 9) José Luis Alonso, 10) José Angel Sordo Gonzalo, 11) Juan Carlos Lopez, 12) Gastone Gilli, 13) Christian Pomelli, 14) Chiara Capelli, 15) Carles Curutchet, 16) Benedetta Mennucci, 17) Werner Reckien, 18) Klaus Müller-Detlefs, 19) Paola Gilli, 20) Gareth Tribello, 21) Sonia Melandri, 22) Elangannan Arunan, 23) Joe Dannenberg, 24) Caterina Ghio, 25) Hendrik Kjaergaard, 26) Joanna Sadlej, 27) Mark Rozenberg, 28) Jann Frey Benn, 29) Wouter Herrebout, 30) Gautam Desiraju, 31) Tony Legon, 32) David Clary.

as happens in exercises of this kind, no one wanted to be wrong and the finalization of the new definition was delayed until mid-2009. But the task force was not idle during this interim time period. In typical scientific fashion, the members questioned each and every proposed word (sometimes even single letters) in the new definition. Unsurprisingly, various aspects of the proposed changes were of greater or lesser interest to crystallographers, spectroscopists, and theoreticians, respectively, and in this regard attracted a greater or lesser degree of stringent criticism from each of these three groups of scientists in the IUPAC group. This is, of course, highly desirable in a scientific dialogue but it greatly added to the time invested in the exercise.

Personally, I found the whole process to be very educational. For example, I learned that to spectroscopists, D–H always refers to a diatomic molecule in which an atom of deuterium is bonded to an atom of hydrogen. To my way of thinking as a structural chemist, D–H signified an atom of hydrogen bonded to some atom D such that the molecule is a hydrogen-bond donor. More serious questions that assailed the group were: 1) How does one characterize a hydrogen bond: by what it is or by what it does? 2) What does one call the interaction, if it passes one test for hydrogen bonding but fails another? 3) Are some indicators of hydrogen bonding mandatory for an interaction to be so classified?

The new definition, in its formal trappings, was submitted for publication in *Pure and Applied Chemistry* in the form of two manuscripts. One contains the recommendation proper while the other gives a detailed background of hydrogen bonding itself and in the context of the present recommendation. These papers have been accepted and will now appear shortly in that journal.^[14]

What follows are the recommendations and my comments on some of them: these comments are reflective of my own background as a crystallographer and a chemist interested in crystal packing, and are not necessarily always revealing of other opinions within the task force. In the best spirit of the committee system, I stand formally and informally by the recommendations made to the IUPAC by the task force. Some of my annotations and comments below may be considered by the reader to be subjective. They are given so that one might appreciate that any such recommendation by a large group of scientists is associated with a lot of underlying discussion that usually does not see the light of day. It is my intention to provide some of the reasoning and thought processes—also divergences—that accompanied our recommendation on an updated definition of the hydrogen bond.

5. Definition

The definition begins with a preamble: *The hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment X–H in which X is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.*

Some aspects of the primary definition need attention:

1) The hydrogen bond is always attractive. 2) Atom X must be

more electronegative than H, as stipulated in the Steiner–Saenger definition.^[11] This condition rules out say, B–H–B bonding in diboranes from the scope of hydrogen bonding. 3) There is an emphasis on “evidence”, that echoes the Pimentel–McClellan definition.^[1b] 4) No electronic condition is placed, as such, on the acceptor but the implication is that for the interaction to be attractive, the acceptor must be electron rich. 5) The word “bond” is not defined. It is used as a trivial name in the finest chemical tradition.

There was some discussion as to whether a bond *is* an interaction, or whether a bond can only *result* from an interaction. I viewed such discussion as limiting and as arising from a very restrictive idea as to what constitutes a chemical bond. This distinction between a bond and an interaction could also be of linguistic origin. I did not feel that there was any linguistic contradiction in English in calling a bond an interaction, although it was held by some that there might be problems in other languages.

This primary definition can, in my view, stand alone, without the rest of the preamble, which now continues.

A typical hydrogen bond may be depicted as X–H···Y–Z, where the three dots denote the bond. X–H represents the hydrogen-bond donor. The acceptor may be an atom or an anion Y, or a fragment or a molecule Y–Z, where Y is bonded to Z. In specific cases X and Y can be the same with both X–H and Y–H bonds being equal. In any event, the acceptor is an electron-rich region such as, but not limited to, a lone pair in Y or a π -bonded pair in Y–Z.

I was rather unhappy with the phrase “the three dots denote the bond”, but this was a stipulation from the IUPAC. As stated in Section 1 I do believe that the entire fragment X–H···Y–Z constitutes the hydrogen bond. In multifurcated hydrogen bonds, such as in crystalline ammonia, the entire assemblage $X-H \cdots \sum_{i=1}^n (Y-Z)_n$ would constitute the entity termed *the hydrogen bond*. This is a philosophical matter. I do not want to argue about what the word “denote” means here. As a matter of incidental interest, the letters X, Y, and Z were selected after much discussion.

The acceptor is now specified as being electron rich.

The evidence for hydrogen-bond formation may be experimental or theoretical, or ideally, a combination of both. Some criteria useful as evidence and some typical characteristics for hydrogen bonding, not necessarily exclusive, are listed in Sections 5.1 and 5.2, numbered E# and C#, respectively.^{F1} (The footnotes denoted F1–F9 are collected in Section 5.3.) The greater the number of criteria satisfied, the more reliable is the characterization as a hydrogen bond.

Theory and experiment have been given equal status. The fact that the evidence for hydrogen bonding may be conflicting is not ruled out. Some subjectivity in defining a particular weak interaction as a hydrogen bond is also not precluded. The task force did not fight shy of the fact that in order to attain both accuracy and generality, a definition may have to become lengthy. In practical terms, this difficulty was resolved by addressing the generality issues in the preamble, and by addressing the accuracy issues in the list of criteria, the list of characteristics and in the footnotes.

5.1. List of Criteria Useful as Evidence

For a hydrogen bond $X-H\cdots Y-Z$:

- (E1) The forces involved in the formation of a hydrogen bond include those of an electrostatic origin,^{F2} those arising from charge transfer between the donor and acceptor leading to partial covalent-bond formation between H and Y, and those originating from dispersion.
- (E2) The atoms X and H are covalently bonded to one another and the X–H bond is polarized, the $H\cdots Y$ bond strength increasing with the increase in electronegativity of X.^{F3}
- (E3) The $X-H\cdots Y$ angle is usually straight (180°) and the closer the angle is to 180° , the stronger the hydrogen bond^{F4} and the shorter the $H\cdots Y$ distance.^{F5}
- (E4) The length of the X–H bond usually increases on hydrogen-bond formation leading to a redshift in the infrared X–H stretching frequency and an increase in the infrared absorption cross section for the X–H stretching vibration. The greater the lengthening of the X–H bond in $X-H\cdots Y$, the stronger the $H\cdots Y$ bond. Simultaneously, new vibrational modes associated with the formation of the $H\cdots Y$ bond are generated.^{F6}
- (E5) The $X-H\cdots Y-Z$ hydrogen bond leads to characteristic NMR signatures that typically include pronounced proton deshielding for H in X–H, through hydrogen-bond spin–spin couplings between X and Y, and nuclear Overhauser enhancements.
- (E6) The Gibbs energy of formation for the hydrogen bond should be greater than the thermal energy of the system for the hydrogen bond to be detected experimentally.^{F7}

These criteria are all very well known and are generally observed for the vast majority of hydrogen bonds. However, they may not be used as rigorous indicators of hydrogen bonding and they are not exclusive to this interaction. For example, criteria E1 and E2 also hold for halogen bonds;^[15] criterion E4 does not hold for hydrogen bonds with a blueshifted infrared absorption, which are genuine hydrogen bonds with a high dispersive component.^[16] Criterion E3 reaffirms the length–strength analogy that has for long been an article of faith in hydrogen bond research. Criterion E6 is important especially because one may now be dealing with very weak hydrogen bonds which are at this limiting energy. The reader will notice that no numerical cutoffs have been specified for energies, distances, and spectroscopic parameters.

5.2. Some Characteristics of Hydrogen Bonds

- (C1) The pK_a of X–H and pK_b of Y–Z correlate strongly with the energy of the hydrogen bond formed between them.
- (C2) Hydrogen bonds are involved in proton-transfer reactions ($X-H\cdots Y \rightarrow X\cdots H-Y$) and may be considered the partially activated precursors to such reactions.
- (C3) Networks of hydrogen bonds show the phenomenon of cooperativity, leading to deviations from pairwise additivity in hydrogen-bond properties.
- (C4) Hydrogen bonds show directional preferences and influence packing modes in crystal structures.^{F8}

- (C5) Estimates of charge transfer in hydrogen bonds show that the interaction energy correlates well with the extent of charge transfer between the donor and the acceptor.
- (C6) Analysis of the electron-density topology of hydrogen-bonded systems usually shows a bond path connecting H and Y and a (3,–1) bond critical point between H and Y.^{F9}

The characteristics may be derived from the preamble and the criteria mentioned above. They are useful guidelines that are applicable to a greater or lesser extent in specific research areas. The first and second are of interest to physical chemists while the third and fourth are important in crystal engineering and structural chemistry.^[17] The last one (C6) is invoked especially often.^[18] It is my view that while all hydrogen bonds will show a (3,–1) bond critical point, not all such points in the bond path between an H atom and another atom need be indicative of hydrogen bonding.

5.3. Footnotes to Definition, Criteria, and Characteristics of Hydrogen Bonds

These footnotes form part of the new IUPAC definition and are given here with a few additional comments:

- (F1) It is understood that there will be borderline cases for which the interpretation of the evidence might be subjective. In any case, there should be no gross deviations from the above-mentioned criteria. It may be noted that a given donor or acceptor may form hydrogen bonds with more than one acceptor or donor, respectively, in a hydrogen-bonded network. When such multiple interactions are present, some of the correlations given above may not follow. Moreover, the correlations work better when the donor or acceptor is fixed while varying acceptors or donors.

This well takes into account the enormous body of work that now exists on weak hydrogen bonds (X, Y of moderate to low electronegativity and bond energy $< 4 \text{ kcal mol}^{-1}$).^[8]

- (F2) Attractive interactions arise from electrostatic forces between permanent multipoles, inductive forces between permanent and induced multipoles, and London dispersive forces. If an interaction is primarily due to dispersive forces, then it would not be characterized as a hydrogen bond. Thus neither $Ar\cdots CH_4$ nor $CH_4\cdots CH_4$ are hydrogen-bonded systems. The importance of various components of hydrogen bonding may vary quite widely from system to system.

Not all groups X–H that point to any atom Y constitute a hydrogen bond. We affirm that London forces are of dispersive origin. We have avoided the use of the term “van der Waals interactions”, which may mean different things to different groups of chemists.

- (F3) It should be remembered that the electronegativity of the elements could change depending on the chemical environment. This is particularly true of organometallic

and other highly polarizable systems. However, it is recommended that no system in which X is less electronegative than H be considered as hydrogen bonded.

As mentioned earlier, the first two sentences are reflective of a condition that is inherent in a complex system.^[4] The third sentence states a practically mandatory condition. All hydrogen bonds are three-center four-electron systems (3c–4e), and for there to be any interaction between electron density on the acceptor with the donor fragment such as would lead to a 4e arrangement, H must be electron deficient with respect to X . The 3c–4e condition is helpful, for example, in distinguishing a hydrogen bond from an agostic interaction, $C-H\cdots M$, which is a 3c–2e interaction.^[19]

(F4) *The $X-H\cdots Y$ bond angle tends toward 180° and should preferably be above 110° . For example, the hydrogen fluoride dimer has $F-H\cdots F$ nearly straight and is a hydrogen-bonded system. However, the lithium fluoride dimer has both LiF molecules oriented antiparallel because of dipole–dipole interactions and would not be considered as being (analogously) lithium bonded.*

Phenomena similar to hydrogen bonding could occur with very small atoms (Li , Be) and with polarizable atoms (halogen bonding). Lithium bonding is seen in $Li^{\delta+}-H^{\delta-}\cdots Li^{\delta+}-H^{\delta-}\cdots Li^{\delta+}-H^{\delta-}\cdots$ in which Li plays the role of H (electropositive atom) in a hydrogen bond. The H atom in this arrangement plays the role of the electronegative atom in a hydrogen bond. This could also be termed as an inverse hydrogen bond with respect to the hydrogen atom. In a halogen bond, $X-Hal\cdots Y-Z$, Hal is an electropositive halogen atom while X , Y , and Z fulfill the same roles as they do in a hydrogen bond.^[15]

(F5) *Historically, the X to Y distance was found to be less than the sum of the van der Waals radii of X and Y , and this shortening of the distance was taken as an infallible indicator of hydrogen bonding. However, this empirical observation is true only for strong hydrogen bonds. This criterion is not recommended. It should be noted that the experimental distances are vibrational averages and would differ from such distances calculated from potential energy minimization.*

The distance cutoff criterion is used typically with reference to the $X-Y$ distance. I am of the view that the use, perhaps unintended, of this criterion has caused more havoc to the field of hydrogen bonding than any other factor. To look at things in perspective, the use of this criterion arose in former times when hydrogen atoms could be not easily observed in X-ray crystallography. Their presence at particular places in crystal structures was inferred if two electronegative atoms were closer to each other than they might otherwise have been if there were no hydrogen between them. Further, many if not most of the old crystal structure analyses in which this criterion was invoked were conducted with some objective other than understanding hydrogen bonding itself (e.g., studying peptide structures). Unfortunately, the use of this criterion got perpetrated in modern times by some computer programs that create lists of possible hydrogen bonds.

Conversely and even more unfortunately, some macromolecular crystal structure refinement programs applied geometrical constraints that stretched $C\cdots O$ nonbonded distances, which appeared to be short, to the van der Waals value—even when this contraction genuinely resulted from $C-H\cdots O$ hydrogen bonding! When the criterion is used with respect to the $H\cdots Y$ distance, the discrepancies are not obvious but in general, the use of van der Waals radii ought to be avoided.

In any event, the hydrogen bond is not a van der Waals interaction (at least in the crystallographic literature), and one should not apply a criterion based on van der Waals radii of the atoms X and Y to evaluate hydrogen bonding. It must be clearly and unambiguously stated that the use of the van der Waals cutoff in assessing a hydrogen bond is without scientific basis. This empirical observation holds only for strong hydrogen bonds, like $O-H\cdots O$ and $N-H\cdots O$, for which the van der Waals cutoff distance is much longer than the hydrogen-bond distance. As the hydrogen bond becomes weaker, the cutoff distance becomes comparable to the hydrogen-bond distance. For $C-H\cdots O$ and $C-H\cdots N$ bonds, the van der Waals cutoff roughly bisects the distance distribution and the use of such a cutoff is definitely ambiguous. For the even weaker $C-H\cdots \pi$ hydrogen bond, the van der Waals cutoff is nearly at the beginning of the distance distribution. Here, the use of such a cutoff is catastrophic. Weak hydrogen bonds are just that, and they do not become van der Waals interactions simply because they are long.^[20]

(F6) *In general, for the donor, the $X-H$ bond length increases and there is an associated redshift in the $X-H$ stretching frequency. There are, however, certain hydrogen bonds in which the $X-H$ bond length decreases and a blueshift in the $X-H$ stretching frequency is observed. It is conceivable that a hydrogen bond could exist without a red or a blue shift. To a lesser extent, in the acceptor, the $Y-Z$ bond deviates from the length of the $Y-Z$ bond in the isolated subunit. The $Y-Z$ bond vibrational frequencies and spectral band intensities also show corresponding changes on hydrogen-bond formation.*

As stated in Section 5.1, hydrogen bonds with blueshifted absorption are genuine hydrogen bonds^[16] and reflect the fact that a hydrogen bond is a complex interaction with electrostatic, dispersive, covalency, and polarization components. In this case, the dispersive component is dominant.

(F7) *For hydrogen bonding to have any practical significance, it should be thermally stable. Hence, a hydrogen-bonded complex, between donor and acceptor molecules, produced in a supersonic beam or a cryogenic matrix, may not be found in a room-temperature mixture of the two molecules. Moreover, the thermal energy along vibrational coordinates that can destroy the orientational preference should be less than the barrier along those coordinates. This explains why H_2S has 12 neighbors and is not hydrogen bonded when it freezes at $-60^\circ C$ but shows features of hydrogen bonding at much lower temperatures.*

Hydrogen bonds are defined based on one's ability to detect them, and this ability is a function of the temperature of measurement.

- (F8) *Hydrogen bonds are directional and influence crystal packing modes in chemically understandable ways. The crystal packing of a non-hydrogen-bonded solid (say naphthalene) is often determined by the principle of close-packing, and each molecule is surrounded by a maximum number of other molecules. In hydrogen-bonded solids, there are deviations from this principle to a greater or lesser extent depending upon the strengths of the hydrogen bonds that are involved. Correspondingly, the hydrogen-bond geometries are conserved with fidelities that depend on their strengths.*

This is a fundamental principle of crystal engineering.^[18] Interaction directionality always leads to loss of close packing in a solid. This fact was not appreciated in the early days of crystal engineering when it was felt that all molecular solids approximate to some close-packed situation as described by Kitaigorodskii.^[21] Today, however, there is a greater awareness of deviations from the Kitaigorodskii model and about the fact that any directional interaction leads one away from an ideally three-dimensionally close-packed arrangement. These deviations could be mediated by differences in local packing densities or by the formation of layered and other lower dimensional crystal structures. That hydrogen-bond geometries are conserved depending on their strengths follows from the fact that all crystal structures are the result of compromise between many interactions of differing strengths, directionalities and distance-dependent characteristics.

- (F9) *Critical points in electron-density topology refer to the points where the electron density is an extremum, that is, a minimum or a maximum. The first derivative of electron density is zero in these points and the second derivative would be positive for a minimum and negative for a maximum. A (3,−1) critical point implies that the electron density is an extremum in all three directions leading to the first digit in parenthesis, 3. The second digit is obtained by adding 1 for directions in which the electron density is minimum and −1 for directions in which the electron density is maximum. A (3,−1) critical point is usually found between two atoms that are bonded that is, along the bond between the two atoms the electron density is a minimum at this point and in the two directions away from the bond, it is maximum thus leading to −1 as the second digit. All the atoms appear as (3,−3) critical points in this analysis as the electron density is maximum at the atoms in all three directions.*

One might only say that great care is needed while examining bond critical points in extremely weak hydrogen bonds. While these points always occur at the sites of non-translational symmetry elements in crystal structures, the typical (unsymmetrical) hydrogen bond $X-H\cdots Y-Z$ cannot lie on such a symmetry location in an ordered crystal structure. More needs to be done to examine this condition for the weakest hydrogen bonds.

6. Summary and Outlook

Research on hydrogen bonds, what they are, and what they can do has been going on for nearly a hundred years. Given certain arbitrary parameters such as the typical temperatures that prevail on the earth's surface and the energy range of covalent bonds, we are able to isolate stable entities that we call molecules. Biological processes take place by reactions between these molecules. A necessary precondition for such reactions is that there should be some kind of interaction between molecules. For these reactions to take place rapidly at moderate temperatures, the catalyzing interactions need to be in a certain energy range. The hydrogen bond fits this energy bill and it is therefore of enormous significance. It also has an optimal directionality for this facilitating role, being neither as directionless as a van der Waals interaction nor as directed as a covalent bond. The surface of the water molecule is composed almost exclusively of hydrogen-bond-donor and -acceptor areas—there is nothing else. The fact that life on earth is based on water also adds enormously to the importance of the hydrogen bond (or did life on earth become water-based because the hydrogen bond was the only “interaction of choice” to facilitate life?). The last century has seen huge advances in our understanding of this interaction and a very wide variety of donors and acceptors are now accepted as being able to form hydrogen bonds.

While the importance of the interaction in biological processes and in other phenomena that involve the study of complex chemical systems is acknowledged and the interest generated by the hydrogen bond will continue unabated, have we stretched the limits of this interaction to the maximum of chemical diversity? Interactions that are of energy less than kT are not viable because they cannot be detected. Interactions stronger than 40 to 50 kcal mol^{−1} cannot easily be called hydrogen bonds; the strongest quasi-covalent hydrogen bonds known today are in this energy range, and anything stronger than this will slip into the domain of covalent bonding. A very large number of chemical elements, including transition metals, now come within the scope of this interaction. Even the peripheral regions in which this interaction overlaps with other types of interaction, for example the region between a hydrogen bond and a van der Waals interaction,^[20] are beginning to be well understood.

Definitions of the hydrogen bond have progressed with our increasing appreciation of this phenomenon. Strong hydrogen bonds pose no problems and will fit all definitions, from those that hark back to the earliest times. As interactions that were progressively weaker and more complex have come to be accepted as hydrogen bonds, the definition of the phenomenon has evolved. It is difficult in science to accept that one knows all there is to know about anything, but even so it seems that we are now at a stage where we do know quite a lot about the hydrogen bond. Perhaps the definition that has been proposed currently to IUPAC will be around for a while.

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