J. Indian Inst. Sci.
A Multidisciplinary Reviews Journal
ISSN: 0970-4140 Coden-JIISAD

REVIEW ARTICLE

Hydrogen Bonding: A Coulombic σ-Hole Interaction

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Abstract | Molecular electrostatic potentials, in conjunction with polarization, provide the key to understanding hydrogen bonding. As required by the Hellmann–Feynman theorem, hydrogen bonding is a Coulombic interaction between (a) a positive electrostatic potential associated with a region of lower electronic density on the hydrogen (a σ-hole), and (b) a negative site on the hydrogen-bond acceptor. The charge distributions of both the hydrogen-bond donor and the acceptor reflect the polarizing effects of each other's electric fields. The greater the polarization, the stronger the interaction. This interpretation of hydrogen bonding applies to all of the different categories into which it has been subdivided; they are fundamentally similar. We show that if polarization is minor and the hydrogen bonds relatively weak, then their interaction energies correlate well with the product of the most positive electrostatic potential on the hydrogen and the most negative one on the negative site. It is argued that the partial covalent character that is often attributed to hydrogen bonds simply reflects a greater degree of polarization.

Keywords: *Hydrogen bonding, σ-hole interactions, Electrostatic potentials, Coulombic interactions*

1 The Overanalyzed Hydrogen Bond

As Grabowski et al. have pointed out,[1] until about 30 years ago, hydrogen bonding was viewed as a relatively straightforward electrostatic interaction between a proton donor A–H and an acceptor B, i.e., A-H···B, the interaction energy being in the approximate range of − 2 to − 10 kcal/mol. It was expected that the hydrogen would be linked to an electronegative atom in A and that the hydrogen bond would be with an electronegative atom in B that had at least one unshared electron pair. The hydrogen-bonding interaction caused the A-H bond to become longer and to have a lower stretching frequency (red shift).

It gradually became evident that this description was too limited and needed to be modified. This led to an enormous amount of analysis of hydrogen bonding. Arunan et al. have reported that more than 31,000 publications mentioned “hydrogen bond” or “hydrogen bonding” during just the 3 years 2006–2008[2]—an average of better than 28 publications every 24 h!

A consequence of all of this activity has been to subdivide hydrogen bonding into a bewildering array of categories: classical or nonclassical, proper or improper, blue-shifted or red-shifted, dihydrogen, anti-hydrogen, H-σ and H-π, positive and negative charge-assisted, resonance-assisted, polarization-assisted, induction-assisted, inverse, and charge-inverted. Arunan et al. provide a good overview of these categories,[2] some of which overlap; see also Grabowski et al.[1] and Anslyn and Dougherty.[3] A given proton donor can fit into different categories with different acceptors.

Lest the preceding not be sufficiently confusing, varying degrees of covalent character are asserted to be present in hydrogen bonds. Again see Arunan et al. for an overview.[2] Covalent character has not been rigorously or uniquely defined, but nonetheless it is widely invoked in relation to hydrogen bonding and even quantified. Bader's Quantum Theory of Atoms in Molecules (QTAIM),[4],[5] is often used to show and quantify

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covalent character, but the usefulness and reliability of QTAIM, from a chemical standpoint, are increasingly being questioned.[6–19]

In this paper, we argue that while hydrogen bonds in various systems may differ in details, they are fundamentally similar and rather straightforward interactions. The unifying concepts are the electrostatic potential and the σ-hole.

2 Electrostatic Potentials

The nuclei and electrons of a molecule (or other system) produce an electrostatic potential $V(\mathbf{r})$ at every point $\mathbf{r}$ in the surrounding space. It is given rigorously by Eq. (1):

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - r|} - \int \frac{\rho(\mathbf{r}\prime)\mathrm{d}\mathbf{r}\prime}{|\mathbf{r}\prime - \mathbf{r}|}, \tag{1}$$

in which Z_A is the charge on nucleus A, located at $\mathbf{R}_\mathbf{A}$, and $\rho(\mathbf{r})$ is the molecule's electronic density. The electrostatic potential is a real physical property of a molecule, an observable, which can be determined experimentally using diffraction methods[20–22] as well as computationally.

The significance of $V(\mathbf{r})$ is that if a charge Q is placed at the point $\mathbf{r}$, then the energy of the interaction between the molecule and Q is $\Delta E = QV(\mathbf{r})$. Thus, portions of the molecule in which $V(\mathbf{r})$ is positive will interact attractively ($\Delta E < 0$) with negative charges or sites, while portions in which $V(\mathbf{r})$ is negative will interact favorably with positive charges or sites.

$V(\mathbf{r})$ is commonly computed on molecular "surfaces," which are usually taken to be the 0.001 au contours of the molecules' electronic densities, as suggested by Bader et al.[23] The most positive and most negative values of $V(\mathbf{r})$ on a molecular surface (its local maxima and minima, of which there may be several) are designated by $V_{S,\,\max}$ and $V_{S,\,\min}$, respectively.

2.1 Electrostatic Potentials and Hydrogen Bonding

Figures 1, 2, and 3 are the computed electrostatic potentials on the 0.001 au surfaces of seven hydrogen-containing molecules. The geometries were optimized at the MP2/aug-cc-pVDZ level,[24] and the electrostatic potentials were obtained with the density functional B3PW91/6-31G(d,p) procedure and the WFA-SAS code.[25]

The three molecules in Fig. 1 (NH_3, H_2O, and HF) fit the traditional description of a proton donor in that the hydrogens are bonded to electronegative atoms. In contrast, the hydrogens in the molecules in Fig. 2 (HCF_3 and HCN) and Fig. 3a (C_2H_2) are bonded to carbons, which are significantly less electronegative. The hydrogens in BeH_2, Fig. 3b, differ even more, being bonded to an electropositive atom.

Each hydrogen in Figs. 1, 2, and 3, other than those in BeH_2, has a roughly hemispherical region of positive electrostatic potential, on the outer

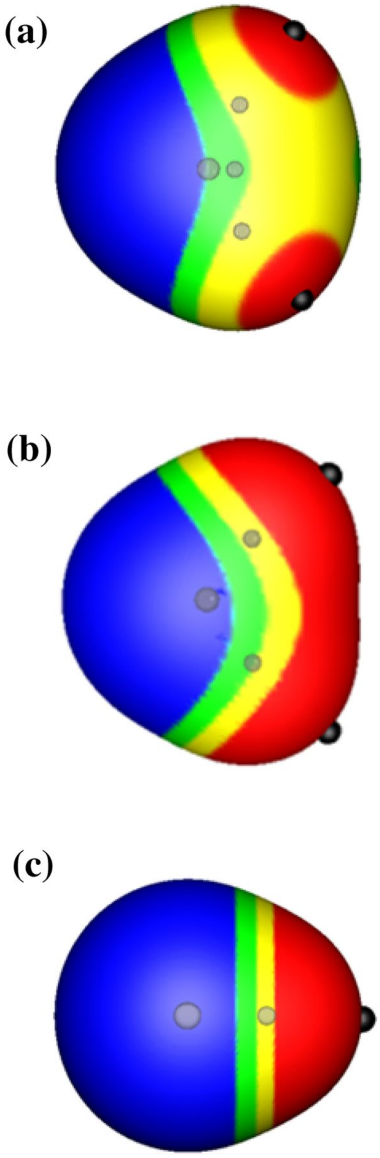

Figure 1: Computed electrostatic potentials on 0.001 au molecular surfaces of (a) NH_3, (b) H_2O, and (c) HF. In each molecule, the hydrogens are at the right. Gray circles show positions of atoms. Black hemispheres indicate most positive potentials, the $V_{S,\,\max}$. They are approximately on the extensions of the bonds to the hydrogens. Color ranges, in kcal/mol: Red, more positive than 20; yellow, between 20 and 10; green, between 10 and zero; blue, negative.

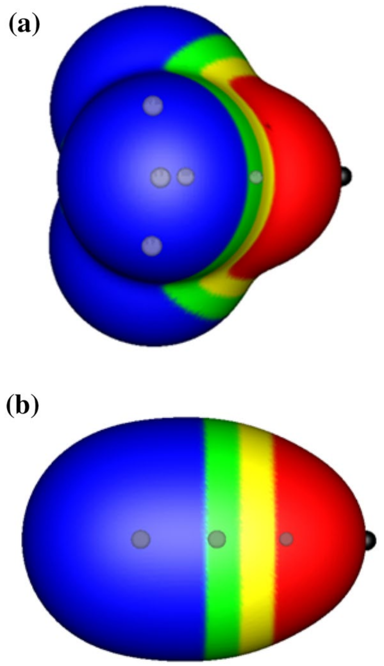

Figure 2: Computed electrostatic potentials on 0.001 au molecular surfaces of (a) HCF_3 and (b) HCN. In each molecule, the hydrogens are at the right. Gray circles show positions of atoms. Black hemispheres indicate most positive potentials, the $V_{S,\ \max}$. They are approximately on the extensions of the bonds to the hydrogens. Color ranges, in kcal/mol: Red, more positive than 20; yellow, between 20 and 10; green, between 10 and zero; blue, negative.

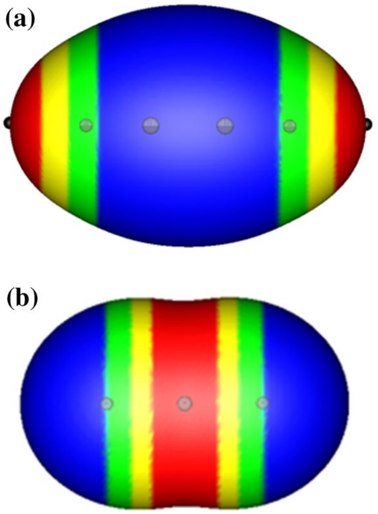

Figure 3: Computed electrostatic potentials on 0.001 au molecular surfaces of (a) C_2H_2 and (b) BeH_2. The hydrogens are at the left and right ends of the molecules. Gray circles show positions of atoms. Black hemispheres indicate most positive potentials, the $V_{S,\ \max}$, on C_2H_2. They are approximately on the extensions of the bonds to the hydrogens. Color ranges, in kcal/mol: Red, more positive than 20; yellow, between 20 and 10; green, between 10 and zero; blue, negative.

side of the hydrogen, opposite to its bond. The most positive value, the $V_{S,\ \max}$, is approximately along the extension of the bond. This positive region reflects the fact that the single electron of the hydrogen is involved in the bond, leaving a low electronic density and hence positive potential on the opposite side. In BeH_2, on the other hand, the hydrogens have roughly hemispherical regions of *negative* electrostatic potential on their outer sides; they have gained electronic density from the electropositive beryllium atom.

Each of the other molecules in Figs. 1, 2, and 3 also has a region or regions of negative electrostatic potential. Most of these are due to lone pairs, but in C_2H_2, Fig. 3a, the negative potential is associated with the C≡C triple bond.

Figures 1, 2, and 3 are certainly consistent with an electrostatic interpretation of hydrogen bonding as an attractive interaction between the positive potential on the hydrogen and the negative one on the acceptor. BeH_2 fits into this picture perfectly well; the acceptor is a hydridic hydrogen, which has a negative electrostatic potential, as shown in Fig. 3b. This is the key to the so-called dihydrogen bonding.

An early application of molecular electrostatic potentials to hydrogen bonding was by Kollman et al.[26] They concluded that "electrostatic potentials appear to be a useful tool in understanding and rationalizing H-bond energies and geometries." Other electrostatic treatments of hydrogen bonding followed.[21,27–29]

In 1991, we showed[30–32] that the most positive potentials ($V_{S,\ \max}$) on donor hydrogens and the most negative potentials ($V_{S,\min}$) on acceptor sites correlate well with experimentally determined measures of, respectively, hydrogen-bond donating tendencies (α) and hydrogen-bond accepting tendencies (β).[33,34] This was demonstrated again by Hunter in 2004,[35] who concluded that "there is good experimental evidence for the dominant role of electrostatics in intermolecular interactions." The fact that electrostatic potentials can identify and rank hydrogen-bond donating and accepting sites has been shown[36] to complement Etter's empirical rules for predicting hydrogen-bonding patterns in organic solids.[37,38] All of this supports the original electrostatic view of hydrogen bonding.

2.2 The σ-Hole

It is not only hydrogen atoms that have regions of lower electronic density on their outer sides, opposite to their bonds. Atoms of Groups IV–VII have also been found to frequently have lower electronic densities opposite to their bonds, on the extensions of the bonds.

Such regions of lower electronic density are called "σ-holes".[39] There is often a positive electrostatic potential associated with the lower electronic density of a σ-hole, and through this positive potential, the atom can interact favorably with a negative site,[40–43] such as a lone pair, π-electrons, an anion, etc. This explains numerous interactions involving atoms of Groups IV–VII that have been observed experimentally over many years.[40,42,44–46]

These are commonly called σ-hole interactions, even though the interaction is actually with the positive electrostatic potential that results from the σ-hole. Hydrogen bonding is simply another type of σ-hole interaction, as has been discussed in detail on several occasions.[41,43,47,48] Hydrogen bonding, A-H···B, has indeed been compared to halogen bonding, A-X···B, where X is a halogen. This is the name given to the σ-hole interactions of Group VII.[48,49] However, the positive regions on bonded hydrogens tend to be almost hemispherical, because of hydrogen having only one electron, while those on halogens are more narrowly focused. Accordingly A-H···B interactions are often less linear than A-X···B.

The discussion so far has viewed hydrogen-bonding and other σ-hole interactions purely in terms of electrostatics involving the unperturbed molecules in their equilibrium states, unaffected by the interactions. This is often sufficient on at least a qualitative level.

However, it is basically not realistic to consider just the electrostatic potentials of the free molecules prior to interaction. This cannot be more than an approximation (albeit often a good one), because it ignores the polarization of each molecule's charge distribution by the electric field of the other.[41,43,50–53] This changes to some extent the electrostatic potentials of the molecules, including both the magnitudes and locations of their $V_{S,\max}$ and $V_{S,\min}$.

Polarization is an intrinsic complement to an electrostatic interaction and always accompanies it, unless only point charges are involved. Sometimes, the polarization is minor and the electrostatic potentials of the free molecules; specifically, their $V_{S,\max}$ and/or $V_{S,\min}$ may allow a reasonable description of the interaction. For instance, the $V_{S,\max}$ of a series of σ-hole molecules interacting with a given negative site may correlate well with the interaction energies.[40,54,55] However, the stronger is an interaction, the more does polarization need to be taken into account.[18,40,56–59] We use the term "Coulombic interaction" to describe the combination of electrostatics plus polarization.

Hydrogen-bonding and other σ-hole interactions are Coulombic in nature. This follows from the rigorous Hellmann–Feynman theorem,[60,61] which shows that the forces exerted upon any nucleus in a system of nuclei and electrons are purely classical Coulombic, the interactions of the nucleus with the electrons and other nuclei. How could it be otherwise, since the potential energy terms in the Schrödinger equation are all Coulombic?

Nevertheless, many theoreticians do not accept the straightforward Coulombic interpretation of hydrogen bonding and other noncovalent interactions. This is partly because they equate Coulombic with just the electrostatics between the free unperturbed molecules prior to interaction, and do not consider polarization. They find examples of interactions that cannot be explained by electrostatics alone and argue from this that the Coulombic σ-hole interpretation is defective.[62–66] They claim that other factors must also be included, not just polarization but also exchange, Pauli repulsion, correlation, dispersion, and charge transfer.

These issues have been addressed at length elsewhere,[41, 43, 50–53] Here, we will simply point out that while exchange and Pauli repulsion are indeed important in the mathematical formulation of a wave function, they do not correspond to physical forces.[67–70] As for correlation and dispersion, these are part of the Coulombic interaction, as Feynman showed for the latter.[61] Finally, charge transfer in this context is no more than mathematical modeling of the physical reality, which is polarization; it is not a separate effect.[17,18,43,51–53,71–77] Brinck and Borrfors put it clearly, after a detailed study of Group VII σ-hole interactions, concluding that they "are governed by electrostatics and polarization, and that charge transfer is of negligible importance."[77]

The deficiencies that have been attributed to the Coulombic interpretation of noncovalent interactions are removed when polarization is taken into account.[47,51,78] How can this be done? One approach is to use a negative point charge to represent the negative site and show the polarizing effect of its presence upon the positive potential associated with the σ-hole.[47,51,77–79] This has the advantage that the results cannot be attributed to charge transfer from the negative site, since the negative site (the point charge) has no electronic charge to transfer. Another approach is to explicitly introduce the electric field of the σ-hole molecule and the polarizability of the negative site into a regression equation for the interaction energy. This is currently being explored for a variety of noncovalent interactions,[58],[59] including hydrogen bonding.

3 Analysis and Discussion

Table 1 lists 24 hydrogen-bonded complexes involving the molecules in Figs. 1, 2, and 3. For each hydrogen-bond donor A-H is given the $V_{S,\max}$ of the positive potential associated with its hydrogen σ-hole, and for each acceptor B is given the $V_{S,\min}$ of its negative site. These were computed for free A–H and B, prior to interaction; for present purposes, polarization is not being taken into account.

The computed interaction energies ΔE(int) are also listed in Table 1; these are defined in terms of the energies of the complexes and the reactants by:

$$\Delta E(\text{int}) = E(\text{A-H}\cdots\text{B}) - [E(\text{A-H}) + E(\text{B})]. \tag{2}$$

The more negative is ΔE(int), the stronger is the interaction. Table 1 shows that for any series of hydrogen bonds with the same acceptor, ΔE(int) becomes more negative as the $V_{S,\max}$ of the hydrogen-bond donor becomes more positive (consistent with electrostatics).

It has been demonstrated on several occasions that hydrogen-bonding equilibrium constants K, both gas phase and in solution, correlate very well with the product of the experimental measures of

Table 1: Computed interaction energies ΔE(int) of hydrogen complexes A-H···B, most positive electrostatic potentials $V_{S,\max}$ on 0.001 au surfaces of hydrogens, and most negative electrostatic potentials $V_{S,\min}$ on 0.001 au surfaces of proton acceptors B. The negative site on C_2H_2 is the C≡C bond and the complex is T-shaped. Computational levels were MP2/aug-cc-pVDZ for ΔE(int) and B3PW91/6-31G(d,p) for $V_{S,\max}$ and $V_{S,\min}$.

Complex	ΔE(int), kcal/mol	$V_{S,\max}$, kcal/mol	$V_{S,\min}$, kcal/mol
HC≡CH···HBeH	– 1.71	30.7	– 10.4
$F_3CH\cdots HBeH$	– 1.99	31.2	– 10.4
HC≡CH···C_2H_2(T-shape)	– 2.45	30.7	– 17.7
$H_2NH\cdots NCH$	– 2.50	25.5	– 32.2
HCN···HBeH	– 2.57	50.0	– 10.4
$F_3CH\cdots C_2H_2$(T-shape)	– 2.65	31.2	– 17.7
HCN···C_2H_2(T-shape)	– 3.25	50.0	– 17.7
HC≡CH···NCH	– 3.58	30.7	– 32.2
HC≡CH···OH_2	– 3.61	30.7	– 39.6
$H_2NH\cdots NH_3$	– 3.62	25.5	– 46.2
FH···HBeH	– 3.92	66.6	– 10.4
$F_3CH\cdots NCH$	– 4.13	31.2	– 32.2
HOH···NCH	– 4.41	43.4	– 32.2
HC≡CH···NH_3	– 4.71	30.7	– 46.2
FH···C_2H_2(T-shape)	– 4.78	66.6	– 17.7
HOH···OH_2	– 5.26	43.4	– 39.6
$F_3CH\cdots NH_3$	– 5.33	31.2	– 46.2
NCH···NCH	– 5.55	50.0	– 32.2
NCH···OH_2	– 5.66	50.0	– 39.6
HOH···NH_3	– 6.96	43.4	– 46.2
NCH···NH_3	– 7.35	50.0	– 46.2
FH···NCH	– 7.79	66.6	– 32.2
FH···OH_2	– 9.03	66.6	– 39.6
FH···NH_3	– 13.14	66.6	– 46.2

hydrogen-bond donating and accepting tendencies, α and β, respectively[80–82]:

$$\log K \sim \alpha\beta. \tag{3}$$

Since α correlates with the $V_{S.max}$ of hydrogen-bond donors and β with the $V_{S,\ min}$ of acceptors,[30–32,35] Hunter suggested that Eq. (3) is equivalent to expressing the free energy of the hydrogen-bonding interaction in terms of the product of $V_{S,\max}$ and $V_{S,\min}$.[35]

We have tested a modified version of what Hunter suggested, Eq. (4), which uses ΔE(int) (instead of the change in free energy) and the absolute value of the product of $V_{S,\max}$ and $V_{S,\min}$:

$$\Delta E(int) = c_1\left|\left(V_{S,max}\right)\left(V_{S,min}\right)\right| + c_2. \tag{4}$$

Equation (4) was tested in terms of the data in Table 1.

The best least-squares fit of the data to Eq. (4) gave the result shown in Fig. 4a. There is definitely a correlation, with $R^2 = 0.908$, but there is also a major outlier, corresponding to the interaction $FH\cdots NH_3$. This is the most strongly bound complex in Table 1, with ΔE(int) = − 13.14 kcal/mol; it is the only one with an interaction energy more negative than -10 kcal/mol. When $FH\cdots NH_3$ is omitted from the database, in Fig. 4b, the correlation clearly improves; $R^2 = 0.931$. Figure 4a and b illustrates the points that (a) weak interactions can often be represented reasonably well in terms of the electrostatic potentials of the free molecules, prior to interaction, but (b) the stronger is the interaction, the more does polarization need to be considered. The $FH\cdots NH_3$ outlier exemplifies this.

We have also investigated the possibility of representing ΔE(int) in terms of an additive

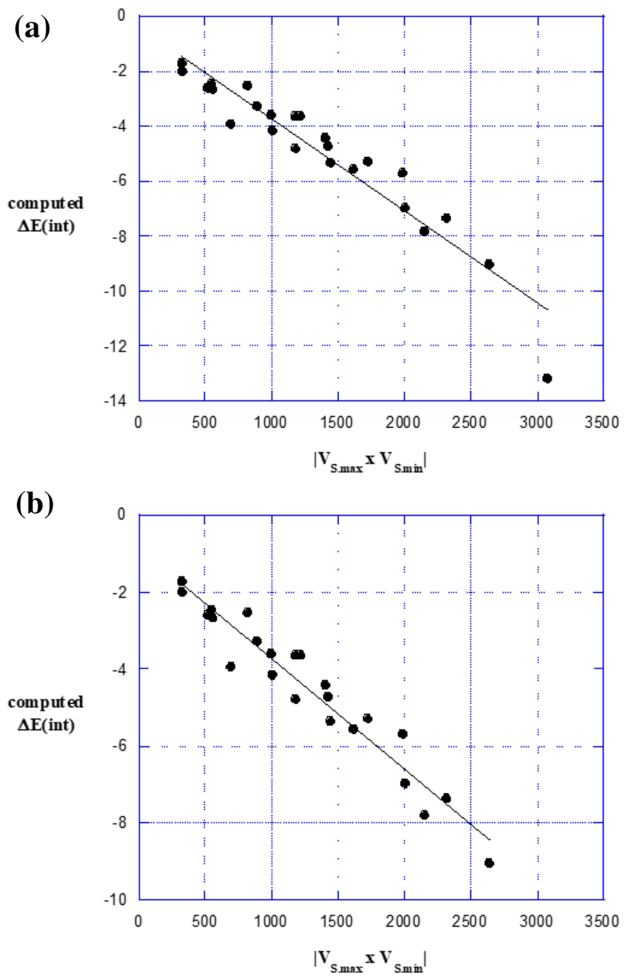

Figure 4: Relationship between computed ΔE(int) and absolute value of product $(V_{S,\max})(V_{S,\min})$ for (a) all 24 complexes in Table 1, and (b) all complexes in Table 1 except $FH\cdots NH_3$. ΔE(int), $V_{S,\max}$ and $V_{S,\min}$ are all in kcal/mol. For (a), $R^2 = 0.908$; for (b), $R^2 = 0.931$.

rather than multiplicative relationship, i.e., the two-parameter regression Eq. (5):

$$\Delta E(\text{int}) = c_1\left(V_{S,\max}\right) + c_2\left(V_{S,\min}\right) + c_3. \quad (5)$$

Abraham et al. had mentioned the possibility of an additive version of Eq. (3).[83] When Eq. (5) is tested for all 24 complexes in Table 1, $R^2 = 0.841$. When FH···NH$_3$ is excluded, R^2 improves 0.899. Both are less than the corresponding values for Eq. (4), indicating that Eq. (4) is more effective, at least for the interactions in Table 1. Abraham et al. came to a similar conclusion in the context of Eq. (3), involving other hydrogen-bonded complexes.[83]

The interactions in Table 1 include several of the categories into which hydrogen bonding has been divided, for example classical and nonclassical, proper and improper, blue-shifted and red-shifted, dihydrogen, anti-hydrogen, and H–π. Note for instance the dihydrogen interactions involving a negative hydridic hydrogen in BeH$_2$, which has $V_{S,\ \min} = -10.4$ kcal/mol, or the H–π interactions with the triple-bond region of C$_2$H$_2$, which has $V_{S,\ \min} = -17.7$ kcal/mol.

The key point is that all of the interactions in Table 1, regardless of category, obey Eq. (4). They are Coulombic σ-hole interactions, fundamentally similar to each other and to σ-hole interactions of Groups IV–VII of the Periodic Table. There can of course be hydrogen bonding that differs in detail, e.g., the positive potentials due to σ-holes on hydrogens in close proximity may overlap, resulting in just one intermediate $V_{S,\ \max}$.[36,42] However, this is simply a variation on the common theme of Coulombic σ-hole interaction. Aakeröy et al. concluded that "the use of calculated molecular electrostatic potential surfaces for competing hydrogen-bond donors provide a reliable and practical tool for predicting the resulting molecular recognition events."[84] It is unfortunate that many analyses of hydrogen bonding and other noncovalent interactions do not look at the relevant molecular electrostatic potentials.

We will conclude with a comment concerning covalent character in relation to hydrogen bonds and other σ-hole interactions. It is often implied that covalency and electrostatics are distinctly separate features of bonding. However, the Schrödinger equation and the Hellmann–Feynman theorem apply to *any* system of nuclei and electrons, including what we call covalent molecules, and they tell us that the forces involved are Coulombic: electrostatics and polarization. These are the components of covalence as well as noncovalence, the difference being one of degree: covalence increases as polarization increases.[18,40,56–59] Lennard-Jones and Pople pointed out already in 1951 that "There is only one source of attraction between two atoms, and that is the force between electrons and nuclei."[85]

It is frequently argued that charge transfer is a measure of covalence. However, this brings us back to what was mentioned earlier: charge transfer in the present context is simply mathematical modeling of the physical reality of polarization.[17,18,43,51–53,71–77] Polarization is the basis for what is called covalent character.

Slater suggested that chemical bonding is a continuum from van der Waals to covalent.[86] Similar sentiments have been expressed by others.[19,87–89] Anslyn and Dougherty summarized the whole matter very nicely: "regions of negative charge, no matter what their nature, will in general be attracted to regions of positive charge, no matter what their nature. It is the character of the partners that leads to our definitions and discussions of the forces."[3]

Publisher's Note

Acknowledgements

We are happy to acknowledge very fruitful and enjoyable collaborations over many years with Tore Brinck and Tim Clark.

Received: 10 September 2019 Accepted: 30 October 2019

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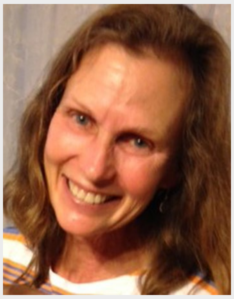

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