

σ -Hole Bonding: A Physical Interpretation

Peter Politzer, Jane S. Murray, and Timothy Clark

Abstract The anisotropic electronic densities of covalently-bonded Group IV–VII atoms frequently give rise to regions of positive electrostatic potential on the extensions of covalent bonds to these atoms. Through such positive “ σ -holes,” the atoms can interact attractively and highly directionally with negative sites such as the lone pairs of Lewis bases, anions, π electrons, etc. In the case of Group VII this is called “halogen bonding.” Hydrogen bonding can be viewed as a less directional subset of σ -hole interactions. Since positive σ -holes often exist in conjunction with regions of negative potential, the atoms can also interact favorably with positive sites. In accordance with the Hellmann–Feynman theorem, all of these interactions are purely Coulombic in nature (which encompasses polarization and dispersion). The strength of σ -hole bonding increases with the magnitudes of the potentials of the positive σ -hole and the negative site; their polarizabilities must sometimes also be taken explicitly into account.

Keywords Coulombic interactions · Halogen bonding · σ -Hole bonding

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1 Newton, the Hellmann–Feynman Theorem and Coulomb’s Law

The formation of chemical bonds, wherever they may fall in the continuum between covalent and non-covalent, involves a balancing of attractive and repulsive forces within the system. At equilibrium, according to Newton, the resultant force on each nucleus must be zero (within the Born–Oppenheimer approximation of treating the nuclei as fixed, with the electrons moving among them [1, 2]). What are the natures of the forces felt by the nuclei?

The Hellmann–Feynman theorem [3, 4] tells us that these forces are given rigorously by purely classical electrostatics – the Coulombic repulsion of the other nuclei and the Coulombic attraction of the electrons. As Levine put it [5]: “The fact that the effective forces on the nuclei are electrostatic affirms that there are no ‘mysterious quantum-mechanical forces’ acting in molecules.” All that is required are the positions of the nuclei, the electronic density distribution $\rho(\mathbf{r})$, and Coulomb’s Law – a distressingly simple conclusion. It provoked some objections [6], but these were refuted [7] and the theorem is alive and well.

However, what about such hallowed quantum-mechanical concepts as exchange, antisymmetry, correlation, Pauli repulsion, etc.? These are important, but their role is in obtaining the electronic density of the system computationally. Once it is available, along with the nuclear positions, only Coulomb’s Law is needed. (For further discussion of this, see Berlin [7] and Bader [8].) The Hellmann–Feynman theorem can in fact be regarded as a forerunner to Hohenberg and Kohn showing that the electronic density is the fundamental determinant of the properties of a system of nuclei and electrons [9].

Coulomb’s law states that the force \mathbf{F} between two point charges Q_a and Q_b separated by a distance R is given by

$$\mathbf{F}(R) = k \frac{Q_a Q_b}{R^2}, \quad (1)$$

where k is a constant. The energy $\Delta E(R)$ of the interaction between Q_a and Q_b can be obtained by integrating $\mathbf{F}(R)$ from infinite separation to R :

$$\Delta E(R) = \int_{R=\infty}^R \mathbf{F}(R) \cdot d\mathbf{R} = \int_{R=\infty}^R k \frac{Q_a Q_b}{R^2} \cos\theta dR, \quad (2)$$

where θ is the angle between the vector \mathbf{F} and the vector \mathbf{R} representing the path of Q_b . If Q_a and Q_b have the same sign, then \mathbf{F} is repulsive and opposite in direction to \mathbf{R} ; thus $\theta = 180^\circ$. If Q_a and Q_b have different signs, then \mathbf{F} is attractive and in the same direction as \mathbf{R} ; $\theta = 0^\circ$. Either way,

$$\Delta E(R) = k \frac{Q_a Q_b}{R}, \quad (3)$$

where $\Delta E(R) > 0$ when Q_a and Q_b have the same sign, and $\Delta E(R) < 0$ when they have opposite signs.

A point charge Q_a creates both an “electric field” $\boldsymbol{\varepsilon}(R)$ and an “electrical potential” $V(R)$ in the surrounding space:

$$\boldsymbol{\varepsilon}(R) = k \frac{Q_a}{R^2}, \quad (4)$$

$$V(R) = k \frac{Q_a}{R}. \quad (5)$$

Their significance is that another point charge Q placed at a distance R from Q_a feels a force $\mathbf{F}(R) = Q\boldsymbol{\varepsilon}(R)$ and the interaction energy with Q_a is $\Delta E(R) = QV(R)$. Both \mathbf{F} and $\boldsymbol{\varepsilon}$ are vectors.

In extending Coulomb’s Law to molecules, complexes, etc., the nuclei and electrons can normally be viewed as point charges. The electrical potential $V(\mathbf{r})$ which they create at any point \mathbf{r} can therefore be obtained, in principle, by summing (5) over all of the nuclei and electrons. However, the electrons, unlike the nuclei, cannot be treated as having fixed positions; accordingly, instead of summing (5) over the electrons, it is necessary to integrate over the electronic density $\rho(\mathbf{r})$:

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}') d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|}. \quad (6)$$

In (6), Z_A is the charge on nucleus A, located at \mathbf{R}_A . The denominators are the distances from each nucleus A and each unit of electronic charge $\rho(\mathbf{r}')d\mathbf{r}'$ from the point of interest \mathbf{r} . Equation (6) is written in atomic units (au), in which the Coulomb’s Law constant k and the charge on an electron or proton are equal to one. A potential $V(\mathbf{r})$ of 1 au is equivalent to 27.21 V (a more common unit for potential).

We emphasize that $V(\mathbf{r})$ is a real property of a system, a physical observable. It can be determined both experimentally, by diffraction methods [10–12], and computationally. The sign of $V(\mathbf{r})$ in any region depends upon whether the positive contribution of the nuclei or the negative contribution of the electrons is dominant there. In the absence of any perturbing effect, $\rho(\mathbf{r})$ is static and $V(\mathbf{r})$ is then commonly known as the “electrostatic” potential.

If a point charge Q is placed at \mathbf{r} , then its interaction energy with the system is, by extension of the earlier discussion, $\Delta E(\mathbf{r}) = QV(\mathbf{r})$. When Q and $V(\mathbf{r})$ are of the same sign, then the interaction is repulsive, $\Delta E(\mathbf{r}) > 0$; when they are of different signs, it is attractive, $\Delta E(\mathbf{r}) < 0$. It is important to recognize, however, that the electric field of Q perturbs (i.e., polarizes) the electronic density of the system and the $V(\mathbf{r})$ appropriate for calculating $\Delta E(\mathbf{r})$ is not the same as $V(\mathbf{r})$ in the absence of Q .

(Traditionally, molecular electrostatic potentials have often been expressed in energy units, e.g., kcal/mol. When this is done, the stated value of $V(\mathbf{r})$ actually corresponds to the interaction energy of the molecule with a positive point charge at the position \mathbf{r} . However, this is misleading because the electric field of the positive point charge would perturb the electronic density of the system and hence change $V(\mathbf{r})$ from what it is for the isolated molecule, for which it was computed. To avoid this unfortunate confusion, we give $V(\mathbf{r})$ in units of potential, i.e., volts (V).)

The electrostatic potential is a property of fundamental significance [13–15], as well as being very useful in interpreting and predicting non-covalent interactions [13, 15, 16]; regions of positive $V(\mathbf{r})$ on one molecule are attracted to regions of negative $V(\mathbf{r})$ on another. For such purposes, $V(\mathbf{r})$ is frequently computed on the surface of the molecule, which is taken to be defined by the 0.001 au (electrons/bohr³) contour of its $\rho(\mathbf{r})$, as suggested by Bader et al. [17]. This surface encompasses approximately 97% of the electronic charge, and has the important feature of being specific to the particular molecule, reflecting lone pairs, π electrons, strained bonds, atomic anisotropies, etc. The electrostatic potential on the surface is labeled $V_S(\mathbf{r})$. Its locally most positive and most negative values are designated by $V_{S,\max}$ and $V_{S,\min}$, respectively, and there may be several of each.

2 The σ -Hole: Halogens

Consider a free halogen atom. Its electronic density distribution is, on average, spherically symmetrical [18] and the electrostatic potential $V(\mathbf{r})$ created by its nucleus and electrons is positive for all $r < \infty$ [19]; the positive contribution of the nucleus, which is usually treated as a point charge, outweighs the negative contribution of the dispersed electrons. When the atom participates in forming a covalent bond, however, its electronic density undergoes a redistribution which causes it to become anisotropic [20–25], less on the outer side of the atom (i.e., along the extension of the bond) than on the lateral sides. This can be seen, for instance, for the chlorine in Cl-OH in Fig. 1. The term “polar flattening” has

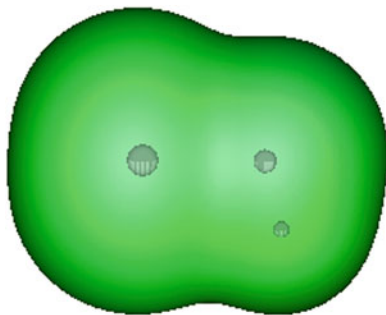


Fig. 1 Calculated 0.001-au molecular surface of ClOH. The positions of the nuclei are shown by *light circles*; chlorine is on the *left*. Distance from chlorine nucleus to surface along extension of O–Cl bond is 1.85 Å; distance from chlorine nucleus to lateral surface is 2.10 Å. Computational level: M06-2X/aug-cc-pVTZ

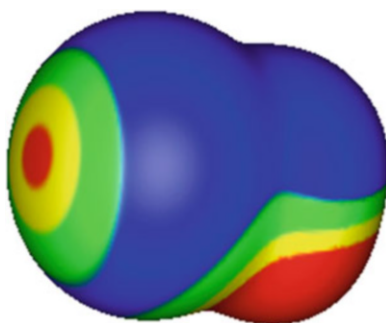


Fig. 2 Calculated electrostatic potential on the 0.001-au molecular surface of ClOH. Chlorine is on the *left*. Color ranges, in volts: *red*, greater than 0.87; *yellow*, from 0.87 to 0.43; *green*, from 0.43 to 0; *blue*, less than 0 (negative). The most positive potential on the chlorine surface (*red*) has a $V_{S,\max}$ of 0.99 V, and corresponds to a σ -hole on the extension of the O–Cl bond. Note also the positive region associated with the hydrogen (*lower right*); the $V_{S,\max}$ is 2.51 V. Computational level: M06-2X/aug-cc-pVTZ

sometimes been used to describe this. The outer region of diminished electronic density has been labeled a “ σ -hole” [26].

This rearrangement of electronic density is, of course, reflected in the electrostatic potential $V_S(\mathbf{r})$ on the surface of the covalently-bonded halogen. What is often found is that $V_S(\mathbf{r})$ is positive in the σ -hole region, which has the lesser electronic density, and is negative on the lateral sides, which have the greater electronic densities. This is shown in Fig. 2 for the chlorine in Cl–OH. The σ -hole corresponds to a local maximum in the molecular surface electrostatic potential, a $V_{S,\max}$. (It should be remembered that the σ -hole is a region in space, not simply a point.)

In general, the more polarizable the halogen atom and the more electron-attracting the remainder of the molecule, the more positive is the halogen σ -hole [27–30]. This is illustrated by the computed $V_{S,\max}$ in Table 1. For instance, the

Table 1 Most positive σ -hole potentials ($V_{S,max}$) and most negative potentials ($V_{S,min}$) on 0.001-au surfaces of indicated halogen atoms, in volts. Computational method: M06-2X/6-311G(d)

Molecule	Atom	Bond producing σ -hole	$V_{S,max}$	$V_{S,min}$	References
<i>Focus on general trends</i>					
H ₃ C-F	F	C-F	-1.07	-1.10	[31]
H ₃ C-Cl	Cl	C-Cl	-0.04	-0.68	[31]
H ₃ C-Br	Br	C-Br	0.25	-0.65	[31]
H ₃ C-I	I	C-I	0.56	-0.56	[31]
F ₃ C-F	F	C-F	-0.06	-0.12	[31]
F ₃ C-Cl	Cl	C-Cl	0.86	-0.03	[31]
F ₃ C-Br	Br	C-Br	1.10	-0.09	[31]
F ₃ C-I	I	C-I	1.38	-0.08	[31]
NC-F	F	C-F	0.56	0.47	Present work
NC-Cl	Cl	C-Cl	1.56	0.45	Present work
NC-Br	Br	C-Br	1.85	0.37	Present work
NC-I	I	C-I	2.11	0.31	Present work
<i>Dihalogens</i>					
F-F	F	F-F	0.49	-0.11	Present work
Cl-Cl	Cl	Cl-Cl	1.11	-0.12	[30]
Br-Br	Br	Br-Br	1.26	-0.18	[30]
<i>Focus on bromine</i>					
H ₃ Ge-Br	Br	Ge-Br	-0.07	-0.58	[31]
H ₃ Si-Br	Br	Si-Br	0.02	-0.51	[31]
H ₂ P-Br	Br	P-Br	0.15	-0.62	[30]
H ₃ C-Br	Br	C-Br	0.25	-0.65	[31]
F ₂ P-Br	Br	P-Br	0.42	-0.33	[30]
HS-Br	Br	S-Br	0.75	-0.42	[30]
H ₂ N-Br	Br	N-Br	0.77	-0.35	[30]
F ₃ Si-Br	Br	Si-Br	0.79	0.09	[31]
FS-Br	Br	S-Br	0.98	-0.20	[30]
Br ₂ C=CBr ₂	Br	C-Br	1.05	-0.25	Present work
F ₃ C-Br	Br	C-Br	1.10	-0.09	[31]
Br-Br	Br	Br-Br	1.26	-0.18	[30]
Br-C≡C-Br	Br	C-Br	1.31	-0.09	Present work
HO-Br	Br	O-Br	1.42	-0.46	[30]
F ₂ N-Br	Br	N-Br	1.48	-0.07	[30]
Cl-Br	Br	Cl-Br	1.54	-0.10	[30]
FO-Br	Br	O-Br	1.99	-0.02	[30]
F-Br	Br	F-Br	2.31	-0.004	[30]

$V_{S,max}$ of iodine is greater in H₃C-I than that of bromine in H₃C-Br but it is less than that of iodine in NC-I. Table 1 also gives the value of the most negative surface potential, $V_{S,min}$, on the portion of the surface attributable to the indicated halogen atom.

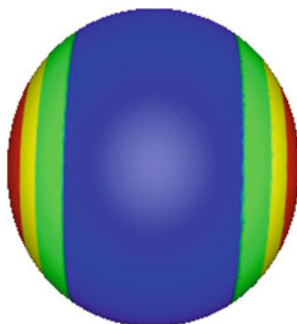


Fig. 3 Calculated electrostatic potential on the 0.001-au molecular surface of a chlorine atom in the $s^2p_x^2p_y^2p_z^1$ valence state configuration. Color ranges, in volts: *red*, greater than 0.43; *yellow*, from 0.43 to 0.22; *green*, from 0.22 to 0; *blue*, less than 0 (negative). The most positive potentials on the chlorine surface, shown in *red* at *left* and *right*, have $V_{S,\max}$ of 0.95 V. Computational level: M06-2X/aug-cc-pVTZ

The less polarizable and more electronegative halogens, fluorine and chlorine, tend to have less positive σ -holes than the others. In fact, they are sometimes negative (although less so than their surroundings); see Table 1. On the other hand, a very strongly electron-attracting bonding partner can cause the potential $V_S(\mathbf{r})$ of the entire surface of the halogen to be positive (the σ -hole being still more so). This can be the case even for fluorine. In F-CN, for instance, the $V_S(\mathbf{r})$ of fluorine is entirely positive (Table 1), with the maximum being in the σ -hole [32]; the $V_{S,\min}$ of fluorine is also positive.

It is interesting that positive σ -holes can even be seen in a free halogen atom if it is in the asymmetric valence state configuration $s^2p_x^2p_y^2p_z^1$ which it has when participating in a covalent bond [26, 28, 33, 34]. The half-filled p_z orbital is the one that is directly involved in the bonding and, in Fig. 3, positive σ -holes are clearly visible in both the $+z$ and $-z$ directions for the valence state of chlorine. In contrast, there is an equatorial ring of negative potential caused by the doubly-occupied p_x and p_y orbitals.

3 σ -Holes: Groups IV–VI

σ -Holes are not limited to halogens. This has been demonstrated for covalently-bonded atoms of Group VI [35], Group V [36], and Group IV [37]. This is again caused by the anisotropic charge distributions of the atoms [21, 25, 38, 39], which result in σ -holes on the extensions of single (and sometimes multiple) bonds to these atoms. Accordingly Group VI, V, and IV atoms can have two, three, and four σ -holes, respectively (or more if the atoms are hypervalent [37, 40]). The electrostatic potentials of these σ -holes show the same trends as for the halogens: within a

given Group, the σ -hole $V_{S,max}$ becomes more positive in going from the lighter to the heavier (more polarizable) atoms and as the bonding partner is more electron-attracting. The latter factor means that the σ -holes on a given atom may have different $V_{S,max}$, depending upon the partners in the covalent bonds; see Figs. 4, 5, and 6. For a more general discussion of factors affecting σ -hole potentials, see Murray et al. [30].

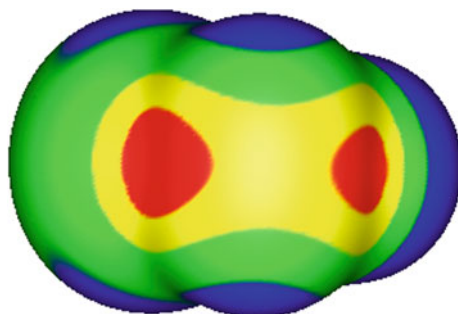


Fig. 4 Calculated electrostatic potential on the 0.001-au molecular surface of BrSF. Sulfur is *in the middle facing the viewer*, bromine is *on the left* and fluorine is *on the right*. Color ranges, in volts: *red*, greater than 0.87; *yellow*, from 0.87 to 0.43; *green*, from 0.43 to 0; *blue*, less than 0 (negative). The most positive potentials on the sulfur surface, shown in *red*, have $V_{S,max}$ of 1.31 V (*left*) and 1.10 V (*right*). These correspond to σ -holes on the extensions of the F–S and Br–S bonds, respectively. Computational level: M06-2X/aug-cc-pVTZ

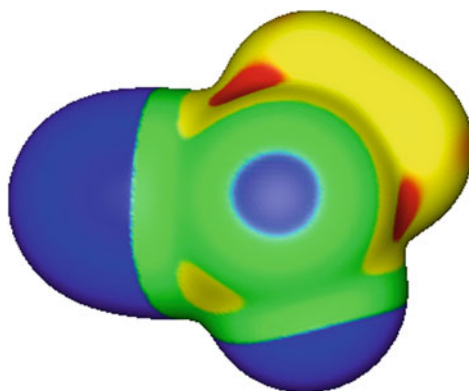


Fig. 5 Calculated electrostatic potential on the 0.001-au molecular surface of PF(CH₃)(CN). Phosphorus is *in the middle facing the viewer*, the cyano group is *on the left*, the methyl group is *at the top right*, and fluorine is *at the bottom right*. Color ranges, in volts: *red*, greater than 1.26; *yellow*, from 1.26 to 0.65; *green*, from 0.65 to 0; *blue*, less than 0 (negative). The most positive potentials on the phosphorus surface, shown in *red* or *yellow*, have $V_{S,max}$ of 1.52 V (*top*), 1.41 V (*right*), and 0.95 V (*bottom left*). These correspond to σ -holes on the extensions of the F–P, NC–P and H₃C–P bonds, respectively. Note that the phosphorus has a negative region facing the viewer. Computational level: M06-2X/aug-cc-pVTZ

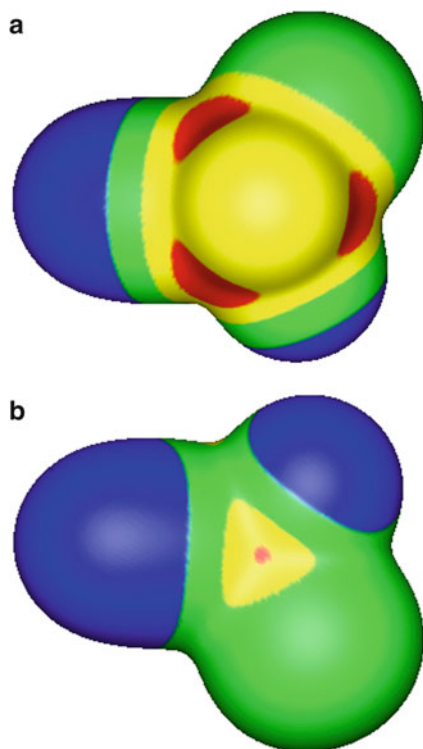


Fig. 6 Calculated electrostatic potential on the 0.001-au molecular surface of HSiF(Cl)(CN). Color ranges, in volts: *red*, greater than 1.26; *yellow*, from 1.26 to 0.65; *green*, from 0.65 to 0; *blue*, less than 0 (negative). Two views are shown: In (a), hydrogen is in the middle facing the viewer, the cyano group is *on the left*, chlorine is *at the top right* and fluorine is *at the bottom right*. The most positive potentials on the silicon surface, shown in *red*, have $V_{S,\max}$ of 1.76 V (*right*), 1.90 V (*bottom left*), and 1.77 V (*top left*). There correspond to σ -holes on the extensions of the NC-Si, Cl-Si and F-Si bonds, respectively. In (b), silicon is *in the middle*, the cyano group is *on the left*, the chlorine is *at the bottom right*, and fluorine is *at the top right*. The most positive potential on the silicon surface, shown in *red*, has $V_{S,\max} = 1.31$ V. It is on the extension of the H-Si bond. Computational level: M06-2X/aug-cc-pVTZ

As with the halogens, positive σ -holes on Group V and VI atoms (but not Group IV) are often found in conjunction with regions of negative potential. This is evident in Figs. 4 and 5 and in Table 2, which lists the σ -hole $V_{S,\max}$ and the $V_{S,\min}$ of various covalently-bonded Group IV–VI atoms. For the first-row members of each Group, which are the least polarizable and most electronegative, the $V_{S,\max}$ are often negative, just as for fluorine. At the other extreme, the surface potential of the Group V or Group VI atom may be completely positive if the atom is bonded to highly electron-withdrawing partners, e.g., in AsF₂Br (Table 2); however the σ -holes are still local maxima. With tetravalent Group IV atoms, our experience has been that their $V_S(\mathbf{r})$ are always entirely positive, regardless of the bonding partners (Fig. 6), with four σ -holes as local maxima.

Table 2 Most positive σ -hole potentials ($V_{S,max}$) and most negative potentials ($V_{S,min}$) on 0.001-au surfaces of indicated atoms from Groups IV–VI, in volts. (The Group IV atoms have no local minima.) Computational method: M06-2X/6-311G(d)

Molecule	Atom	Bond producing σ -hole	$V_{S,max}$	$V_{S,min}$	References
FOBr	O	F–O	0.46	–0.51	Present work
	O	Br–O	–0.15	–0.51	Present work
FSBr	S	F–S	1.56	–0.17	Present work
	S	Br–S	1.18	–0.17	Present work
FSeBr	Se	F–Se	1.89	–0.22	Present work
	Se	Br–Se	1.52	–0.22	Present work
F ₂ NBr	N	F–N	0.57	–0.40	Present work
	N	Br–N	0.52	–0.40	Present work
F ₂ PBr	P	F–P	1.40	0.49	Present work
	P	Br–P	1.53	0.49	Present work
F ₂ AsBr	As	F–As	1.72	0.91	Present work
	As	Br–As	1.67	0.91	Present work
F ₃ CBr	C	F–C	0.69	–	[31]
	C	Br–C	0.94	–	[31]
F ₃ SiBr	Si	F–Si	1.76	–	[31]
	Si	Br–Si	2.06	–	[31]
F ₃ GeBr	Ge	F–Ge	1.96	–	[31]
	Ge	Br–Ge	1.93	–	[31]

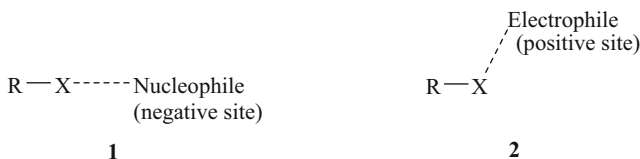
4 σ -Hole Interactions

The existence of positive σ -holes on many covalently-bonded atoms suggests that these can give rise to attractive non-covalent interactions, both inter- and intramolecular, with negative sites such as the lone pairs of Lewis bases, π electrons, anions, etc. Because of the focused nature of the positive region, the σ -hole, these interactions should be highly directional, approximately along the extensions of the covalent bonds giving rise to the σ -holes. They should also be stronger as the σ -hole is more positive. Interactions of this sort have in fact been known experimentally for Groups IV–VII for decades, as summarized elsewhere [28, 29, 41]. However, these were not described as σ -hole interactions until 2007 [26, 32, 35–37].

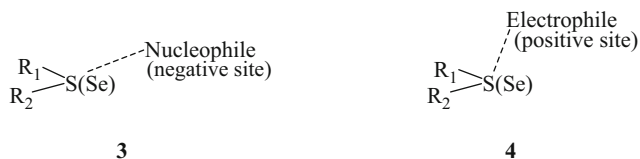
When Group VII is involved, this has been labeled “halogen bonding,” and it was often viewed as puzzling that a covalently-bonded halogen – normally presumed to be negative in character – would be attracted to a negative site. Much of the evidence for this involved crystallographic observations of close contacts in organic halides and in complexes between halides and oxygen/nitrogen Lewis bases. A series of the latter studies, particularly by Hassel et al., was reviewed by Bent in 1968 [42].

Especially significant were surveys of organic halide crystal structures in the Cambridge Structural Database by Murray-Rust et al. [43–45]. They found numerous halogen close contacts, which were highly directional. For a halogen X in a

molecule R–X, close contacts with nucleophilic components of other molecules (negative sites) were approximately linear, along the extension of the R–X bond (**1**), while close contacts with electrophilic components (positive sites) involved the lateral sides of the halogen (**2**).



At roughly the same time, analogous findings were reported by Parthasarathy et al. for sulfides and selenides [38, 39, 46]. For compounds $R_1R_2S(\text{Se})$, crystallographic surveys showed that close contacts with nucleophilic (negative) sites were along the extensions of the R_1 –S(Se) and/or R_2 –S(Se) bonds (**3**), and those with electrophilic (positive) sites were above or below the R_1 –S(Se)– R_2 plane (**4**).



It is clear that the close contacts with nucleophiles, **1** and **3**, can readily be explained as positive σ -holes interacting with negative sites, while **2** and **4** involve the negative lateral sides of the halogen, sulfur, or selenium (Figs. 1 and 4). This was first pointed out by Brinck et al. for halogen bonding [47, 48] and by Burling and Goldstein for S–O and Se–O close contacts [49]; Auffinger et al. [50] and Awwadi et al. [23] subsequently offered similar interpretations of halogen bonding. However, none of these persons used the term “ σ -hole,” which was introduced later, in 2007 [26].

Numerous Group IV–VII non-covalent interactions which fit the characteristic directional criterion for σ -hole bonding have now been documented, both computationally and experimentally; several overviews are available [27–29, 41]. Some computational examples are presented in Table 3. The interactions are all approximately linear (i.e., along the extension of the covalent bond to the atom) and the separations between the atoms with the σ -holes and the negative sites are less than or similar to the sums of the respective van der Waals radii. The interaction energies ΔE were obtained via (7):

$$\Delta E = E(\text{A–B}) - [E(\text{A}) + E(\text{B})], \quad (7)$$

in which $E(\text{A–B})$ is the energy of the complex A–B and $E(\text{A})$ and $E(\text{B})$ are the energies of the isolated components.

Table 3 σ -Hole $V_{S,\max}$ for atoms shown in bold and interaction energies ΔE for some gas phase complexes with NH_3 and HCN .^a Computational methods: electrostatic potentials, M06-2X/6-311G(d); interaction energies, M06-2X/aug-cc-pVTZ

Complex	Bond producing σ -hole	σ -Hole $V_{S,\max}$ (volts)	ΔE (kcal/mol)	Separation ^b (Å)	Angle (deg)
F-F— NH_3	F-F	0.49	-1.5	2.59 (3.0)	179.9
F ₃ C-Cl— NH_3	C-Cl	0.86	-2.5	3.03 (3.3)	180.0
F ₃ C-Br— NH_3	C-Br	1.10	-3.7	3.07 (3.5)	179.9
BrC≡C-Br— NH_3	C-Br	1.31	-4.2	2.99 (3.5)	179.8
H ₂ FP— NH_3	F-P	1.68	-7.2	2.71 (3.4)	166.5
H ₂ FAs— NH_3	F-As	1.93	-8.7	2.73 (3.5)	165.0
F-Cl— NH_3	F-Cl	1.98	-10.3	2.59 (3.3)	179.9
F ₃ C-Cl—NCH	C-Cl	0.86	-1.6	3.13 (3.3)	179.1
BrC≡C-Br—NCH	C-Br	1.31	-2.7	3.05 (3.5)	180.0
Cl ₂ Se—NCH	Cl-Se	1.57	-4.0	2.92 (3.5)	176.1
H ₂ FP—NCH	F-P	1.68	-4.7	2.81 (3.4)	164.0
H ₃ FGe—NCH	F-Ge	1.87	-4.9	2.89 (-)	179.8
F-Br—NCH	F-Br	2.31	-7.1	2.60 (3.5)	180.0

^aComputed $V_{S,\max}$ and ΔE were reported in [29]

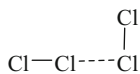
^bValues in parentheses are the sums of the van der Waals radii of the σ -hole-containing atom and nitrogen [108, 109]. No van der Waals radius was found for germanium

For a given negative site, ΔE has been found to correlate reasonably well with the $V_{S,\max}$ of the σ -hole [28, 29, 31, 51, 52]; ΔE becomes more negative (stronger interaction) as $V_{S,\max}$ is more positive. When the ΔE correspond to two or more different negative sites, as in Table 3, then their $V_{S,\min}$ must be taken into account. One way of doing this is by plotting ΔE against the product of $V_{S,\max}$ (σ -hole) and $V_{S,\min}$ (negative site). When this was done for a series of 20 complexes with NH_3 and HCN , including the 13 in Table 3, the R^2 was a very satisfactory 0.96 [29].

The first-row atoms of Groups IV–VII (carbon, nitrogen, oxygen, and fluorine) tend to have relatively weakly-positive or negative σ -holes, because of their lower polarizabilities and higher electronegativities compared to the other members of their groups. Attractive σ -hole interactions are therefore less common for these four atoms. Thus it was formerly thought that fluorine does not form halogen bonds. This has been disproved [32, 53, 54]. It was in fact shown some years ago that carbon [37], nitrogen [36], oxygen [35], and fluorine [32] can all have positive σ -holes if covalently bonded to strongly electron-attracting partners. From this it follows that they can indeed form σ -hole bonds, and this has been demonstrated computationally [31, 32, 35–37] and to some extent experimentally [41, 53, 54].

Since a positive σ -hole is frequently surrounded by a negative surface potential (except for Group IV), a given atom can interact favorably and directionally with both negative and positive sites, as is seen in the crystallographic close contacts discussed above, 1–4. It is even possible to have “like attracting like,” whereby the positive σ -hole on an atom in one molecule interacts with the negative potential on

the same atom in another identical molecule. This has been observed both computationally [25, 29, 55, 56] and experimentally [22, 38, 57, 58]. Examples are crystalline Cl_2 , **5** [22], and $\text{ClH}_2\text{P}-\text{PH}_2\text{Cl}$ [56]. (Note that “like attracting like” cannot happen with tetravalent Group IV atoms, which have entirely positive surface potentials.)



5

The fact that many atoms have surface regions of both positive and negative potentials, and can interact through either or both, demonstrates anew the fallacy of trying to assign a point positive or negative charge to an atom in a molecule (i.e., an atomic monopole). While numerous different procedures for doing so have been invented [59] (including one by an author of this paper [60], a youthful folly), there is no rigorous basis for doing so, and the results are likely to be physically misleading, as shown by Figs. 2, 4, 5, and 6, and Tables 1 and 2. For example, traditional atomic charges cannot in general account for or predict halogen bonding and other σ -hole interactions. In this respect, as has been pointed out [50, 55], force fields that assign single charges to atoms in molecules are inadequate; recognition of this has led to efforts to make them more realistic [61–65].

5 The Nature of σ -Hole Interactions

The interaction energy ΔE of a σ -hole-bonded complex A—B can be determined by (7). ΔE is a real physical property, an observable which can be obtained experimentally. It tells us how much energy is released when the complex is formed, or alternatively, the negative of ΔE tells us how much energy is required to break the A—B bond and separate A and B, i.e., the binding energy.

Unfortunately, it has become quite popular in recent years to dissect ΔE into various components. This is viewed as a means of better “understanding” the interaction; the fact that the process is physically meaningless is not taken to be a deterrent. The assumed components are usually some subset of a group which includes electrostatics, dispersion, polarization, charge transfer, exchange repulsion (which Bader called an oxymoron [8]), induction, orbital interaction, Pauli repulsion, exchange, distortion, etc. While each of these can be claimed to have some conceptual significance, they are not observables, are not uniquely defined, and are not independent of each other.

There is no physically rigorous or “correct” way to make such a dissection of ΔE , which has the advantage that everyone can feel free to invent their own scheme (a situation akin to that of atomic charges) and their own set of assumed components. A recent summary by Mo et al. [66] lists at least 16 different procedures

which have been proposed, and they invoke different subsets of the group of supposed components listed above. They can be quite contradictory, as exemplified by two separate dissections of the interaction energies of the complexes $\text{H}_3\text{C-X-OCH}_2$ and $\text{F}_3\text{C-X-OCH}_2$. By one procedure, the primary stabilizing components were found to be electrostatics and dispersion [67]. The other energy dissection scheme concluded, *for the same complexes*, that charge transfer and polarization are dominant and that electrostatics contributes only “slightly” [68]. (So what causes the polarization?)

The Hellmann–Feynman theorem tells us that the forces acting within the complex A—B are purely Coulombic attractions and repulsions involving the nuclei and electrons, and can be determined exactly from the electronic density and the positions of the nuclei [3, 4]. How do we reconcile this rigorous statement with the various interaction components commonly invoked in different analyses of non-covalent bonding, even if we resist the urge to try to quantify them?

The answer to this lies in the fact that the Hellmann–Feynman theorem refers to the actual electronic density of the system; this is what is to be used in evaluating the Coulombic interactions of the electrons. In energy dissection schemes, on the other hand, the electrostatic term pertains to an imaginary situation: A and B being at the separation that they have in the complex but with the unperturbed charge distributions that they would have at infinite separation. Accordingly, the electrostatic component of the interaction energy is typically computed without including the polarizing effects that A and B have upon each other and that perturb their electronic densities and hence their electrostatic interactions. Polarization is treated as another component, separate from the electrostatic, which is completely unrealistic.

Polarization is an intrinsic part of any Coulombic interaction (unless only point charges are involved) [25, 28, 29, 69, 70]; it cannot be viewed separately. The electric fields of the participants polarize each other’s charge distributions. Consider the formation of a σ -hole complex A—B in which the positive σ -hole is on A and the negative site on B. Then the shifting (polarization) of the electronic densities of A and B are as shown in **6**.



The importance of polarization is confirmed by plots showing the difference between the computed electronic density of a σ -hole complex A—B and that of the imaginary unperturbed system mentioned above: free A and free B placed at the same separation as in the complex [25, 69, 71, 72]. Such plots all show the qualitative features depicted in **6**: the electric field of the negative site on B polarizes the electronic density near the σ -hole of A away from B, while the electric field of the σ -hole polarizes the electronic charge of B toward A.

The polarization shown in **6** helps to interpret the “cooperativity” sometimes observed in systems involving more than one non-covalent interaction [32, 71, 73, 74]. For example, ΔE for the formation of NC-Br-NC-Br-NC-Br has more than

twice the magnitude of that for NC-Br—NC-Br [32], because each NC-Br—NC-Br interaction in the trimer strengthens either the σ -hole or the negative site for the other.

Polarization also nicely explains the changes that σ -hole interactions produce in the stretching frequencies of the covalent bonds to the atoms having the σ -holes (i.e., the bonds that give rise to them). In some complexes these frequencies increase (blue shifts) but more often they decrease (red shifts) [75, 76]. These observations have frequently been rationalized in terms of “charge transfer” from orbitals on the negative sites B to various orbitals on the σ -hole molecules A. However it has been demonstrated [75, 76] that both blue and red shifts can be explained and predicted, using the formalisms of Hermansson [77] or Qian and Krimm [78], from the electric field produced by B and the permanent and induced dipole moments of A. No orbital factors need be invoked.

Dispersion is an intrinsic part of the Coulombic interaction in a complex A—B, as is polarization. Dispersion is commonly considered to be associated with electronic correlation [79–81], i.e., the instantaneous correlated movements of the electrons in response to their mutual Coulombic repulsions. These movements create temporary dipoles which interact attractively, accounting for the stabilizing contribution of dispersion.

Feynman proposed a different (often overlooked) interpretation of dispersion [4], involving nuclear-electronic rather than dipole interactions. Support for his conjecture was reported by Hirschfelder and Eliason [82], and a proof was offered by Hunt [83].

Either explanation is consistent with the Hellmann–Feynman theorem: The forces acting within the complex are purely Coulombic and can be determined from the electronic density and the nuclear positions. What the energy dissection procedures view as three separate components of ΔE – electrostatics, polarization, and dispersion – are really just one, the Coulombic, which rigorously encompasses all the forces within the complex.

The electronic density and the nuclear positions can in principle be obtained either experimentally or computationally. It is in doing the latter that factors such as antisymmetry, exchange, Pauli repulsion, etc., enter the picture, as consequences of the mathematical model being used. However, the distinction between physical reality and a mathematical model should always be kept in mind.

An example of a frequent failure to do this relates to the notion of charge transfer. This is often invoked in regard to non-covalent bonding, although without explaining how, physically, this is stabilizing. (On the other hand, some energy dissection schemes do not even include it in their subsets of components.) Charge-transfer formalism was introduced by Mulliken to describe the electronic transition from the ground state of a complex to an excited state, which is largely dative [84]; his focus was upon this transition, not upon the physical nature of the bonding in the ground state. The idea that a σ -hole interaction involves some small fraction of an electron being transferred from the negative site on B into an orbital on the molecule A having the positive σ -hole is purely mathematical modeling, not physical reality. Orbitals are not real, they are mathematical expressions which

are useful in constructing wave functions [85]; electrons cannot be sliced up into fragments. The overlap of an occupied orbital of the “donor” with an unoccupied orbital of the “acceptor” is simply one mathematical technique (not the only one) for describing the physical event, which is the mutual polarization of A and B, as in **6**.

This point can be illustrated by considering another perfectly valid mathematical approach, discussed by Stone and Misquitta [86]. Quite a satisfactory quantum chemical representation of the complex A—B could be obtained using only orbitals of either A or B, provided that enough of them were used. The polarization depicted in **6** would be adequately described. However, the charge transfer, as evaluated by any orbital-based method, would necessarily be zero, since one of the participants was not assigned any orbitals! It is indeed increasingly becoming recognized that the distinction between polarization and charge transfer is an artificial one [87–90].

6 Hydrogen Bonding

There is an obvious structural similarity between hydrogen bonding, R—H—B, and halogen bonding, R—X—B, in that both involve a univalent covalently-bonded atom interacting with a negative site. For a given R and B, hydrogen bonding is generally the stronger if X=F or Cl, but they are comparable when X=Br and halogen bonding is often the stronger when X=I [91–93]. Halogen bonding dominating over hydrogen bonding has been observed experimentally, for instance in solution studies [94] and in co-crystallization [95].

In recent years, hydrogen bonding has fallen victim to intense theoretical scrutiny, and so one can now find references to classical and nonclassical hydrogen bonding, proper and improper, blue shifted and red shifted, dihydrogen bonding, anti-hydrogen bonding, H— σ and H— π hydrogen bonding, positive and negative charge-assisted hydrogen bonding, resonance-assisted and polarization-assisted hydrogen bonding, etc. However, all of these fit the same basic pattern: a Coulombic interaction involving a region of positive electrostatic potential on the hydrogen and a negative site.

It is in fact justifiable to view hydrogen bonding as a subset of σ -hole interactions [25, 28, 33, 34]. Since a hydrogen atom has only one valence electron, and that is participating in the R—H bond, it can be anticipated that the outer portion of the hydrogen has a positive potential with its maximum along the extension of the R—H bond (a σ -hole). Because of the absence of any other valence electrons on the hydrogen, its lateral sides also have relatively low electronic densities and therefore the positive σ -hole potential extends farther back toward the bonding partner than is typical of Group V–VII atoms. Hydrogen σ -holes are more hemispherical and less narrowly focused. These features are clearly apparent in Fig. 2 and especially in Fig. 7, and can also be seen in earlier reports [27, 28, 33, 81]. They help to explain why hydrogen bonds tend overall to be less directional than other σ -hole interactions [33, 96, 97].

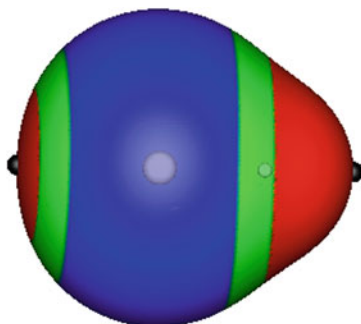
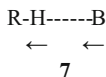


Fig. 7 Calculated electrostatic potential on the 0.001-au molecular surface of HI. The hydrogen is *on the right*. The positions of the nuclei are indicated by the *light circles*. Color ranges, in volts: *red*, greater than 0.43; *green*, between 0.43 and 0; *blue*, less than 0 (negative). The most positive values of the electrostatic potential, the $V_{S,max}$, are shown by *black hemispheres*; they are 1.26 V (hydrogen) and 0.91 V (iodine). Note that these surface maxima are along the extensions of the covalent bond. Computational level: M06-2X/6-311G(d)

Plots of electronic-density changes accompanying hydrogen bond formation show polarization as represented in 7 [98–100]. This is fully analogous to what is observed for other σ -hole interactions, discussed earlier and depicted in 6.



Both the minor differences in directionality and the fundamentally similar Coulombic natures of hydrogen bonding and halogen bonding in particular were brought out in a recent computational study [33]. This involved the halogen-bonded complexes of NC-Br and F₃C-Br with the two bases NH₃ and HCN, and the hydrogen-bonded complexes of NC-H and F₃C-H with the same two bases. For each complex, the interaction energy ΔE was computed as a function of the C-Br—N or C-H—N angle over the range 100°–180°. The most negative ΔE (strongest interactions) were for angles of 180°, since these involved the most positive potentials (the $V_{S,max}$) of the σ -holes of both the bromines and the hydrogens. ΔE was more negative for the hydrogen bonds than for the corresponding halogen bonds, reflecting the more positive potentials of the hydrogens compared to the bromines, and the NH₃ interactions were stronger than the HCN, caused by the nitrogen in the former having a more negative $V_{S,min}$.

The results showed the greater tendency of halogen bonding for linearity: the halogen bond ΔE rapidly became more negative as angles of 180° were approached, even in the NC-Br complexes, in which the bromine is completely positive (Table 1), whereas the hydrogen bond ΔE variation was more gradual. This demonstrates the role of the nonbonding valence electrons on the lateral sides of the halogen in focusing the interaction.

Particularly striking were plots of ΔE vs the positive potentials created by the four isolated R-Br and R-H molecules at the various distances and angles where the nitrogens of NH_3 and HCN were situated in the complexes; these were the potentials felt by the nitrogens in the complexes. Excellent linear correlations were obtained: $R^2 = 0.986$ for the NH_3 complexes and $R^2 = 0.990$ for the HCN. In each case, and for both $\text{R}=\text{NC}$ and $\text{R}=\text{F}_3\text{C}$, the hydrogen-bonded and the halogen-bonded complexes fit on the *same* correlation! All of this certainly strengthens the argument that these are basically similar Coulombic interactions.

7 Thermodynamic Stability

It is customary to use the energy change ΔE or the enthalpy change ΔH as a measure of the strength of the interaction in forming a complex A—B. The more negative are ΔE and ΔH , the more strongly bound is the complex.

From a thermodynamic standpoint, however, it is the free energy change ΔG that is important. Thermodynamic stability requires that ΔG be negative. Since at a fixed absolute temperature T ,

$$\Delta G = \Delta H - T\Delta S, \quad (8)$$

this introduces the entropy change ΔS as an additional factor. The formation of A—B diminishes the degrees of freedom of A and B, causing ΔS to be negative. Accordingly, even for an attractive interaction having $\Delta H < 0$, if $|T\Delta S| > |\Delta H|$, then $\Delta G > 0$ and the complex is thermodynamically unstable.

This is in fact the case for the formation of many σ -hole complexes in the gas phase at 298 K [29, 101, 102]. In solution or a solid phase, additional factors are involved which may make ΔG negative even when it is positive in the gas phase. However, it should be remembered that $\Delta G > 0$ does not completely preclude the formation of a complex; it simply means that the equilibrium constant for the process is less than one. (More extensive discussions of the thermodynamic stabilities of σ -hole complexes are given elsewhere [28, 29, 102].)

8 “Anomalously” Strong Interactions

There have sometimes been encountered, at least computationally, σ -hole complexes having properties suggesting unusually strong interactions – e.g., significantly more negative ΔE and shorter A—B separations than are commonly obtained. It might be inferred that the bonding in these systems differs in some fundamental manner from that in the weaker complexes; however, that is not the case. These “anomalously” strong interactions can be explained quite well in terms

of the usual suspects: the $V_{S,\max}$ of the σ -hole, the $V_{S,\min}$ of the negative site, and the polarizabilities of both.

For example, the computed ΔE of the complexes F-Cl—CN-Q and F-Cl—SiN-Q, where Q is an atom or group, range from -1.9 to -33.4 kcal/mol [103, 104]. This remarkably large variation must reflect the properties of the negative sites, since the σ -hole molecule is in all instances the same. Indeed, when the ΔE were expressed by double regression analysis as functions of the $V_{S,\min}$ and the local ionization energies of the CN-Q carbons and the SiN-Q silicons, the relationship between predicted and computed ΔE had $R^2 = 0.99$ [104]. (The local ionization energy was being used as a measure of polarizability [105].) The combination of a strong electric field produced by a large positive σ -hole $V_{S,\max}$ plus a highly polarizable negative site (as indicated by a low local ionization energy) can result in polarization to an extent which might be described (in less physical and more ambiguous terms) as a significant degree of dative sharing of electrons, or coordinate covalence. However, this is just terminology and does not imply a “transfer” of electronic charge or some other new factor; it is still a Coulombic interaction, but with a higher level of polarization. (An analogous explanation applies to “anomalously strong” π -hole interactions, in which the region of positive electrostatic potential is perpendicular to an atom in a planar portion of a molecular framework, e.g., the boron in BCl_3 and the sulfur in SO_2 [106]). For more detailed discussions, see Politzer et al. [29].

9 William of Occam, Einstein, and Newton

A great many non-covalent interactions of covalently-bonded atoms of Groups IV–VII, as well as hydrogen bonding, can be explained as Coulombic interactions (which encompasses polarization and dispersion) involving positive σ -holes and negative sites. We resist forlornly the current tendency to subject σ -hole bonding to the fate of compartmentalization which has befallen hydrogen bonding. Thus we do not separate σ -hole interactions on the basis of the atom having the σ -hole (i.e., chalcogen bonding, pnicogen bonding, tetrel bonding, carbon bonding, etc.) nor on the basis of the negative site (lone pair, anion, π electrons, etc.). They are all σ -hole interactions, and we believe that it is important to focus upon this fundamental unifying similarity rather than upon differences in detail. In the spirit of William of Occam: *Lex parsimoniae: Pluralitas non est ponenda sine necessitate* (plurality is not to be posited without necessity), Occam’s Razor.

We have tried to emphasize the importance of distinguishing between mathematical models and physical reality. This can be challenging, because mathematical models are often pleasingly elegant and complex, whereas physical reality may be distressingly simple and straightforward. Newton was aware of this failing on the part of Nature; he observed, “Nature is pleased with simplicity.” [107]. Einstein concurred: “Nature is the realization of the simplest conceivable mathematical ideas.” [107]. (To Newton and Einstein, “Nature” meant physical laws. Biological

“Nature” often finds seemingly unnecessarily complicated solutions to problems; evolution simply stops changing what works well enough.) Newton, Einstein, and William of Occam provide excellent guiding principles for those wishing to understand physical phenomena.

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