

The σ -Hole Revisited

Peter Politzer,^{*a} Jane S. Murray,^a Timothy Clark^b and Giuseppe Resnati^c

^aDepartment of Chemistry, University of New Orleans, New Orleans, LA 70148 USA

^bComputer-Chemie-Centrum and Interdisciplinary Center for Molecular Materials, Department of Chemistry and Pharmacy, Friedrich-Alexander-Universität, Erlangen-Nürnberg, Nagelbachstrasse 25, 91052 Erlangen, Germany

^cLaboratory of Nanostructured Fluorinated Materials (NFMLab), Department of Chemistry, Materials, and Chemical Engineering “Giulio Natta”, Politecnico di Milano, Via L. Mancinelli 7, 20131 Milano, Italy

Abstract

A covalently-bonded atom typically has a region of lower electronic density, a “ σ -hole,” on the side of the atom opposite to the bond, along its extension. There is frequently a positive electrostatic potential associated with this region, through which the atom can interact attractively but noncovalently with negative sites. This positive potential reflects not only the lower electronic density of the σ -hole but also contributions from other portions of the molecule. These can significantly influence both the value and also the angular position of the positive potential, causing it to deviate from the extension of the covalent bond. We have surveyed these effects, and their consequences for the directionalities of subsequent noncovalent intermolecular interactions, for atoms of Groups IV-VII. The overall trends are that larger deviations of the positive potential result in less linear intermolecular interactions, while smaller deviations lead to more linear interactions. We find that the deviations of the positive potentials and the nonlinearities of the noncovalent interactions tend to be greatest for atoms of Groups V and VI. We also present arguments supporting the use of the 0.001 au contour of the electronic density as the molecular surface on which to compute the electrostatic potential.

Keywords:

Noncovalent interactions, the σ -hole, electrostatic potentials, electronic densities, halogen bonding, molecular surfaces, deviations from linearity in noncovalent interactions.

The σ -Hole

About 25 years ago, Brinck *et al.* reported finding computationally that many covalently-bonded halogen atoms have regions of positive electrostatic potential on their outer sides, opposite to the covalent bonds and approximately along the extensions of the bonds.^{1,2} The lateral sides of the halogen atoms had negative potentials, which was expected, but the presence of the positive regions was rather surprising. Since halogens are electronegative, then it was anticipated that the halogen atoms would be negative in character. (It should be noted, however, that Kollman had already in 1977 computed the electrostatic potentials at single points around some diatomic molecules and obtained positive values at the ends of F₂ and Cl₂.³)

Brinck *et al.* pointed out that the positive regions allow the halogens to interact attractively with negative sites,^{1,2} and thus explain the basis for the noncovalent interaction known as halogen bonding. Halogen bonding had long been known⁴⁻¹¹ but was little understood; in fact it was often viewed as enigmatic. Since halogen atoms in molecules are expected to be negative, why would they interact attractively with negative sites? The positive regions found by Brinck *et al.* resolve the enigma in a very straightforward fashion (although some theoreticians continue to be dissatisfied with straightforward explanations).

The Coulombic explanation of halogen bonding gradually gained adherents.¹²⁻¹⁵ Then at a conference in 2005,¹⁶ the term “ σ -hole” was introduced, although it did not appear in the literature until 2007.¹⁷ The term was initially used to denote the localized positive potentials on the outer sides of many univalent halogen atoms. However it was soon recognized that it was more appropriate to use “ σ -hole” to describe the lower electronic densities that are found on the extensions of σ bonds^{18,19} (to be discussed in a later section).

At about the same time (2007), it was demonstrated that regions of positive potential can also exist on covalently-bonded atoms of Group VI,¹⁸ Group V¹⁹ and Group IV,²⁰ on the extensions of their bonds. These explained the noncovalent interactions of these atoms with negative sites that had been known for many years, and are surveyed in several overviews.²¹⁻²³

The decade since the formal “birth” of the σ -hole has coincided with an explosion of related research activity. For example, during the five years 2002-2006, there were 122 papers that mentioned halogen bonding; during the following five years, 2007-2011 there were 435.²⁴

Interest has undoubtedly increased exponentially in recent years, with the growing recognition of σ -holes and their related positive potentials in covalently-bonded Group IV-VI atoms.

Our purpose in this paper is to look at the relationship between σ -holes and noncovalent interactions from the perspective of the past ten years. Since σ -holes are intimately related to electronic densities and electrostatic potentials, we shall begin by briefly discussing these properties.

Electronic densities and electrostatic potentials

The electronic density $\rho(\mathbf{r})$ of a system of nuclei and electrons is the number of electrons in an infinitesimal volume $d\mathbf{r}$ at the point \mathbf{r} . Since the electrons are in constant rapid motion, $\rho(\mathbf{r})$ refers, in practice, to the average electronic density at \mathbf{r} .

The electrostatic potential is related to Coulomb's Law. Any point charge Q_a creates an electrostatic potential in the surrounding space; at a distance R , the value of this potential $V(R)$ is,

$$V(R) = Q_a/R \quad (1)$$

(in atomic units). The significance of the potential is that the interaction energy $\Delta E(R)$ between Q_a and a second point charge Q_b at a distance R is given by,

$$\Delta E = Q_a Q_b / R \quad (2)$$

When Q_a and Q_b have the same sign, ΔE is positive and the interaction is repulsive; when they have opposite signs, ΔE is negative and the interaction is attractive.

By classical physics, the negative gradient of a potential energy is a force. Accordingly the force $\mathbf{F}(R)$ exerted by Q_a upon Q_b is,

$$\mathbf{F}(R) = Q_a Q_b / R^2 \quad (3)$$

When Q_a and Q_b have the same sign, a repulsive interaction, then $\mathbf{F}(\mathbf{R})$ is positive and Q_b is being repelled from Q_a ; when they have opposite signs, an attractive interaction, then $\mathbf{F}(\mathbf{R})$ is negative and Q_b is attracted toward Q_a . Eq. (3) is Coulomb's Law.

When dealing with a molecule, complex, etc., the nuclei and electrons are normally treated as point charges. The electrostatic potential that they create at any \mathbf{r} in the surrounding space can then be obtained, in principle, by summing eq. (1) over all of the nuclei and electrons. In doing this, the Born-Oppenheimer approximation is invoked and the nuclei are assumed to have fixed positions. However this cannot be extended to the rapidly-moving electrons, and so summation of eq. (1) is replaced for the electrons by integration over the average electronic density $\rho(\mathbf{r}')$:

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|} \quad (4)$$

Z_A is the charge on nucleus A, located at \mathbf{R}_A . In eq. (4), the denominators are the distances from the point \mathbf{r} to each nucleus A and to each element of electronic charge $\rho(\mathbf{r}')d\mathbf{r}'$.

An important feature of both the electronic density and the electrostatic potential is that they are real physical properties, *observables*. They can be determined experimentally, by diffraction methods,²⁵⁻²⁷ as well as computationally. This distinguishes them from defined properties such as atomic charges and bond orders, which are not physical observables.

In analyzing and interpreting a molecule's noncovalent interactions, $V(\mathbf{r})$ is now commonly computed on the molecule's "surface;" following the suggestion of Bader *et al.*,²⁸ this is frequently taken to be an outer contour of the molecule's electronic density, usually the 0.001 au. Using an electronic density contour to define the surface has the advantage that it reflects the specific features of the particular molecule, *e.g.* lone pairs, atomic anisotropy, π electrons, *etc.* It has been demonstrated that the 0.001 au contour typically lies beyond the van der Waals radii of the atoms in the molecule,²⁹ so that $V(\mathbf{r})$ on this surface is relevant to the onset of noncovalent interactions.

A word about units: It has long been customary to report $V(\mathbf{r})$ in energy units, *e.g.* kcal/mol, rather than units of potential, *e.g.* volts. We shall follow this well-established procedure. When given in energy units, $V(\mathbf{r})$ corresponds to the interaction energy with a +1 point charge located at \mathbf{r} .

When plotted on an outer contour of the electronic density (typically the 0.001 au), $V(\mathbf{r})$ is labeled $V_S(\mathbf{r})$ and its most positive and most negative values on this contour, of which there may be several, are designated as the $V_{S,\max}$ and $V_{S,\min}$, respectively. In general, regions of positive (negative) $V_S(\mathbf{r})$ are expected to interact attractively with negative (positive) sites.

Electrostatic potentials: Some words of caution

There is clearly a relationship between the electrostatic potential and the electronic density, as shown by eq. (4). However there is a fundamental and very significant difference between these two properties. $\rho(\mathbf{r})$ depends explicitly only on the point \mathbf{r} . In contrast, $V(\mathbf{r})$ is the result of integrating over the whole space of the molecule, and it also explicitly reflects the contributions of all of the nuclei as well as all of the electrons. Since the nuclear charges are concentrated rather than dispersed like those of the electrons, the former are sometimes unexpectedly dominant. For instance, the electrostatic potential of a neutral spherically-symmetrical ground-state atom is positive everywhere,³⁰ despite the number of electrons being equal to the nuclear charge. The effect of the nucleus prevails over that of the electrons. Another example is the bond regions of molecules; these generally feature buildups of electronic density,^{27,31,32} yet the electrostatic potentials in these regions are usually positive^{26,33,34} due to the nearby nuclei. Accordingly it should not be assumed, as is often done, that regions with positive $V(\mathbf{r})$ are “electron-poor” while negative $V(\mathbf{r})$ implies “electron-rich.” This ignores the contributions of the nuclei, as has been discussed on several occasions.³⁵⁻⁴⁰

It is also very important to stress the role of polarization. Electrostatic potentials are generally computed for molecules in their unperturbed ground states. However as soon as a molecule comes into the vicinity of another molecule (or atom, ion, *etc.*), the charge distribution of each begins to undergo some polarization in response to the electric field of the other. This increases as they approach, with the consequence that their ground-state electrostatic potentials gradually become less meaningful, although strongly-positive and strongly-negative regions continue to be relevant. Polarization is an intrinsic part of a Coulombic interaction.⁴¹⁻⁴⁶ It is inherently stabilizing, and will sometimes make possible a favorable interaction that would have appeared to be prohibited on the basis of the ground state electrostatic potentials. For instance, the π region of 1,4-difluorobenzene has a weakly negative potential, yet it interacts attractively

with the lone pair of the nitrogen of HCN;³⁷ the π region of 1,3,5-trifluorobenzene has a weakly positive potential but interacts attractively with the acidic hydrogen of HCN. These and other examples show that weakly unfavorable electrostatic potentials can sometimes be overcome by polarization.^{35-39,41-46}

Finally we want to point out that the labels $V_{S,\max}$ and $V_{S,\min}$ refer specifically to the local maxima and minima of $V(\mathbf{r})$ on a specified outer contour of the molecular electronic density. They are not global local maxima and minima of the electrostatic potential. In fact, while a molecule's electrostatic potential can have one or more global minima, it has been proven that the only global maxima are by the nuclei.⁴⁷ Thus while $V_{S,\max}$ and $V_{S,\min}$ on the 0.001 au contour have proven to be very useful indicators of the relative strengths of positive and negative potentials on molecular surfaces, they should not be viewed as global positive and negative sites. One of our specific aims in this study of the electrostatic potentials arising from σ -holes has been to assess the relevance of the $V_{S,\max}$ on 0.001 au molecular surfaces to the actual interactions. Note that all $V_{S,\max}$ presented and discussed in this paper will be on the 0.001 au contours, except where otherwise specified.

Origins of σ -holes

The σ -hole concept evolved within the context of halogen bonding.¹⁷ This was *fortunate* in that it is more straightforward for univalent halogens. It was also *unfortunate* in that the concept is more straightforward for univalent halogens; its extension to other Groups can be misleading if not done cautiously, as will be demonstrated.

What is the origin of the regions of positive electrostatic potential that are found on many covalently-bonded atoms, on the extensions of the bonds? Any ground state neutral atom has, on the average, a spherically-symmetrical charge distribution,⁴⁸ and this produces an electrostatic potential that is positive everywhere.³⁰ What is new, therefore, is the development of regions of negative potential, if this occurs. These must result from the interactions to form bonds.

These interactions involve the polarization and rearrangement of the atoms' electronic densities, some moving into the bond regions, some possibly forming lone pairs on lateral sides of the atoms, *etc.* The atoms' electronic densities thus become anisotropic. This is readily apparent in density difference plots that compare a molecule's electronic density to that of the

superposed free atoms.^{27,31,32} In particular, the electronic density on the side of an atom opposite to a covalent bond (along its extension) is generally less than in other nonbonding directions from the nucleus.^{12,15,49-56}

The term σ -hole refers to this region of lower electronic density opposite to a covalent bond, approximately on the extension of the bond. There is usually (but not always) a positive electrostatic potential associated with this lower electronic density, *i.e.* with a σ -hole, as was found initially by Brinck *et al* for univalent halogens.^{1,2} It is through this positive potential that attractive interactions with negative sites occur.

For example, Figure 1 shows the computed electrostatic potential on the 0.001 au surface of FSeI. The outer side of the iodine, opposite to the Se-I bond, is positive, with negative potentials on its lateral sides, Figure 1(a). The presence of an iodine σ -hole is indicated by the fact that the distance from the iodine nucleus to the 0.001 au contour along the extension of the Se-I bond is 2.21 Å, less than the distance to the lateral sides of the iodine, 2.44 Å. This shows that there is less electronic density along the extension of the bond. [All calculations carried out in this work were at the density functional M06-2X/6-311G(d) level, using Gaussian 09;⁵⁷ electrostatic potentials were obtained with the WFA-SAS code.⁵⁸]

In Figure 1(b) can be seen positive potentials on the selenium that are opposite to the F-Se and I-Se bonds. These are confirmed to reflect selenium σ -holes; the distances to the 0.001 au contour along the extensions of the F-Se and I-Se bonds, 2.02 Å and 2.05 Å respectively, are less than the distances to the negative surfaces above and below the selenium nucleus, 2.37 Å.

Note that both the iodine and the selenium can also interact favorably with positive sites, the iodine through the negative potentials on its lateral sides and the selenium through the negative potentials above and below the molecular plane. The ability of covalently-bonded atoms to interact in different directions with both positive and negative sites (electrophiles and nucleophiles) was observed many years ago in surveys of crystal structures, for halogens by Murray-Rust *et al.*⁵⁹⁻⁶¹ and for sulfur and selenium by Parthasarathy *et al.*^{52,54,62} For further discussion of this, with examples, see Politzer *et al.*^{63,64}

Univalent halogen atoms are on the peripheries of molecules and the larger ones (chlorine, bromine and iodine) often protrude somewhat from the molecular frameworks, with only one close neighbor (the atom to which they are bonded). As a result of the relatively isolated positions of univalent halogens, their electrostatic potentials tend to be less affected by other

portions of their molecules than is the case for atoms with several bonding partners. One consequence of this is that the regions of positive potential of univalent halogens are usually quite close to the extensions of the bonds to the halogen atoms. In FSeI, for instance, the positive potential opposite to the Se-I bond is essentially along the extension of that bond; the most positive value on the 0.001 au contour, the $V_{S,max}$ of 29 kcal/mol, deviates from the bond extension by only 3°.

In contrast to the halogens, covalently-bonded Group IV-VI atoms are linked to four, three and two other atoms (or more if hypervalent), and are therefore enclosed within the frameworks of the molecules. This means that the electrostatic potentials of the Group IV-VI atoms are much more likely to reflect contributions from other parts of the molecules and will often diverge somewhat from the extensions of the bonds that gave rise to the σ -holes. In F₂PCl, for example, the three phosphorus $V_{S,max}$ on the extensions of the two F-P and the Cl-P bonds deviate from them by 17°, 17° and 22°, respectively.

The additional bonds in which Group IV-VI atoms are involved also result in another difference from halogens. The positive potentials on univalent halogens are usually surrounded, or nearly surrounded as in Figure 1(a), by negative potentials.^{1,2,15,64,65} This is what allows directional interactions with both negative and positive sites.^{59-61,63-65} However as more of an atom's valence electrons are involved in covalent bonds, the negative regions on its surface become less extensive, now primarily reflecting the atom's lone pairs (if any). Thus while Group VI and to a lesser extent Group V atoms are still able to have directional interactions of both types,^{52,54,62,63} tetrahedrally-bonded Group IV atoms have no negative surface potentials;²⁰ their valence electrons are all in bonds.

Strengths of electrostatic potentials associated with σ -holes of Group IV-VII atoms

What determines the magnitude of the electrostatic potential associated with a σ -hole? For halogens, some generalizations can be made. For a molecule R-X, where X is a halogen, the strength of the positive potential appears to be related to (a) the polarizability and the electronegativity of X and (b) the electron-attracting power of R. If R is held constant, then the more polarizable and less electronegative is X, the more positive will be the potential due to its σ -hole.^{64,65}

Table 1 lists the values of the 0.001 au $V_{S,max}$ corresponding to the σ -holes of some covalently-bonded halogen atoms. Note, for instance, that the $V_{S,max}$ of the XCN and the H_3CX molecules increase as X goes from fluorine to iodine. Iodine is the most polarizable and least electronegative of the halogens, and so iodides tend to have the most positive potentials and form the strongest halogen bonds. This is why much of the crystal engineering involving halogen bonding has been with iodides.⁶⁶⁻⁶⁹ The R portions of the molecules were often fluorinated, to make the iodine potentials even more positive, since a halogen's positive potential increases as the remainder of the molecule is more electron-attracting. For example, the $V_{S,max}$ of the cyanohalides, XCN, are much greater than those of the corresponding methyl halides, H_3CX , because the cyano group is so strongly electron-attracting.

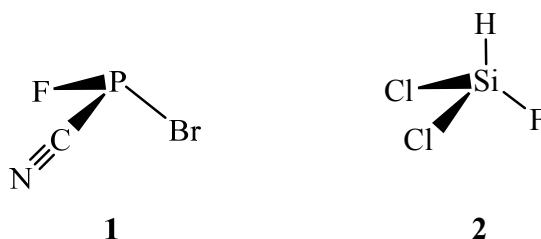
Fluorine, the least polarizable and most electronegative halogen, tends to have the least positive potentials; in fact the potentials due to its σ -holes are often negative, although less so than the surrounding 0.001 au contour. The fluorines then have negative $V_{S,max}$.^{43,64} In Table 1, this is the case for H_3CF , C_6H_5F and H_3COF . Nevertheless these fluorines do have σ -holes; the distances from the fluorine nuclei to the 0.001 au contours along the extensions of the bonds are less than to the lateral sides of the fluorines by 0.03 Å, 0.04 Å and 0.08 Å, respectively. However when the remainder of the molecule is strongly electron-attracting, as in FCN or FOF, then the σ -hole of a fluorine does have a positive potential (Table 1).⁷⁰⁻⁷²

We will proceed now to the $V_{S,max}$ on the 0.001 au surfaces of atoms having increasing numbers of covalent bonds. In Table 2 is Group VI (two covalent bonds), in Table 3 is Group V (three) and in Table 4 is Group IV (four). We will focus only upon those $V_{S,max}$ that are relevant in the present context.

For atoms in the same Group, the relative values of the $V_{S,max}$ can sometimes again be explained simply in terms of polarizabilities and electronegativities, as for the halogens. Thus the $V_{S,max}$ increase in going from SF_2 to SeF_2 to TeF_2 , as the Group VI atom becomes more polarizable and less electronegative. In $(H_3C)_2SiF_2$ and $(H_3C)_2GeF_2$, the $V_{S,max}$ opposite to the bonds to the more electronegative fluorines are more positive than those opposite to the bonds to the methyl groups.

On the other hand, there are numerous examples in which the polarizability/electronegativity explanation is inadequate, among them being:

- (a) In F_3SiCl , the silicon $V_{S,max}$ opposite to the bonds to the fluorines are less positive than the one opposite the bond to the less electronegative chlorine (Table 4).
- (b) Similarly, in F_2PCl , the phosphorus $V_{S,max}$ opposite to the bonds to the fluorines are less positive than that opposite the bond to the less electronegative chlorine (Table 3).
- (c) In $FPBr(CN)$, **1**, the phosphorus $V_{S,max}$ on the extensions of the F-P and Br-P bonds are 38 and 40 kcal/mol, respectively, even though fluorine is significantly more electronegative than bromine (Table 3). Furthermore, the $V_{S,max}$ on the extension of the NC-P bond is less than either of the above, despite the cyano group being much more electron-attracting than either fluorine or bromine.
- (d) In $Cl_2SiH(F)$, **2**, the silicon $V_{S,max}$ opposite to the Cl-Si bonds are slightly more positive than that opposite the bond to the more electronegative fluorine (Table 4).

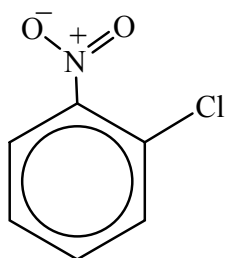
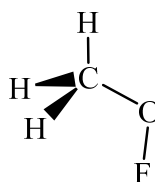


There are also inconsistencies when comparing the values for atoms in different Groups, as was discussed in earlier work.^{73,74} The $V_{S,max}$ of the difluorides of Se and Te (Table 2) are greater than the $V_{S,max}$ of the trifluorides of As and Sb (Table 3), even though the Group V atoms are more polarizable and less electronegative than the corresponding Group VI and have three electron-attracting fluorines instead of two. But the tetrafluorides of Si and Ge reverse the trend and have more positive $V_{S,max}$ than either the respective Group VI or Group V atoms (Table 4).

Overall, for Groups IV-VI, it seems fair to repeat our earlier conclusion:⁷⁴ “While reasonably reliable predictions of relative $V_{S,max}$ can often be made, in the final analysis the safest approach is to simply compute them.”

Locations of $V_{S,\max}$ associated with σ -holes of Group IV-VII atoms

Tables 1-4 also include the locations of the $V_{S,\max}$ of the Group IV-VII atoms relative to the extensions of the covalent bonds responsible for their σ -holes. It was already pointed out that the relatively isolated positions of the halogens, Group VII, diminishes the effects of the other portions of their molecules upon their σ -hole potentials. As a result, these are usually centered quite close to the extensions of the halogens' covalent bonds. Table 1 shows that the $V_{S,\max}$ on the 0.001 au surfaces are usually within 5° of the bond extensions. This is true even for *ortho*-chloronitrobenzene, **3**, in which it might be expected that the nearby oxygen would affect the chlorine $V_{S,\max}$. But its $V_{S,\max}$ is 1.91 Å beyond the chlorine nucleus, along the extension of the C-Cl bond; it is fully 3.93 Å from the closest oxygen nucleus.

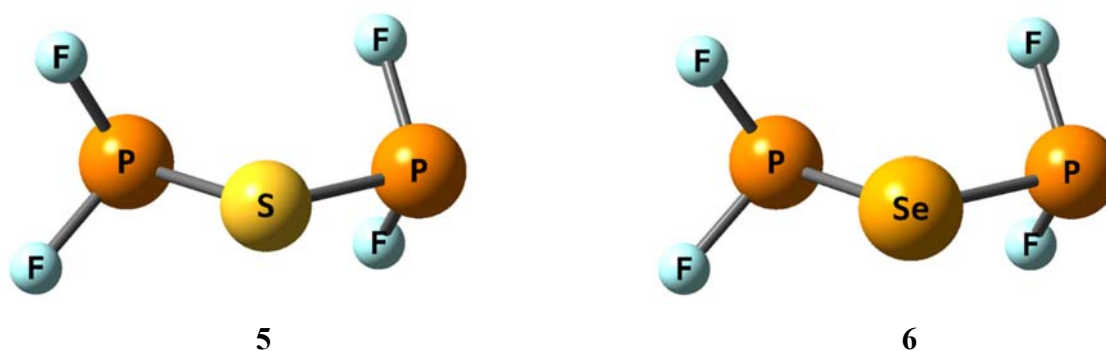
**3****4**

The greatest deviation shown by a halogen $V_{S,\max}$ in Table 1 is 10° , for the fluorine in H_3COF , **4**. This is because of the small size of the fluorine atom, which does not protrude from molecular frameworks as much as do the other halogens. The $V_{S,\max}$ of the fluorine in H_3COF is 3.45 Å from two hydrogen nuclei, and accordingly is somewhat influenced by them.

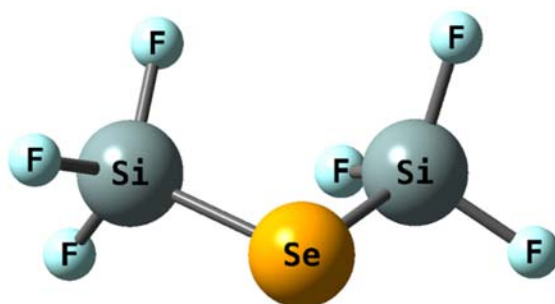
The overall effect of a second covalent bond, in Group VI, is to increase the deviations of the atoms' $V_{S,\max}$ from the extensions of the bonds (Table 2). Most of the deviations listed in the table are in the range 6° - 24° . The tendency is for the two $V_{S,\max}$ on the Group VI atom to move away from each other. Thus for the sulfide $BrS(CN)$, the sulfur $V_{S,\max}$ opposite to the $NC-S$ bond moves toward the bromine and the one opposite to the $Br-S$ bond toward the cyano group. This is because these $V_{S,\max}$, unlike those of halogens, are relatively close to other parts of the

molecule. Their separations from the bromine and the cyano carbon nuclei are just 2.50 Å and -2.15 Å, respectively.

Some molecules in Table 2 merit special consideration. Why do the two $V_{S,max}$ on the sulfur in $S(PF_2)_2$ have such different magnitudes, since they are both opposite to F_2P-S bonds? The same is observed for the selenium $V_{S,max}$ in $Se(PF_2)_2$. These are conformational issues. The optimized geometries of the two molecules are as shown in **5** and **6**. One $V_{S,max}$ on both the sulfur and the selenium is relatively close to the fluorines of a PF_2 group. The negative potentials of these fluorines overlap the nearby positive potentials on the sulfur and selenium and diminish the magnitudes of those $V_{S,max}$ (see Figure 2).



One may also ask: Why are there no $V_{S,max}$ on the selenium in $Se(SiF_3)_2$, on the extensions of the Si-Se bonds? This is because each positive region on the selenium overlaps with the positive region on a silicon opposite to one of the F-Si bonds [see the optimized structure **7** and Figure 3(a)]. The result is just a single $V_{S,max}$ for the overlapping regions. Because of the electronegativities of the fluorines, the potential associated with the F-Si bond dominates and this single $V_{S,max}$ is only 5° from the extension of the F-Si bond.



7

Proceeding to Group V, atoms with three covalent bonds, there is a further increase in the deviations of the atoms' $V_{S,max}$ from the extensions of the bonds. They are between 15° and 26° for nearly all of the molecules in Table 3. These larger deviations can be attributed to the pyramidal structures of the molecules, which result in the positive regions arising from their σ -holes all being on the same side of the molecule. There is accordingly considerable overlap of these positive potentials, and significant shifting of the $V_{S,max}$ away from the extensions of the bonds. Thus Figure 4 shows that the phosphorus in H_2PBr has a large and continuous positive region opposite to the Br-P and the two H-P bonds; it does have three $V_{S,max}$ but they diverge from the extensions of these bonds by 26° , 33° and 33° , respectively.

Finally, for Group IV, we find in Table 4 – perhaps surprisingly – that the deviations of the $V_{S,max}$ from the extensions of the bonds are almost as small as for the halogens, mostly between 0° and 8° . One reason for this may be that each $V_{S,max}$ is now within a cone formed by three atoms or groups; even when these are not all the same, their effects appear to partially cancel.

The $Se(SiF_3)_2$ molecule again needs further comment. It has a large number of atoms in a relatively small space; see structure 7 and Figure 3. This can be expected to significantly affect the values and locations of the $V_{S,max}$. We have already mentioned the overlapping of selenium and silicon positive potentials, resulting in single $V_{S,max}$ opposite to F-Si bonds. Now Table 4 and Figure 3(b) reveal a very striking anomaly: The $V_{S,max}$ on the right silicon (in the green region) that is roughly opposite to an F-Si bond diverges from the extension of that bond by 35° ; this is a much greater divergence than any other in Table 4. [There is an analogous $V_{S,max}$ on the left silicon surface which is not visible in Fig. 3(b).] These large divergences are simply due to the structure of the molecule, the crowding of the atoms in its central portion and their mutual effects upon each other's electrostatic potentials on the 0.001 au molecular surface.

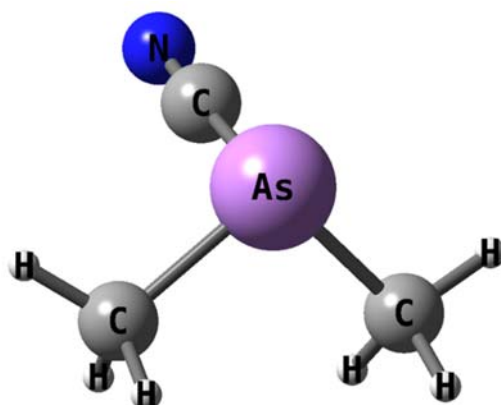
In summary, Tables 1-4 show that as the intramolecular environment of an atom becomes more crowded and less symmetrical, the positive potential arising from its σ -hole will be more affected by its neighbors and may deviate quite significantly from the extension of the bond that gave rise to the σ -hole. In some instances, *e.g.* the selenium in $Se(SiF_3)_2$, an anticipated $V_{S,max}$ may not even appear. Some interesting examples of this will be given in a later section dealing with heterocyclic molecules.

Variation of $V_{S,max}$ with contour of electronic density

The effects of nearby atoms upon the electrostatic potential associated with a σ -hole can be seen by computing the potential on different outer contours of the electronic density. We have done this for some covalently-bonded atoms of Group VI and Group V, since these have the largest deviations from the extensions of the bonds (Tables 2 and 3). For two molecules from each of these Groups, Table 5 presents the values and locations of the σ -hole $V_{S,max}$ on a series of different contours, some with magnitudes greater than 0.001 au and others with magnitudes less than 0.001 au. For each contour is given the deviation of the $V_{S,max}$ from the extension of the covalent bond that gave rise to it and its distance from the nucleus of the atom.

Contours with magnitudes larger than 0.001 au are closer to the nuclei of the molecule and so the σ -hole $V_{S,max}$ becomes more positive. Usually it is also more subject to the influence of nearby atoms, which causes it to increasingly deviate from the extension of the bond. Contours with magnitudes smaller than 0.001 au are farther from the nuclei; their $V_{S,max}$ become less positive and usually less subject to the influence of nearby atoms, so that they deviate less from the extension of the bond.

Table 5 includes one molecule, $(H_3C)_2AsCN$, that is an exception to these general tendencies. The spatial extent of the methyl groups, shown in optimized structure **8**, is such that the $V_{S,max}$ on the extension of the NC-As bond is affected by them roughly equally for all of the contours considered. The deviation of the $V_{S,max}$ from the extension of the bond simply fluctuates within the range 156° - 160° .



8

Locations of $V_{S,max}$ of heterocyclic molecules

In Table 6 are eight heterocyclic molecules, labeled **9-16**. In **9-13** the rings are four-membered and planar, in **14** and **15** they are four-membered but puckered, and in **16** the ring is five-membered and planar. The computed electrostatic potentials on the 0.001 au surfaces of all of these molecules except **14** are displayed in the indicated references.

For **14**, the electrostatic potential on the 0.001 au surface is in Figure 5. It might be anticipated that each of the sulfur and phosphorus atoms that constitute the ring would have two $V_{S,max}$ corresponding to its two bonds within the ring, for a total of eight $V_{S,max}$ associated with the ring. Instead Figure 5 reveals only four ring $V_{S,max}$, and they are located *between* the extensions of the bonds linking the sulfur and phosphorus atoms. There is one such $V_{S,max}$ on each side of the ring, and they deviate by 41° from the bonds to the sulfurs and by about 29° from the bonds to the phosphorus atoms (Table 6).

Analogous situations are found in **9-13** and **15**. Each of them has just four $V_{S,max}$ associated with the ring, and the deviations of these from the extensions of the respective bonds, given in Table 6, indicate that most of the $V_{S,max}$ are somewhere between the bond extensions.

These observations can be explained by recalling that the $V_{S,max}$ of Group VI and Group V atoms tend to diverge significantly from their bond extensions (Tables 2 and 3), as do also the $V_{S,max}$ of Group IV atoms to a small extent (Table 4). These tendencies promote overlapping of the positive potentials of the neighboring atoms of the rings, which results in just one $V_{S,max}$ between each pair of neighbors. Note, in **9-13**, that the $V_{S,max}$ usually diverge less from the bonds to the Group IV atoms (carbons and silicons) than from the bonds to the Group VI (sulfurs and seleniums). In **13**, the divergences from the bonds to the Group IV silicons are only 4° . In **9**, **10** and **13**, the dominance of the Group IV atoms' positive potentials is promoted by the highly electronegative fluorines on these atoms.

The molecule with the five-membered ring, **16**, has an interesting feature. Because of the shape of the ring, the extensions of the bonds to adjacent carbon atoms intersect. There are $V_{S,max}$ located essentially at the three points of intersection. Thus these three $V_{S,max}$ are simultaneously on the extensions of two different bonds, deviating from these by only 2° - 4° . Each of these $V_{S,max}$ can be regarded as associated with σ -holes on two adjacent carbons.

There are also two $V_{S,max}$ corresponding to the overlap of each of the two positive regions on the sulfur with the positive potential of its neighboring carbon. The contributions of the carbons, each bearing two fluorines, are again the stronger ones since these two $V_{S,max}$ deviate by only 4° from the extensions of the C-C bonds but by 22° from the extensions of the C-S.

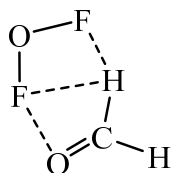
$V_{S,max}$ and noncovalent interactions

It was emphasized earlier that $V_{S,max}$ are local maxima only on the specified contours of the electronic density, not globally, and therefore are not really positive sites. The only positive sites in a molecule in a global sense are the nuclei.⁴⁷ To what extent, therefore, are the $V_{S,max}$ on the widely-used 0.001 au contours of individual (*i.e.* gas phase) molecules related to the strengths and directionalities of noncovalent interactions?

In addressing this, we point out first that in the gas phase, the strengths of the interactions with a given negative site correlate quite well with the magnitudes of the 0.001 au $V_{S,max}$.^{65,73,77,78} Furthermore, for a group of 20 complexes involving the positive regions of various Group IV-VII atoms and the nitrogen lone pairs of HCN and NH₃, the computed interaction energies plotted against the product of the $V_{S,max}$ and the respective nitrogen $V_{S,min}$ (prior to interaction) had an R^2 of 0.96.⁷⁸ The interactions become stronger as $V_{S,max}$ is more positive and $V_{S,min}$ more negative.

Proceeding to directionality, we have already noted that univalent halogens are usually on the peripheries of molecules, so that their positive potentials and their $V_{S,max}$ are little influenced by intramolecular effects. They are generally quite close to the extensions of the bonds to the halogens (Table 1). Accordingly, as is shown in Table 7, gas phase halogen bonding interactions are often nearly linear;^{64,65} in a complex R-X---B, in which X is a halogen and B is a negative site, the R-X---B angle is usually close to 180° . However this near-linearity can be affected by secondary interactions involving other portions of R-X and B. Halogen bonds to formaldehyde, for instance, are often accompanied by secondary attractive interactions between a formaldehyde hydrogen and a negative lateral side of the halogen atom. These result in the R-X---O angles being $167^\circ - 173^\circ$ for the complexes H₃C-X---O=CH₂ (X = Cl, Br and I),^{64,79} and 151° for FO-F---O=CH₂ (structure **17**).⁷² The deviation from linearity of the F---O halogen

bond is particularly large in **17** because the upper hydrogen can interact attractively with both fluorines, as shown.



17

For atoms of Groups VI and V, Tables 2 and 3 show that the $V_{S,max}$ generally deviate significantly from the extensions of the bonds and, by Table 7, the gas phase interactions are correspondingly nonlinear. For the molecules in Table 7, the nonlinearities are somewhat less than the deviations of the $V_{S,max}$ prior to the interactions, possibly reflecting secondary interactions between other portions of the two molecules. In H_2AsF , for instance, the $V_{S,max}$ diverges from the extension of the F-As bond by 22° but in the interaction with NH_3 the nonlinearity of the F-As---N bond is just 15° .

Group IV is more like the halogens. The $V_{S,max}$ are close to the extensions of the bonds (Table 4) and the interactions are near-linear (Table 7).

In the gas phase, therefore, the $V_{S,max}$ on the 0.001 au contours are indicative of the strengths of the interactions and are approximately consistent with their directionalities: Table 7 shows that larger deviations of $V_{S,max}$ result in greater nonlinearities of the interaction angles; smaller deviations result in lesser nonlinearities. What is the situation with respect to directionality in crystalline phases? We shall look at some examples.

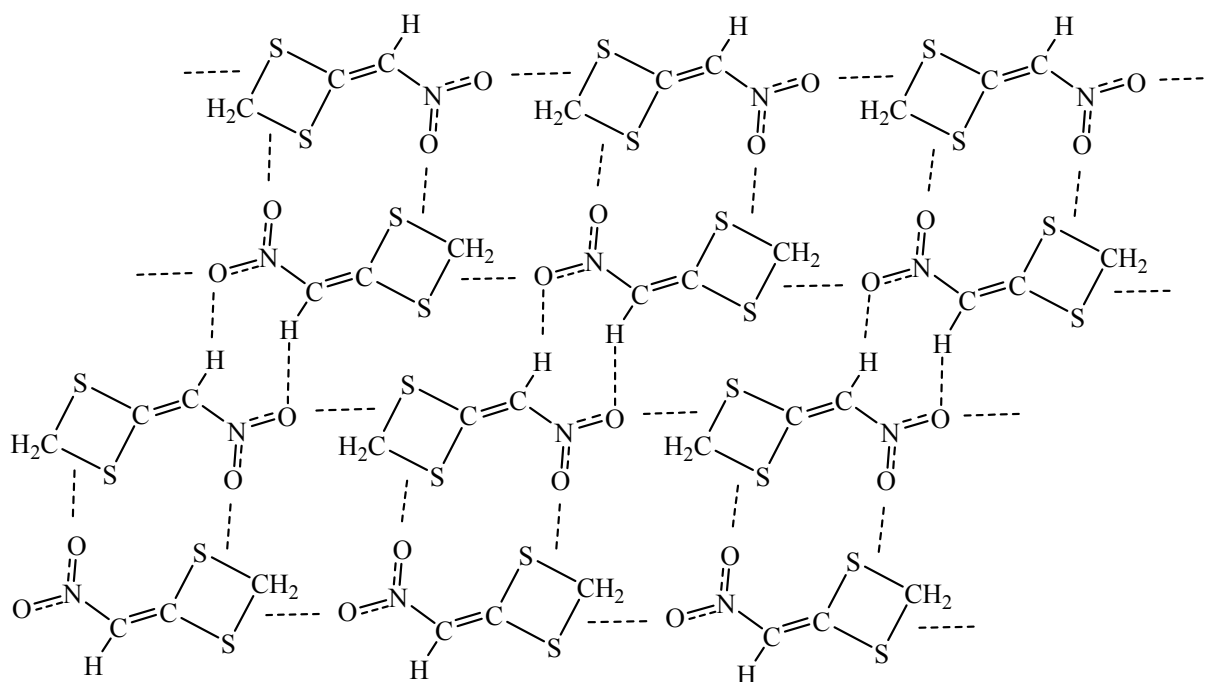
In crystal lattices, the proximities of other molecules increase the likelihood of secondary effects. Surveys of crystal structures for halides by Murray-Rust *et al.*⁵⁹⁻⁶¹ and for sulfides by Parthasarathy *et al.*^{52,62} found most intermolecular interactions to be within 15° of linearity, but greater nonlinearities were common, especially for chlorine. Some other observations:

- (a) The crystal lattices of selenium cyanide and tellurium cyanide consist of networks of $Se(CN)_2$ and $Te(CN)_2$ molecules linked through NC-Se---NC-Se and NC-Te---NC-Te interactions, respectively.^{80,81} The C-Se---N angles diverge from linearity by about 14° and 10° , quite consistent with the deviation of the $V_{S,max}$ of selenium in $Se(CN)_2$ from the extensions of the C-Se bonds by 11° (Table 2). Similarly, the C-Te---N angles in

Te(CN)₂ diverge from linearity by about 17°, which exactly agrees with the deviations of the $V_{S,max}$ of tellurium from the extensions of the C-Te bonds.

- (b) Scilabra *et al.* have presented the crystal structures of complexes in which SbF₃ is linked to various organic bases B through F-Sb---B interactions.⁸² The F-Sb---B angles are nonlinear by 15° – 27°. From Table 3, the antimony $V_{S,max}$ in SbF₃ deviate from the extensions of the F-Sb bonds by 25°, which is within the range of the observed nonlinearities but near its upper end.
- (c) The crystal structure of FSb(C₆H₅)₂ features F-Sb---F interactions, the F-Sb---F angle being nonlinear by 15°.⁸² The deviation of the antimony $V_{S,max}$ from the extension of the F-Sb bond is somewhat greater, 26° (Table 3).
- (d) In complexes between SiF₄ and two nitrogen bases (2,2'-dipyridyl and a diamine), which involve F-Si---N interactions, the F-Si---N angles are nonlinear by about 9° and 6°.⁸² The silicon $V_{S,max}$ deviate by 2° from the extensions of the F-Si bonds (Table 4).
- (e) The crystal structure of (H₃C)₃GeCN is comprised of linear chains of molecules, “with the cyanide group in one molecule pointing directly toward the germanium atom in the next.”⁸³ In good agreement with this, the germanium $V_{S,max}$ deviates by only 2° from the extension of the NC-Ge bond (Table 4).
- (f) A particularly interesting example involves the crystal structure of the heterocyclic compound **12**. As indicated in Table 6, the only $V_{S,max}$ associated with the four-membered ring are located *between* the extensions of the bonds that form the ring. In the crystal lattice, each four-membered ring is interacting with nitro oxygens from each of two neighboring molecules,⁸⁴ as shown in structure **18**. The positions of these oxygens are consistent with the interactions involving positive regions that are between the extensions of the ring bonds, as indicated by the locations of the $V_{S,max}$. Note that each molecule is also participating in two O---H hydrogen bonds, as shown between the second and third rows in **18**.

These examples suggest that the $V_{S,max}$ on 0.001 au contours may often provide some *qualitative* insight into the directionalities of noncovalent interactions in crystalline phases.



18

Discussion and summary

A σ -hole is a feature of the electronic density of a covalently-bonded atom in a molecule. It is a region of lower electronic density on the side of the atom opposite to the bond, approximately along the extension of that bond, and is a consequence of the rearrangement of electronic density that accompanies the formation of the bond. A σ -hole often gives rise to a positive electrostatic potential, through which the atom can interact attractively (noncovalently) with negative sites.

However this positive potential, given rigorously by eq. (4), reflects not only the lower electronic density of the σ -hole but also contributions from the electrons and nuclei of the entire molecule. These can considerably affect the magnitude and the location of the positive potential. In particular, they may cause the strongest portion of it to deviate to some extent from the extension of the bond that resulted in the σ -hole.

For univalent halogens, such intramolecular effects are usually relatively unimportant because a halogen atom normally has only one close neighbor within a molecule (the atom to which it is bonded). Atoms of Groups IV-VI, on the other hand, have two or more bonds and are

embedded within the molecular frameworks, making their σ -hole potentials more subject to contributions from other portions of their own molecules.

A common practice is to plot the electrostatic potential of a molecule on an outer contour of its electronic density, usually the 0.001 au, and to locate the most positive values associated with the σ -holes. These are labeled the $V_{S,\max}$. It is important to realize, however, that these are not global maxima of the potential; they are simply local maxima on the 0.001 au contour.

Accordingly they do not correspond to global positive sites.

Since the positive potentials of univalent halogens are often little influenced by intramolecular effects, their $V_{S,\max}$ on the 0.001 au contours tend to be close to the extensions of the bonds to the halogen atoms (Table 1). In contrast, the 0.001 au $V_{S,\max}$ of atoms of Groups IV-VI may deviate significantly from the extensions of the bonds (Tables 2-4 and Table 6). This is especially likely for Groups V and VI.

The importance of intramolecular effects is illustrated by determining the $V_{S,\max}$ for contours other than the 0.001 au (Table 5). On contours of higher values, which are closer to the central portion of the molecule, the deviations of the $V_{S,\max}$ from the extensions of the bonds usually increase, as they are more influenced by the other nuclei and electrons. In going to contours of lower values, which are farther out, these influences generally diminish and the $V_{S,\max}$ on these contours usually approach the extensions of the bonds.

It is accordingly reasonable to ask whether the 0.001 au contour in particular is relevant to analyzing noncovalent interactions. We respond as follows:

- (a) The $V_{S,\max}$ on 0.001 au contours tend to be about 0.2 Å beyond typical van der Waals radii.²⁹ This seems appropriate for the early stages of noncovalent interactions, particularly since both Dance⁸⁵ and Alvarez⁸⁶ have argued convincingly that a significant number of noncovalent interactions are at separations greater than the sums of these van der Waals radii.
- (b) The magnitudes of the $V_{S,\max}$ on 0.001 au contours correlate well with the interaction energies of complex formation in the gas phase.^{65,73,78}
- (c) It has been demonstrated that the detailed features of the electrostatic potentials on 0.001 au molecular surfaces can be related quantitatively to a variety of condensed phase properties that depend upon noncovalent interactions.^{87,88} Such properties include heats

of phase transitions, boiling points and critical constants, partition coefficients, viscosities, solubilities and solvation energies, diffusion constants, *etc.*

- (d) In the gas phase, the 0.001 au $V_{S,max}$ are qualitatively correct in indicating that the interactions of Group IV and the halogens with negative sites will frequently be close to linear, while those of Groups V and VI are likely to deviate to some extent from linearity. To a lesser degree, these observations also apply in crystalline phases.

We conclude this “revisit” of the σ -hole by emphasizing that while the positive potentials that have been discussed originate with σ -holes, *it is the potentials – not the σ -holes – that are responsible for halogen bonding and the analogous interactions of Group IV-VI atoms.* As shown rigorously by the Hellmann-Feynman theorem,^{89,90} the interactions are Coulombic – which includes electrostatics and polarization (and encompasses dispersion, as was demonstrated explicitly by Feynman⁹⁰).

References

1. T. Brinck, J. S. Murray and P. Politzer, *Int. J. Quantum Chem.*, 1992, **44**(Suppl. 19), 57-64.
2. T. Brinck, J. S. Murray and P. Politzer, *Int. J. Quantum Chem.*, 1993, **48**(Suppl. 20), 73-88.
3. P. Kollman, *J. Am. Chem. Soc.*, 1977, **99**, 4875-4894.
4. F. Guthrie, *J. Chem. Soc.*, 1863, **16**, 239-244.
5. I. Remsen and J. F. Norris, *Am. Chem. J.*, 1896, **18**, 90-96.
6. H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2703-2727.
7. O. Hassel and C. Rømming, *Q. Rev. Chem. Soc.*, 1962, **16**, 1-18.
8. H. A. Bent, *Chem. Rev.*, 1968, **68**, 587-648.
9. T. Di Paolo and C. Sandorfy, *Can. J. Chem.* 1974, **52**, 3612-3622.
10. J.-M. Dumas, M. Kern and J. L. Janier-Dubry, *Bull. Soc. Chim. Fr.*, 1976, 1785-1787.
11. S. C. Blackstock, J. P. Lorand and J. K. Kochi, *J. Org. Chem.*, 1987, **52**, 1451-1460.
12. J. P. M. Lommerse, A. J. Stone, R. Taylor, F. H. Allen, *J. Am. Chem. Soc.*, 1996, **118**, 3108-3116.

13. P. Auffinger, F. A. Hays, E. Westhof and P. Shing Ho, *Proc. Natl. Acad. Sci. U.S.A.*, 2004, **101**, 16789-16794.
14. F. Zordan, L. Brammer and P. Sherwood, *J. Am. Chem. Soc.*, 2005, **127**, 5979-5989.
15. F. F. Awwadi, R. D. Willett, K. A. Peterson and B. Twamley, *Chem.-Eur. J.*, 2006, **12**, 8952-8960.
16. *Modeling Interactions in Biomolecules II*, Prague, Sept. 5-9, 2005.
17. T. Clark, M. Hennemann, J. S. Murray and P. Politzer, *J. Mol. Model.*, 2007, **13**, 291-296.
18. J. S. Murray, P. Lane and T. Clark, *J. Mol. Model.*, 2007, **13**, 1033-1038.
19. J. S. Murray, P. Lane and P. Politzer, *Int. J. Quantum Chem.*, 2007, **107**, 2286-2292.
20. J. S. Murray, P. Lane and P. Politzer, *J. Mol. Model.*, 2009, **15**, 723-729.
21. P. Politzer, J. S. Murray and T. Clark, *Phys. Chem. Chem. Phys.*, 2013, **15**, 11178-11189.
22. P. Politzer, J. S. Murray, G. V. Janjić and S. D. Zarić, *Crystals*, 2014, **4**, 12-31.
23. A. Bauzá, T. J. Mooibroek and A. Frontera, *ChemPhysChem*, 2015, **16**, 2496-2517.
24. P. Metrangolo and G. Resnati, *Cryst. Growth Des.*, 2012, **12**, 5835-5838.
25. R. F. Stewart, *Chem. Phys. Lett.*, 1979, **65**, 335-342.
26. *Chemical Applications of Atomic and Molecular Electrostatic Potentials*, ed. P. Politzer and D. G. Truhlar, Plenum Press, New York, 1981.
27. C. L. Klein and E. D. Stevens, in *Structure and Reactivity*, eds. J. F. Liebman and A. Greenberg, VCH, New York, 1988, ch. 2, pp. 25-64.
28. R. F. W. Bader, M. T. Carroll, J. R. Cheeseman and C. Chang, *J. Am. Chem. Soc.*, 1987, **109**, 7968-7979.
29. J. S. Murray and P. Politzer, *Croat. Chem. Acta*, 2009, **82**, 267-275.
30. K. D. Sen and P. Politzer, *J. Chem. Phys.*, 1989, **90**, 4370-4372.
31. P. Coppens, *Angew. Chem. Int. Ed.*, 1977, **16**, 32-40.
32. D. Feil, *Chem. Scripta*, 1986, **26**, 395-408.
33. P. Politzer and K. C. Daiker, in *The Force Concept in Chemistry*, ed. B. M. Deb, Van Nostrand Reinhold, New York, 1981, ch. 6, pp. 294-387.
34. P. Politzer and J. S. Murray, in *Reviews in Computational Chemistry*, vol. 2, eds. K. B. Lipkowitz and D. B. Boyd, VCH, New York, 1991, ch. 7, pp. 273-312.

35. S. E. Wheeler and K. N. Houk, *J. Chem. Theory Comput.*, 2009, **5**, 2301-2312.
36. S. E. Wheeler and J. W. G. Bloom, *J. Phys. Chem. A*, 2014, **118**, 6133-6147.
37. J. S. Murray, Z. P.-I. Shields, P. G. Seybold and P. Politzer, *J. Comput. Sci.*, 2015, **10**, 209-216.
38. J. S. Murray and P. Politzer, *WIREs Comput. Mol. Sci.*, 2017, DOI: 10.1002/wcms.1326.
39. P. Politzer and J. S. Murray, *J. Comput. Chem.*, 2017, DOI: 10.1002/jcc.24891.
40. P. Politzer and J. S. Murray, *Crystals*, 2017, **7**, 212(1-14).
41. P. Politzer, K. E. Riley, F. A. Bulat and J. S. Murray, *Comput. Theoret. Chem.*, 2012, **998**, 2-8.
42. T. Clark, J. S. Murray and P. Politzer, *Aust. J. Chem.*, 2014, **67**, 451-456.
43. P. Politzer, J. S. Murray and T. Clark, *Top. Curr. Chem.*, 2015, **358**, 19-42.
44. T. Clark, P. Politzer and J. S. Murray, *WIREs Comput. Mol. Sci.*, 2015, **5**, 169-177.
45. P. Politzer, J. S. Murray and T. Clark, *J. Mol. Model.*, 2015, **21**, 52(1-10).
46. D. J. R. Duarte, G. L. Sosa, N. M. Peruchena and I. Alkorta, *Phys. Chem. Chem. Phys.*, 2016, **18**, 7300-7309.
47. R. K. Pathak and S. R. Gadre, *J. Chem. Phys.*, 1990, **93**, 1770-1773.
48. G. Delgado-Barrio and R. F. Prat, *Phys. Rev. A*, 1975, **12**, 2288-2297.
49. H. A. Bent, *Chem. Rev.*, 1968, **68**, 587-648.
50. E. D. Stevens, *Mol. Phys.*, 1979, **37**, 27-45.
51. V. G. Tsirelson, P. F. Zou, T.-H. Tang and R. F. W. Bader, *Acta Cryst.*, 1995, **A51**, 143-153.
52. T. N. Guru Row and R. Parthasarathy, *J. Am. Chem. Soc.*, 1981, **103**, 477-479.
53. S. C. Nyburg and C.H. Faerman, *Acta Cryst.*, 1985, **B41**, 274-279.
54. N. Ramasubbu and R. Parthasarathy, *Phosphorus Sulfur*, 1987, **31**, 221-229.
55. S. S. Batsanov, *Struct. Chem.*, 2000, **11**, 177-183.
56. H. Eramian, Y.-H. Tian, Z. Fox, H. Z. Beneberu and M. Kertesz, *J. Phys. Chem. A*, 2013, **117**, 14184-14190.
57. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, *et al.*, *Gaussian 09*, Revision A.1, Gaussian, Inc., Wallingford, CT, 2009.
58. F. A. Bulat, A. Toro-Labbé, T. Brinck, J. S. Murray and P. Politzer, *J. Mol. Model.*, 2010, **16**, 1679-1691.

59. P. Murray-Rust and W. D. S. Motherwell, *J. Am. Chem. Soc.*, 1979, **101**, 4374-4376.
60. P. Murray-Rust, W. C. Stallings, C. T. Monti, R. K. Preston and J. P. Glusker, *J. Am. Chem. Soc.*, 1983, **105**, 3206-3214.
61. N. Ramasubbu, R. Parthasarathy and P. Murray-Rust, *J. Am. Chem. Soc.*, 1986, **108**, 4308-4314.
62. R. E. Rosenfield, Jr., R. Parthasarathy and J. D. Dunitz, *J. Am. Chem. Soc.*, 1977, **99**, 4860-4862.
63. P. Politzer, J. S. Murray and M. C. Concha, *J. Mol. Model.*, 2008, **14**, 659-665.
64. P. Politzer, J. S. Murray and T. Clark, *Phys. Chem. Chem. Phys.*, 2010, **12**, 7748-7757.
65. P. Politzer and J. S. Murray, *ChemPhysChem*, 2013, **14**, 278-294.
66. T. Imakubo, H. Sawa and R. Kato, *Synth. Meth.*, 1995, **73**, 117-122.
67. V. Amico, S. V. Meille, E. Corradi, M. T. Messina and G. Resnati, *J. Am. Chem. Soc.*, 1998, **120**, 8261-8262.
68. P. Metrangolo, H. Neukirch, T. Pilati and G. Resnati, *Acc. Chem. Res.*, 2005, **38**, 386-395.
69. P. Metrangolo, F. Meyer, T. Pilati, G. Resnati and G. Terraneo, *Angew. Chem. Int. Ed.*, 2008, **47**, 6114-6127.
70. P. Politzer, J. S. Murray and M. C. Concha, *J. Mol. Model.*, 2007, **13**, 643-650.
71. D. Chopra and T. N. Guru Row, *CrystEngComm*, 2011, **13**, 2175-2186.
72. P. Metrangolo, J. S. Murray, T. Pilati, P. Politzer, G. Resnati and G. Terraneo, *Cryst. Growth Des.*, 2011, **11**, 4238-4246.
73. A. Bundhun, P. Ramasami, J. S. Murray and P. Politzer, *J. Mol. Model.*, 2013, **19**, 2739-2746.
74. J. S. Murray, L. Macaveiu and P. Politzer, *J. Comput. Sci.*, 2014, **5**, 590-596.
75. J. S. Murray, G. Resnati and P. Politzer, *Faraday Discussions*, 2017, **203**, 113-130.
76. S. K. Nayak, V. Kumar, J. S. Murray, P. Politzer, G. Terraneo, T. Pilati, P. Metrangolo and G. Resnati, *CrystEngComm*, 2017, **19**, 4955-4959.
77. K. E. Riley, J. S. Murray, J. Fanfrlík, J. Řezáč, R. J. Solá, M. C. Concha, F. M. Ramos and P. Politzer, *J. Mol. Model.*, 2011, **17**, 3309-3318.
78. P. Politzer, J. S. Murray and T. Clark, *Phys. Chem. Chem. Phys.*, 2013, **15**, 11178-11189.

79. K. E. Riley and P. Hobza, *J. Chem. Theory Comput.*, 2008, **4**, 232-242.
80. T. M. Klapötke, B. Krumm and M. Scherr, *Inorg. Chem.*, 2008, **47**, 7025-7028.
81. T. M. Klapötke, B. Krumm, J. C. Gálvez-Ruiz, H. Nöth and I. Schwab, *Eur. J. Inorg. Chem.*, 2004, 4764-4769.
82. P. Scilabra, G. Terraneo and G. Resnati, *J. Fluorine Chem.*, 2017, DOI: 10.1016/j.jfluchem.2017.10.002.
83. E. O. Schlemper and D. Britton, *Inorg. Chem.*, 1966, **5**, 511-514.
84. S. S. S. Raj, H. S. P. Rao, L. Sakthikumar and H.-K. Fun, *Acta Cryst.*, 2000, **C56**, 1113-1114.
85. I. Dance, *New J. Chem.*, 2003, **27**, 22-27.
86. S. Alvarez, *Dalton Trans.*, 2013, **42**, 8617-8636.
87. J. S. Murray and P. Politzer, *J. Mol. Struct. (Theochem)*, 1998, **425**, 107-114.
88. P. Politzer and J. S. Murray, *Fluid Phase Equil.*, 2001, **185**, 129-137.
89. H. Hellmann, *Einführung in die Quantenchemie*, 1937, Deuticke, Leipzig.
90. R. P. Feynman, *Phys. Rev.*, 1939, **56**, 340-343.

Table 1. Values and angular positions of 0.001 au $V_{S,max}$ associated with σ -holes of covalently-bonded halogen atoms (Group VII).

Molecule	Atom	$V_{S,max}$, kcal/mol	Deviation from extension of indicated bond, degrees
F ₂	F	11	F-F: 0
H ₃ CF	F	-25	C-F: 1
H ₃ CCl	Cl	-1	C-Cl: 1
H ₃ CBr	Br	6	C-Br: 1
H ₃ CI	I	13	C-I: 2
FCN	F	13	NC-F: 0
ClCN	Cl	36	NC-Cl: 1
BrCN	Br	43	NC-Br: 1
ICN	I	49	NC-I: 1
C ₆ H ₅ F	F	-16	C-F: 0
H ₃ COF	F	-10	O-F: 10
FOF	F	4	O-F: 1
FCl	Cl	45	F-Cl: 0
F ₃ CCl	Cl	20	C-Cl: 0
F ₂ PCl	Cl	5	P-Cl: 7
(Cl) ₂ SiH(F)	Cl	6	Si-Cl: 1
<i>o</i> -C ₆ H ₄ (Cl)(NO ₂)	Cl	11	C-Cl: 4
H ₂ PBr	Br	4	P-Br: 1
F ₃ CBr	Br	25	C-Br: 0
FAsBr(CN)	Br	16	As-Br: 6
FPBr(CN)	Br	18	P-Br: 3
FSeBr	Br	20	Se-Br: 5
FSBr	Br	23	S-Br: 4
BrS(CN)	Br	29	S-Br: 1
Br ₂ C=CBr ₂	Br	24	C-Br: 2
BrC≡CBr	Br	30	C-Br: 0
FBr	Br	53	F-Br: 0
FSeI	I	29	Se-I: 3

Table 2. Values and angular positions of 0.001 au $V_{S,max}$ associated with σ -holes of covalently-bonded atoms of Group VI. If the specified atom has two $V_{S,max}$ with the same values, this is indicated in parentheses.

Molecule	Atom	$V_{S,max}$, kcal/mol	Deviation from extension of indicated bond, degrees
SF ₂	S	40 (2)	F-S: 8
SeF ₂	Se	50 (2)	F-Se: 9
TeF ₂	Te	56 (2)	F-Te: 14
S(CN) ₂	S	44 (2)	NC-S: 11
Se(CN) ₂	Se	50 (2)	NC-Se: 11
Te(CN) ₂	Te	55 (2)	NC-Te: 17
S(CF ₃) ₂	S	25 (2)	F ₃ C-S: 17
Se(CF ₃) ₂	Se	28 (2)	F ₃ C-Se: 7
S(PF ₂) ₂	S	21,29	F ₂ P-S: 22
Se(PF ₂) ₂	Se	20,30	F ₂ P-Se: 30
HSF	S	46	F-S: 24
	S	14	H-S: 18
HSeF	Se	51	F-Se: 22
	Se	19	H-Se: 18
FSBr	S	36	F-S: 1
	S	27	Br-S: 10
FSeBr	Se	43	F-Se: 2
	Se	35	Br-Se: 7
FSeI	Se	43	F-Se: 3
	Se	29	I-Se: 9
BrS(CH ₃)	S	25	Br-S: 12
	S	4	H ₃ C-S: 6
BrS(CN)	S	34	Br-S: 9
	S	33	NC-S: 8
SeCl ₂	Se	36 (2)	Cl-Se: 3
Se(SiF ₃) ₂	Se	none	Si-Se: ---

Table 3. Values and angular positions of 0.001 au $V_{S,max}$ associated with σ -holes of covalently-bonded atoms of Group V. If the specified atom has two or three $V_{S,max}$ with the same values, this is indicated in parentheses.

Molecule	Atom	$V_{S,max}$, kcal/mol	Deviation from extension of indicated bond, degrees
PF ₃	P	35 (3)	F-P: 20
AsF ₃	As	44 (3)	F-As: 18
SbF ₃	Sb	52 (3)	F-Sb: 25
H ₂ PF	P	39	F-P: 26
H ₂ AsF	As	44	F-As: 22
(H ₃ C) ₂ PCN	P	30	NC-P: 20
	P	18 (2)	H ₃ C-P: 22
(H ₃ C) ₂ AsCN	As	34	NC-As: 21
	As	20 (2)	H ₃ C-As: 22
FP(C ₆ H ₅) ₂	P	18	F-P: 3
	P	5 (2)	C-P: 19
FAs(C ₆ H ₅) ₂	As	25	F-As: 8
	As	8 (2)	C-As: 20
FSb(C ₆ H ₅) ₂	Sb	37	F-Sb: 26
	Sb	18 (2)	C-Sb: 21
FPBr(CN)	P	38	F-P: 15
	P	40	Br-P: 18
	P	35	NC-P: 19
FAsBr(CN)	As	46	F-As: 15
	As	44	Br-As: 17
	As	40	NC-As: 17
F ₂ PCl	P	34 (2)	F-P: 17
	P	36	Cl-P: 22
H ₂ PBr	P	19 (2)	H-P: 33
	P	35	Br-P: 26
S(PF ₂) ₂	P	32	S-P: 21
Se(PF ₂) ₂	P	31	Se-P: 19

Table 4. Values and angular positions of 0.001 au $V_{S,max}$ associated with σ -holes of covalently-bonded atoms of Group IV. If the specified atom has two or more $V_{S,max}$ with the same values, this is indicated in parentheses.

Molecule	Atom	$V_{S,max}$, kcal/mol	Deviation from extension of indicated bond, degrees
CF ₄	C	24 (4)	F-C: 0
SiF ₄	Si	53 (4)	F-Si: 2
GeF ₄	Ge	61 (4)	F-Ge: 2
HCF(Cl)(CN)	C	16 ^a	H-C: 7
H ₃ SiF	Si	35	F-Si: 0
	Si	22 (3)	H-Si: 2
H ₃ GeF	Ge	43	F-Ge: 0
	Ge	24 (3)	H-Ge: 2
F ₃ SiCl	Si	48	Cl-Si: 0
	Si	41 (3)	F-Si: 21
(H ₃ C) ₂ SiF ₂	Si	28 (2)	F-Si: 3
	Si	18 (2)	H ₃ C-Si: 8
(H ₃ C) ₂ GeF ₂	Ge	36 (2)	F-Ge: 5
	Ge	17 (2)	H ₃ C-Ge: 10
(H ₃ C) ₃ GeCN	Ge	34	NC-Ge: 2
	Ge	21 (3)	H ₃ C-Ge: 4
Se(SiF ₃) ₂	Si	47	Se-Si: 4
	Si	46	F-Si: 5
	Si	36	F-Si: 12
Cl ₂ SiH(F)	Si	14	F-Si: 35
	Si	33	F-Si: 8
	Si	34 (2)	Cl-Si: 8
	Si	23	H-Si: 5

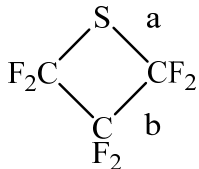
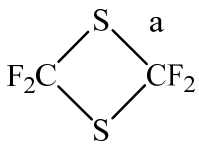
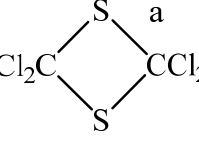
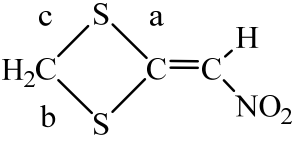
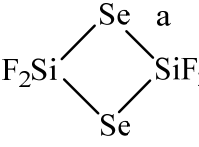
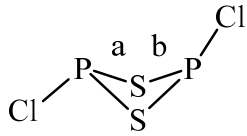
^aThe only $V_{S,max}$ associated with the central carbon is along the extension of the H-C bond.

Table 5. Values and angular positions of $V_{S,max}$ for different contours of the electronic density.

Molecule	Bond and atom ^a	Contour, au	$V_{S,max}$, kcal/mol	Distance from indicated atom to $V_{S,max}$, Å	Deviation from extension of indicated bond, degrees
S(CN) ₂	C-S	0.005	79	1.60	18
		0.003	64	1.73	16
		0.002	56	1.82	14
		0.001	44	1.97	11
		0.0005	37	2.12	10
		0.0001	26	2.47	5
SF ₂	F-S	0.005	79	1.54	14
		0.003	62	1.66	13
		0.002	52	1.75	11
		0.001	40	1.91	8
		0.0005	32	2.07	6
		0.0001	21	2.45	3
PF ₃	F-P	0.005	77	1.59	24
		0.003	59	1.72	23
		0.002	48	1.82	21
		0.001	35	2.00	20
		0.0005	26	2.18	19
		0.0001	15	2.65	10
As(CH ₃) ₂ CN	NC-As	0.005	67	1.67	24
		0.003	52	1.81	22
		0.002	44	1.93	22
		0.001	34	2.14	21
		0.0005	28	2.36	20
		0.0001	20	2.91	23

^aThe interacting atom is in bold.

Table 6. Values and angular positions of 0.001 au $V_{S,max}$ associated with four- and five-membered rings of some heterocyclic molecules.

	Molecule	$V_{S,max}$, kcal/mol	Deviation from extension of indicated bond, degrees	Reference
9		a) 33 b) 34	a) C-S: 41 C-C: 21 b) S-C: 21 C-C: 17	40
10		a) 33	a) C-S: 37 S-C: 16	76
11		a) 28	a) C-S: 24 S-C: 26	76
12		a) 33 b) 33 c) 35	a) C-S: 26 S-C: 18 b) C-S: 37 S-C: 20 c) C-S: 33 S-C: 23	75
13		a) 43	a) Si-Se: 54 Se-Si: 4	75
14		a) 36 b) 32	a) S-P: 29 P-S: 41 b) S-P: 28 P-S: 41	present work

(continued)

Table 6 (continued).

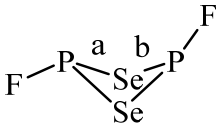
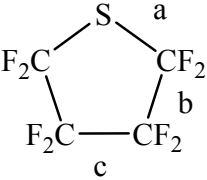
Molecule	$V_{S,max}$, kcal/mol	Deviation from extension of indicated bond, degrees	Reference
15 	a) 34 b) 28	a) Se-P: 28 P-Se: 43 b) Se-P: 28 P-Se: 40	75
16 	a) 35 b) 31 c) 31	a) C-S: 22 C-C: 4 b) S-C: 4 C-C: 2 c) C-C: 2 C-C: 2	75

Table 7. Angular positions of 0.001 au $V_{S,max}$ associated with σ -holes compared to deviations from linearity of gas phase interaction angles. Computational level: M06-2X/6-311G(d).

Complex	Interacting atom and bond ^a	Deviation of $V_{S,max}$ from extension of indicated bond, degrees ^b	Interaction angle and deviation from linearity, degrees
F-F---NH ₃	F-F	0	F-F ---N: 1
F ₃ C-Cl---NH ₃	C-Cl	0	C-Cl ---N: 0
F-Cl---NH ₃	F-Cl	0	F-Cl ---N: 0
F ₃ Si-Cl---NH ₃	Si-Cl	0	Si-Cl ---N: 0
F ₃ C-Br---NH ₃	C-Br	0	C-Br ---N: 0
BrC≡C-Br---NH ₃	C-Br	0	C-Br ---N: 0
HFS---NH ₃	F-S	24	F-S ---N: 10
HFSe---NH ₃	F-Se	22	F-Se ---N: 10
H ₂ FP---NH ₃	F-P	26	F-P ---N: 13
H ₂ FAs---NH ₃	F-As	22	F-As ---N: 15
F ₃ C-Cl---NCH	C-Cl	0	C-Cl ---N: 0
F-Br---NCH	F-Br	0	F-Br ---N: 0
Br ₂ C=CB _{r2} ---NCH	C-Br	2	C-Br ---N: 2
BrC≡C-Br---NCH	C-Br	0	C-Br ---N: 0
F ₂ S---NCH	F-S	8	F-S ---N: 6
Cl ₂ Se---NCH	Cl-Se	3	Cl-Se ---N: 0
H ₂ FP---NCH	F-P	26	F-P ---N: 16
H ₂ FAs---NCH	F-As	22	F-As ---N: 17
H ₃ FSi---NCH	F-Si	0	F-Si ---N: 0
H ₃ FGe---NCH	F-Ge	0	F-Ge ---N: 0

^aInteracting atom is in bold.

^b $V_{S,max}$ deviations are for molecules prior to interaction.

Figure Captions

Figure 1. Computed electrostatic potentials on the 0.001 au molecular surface of FSeI. In (a), the iodine is in the foreground, the fluorine is to the left. In (b), the selenium is in the foreground, the iodine is to the right. Color ranges, in kcal/mol: Red, more positive than 24; yellow, between 24 and 12; green, between 12 and zero; blue, negative. The black hemispheres indicate the locations of the most positive potentials, the $V_{S,max}$. The one in (a) is on the iodine, the two in (b) are on the selenium.

Figure 2. Computed electrostatic potential on the 0.001 au molecular surface of S(PF₂)₂. The sulfur is in the middle, to the left are the fluorines of one of the PF₂ groups. To the right is the phosphorus of the other PF₂. (See structure 5). Color ranges, in kcal/mol: Red, more positive than 24; yellow, between 24 and 12; green, between 12 and zero; blue, negative. The black hemispheres indicate the locations of the most positive potentials, the $V_{S,max}$. Two of them are on the sulfur (at the same horizontal level), the other two on the right are on the phosphorus. The strongly-positive potentials on the right side overlap to form a vertical band.

Figure 3. Computed electrostatic potential on the 0.001 au molecular surface of Se(SiF₃)₂. In (a), the selenium is in the foreground. In (b), the selenium is in the back, and one fluorine from each of the SiF₃ groups is in the foreground. (See structure 7). Color ranges, in kcal/mol: Red, more positive than 24; yellow, between 24 and 12; green, between 12 and zero; blue, negative. The black hemispheres indicate the locations of the most positive potentials, the $V_{S,max}$. The two shown in (a) are on the silicons.

Figure 4. Computed electrostatic potential on the 0.001 au molecular surface of PH₂Br. The phosphorus is in the foreground, the bromine is to the left. Color ranges, in kcal/mol: Red, more positive than 24; yellow, between 24 and 17; green, between 17 and zero; blue, negative. The black hemispheres indicate the locations of the most positive potentials, the $V_{S,max}$. The two shown are on the phosphorus atom.

Figure 5. Computed electrostatic potential on the 0.001 au molecular surface of the four-membered ring molecule **14**; its structure is shown below. One of the sulfurs is in the middle, with a phosphorus on either side of it. Color ranges, in kcal/mol: Red, more positive than 24; yellow, between 24 and 12; green, between 12 and zero; blue, negative. The black hemispheres indicate the locations of the most positive potentials, the $V_{S,max}$; these are located on the four sides of the ring, between the extensions of the bonds linking the sulfur and phosphorus atoms.

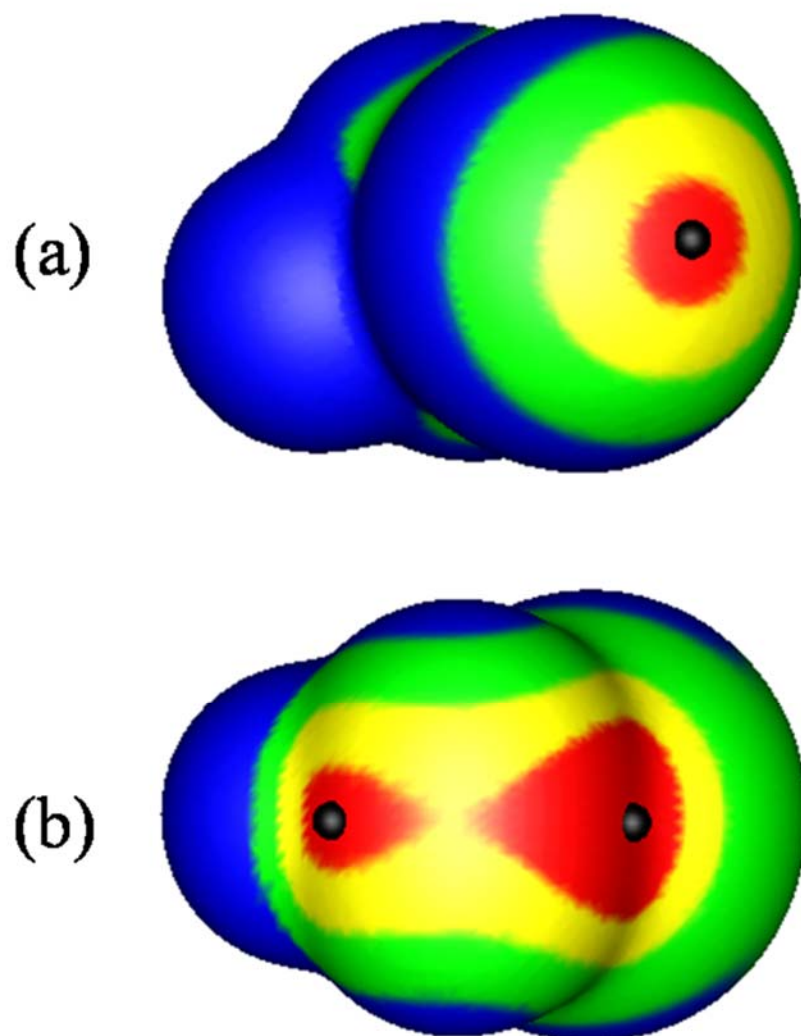


Figure 1.

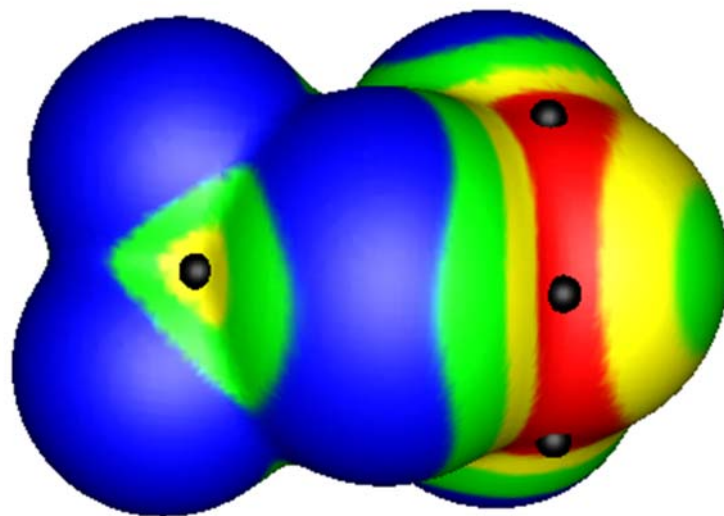


Figure 2.

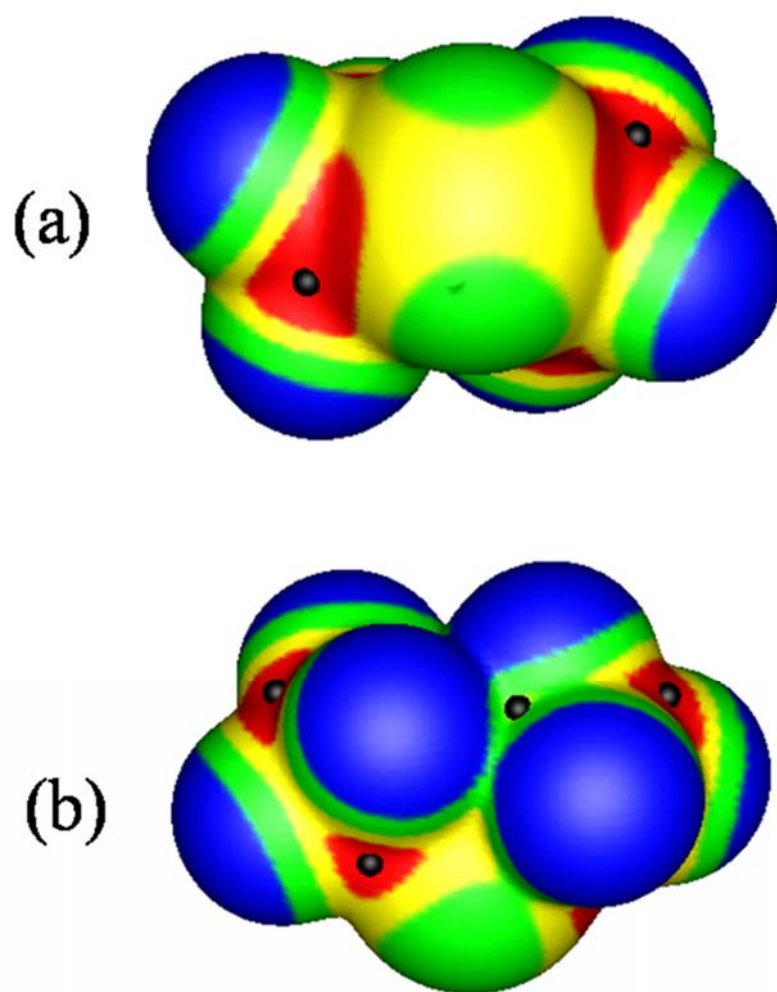


Figure 3.

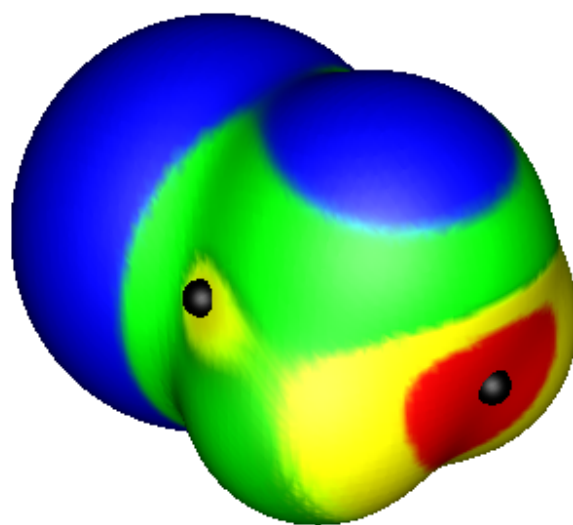


Figure 4.

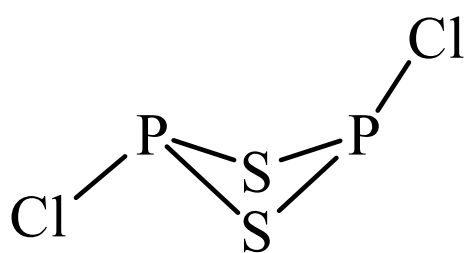
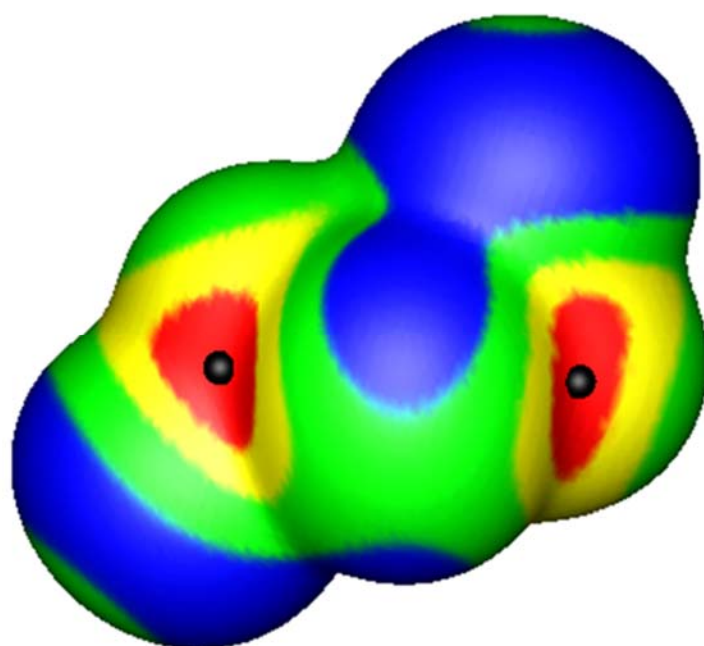


Figure 5.