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Interaction and Polarization Energy Relationships in σ -Hole and π -Hole Bonding

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Abstract: We demonstrate that a wide range of σ - and π -hole interaction energies can be related to (a) the electrostatic potentials and electric fields of the σ - and π -hole molecules at the approximate positions of the negative sites and (b) the electrostatic potentials and polarizabilities of the latter. This is consistent with the Coulombic nature of these interactions, which should be understood to include both electrostatics and polarization. The energies associated with polarization were estimated and were shown to overall be greater for the stronger interactions; no new factors need be introduced to account for these. All of the interactions can be treated in the same manner.

Keywords: noncovalent interactions; σ -holes; π -holes; electrostatics; polarization; interaction energies; polarization energies

1. σ **-Holes and** π **-Holes**

The electronic density of a free atom is, on average, spherically symmetrical [1]. However, in forming a covalent bond and becoming part of a molecule, the atom normally loses this symmetry and becomes anisotropic, with regions of higher and lower electronic density [2–9].

There tends to be a lower electronic density on the side of the atom opposite to the bond, on its extension; the atom's radius in that direction is less than to a lateral side. This region of lower electronic density on the extension of a bond is known as a σ -hole [10]. There is also frequently a region of lower electronic density above and below a planar portion of a molecule, which has been labeled a π -hole [11].

Our present interest is in the effects of σ -holes and π -holes upon the energetics of intermolecular interactions. Since these effects involve molecular electrostatic potentials and electric fields, we will briefly discuss these two properties.

2. Molecular Electrostatic Potentials and Electric Fields

The nuclei and electrons of any molecule create an electrostatic potential $V(\mathbf{r})$ at each point \mathbf{r} in the surrounding space. $V(\mathbf{r})$ is given rigorously by Equation (1),

$$V(\mathbf{r}) = \sum_{A} \frac{Z_{A}}{|\mathbf{R}_{A} - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|}$$
(1)

in which Z_A is the charge on nucleus A, located at \mathbf{R}_A , and $\rho(\mathbf{r})$ is the molecule's electronic density.

The sign of $V(\mathbf{r})$ in any region is the result of the positive contributions of the nuclei and the negative ones of the electrons. It is sometimes incorrectly assumed that the electrostatic potential follows the electronic density and that "electron-rich" and "electron-poor" regions will have negative and positive $V(\mathbf{r})$, respectively. This is sometimes the case but not always; the nuclear contributions must be taken into account as well as the electronic ones. For instance, this is shown by there usually being buildups of electronic density in the internuclear regions of covalent bonds [12–14], but the

electrostatic potentials in those regions are generally positive [15–17], which is due to the proximities of the positive nuclei.

A key feature of the electrostatic potential is that it is a real physical property, an observable. It can be determined experimentally, by diffraction methods [14,15,18], as well as computationally.

The significance of V(**r**) for the present discussion is in relation to interaction energies. If a molecule A has an electrostatic potential $V_A(\mathbf{r})$, then its interaction energy ΔE with a point charge Q placed at the position **R** is $\Delta E = QV_A(\mathbf{R})$. If Q and $V_A(\mathbf{R})$ have opposite signs, then $\Delta E < 0$ and the interaction is attractive; if they have the same sign, $\Delta E > 0$ and the interaction is repulsive. This can readily be extended to the interaction of A with a second molecule B, since B is simply a collection of point charges (nuclei and electrons). Regions of positive (negative) electrostatic potential on A will interact attractively with negative (positive) regions on B.

It might be argued that atomic charges can achieve the same purpose as electrostatic potentials. However, the charge on an atom in a molecule is not a physical observable; it cannot be determined experimentally. Numerous definitions of atomic charge have been proposed, but they are all arbitrary and have no physical basis [19–23]. The perils of atomic charges are illustrated by the case of H₃C-NO₂; seven different definitions of atomic charge assigned values to the carbon that ranged from -0.478 to +0.564 [20]. They do not even agree as to whether it is positive or negative!

In the context of molecular interactions, electrostatic potentials are now commonly presented on molecular surfaces defined by outer contours of the electronic densities [24] and labeled $V_S(\mathbf{r})$. The 0.001 au contour is most often used for this purpose. The local maxima and minima of $V_S(\mathbf{r})$ (its most positive and most negative values) are designated by $V_{S,max}$ and $V_{S,min}$, respectively. There may be several of each.

The electrostatic potential of a molecule creates an electric field $\varepsilon(\mathbf{r})$. From classical physics, this is equal to the negative gradient of the electrostatic potential, $\varepsilon(\mathbf{r}) = -\nabla V(\mathbf{r})$. If a charge Q is placed at the point **R**, then the electric field exerts a force **F**(**R**) upon Q, which is given by $\mathbf{F}(\mathbf{R}) = Q\varepsilon(\mathbf{R}) = -Q\nabla V(\mathbf{R})$. If $\nabla V(\mathbf{R})$ and Q have the same sign, then the electric field attracts Q toward the molecule.

3. σ - and π -Hole Interactions

There are frequently (although not always) positive electrostatic potentials associated with the lower electronic densities of σ -holes and π -holes. Through these positive potentials, the molecule can interact attractively with negative sites such as lone pairs, π electrons, and anions [11,25–27]. These are known as σ - and π -hole interactions, even though they do not actually involve the σ - and π -holes but rather the positive potentials associated with them [28,29]. Such interactions have been widely observed, both experimentally and computationally, for covalently bonded atoms from different groups of the periodic table [2,11,25,26,30–37]. Hydrogen bonding is also a σ -hole interaction [38–42].

As examples of positive potentials associated with σ - and π -holes, Figures 1 and 2 display the computed electrostatic potentials on the 0.001 au molecular surfaces of SeClBr and SeO₃. These were computed at the density functional B3PW91/6-31G(d,p) level using Gaussian 09 [43] and the WFA-SAS code [44].

In SeClBr, Figure 1, there are four positive maxima, arising from two σ-holes on the selenium, and one on each halogen atom, which are on the extensions of the bonds to these atoms. Note that all three atoms have regions of both positive and negative electrostatic potential, which means that they can interact attractively with both negative and positive sites. Such dual reactivity is well-established experimentally [4,6,34,35] and computationally [45,46]. It could not have been predicted on the basis of atomic charges, since each atom in a molecule is assigned a single charge.

Figure 2 shows the positive potential that is above and below the selenium in SeO₃, due to its π -holes. The three oxygens are entirely negative. They do have σ -holes (regions of lower electronic density) on the extensions of the Se–O bonds, but the potentials associated with them are negative, although less so than the surrounding oxygen surfaces.



Figure 1. Computed electrostatic potentials on the 0.001 au molecular surface of SeClBr. In (**a**), the selenium is in the foreground, the chlorine is in the rear left, and the bromine in the rear right. In (**b**), the chlorine is in the foreground left and the bromine in the foreground right. Color ranges, in kcal/mol: red, more positive than 24; yellow, between 24 and 12; green, between 12 and 0; blue, negative. Black hemispheres indicate the most positive potentials ($V_{S,max}$) corresponding to the two σ -holes on the selenium, on the extensions of the Cl–Se and Br–Se bonds, and the σ -holes on the chlorine and bromine, on the extensions of the Se–Cl and Se–Br bonds.



Figure 2. Computed electrostatic potential on the 0.001 au molecular surface of SeO₃. Selenium is in the center. Color ranges, in kcal/mol: red, more positive than 36; yellow, between 36 and 18; green, between 18 and 0; blue, negative. Black hemisphere indicates the most positive potential ($V_{S,max}$) corresponding to the π -holes above and below selenium.

4. Polarization

The electrostatic potentials plotted on molecular surfaces, as in Figures 1 and 2, can reveal positive regions that are likely to interact favorably with negative sites. However, these potentials are typically

computed for the free molecules prior to interaction. They do not reflect that as two molecules approach each other and interact, the charge distribution of each becomes increasingly polarized by the electric field of the other. This is clearly visible in density difference plots [47–50]; the electronic densities of the negative sites are polarized toward the positive potentials of the σ - or π -hole atoms, and the electronic densities of those atoms are polarized away from the negative sites. It follows that the electrostatic potentials computed for the free molecules, e.g., their V_{S,max} and V_{S,min}, become somewhat less relevant as the molecules interact.

Polarization is an intrinsic part of a Coulombic interaction [48,49,51–53], and it is always stabilizing, strengthening the interaction. Hennemann et al have shown how putting a point charge in the vicinity of a σ -hole can affect the magnitude of the electrostatic potential associated with that σ -hole [39]. Polarization can actually result in an interaction becoming favorable even though the electrostatic potentials of the free molecules would predict it to be unfavorable. For instance, the σ -hole potentials of the chlorine in H₃C–Cl and the phosphorus in H₃P are essentially neutral (near-zero or even slightly negative, depending upon the computational procedure). Yet, these molecules were found to computationally to interact favorably with O=CH₂ and NSH to form H₃C-Cl—O=CH₂ [54] and H₃P—NSH [55]. The electric fields of the negative sites *induce* positive potentials on the chlorine and phosphorus.

Substituted aromatic systems provide some dramatic examples of the effects of polarization. 1,4-Difluorobenzene has weakly negative electrostatic potentials above and below the ring; nevertheless, it interacts there with the nitrogen lone pair of HCN to form a T-shaped complex [56]. The negative lone pair induces a positive ring potential. 1,3,5-Trifluorobenzene has weakly positive potentials above and below the ring, but it forms a T-shaped complex with the positive hydrogen of HCN, which induces a negative potential. See also Geronimo et al [57].

The important role that polarization can play has been recognized since the earliest days of using electrostatic potentials to analyze molecular interactions [58–60]. Several approaches have been used to account for it, including perturbation theory [58,60,61] and modeling with point charges [59,62–64]. For overviews of this work, see Politzer et al [17,65].

5. Strengths of σ - and π -Hole Interactions

The strength of noncovalent bonding is typically measured by the interaction energy, ΔE . For the formation of a complex A—B, this is given in terms of the respective energies by

$$\Delta E = E(A - B) - [E(A) + E(B)].$$
(2)

The more negative ΔE is, the stronger the interaction.

 ΔE reflects the contributions of both electrostatics and polarization. Sometimes, the polarization is relatively minor, and ΔE can be related to just electrostatics. Thus, for series of σ -hole interactions with a given negative site, it has on occasion been possible to correlate ΔE quite well with just the V_{S,max} of the σ -hole molecules [25,30,66–68]. If the negative site is not held constant, there has been some success in relating ΔE to combinations of the V_{S,max} of the σ -hole molecules and the V_{S,min} of the negative sites [25,42,52]. For groups of interactions with a given σ - or π -hole molecule, correlations have sometimes been found between ΔE and the V_{S,min} of the negative sites [59,68].

However, polarization does often have a significant effect and cannot be neglected. It has two components in σ - and π -hole interactions: namely, the effect of the electric field of the σ - or π -hole molecule upon the negative site and the effect of the electric field of the negative site upon the σ - or π -hole molecule.

We have recently been investigating possible procedures for expressing σ - and π -hole interaction energies in terms of both electrostatics and polarization. Initially, we used data bases of 20 σ -hole and 21 π -hole interactions, involving a variety of σ - and π -hole molecules and negative sites [69]. We verified that electrostatics—i.e., V_{S,max} or a combination of V_{S,max} and V_{S,min}—is not sufficient for an acceptable correlation with either the σ -hole or the π -hole interaction energies. Polarization needs to be included.

Accordingly, we tested the triple regression relationship given by Equation (3). It represents the electrostatics of the interactions by the most positive electrostatic potentials, the $V_{S,max}$, of the σ - or π -holes on the 0.001 au molecular surfaces. Polarization is taken into account by explicitly including the electric fields $\varepsilon(R)$ that the σ - or π -hole molecules exert upon the negative sites and the average polarizabilities α of these sites [65,69].

$$\Delta E = c_1 [V_{S,max}] + c_2 [\varepsilon(R)]^2 + c_3 [\alpha] + c_4$$
(3)

In Equation (3), R is the intermolecular separation. For a σ -hole molecule, ε (R) is evaluated at the distance R along the extension of the bond that produced the σ -hole, and for a π -hole molecule, it is evaluated at R in the direction perpendicular to the planar portion of the molecule. This should give the magnitudes of the fields at the approximate positions of the negative sites. ε (R) is raised to the second power, because the energy of an induced dipole is $-0.5\alpha\varepsilon^2$ [70]. The coefficients c_1 - c_4 were obtained through the regression procedure for each database separately [71].

The σ -hole and π -hole databases were separately fit to Equation (3) to obtain expressions for predicting the respective interaction energies [69]. The results were encouraging. Therefore, in the present work, we have expanded the analyses, in modified form, to considerably larger databases of σ -hole and π -hole interactions. For each interaction, we have also directly calculated the energy associated with the polarization of the negative site by the electric field of the σ - or π -hole molecule.

6. Present Results

Table 1 lists the computed properties for 54 σ -hole complexes involving σ -hole molecules from Groups IV–VII, with several nitrogen and oxygen Lewis bases as negative sites. About one-fourth of the complexes are hydrogen-bonded. Structures and energies were obtained with the MP2/aug-cc-pVDZ procedure [43], electrostatic potentials, and electric fields with B3PW91/6-31G(d,p) using the MP2 geometries.

Table 1. Computed data for σ -hole interactions. The σ -hole is on the extension of the bond between atoms, and it is indicated in **bold**. Dashed lines show interactions. ΔE is interaction energy, as shown in Equation (2). $V_{S,max}$ is the most positive electrostatic potential of the σ -hole on the 0.001 au molecular surface before interaction. R is equilibrium interaction separation. V(R) and ε (R) are the electrostatic potential and electric field of the σ -hole molecule at the approximate position of the negative site. ΔE (pol) is the energy of polarization of the negative site, as shown in Equation (6).

Interaction	ΔE (kcal/mol)	V _{S,max} (kcal/mol)	R (Å)	V(R) (kcal/mol)	ε(R) (au)	ΔE(pol) (kcal/mol)
FF—OH ₂	-1.68	14.5	2.60	2.7	0.002549	-0.02
FF—O=CH ₂	-2.04	14.5	2.54	2.8	0.002781	-0.05
$H_3C(Cl)Se-NCH$	-2.58	8.8	3.19	1.8	0.001770	-0.02
HF ₂ CBr—NCH	-2.97	16.5	3.12	3.1	0.003319	-0.06
$HF_2CBr - O = CH_2$	-3.47	16.5	3.02	3.5	0.003856	-0.09
HC CH —NCH	-3.58	30.7	2.30	9.1	0.006834	-0.26
H_2 NH— NH_3	-3.62	25.5	2.28	7.7	0.005442	-0.13
$NC-CI-OH_2$	-3.65	35.3	2.88	13.6	0.007823	-0.19
$HF_2CBr-NH_3$	-3.67	16.5	3.06	3.3	0.003621	-0.06
$H_3C(Cl)Se-NH_3$	-3.91	8.8	3.13	1.7	0.001990	-0.02
F ₃ CBr—NCH	-3.92	24.1	3.04	7.1	0.005416	-0.16
F_3 CBr —O=CH ₂	-4.04	24.1	2.94	7.8	0.006187	-0.22
F ₃ CH—NCH	-4.13	31.2	2.33	12.6	0.007259	-0.29

	Tabl	e 1.	Cont.
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Interaction	ΔE (kcal/mol)	V _{S,max} (kcal/mol)	R (Å)	V(R) (kcal/mol)	ε(R) (au)	ΔE(pol) (kcal/mol)
F ₃ CH—O=CH ₂	-4.32	31.2	2.31	12.8	0.007431	-0.32
H OH —NCH	-4.41	43.4	2.11	15.2	0.01097	-0.66
F ₂ (NC)P—NCH	-4.60	36.5	2.98	12.0	0.007417	-0.30
H ₃ (F) Si —NCH	-4.67	34.1	2.91	12.2	0.008482	-0.39
HCCH-NH ₃	-4.71	30.7	2.26	9.5	0.007218	-0.23
F ₃ CBr—NH ₃	-4.97	24.1	2.97	7.6	0.005923	-0.16
HF ₂ CBr—NH ₂ CH ₃	-5.05	16.5	2.98	3.7	0.004098	-0.13
NC-Br—OH ₂	-5.15	42.7	2.87	18.3	0.01112	-0.40
F ₃ CH—NH ₃	-5.33	31.2	2.28	13.1	0.007667	-0.26
HCCH—NH ₂ CH ₃	-5.51	30.7	2.17	10.3	0.008089	-0.52
NC-H—OH ₂	-5.66	50.0	2.05	22.8	0.01439	-0.66
FCl—OH ₂	-5.93	40.3	2.53	16.5	0.01396	-0.62
FC1—NCH	-5.96	40.3	2.60	15.4	0.01256	-0.87
F ₃ As—NCH	-6.01	36.2	2.91	14.6	0.01044	-0.60
HF ₂ CBr—NH(CH ₃) ₂	-6.17	16.5	2.90	4.1	0.004658	-0.25
HCCH—NH(CH ₃) ₂	-6.26	30.7	2.09	11.1	0.009099	-0.95
F ₃ CH—NH ₂ CH ₃	-6.29	31.2	2.24	13.4	0.007994	-0.51
F ₃ CBr—NH ₂ CH ₃	-6.42	24.1	2.88	8.2	0.006701	-0.36
Cl-ClNH ₃	-6.48	24.1	2.55	8.9	0.009112	-0.37
(NC) ₂ S—NCH	-6.65	43.8	2.92	17.0	0.01033	-0.59
HOH-NH ₃	-6.96	43.4	1.97	17.1	0.01325	-0.78
F ₂ (NC)P—NH ₃	-6.98	36.5	2.73	14.7	0.01032	-0.48
H ₃ FSi—NH ₃	-7.26	34.1	2.56	16.8	0.01416	-0.89
F ₃ CBr—NH(CH ₃) ₂	-7.79	24.1	2.80	8.9	0.007504	-0.65
HOH—NH ₂ CH ₃	-8.13	43.4	1.91	18.1	0.01442	-1.65
(NC) ₂ S—O=CH ₂	-8.27	43.8	2.82	18.3	0.01156	-0.79
FBr—OH ₂	-8.43	47.7	2.53	22.3	0.01908	-1.16
F ₃ As—O=CH ₂	-8.44	36.2	2.68	17.8	0.01407	-1.16
(NC) ₂ S—NH ₃	-8.56	43.8	2.86	17.8	0.01104	-0.54
F ₂ (NC)P—NH ₂ CH ₃	-9.45	36.5	2.56	16.9	0.01305	-1.35
$(NC)_2S$ — NH_2CH_3	-10.10	43.8	2.74	19.5	0.01267	-1.28
F ₃ As—NH ₃	-10.13	36.2	2.59	19.4	0.01611	-1.16
H ₃ FSi—NH ₂ CH ₃	-10.35	34.1	2.34	21.1	0.02059	-3.37
FCl—NH ₃	-12.18	40.3	2.27	21.8	0.02138	-2.03
$F_2(NC)P$ —NH(CH ₃) ₂	-12.26	36.5	2.39	20.0	0.01713	-3.38
(NC) ₂ S—NH(CH ₃) ₂	-12.39	43.8	2.66	20.7	0.01393	-2.24
F ₃ As—NH ₂ CH ₃	-13.10	36.2	2.51	21.1	0.01825	-2.65
H ₃ FSi—NH(CH ₃) ₂	-13.22	34.1	2.27	23.0	0.02358	-6.41
F_3As —NH(CH ₃) ₂	-16.29	36.2	2.41	23.5	0.02156	-5.36
FCl—NH ₂ CH ₃	-17.28	40.3	2.15	25.3	0.02697	-5.78
FCl—NH(CH ₃) ₂	-21.96	40.3	2.09	27.4	0.03012	-10.46

Table 2 presents the same properties for 33 π -hole complexes. Table 3 shows the computed V_{S,min} and the experimental polarizabilities [72] of the negative sites. The V_{S,min} are on the 0.001 au surfaces of the negative sites prior to interaction.

Table 2. Computed data for π -hole interactions. Atoms with π -holes are indicated in **bold**. Interactions are with the first atom listed for the negative site. ΔE is interaction energy, as shown in Equation (2). $V_{S,max}$ is the most positive electrostatic potential of the π -hole on the 0.001 au molecular surface before interaction. R is the equilibrium interaction separation. V(R) and ε (R) are the electrostatic potential and electric field of the π -hole molecule at the approximate position of the negative site. ΔE (pol) is the energy of polarization of the negative site, as shown in Equation (6).

π-Hole Molecule	Negative Site	ΔE (kcal/mol)	V _{S,max} (kcal/mol)	R (Å)	V(R) (kcal/mol)	ε(R) (au)	ΔE(pol) (kcal/mol)
SeO ₂	OCO	-2.36	35.4	3.19	10.5	0.007622	-0.36
SeO ₂	СО	-2.42	35.4	3.44	8.5	0.005766	-0.14
Cl ₂ C=O	СО	-2.55	22.8	3.16	3.9	0.003483	-0.05
Cl ₂ C=O	OCO	-2.70	22.8	2.88	5.3	0.005104	-0.16
Cl ₂ C=O	NCH	-3.99	22.8	2.89	5.2	0.005042	-0.14
FPO ₂	OCO	-4.00	58.4	2.71	20.5	0.01795	-1.99
SO ₂	NCH	-4.04	32.9	3.03	10.2	0.007796	-0.33
SeO ₂	NCH	-4.14	35.4	3.08	11.6	0.008652	-0.41
FNO ₂	NCH	-4.38	32.8	2.80	8.5	0.007202	-0.28
Cl ₃ B	NCH	-4.46	24.0	2.84	6.7	0.006555	-0.24
F ₂ C=O	NCH	-4.58	40.9	2.77	9.0	0.007798	-0.33
Cl ₂ C=O	NH ₃	-4.64	22.8	2.85	5.5	0.005332	-0.13
FNO ₂	NH ₃	-5.52	32.8	2.79	8.5	0.007301	-0.24
FPO ₂	СО	-5.91	58.4	2.53	24.9	0.02326	-2.24
SO ₂	NH ₃	-6.00	32.9	2.83	12.3	0.01004	-0.45
F ₂ C=O	NH ₃	-6.14	40.9	2.67	10.0	0.008952	-0.36
$F_3 B$	NCH	-6.94	48.8	2.35	17.9	0.01836	-1.85
H ₃ CPO ₂	NCH	-7.59	47.6	2.68	14.8	0.01361	-1.02
SeO ₂	NH ₃	-7.62	35.4	2.87	14.0	0.01123	-0.56
SO ₂	NH ₂ CH ₃	-9.52	32.9	2.59	15.6	0.01398	-1.55
H ₂ Si=O	NCH	-11.55	43.4	2.18	30.7	0.03635	-7.25
FPO ₂	NCH	-11.88	58.4	2.21	36.3	0.03868	-8.21
SeO ₂	NH ₂ CH ₃	-12.23	35.4	2.58	18.8	0.01693	-2.28
SO ₂	NH(CH ₃) ₂	-12.93	32.9	2.43	18.7	0.01793	-3.71
F ₂ Si=O	CO	-13.52	66.7	2.12	45.9	0.05101	-10.76
SeO ₂	NH(CH ₃) ₂	-16.66	35.4	2.42	22.4	0.02177	-5.47
H ₃ CPO ₂	NH ₃	-18.41	47.6	2.05	32.9	0.04145	-7.65
F ₂ Si=O	NCH	-22.58	66.7	2.01	53.4	0.06293	-21.74
H ₂ Si=O	NH ₃	-26.69	43.4	2.03	38.2	0.04925	-10.80
H ₂ Si=O	NH ₂ CH ₃	-31.91	43.4	2.00	39.7	0.05195	-21.46
FPO ₂	NH ₃	-32.35	58.4	1.95	51.5	0.06246	-17.37
H ₂ Si=O	NH(CH ₃) ₂	-36.39	43.4	1.94	43.7	0.05916	-40.36
F ₂ Si=O	NH ₃	-42.38	66.7	1.95	58.2	0.07063	-22.21

Molecule	V _{S,min} (kcal/mol) ^a	Polarizability, α (Å ³) ^b
CO ₂	-12.6	2.911
СО	-14.0	1.953
H ₂ C=O	-30.2	2.77
HCN	-32.2	2.593
NH(CH ₃) ₂	-39.1	5.447
H ₂ O	-39.6	1.501
NH ₂ CH ₃	-42.9	3.754
NH ₃	-46.2	2.103

Table 3. Computed V_{S,min} and experimental polarizabilities of negative sites.

^a The V_{S,min} are on the nitrogen and oxygen atoms except for CO, for which it is on the carbon atom. ^b Reference [72].

In the present study, in addition to using larger databases, we have modified our approach. In Equation (3), the electrostatics are modeled entirely by the σ - or π -hole V_{S,max}, which is on the 0.001 au surface of that molecule in the free, unperturbed state. However as recently suggested [65], it should be more realistic to use the potential V(R) that the σ - or π -hole molecule creates at the point at which the electric field is evaluated [65]. This should better reflect what the negative site actually experiences, and it would also be consistent with earlier work [38,64].

In order to further improve the representation of the electrostatic contribution, we also introduce the most negative potential $V_{S,min}$ on the 0.001 au surface of the negative site. This should be at least somewhat indicative of what is interacting with V(R).

Accordingly, our regression relationship becomes,

$$\Delta E = c_1 [V(R)] + c_2 [\varepsilon(R)]^2 + c_3 [\alpha] + c_4 [V_{S,min}] + c_5$$
(4)

However, we have found that V(R) and $\varepsilon(R)^2$ are rather closely related for the π -hole interactions in Table 2; the coefficient of determination R^2 for $[\varepsilon(R)]^2$ versus V(R) is 0.918. Therefore, using both of them in the regression relationship would be redundant and statistically undesirable. For the σ -hole interactions, on the other hand, R^2 is just 0.649 for $[\varepsilon(R)]^2$ versus V(R), indicating that both of them are needed. Therefore, we have used Equation (4) for the σ -hole interactions in Table 1 and Equation (5) for the π -hole interactions in Table 2.

$$\Delta E = c_1[\varepsilon(R)]^2 + c_2[\alpha] + c_3[V_{S,min}] + c_4$$
(5)

The results are gratifying. In Figures 3 and 4, the ΔE predicted by Equations (4) and (5), respectively, are plotted against the computed ΔE in Tables 1 and 2. For the σ -hole interactions in Figure 3, $R^2 = 0.938$ and the root-mean-square error is 1.04 kcal/mol. For the π -hole interactions in Figure 4, $R^2 = 0.952$ and the root-mean-square error is 2.51 kcal/mol. There is one major outlier, which is in Figure 4. It is for the π -hole interaction between F₂Si=O and NCH, for which the predicted ΔE is -30.73 kcal/mol, which is much more negative than the computed -22.58 kcal/mol. If this interaction were omitted from the database, R^2 would increase to 0.974, and the root-mean-square error would decrease to 1.89 kcal/mol.



Figure 3. ΔE predicted with Equation (4) plotted against the computed ΔE , in kcal/mol, for the σ -hole interactions in Table 1. $R^2 = 0.938$.



Figure 4. ΔE predicted with Equation (5) plotted against the computed ΔE , in kcal/mol, for the π -hole interactions in Table 2. $R^2 = 0.952$.

The discrepancy between the predicted and computed ΔE for this complex can be attributed largely to the secondary interactions involving portions of the molecules other than the σ - or π -hole and the primary negative site. In the case of F₂Si=O and NCH, the negative fluorines and oxygen of F₂Si=O interact repulsively with the negative nitrogen of NCH; the computed F—N and O—N separations, 2.66 and 2.87 Å, are considerably less than the sums of the respective van der Waals radii, 3.12 and 3.16 Å [73]. The computed ΔE takes these destabilizing repulsions into account, but the

 ΔE predicted by Equation (5) does not. As a result, the predicted ΔE exaggerates the strength of the interaction. Secondary interactions are certainly also implicated in the other discrepancies between predicted and computed ΔE , although their effects are not nearly as great. They are likely to be more significant in π -hole interactions than in σ -hole interactions, because the planar nature of the molecule around the π -hole puts more atoms in closer proximity to the atoms of the negative site.

Could all of the interaction energies in Tables 1 and 2, both σ -hole and π -hole, be represented by a single regression relationship? We investigated this using Equation (4), which was parametrized to fit all 54 σ -hole and 33 π -hole interaction energies. The resulting correlation between predicted and computed ΔE values is shown in Figure 5. It has an R^2 of 0.927 and root-mean-square error of 2.12 kcal/mol. These results are very encouraging, considering that 87 interactions of a variety of types are involved.



Figure 5. ΔE predicted with Equation (4) plotted against the computed ΔE , in kcal/mol, for all of the σ and π -hole interactions in Tables 1 and 2. $R^2 = 0.927$.

The same outlier that appeared in Figure 4 is again shown in Figure 5. It is for the π -hole interaction between F₂SiO and NCH, and it is due to significant secondary interactions, as discussed above.

7. Polarization Energies

For each interaction in Tables 1 and 2, we have calculated the energy of the polarization of the negative site by the electric field of the σ - or π -hole molecule, using Equation (6) [70]:

$$\Delta E(\text{pol}) = -0.5[\alpha][\varepsilon(R)]^2 \tag{6}$$

Note that we are not presently taking into account the polarization of the σ - or π -hole molecule by the negative site.

The calculated $\Delta E(\text{pol})$ values are listed in Tables 1 and 2. The relationship between the computed total interaction energies and the polarization energies is shown in Figure 6 for the σ -hole interactions and in Figure 7 for the π -hole interactions. The overall trends are that the stronger interactions are associated with greater degrees of polarization.





Figure 6. Computed ΔE plotted against ΔE (pol) obtained with Equation (6), in kcal/mol, for the σ -hole interactions in Table 1.



Figure 7. Computed ΔE plotted against ΔE (pol) obtained with Equation (6), in kcal/mol, for the π -hole interactions in Table 2.

However, most of the interactions are weak to moderate, and polarization makes only a minor contribution. In the σ -hole category (Table 1), 69% have ΔE between zero and -8 kcal/mol, and their average polarization energy $\Delta E(\text{pol})$, by Equation (6), is just -0.37 kcal/mol. Among the π -hole (Table 2), 58% have ΔE between zero and -8 kcal/mol, and their average $\Delta E(\text{pol})$ is -0.59 kcal/mol.

This explains why polarization can often be neglected and the interaction energies expressed satisfactorily in terms of just the most positive and/or most negative potentials, $V_{S,max}$ and/or $V_{S,min}$, of the free molecules prior to interaction [25,30,42,52,59,66–68]. On the other hand, there are three π -hole

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complexes in Table 2 (F_3B and NCH, FPO_2 and CO, FPO_2 and OCO) that have interaction energies ΔE between -4 and -7 kcal/mol, but yet have an ΔE (pol) value of about -2 kcal/mol. Thus, a weak or moderate interaction does not necessarily have insignificant polarization. Nevertheless, it seems generally valid to say that the stronger interactions are accompanied by greater degrees of polarization.

Figures 6 and 7 show that strong interactions and high degrees of polarization are more likely for the π -hole interactions in Table 2 than for the σ -hole in Table 1. More than one-third (39%) of the π -holes have ΔE values that are more negative than -10 kcal/mol, reaching -42.38 kcal/mol, and their average ΔE (pol) is -13.8 kcal/mol. In contrast, just 20% of the σ -hole interactions have ΔE values that are more negative is -21.96 kcal/mol, and their average ΔE (pol) is -4.0 kcal/mol.

Why are there such differences between the energetics of the σ -hole and π -hole interactions? One possible factor is that the planar surfaces around π -holes results in more atoms of the interacting molecules being in closer contact. Furthermore, σ -hole interactions are usually accompanied by increases or decreases in the lengths of the bonds that produce the σ -holes [69,74,75], while the π -hole interactions in Table 2 involve bond bending as the π -hole atoms change from trigonal to partial tetrahedral character [11,69]. Since bond stretching or compression requires a greater input of energy than bond bending [76], this would contribute to making σ -hole interactions on the average weaker (i.e., less negative ΔE).

8. Discussion and Summary

We have demonstrated that the energies of σ - and π -hole interactions can be expressed quite well in terms of four properties: the electrostatic potentials V(R) and electric fields ε (R) of the σ - and π -hole molecules at the approximate positions of the negative sites, the most negative potentials V_{S,min} on the 0.001 au surfaces of the negative sites prior to interaction, and the average polarizabilities α of these sites. It would of course be more accurate to use the components of the polarizabilities in the directions of the electric fields, but it is difficult to find reliable values for these [77]. The relative importance of the four properties cited varies somewhat depending upon the particular database; for instance, the interaction energies of the π -hole interactions in Table 2 can be represented without V(R).

The success achieved with Equations (3)–(5) supports the interpretation of these σ - and π -hole interactions as Coulombic in nature, which is consistent with the rigorous Hellmann–Feynman theorem [78,79]. Coulombic should be understood to mean both electrostatics and polarization. Dispersion is included in the polarization contribution, as demonstrated by Feynman [79].

It is noteworthy that interactions with ΔE ranging from -1.7 to -42.4 kcal/mol can be handled in the same manner. No new factors need to be invoked to account for the stronger ones. Overall, they simply involve greater degrees of polarization of the electronic densities of the negative sites toward the σ - or π -hole molecules. It might be suggested that this be described using terms such as "dative" or "coordinate covalent" character [11,25,30,80], but the gradation in interaction energies is in fact simply a manifestation of the continuum nature of chemical bonding, from weak to strong [81–84].

A major cause of deviations from Equations. (3)–(5) is the secondary interactions between portions of the molecules other than the σ - or π -hole potentials and the negative sites. Examples have been discussed earlier in this paper and in other work [11,65,69,85,86]. The problem arises because the actual computed ΔE does reflect secondary interactions, but Equations (3)–(5) do not.

The importance of secondary interactions increases as more atoms of the two molecules are in closer proximity. Thus, they can be expected to be less significant for σ -hole interactions than for π -hole interactions, and least so when the σ -hole atom is hydrogen or a halogen, since these have only one immediate neighbor, which is the atom to which the hydrogen or halogen is bonded. For example, there are 34 interactions in Table 1 in which the σ -hole is on hydrogen or a halogen. If Equation (4) is fit to the data for these 34 interactions, the R^2 is an excellent 0.980, and the root-mean-square error is just 0.60 kcal/mol. This correlation is clearly superior to the one for all 54 σ -hole interactions, as shown in Figure 3, which has an $R^2 = 0.938$ and root-mean-square error = 1.04 kcal/mol.

We conclude by noting again that we have considered only the polarization of the negative site by the σ - or π -hole molecule, not the polarization of the latter by the negative site. It seems reasonable to expect the polarization of the negative site to be the more important, since the negative site is likely to have the higher electronic density and be more polarizable. However, in principle, the present procedure could also be applied to the polarization of the σ - or π -hole molecule.

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