Sensitivity of Noncovalent Bonds to Intermolecular Separation:
Hydrogen, Halogen, Chalcogen, and Pnicogen Bonds

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Abstract
It is well known that noncovalent bonds are weakened when stretched from their equilibrium intermolecular separation. Quantum chemical calculations are used to examine and compare the sensitivity to stretches of hydrogen, halogen, chalcogen, and pnicogen bonds. NH$_3$ was taken as the universal electron donor, paired with HOH and FH in H-bonds, as well as with FPH$_2$, FSH, and FCl. Even though the binding energies span a wide range, stretching the intermolecular separation by 1 Å cuts this quantity by the same proportion, roughly in half, for each system. Taking the sum of van der Waals radii as an arbitrary cutoff, the H-bond energy in FH···NH$_3$ remains at 5.5 kcal/mol while the binding energy of the other three bond types is only slightly smaller at 4.5-4.7 kcal/mol.

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INTRODUCTION

The hydrogen bond has a long and venerated history \(^1\,^2\). From the standpoint of vibrational spectroscopy, the stretching frequency of the AH bond most commonly shifts to the red upon engaging in a AH···D interaction with an electron donor D. This shift is often accompanied by an intensification and broadening of the band. The NMR spectrum is affected as well, most notably a downfield shift of the signal of the bridging proton. Within a structural context, the AH···D arrangement strives toward linearity, and the separation between the H and D atoms is short, frequently described as smaller than the sum of the van der Waals radii of these two atoms. The A-H bond is elongated to a certain degree by the H-bond, and this bond lengthening correlates with the energetic strength of the interaction. The latter weakening of this bond is commonly attributed to the accumulation of charge in the A-H \(\sigma^*\) antibonding orbital.

While perhaps a somewhat later development than the H-bond, the halogen bond has undergone a great deal of scrutiny from both experimental and theoretical directions \(^3\,^9\). The replacement of the bridging H atom by a halogen X results in a number of parallels, but there are also significant differences. Like the H-bond, the A-X···D arrangement prefers a linear configuration, and the attraction between the two subunits results in a short contact distance between X and D, again less than the van der Waals radii sum. The tendency toward linearity is attributed to various factors. There is a decreased repulsive wall in this direction \(^3\). The A-X bond induces a nonspherical shape of the electrostatic potential around the halogen atom, wherein a ring of negative charge surrounds a crown of positive charge directly opposite the A-X bond, an effect sometimes referred to as a \(\sigma\)-hole \(^10\,^13\). The resulting electrostatic attraction to an incoming electron donor, is supplemented by other factors \(^14\,^16\) such as polarization/ charge-transfer effects \(^3\,^17\,^20\), as well as dispersion \(^21\,^23\). A transfer from the D lone pair to the A-X \(\sigma^*\) antibonding orbital, lengthens the A-X bond \(^24\,^26\). As in the case of H-bonds, this lp\(\rightarrow\sigma^*\) shift can be overridden by other factors, so not all halogen bonds result in a lengthening of the C-X bond \(^27\,^30\). Whether a H or X bond, the presence of electron-withdrawing substituents on the electron-acceptor enhances the binding \(^31\,^33\), a direct parallel to what is seen in H-bonds. There is a clear pattern wherein the strength of a halogen bond increases in the order F < Cl < Br < I \(^34\,^35\), and further that a halogen bonded to a sp\(^3\)-hybridized C forms a weaker bond than does one involving sp, with sp\(^2\) intermediate \(^36\). Halogen bonding energies can reach, and even surpass, the strengths of comparable H-bonds \(^37\,^38\).
Evidence has accumulated that H and X bonds are not alone. Work over the years has implicated chalcogen atoms such as O and S as potential replacements for halogens as bridging atoms \(^{39-41}\) and that nucleophiles tend to approach along extensions of the covalent bond by which the chalcogen is bound \(^{42,43}\). Also like halogen bonds, this bonding has been attributed at least in part to charge transfer into a \(\sigma^*\) antibonding orbital \(^{44-47}\), again supplemented by electrostatic attraction \(^{48,49}\), with an additional attraction supplied by dispersion \(^{50}\). There is evidence that like X bonds, chalcogen bonds also strengthen as the bridging atom moves down the pertinent column of the periodic table \(^{27,51-54}\).

Given the ability of atoms of Groups VII and VI to engage in interactions with a nucleophile, it should come as no surprise that the pnicogen (also sometimes referred to as pnictogen or pnigogen) family can do so as well. Most of the evidence for pnicogen bonds arose earliest from crystal structure analyses \(^{55-59}\), but were latter bolstered by computational support \(^{53,60-63}\). There are strong parallels with the halogen and chalcogen bonds, particularly in terms of the preference for a nucleophile to approach the pnicogen atom along an extension of one of its covalent bonds. Recent work from this laboratory \(^{64-68}\) has emphasized the importance of charge transfer from the lone pair of the approaching nucleophile into the PB \(\sigma^*\) antibonding orbital (where B represents the atom bonded to P that is turned away from the nucleophile), and that the strengths of pnicogen bonds are comparable to those of H, X, and chalcogen bonds. Other sets of calculations \(^{63,69,70}\) have confirmed these findings, and in particular the ability of electron-withdrawing substituents to enhance the bond. In contrast to a preponderance of findings that confirm the importance of charge transfer in these sorts of noncovalent bonds \(^{43,69,71-78}\), there are others that assert a dominating role of electrostatic phenomena \(^{79}\).

In addition to H-bonds, halogen bonds have also been recognized as important structural components in biological and non-biological macromolecules alike \(^{8-10,80-82}\), self assembly \(^{83,84}\), liquid crystal formation \(^{85,86}\), nonlinear optical properties \(^{87,88}\), or for recognition processes \(^{89,90}\). Their potential to be incorporated as design elements in pharmaceuticals \(^{91,92}\) or crystal \(^{93,94}\) engineering is also well established. Can the same be said of chalcogen and pnicogen bonds? Perhaps the first issue revolves around the recognition of these interactions when they are present. It is thus important to establish the geometric criteria that are associated with such bonds. A second and related question has to do with the strength of each such noncovalent bond. How much energy can they contribute to a given structure? And how does this maximal contribution diminish if these bonds are distorted from their optimal arrangement due to other
structural restraints within the entire crystal? Is there a set of cutoffs that can be recommended for halogen and other noncovalent bonds, in the same manner as has been done previously for H-bonds? The goal of the present communication is to try to provide answers to these questions, via quantum chemical calculations.

METHODS

Small model chemical systems are chosen by which to simulate H, halogen, chalcogen, and pnicogen bonds. In order to maximize the similarities, all binary complexes incorporate a common electron donor molecule, NH$_3$ in this case. The five complexes considered are illustrated in Fig 1. The Gaussian 09 package $^{95}$ was used to perform all calculations. Geometries were optimized at the ab initio MP2/aug-cc-pVDZ level which has been shown to be of high accuracy, especially for weak intermolecular interactions of the type of interest here $^{96,97}$ where the data are in close accord with CCSD(T) values with larger basis sets $^{22,65,98}$ and in excellent agreement with experimental energetics $^{99}$. Binding energies were computed as the difference in energy between the dimer, and the sum of the optimized energies of the isolated monomers, corrected for basis set superposition error by the counterpoise procedure.

RESULTS

HOH and HF form H-bonds, with total binding energies of 5.81 and 11.64 kcal/mol, respectively, as indicated by the blue numbers below each structure in Fig 1. The second-row atoms P, S, and Cl were chosen to study the pnicogen, chalcogen, and halogen bonds, respectively, as first-row atoms are reluctant participants in such interactions. The other three complexes thus involve electron acceptors H$_2$FP, HFS, and FCl. The fluorosubstituted molecules were selected as they have been found to form strong noncovalent bonds, more easily visible via crystal structures, and also as they facilitate comparison with the H-bonds, as documented below.

The binding energies of these molecules with NH$_3$ enlarge from 6.18 kcal/mol for H$_2$FP···NH$_3$ up to 10.37 kcal/mol for the halogen bond, as indicated in Fig 1. Note that these three values are bracketed by the two H-bonding energies. It might also be noted that the H-bond lengths are quite a bit shorter than the others, due largely to the small size of the bridging H atom. As the strengths of the A···N bonds grow, so do the intermolecular distances shrink, from 2.62 Å for H$_2$FP···NH$_3$ down to 2.27 Å for FCl···NH$_3$.

The effects of stretching each sort of bond on the binding energy is illustrated in Fig 2. The horizontal axis refers to the elongation of the intermolecular separation relative to the fully
optimized complex. This separation was increased in uniform increments, and for each new
distance, the remainder of the geometry of each complex was fully optimized. For all five
systems, one may note a sharp rise in energy as the bond begins to stretch from its equilibrium
distance. Each curve begins to flatten as the stretch continues, as it approaches its asymptote of
zero interaction energy for very long distances.

Any differences between the various curves are fairly subtle. For example, the FH···NH₃ H-
bond energy remains stronger than any of the other complexes for all stretches. It seems to
maintain its separation throughout, suggesting that this H-bond is of longer range than the other
noncovalent bonds. This distinction is likely due to the high proportion of electrostatic attraction
as a contributing factor to this bond, most notably the dipole-dipole attraction which is
distinguished by a perfect alignment of the two molecular dipoles. In contrast, the energy of
FCl···NH₃ appears to rise a bit more sharply than do the other complexes, suggesting that
halogen bonds are perhaps a bit more sensitive to stretching than are the other noncovalent bonds
considered here.

One might introduce an arbitrary quantitative measure of the steepness of each curve, ρ, the
stretch required to reduce the interaction energy to half its maximal value. All five of the
systems considered here have values of ρ between 0.9 and 1.1 Å, as reported in Table 1. In other
words, stretching the intermolecular separation by some 1 Å cuts the binding energy of each
system roughly in half. This required stretch ρ is smallest for FCl···NH₃, making this the system
most sensitive to bond stretch, while FH₂P···NH₃ is the least sensitive. But again, there is not a
large difference of ρ from one system to the next, all within the range of 0.9-1.1 Å.

What might be considered the cutoff or threshold? That is, after how much of a stretch can
one say that a H or other noncovalent bond is “broken”? This is a question that has laid at the
heart of many discussions of H-bonds. The answer clearly depends upon one’s definition of a
bond. A criterion of an attractive force, even if a small one, is probably unsatisfactory as the
attraction persists to even very long distances. A threshold of a particular bond energy would
lead to the idea that the stronger interactions may be stretched a greater amount. Taking 4
kcal/mol as a sample cutoff, the FH···NH₃ H-bond may be stretched by 1.3 Å, while the allowed
stretch in FH₂P···NH₃ is only 0.8 Å. Still another view might envision the stretch required to
reduce the binding energy to half its maximal value, in which case all the systems can sustain a
stretch of some 1.0 ± 0.1 Å.
It might be instructive to consider how particular choices of a bond distance cutoff correlate with binding energy. In the strongly H-bonded FH···NH\textsubscript{3} complex, the equilibrium R(H···N) distance is 1.69 Å. Adding in the r(FH) bond length of 0.96 Å, the R(F···N) distance is 2.65 Å. If one were to assert a R(F···N) cutoff of 3.02 Å, the sum of \( r_F + r_N \) van der Waals radii \(^{101}\), the stretch of 0.37 Å would leave a residual H-bond energy of 10 kcal/mol. Even taking the longer cutoff of 3.2 Å would correspond to a value of 8.5 kcal/mol. A R(H···N) distance of 2.75 Å, corresponding to the sum of r\( _H \) + r\( _N \) van der Waals radii, and representing a stretch of 1.06 Å, is still associated with a rather strong interaction, of some 5.5 kcal/mol. One of the longer H-bond threshold values proposed in the literature sets the R(F···N) distance at 4 Å \(^{102}\), which would reduce the interaction energy to 1.0 kcal/mol.

Turning next to the pnicogen bond in Fig 1c, a threshold of 3.0 Å for the R(P···N) separation corresponds to a stretch of 0.38 Å from its equilibrium value, reducing the bond energy by only 0.6 kcal/mol, from 6.2 down to 5.6. Taking the sum of van der Waals radii \(^{101}\) for this pair of atoms, 3.35 Å, as the threshold leaves a remaining noncovalent bond energy of 4.5 kcal/mol, still quite strong. (The binding energies of the halogen and chalcogen bonds are quite similar, 4.6 and 4.7 kcal/mol, respectively, when the molecules are separated by the sum of van der Waals radii.) Indeed, even a stretch of the intermolecular distance up to 4.0 Å provides a bond energy in excess of 2 kcal/mol. Note that the latter represents a stronger interaction than a H-bond of only 1 kcal/mol with a similar R(F···N) distance. One of the longer thresholds in the literature for interactions of this sort is a value of 4.5 Å \(^{103}\). At this very long distance, the interaction energy remains at roughly 1.5 kcal/mol.

The slow die-off of these interaction energies suggests that there is perhaps a heavy element of electrostatic attraction. And indeed, previous work \(^{64-68}\) from this laboratory has confirmed that electrostatics, along with induction, is a strong contributor to such noncovalent bonds. The electrostatic and induction energies are similar in magnitude to one another, and both correlate very closely with the total interaction energy in pnicogen, chalcogen, and halogen bonds. In the case of H-bonds, electrostatic attraction plays an even more important role, not only in the ground, but also in excited states \(^{104-106}\).

Of course, the systems discussed above may indeed be stretched but all are undistorted in an angular sense. In other words, the two molecules are allowed to adopt their most favorable relative orientations. The proton in FH···NH\textsubscript{3} lies directly along the F···N axis, for example, and the F atom in H\textsubscript{2}FP···NH\textsubscript{3} is turned 167° away from the N atom. But just as crystal forces induce
stretches in these noncovalent bonds, so too are bends quite common. The effects of such misalignments were examined earlier in the same systems illustrated in Fig 1, as well as several others. The calculations showed that pnicogen, as well as chalcogen and halogen bonds, are more sensitive to misorientations than are H-bonds. The dependence of the energy upon the bending angle, $\Delta \theta$, was very close to a parabola, so that it was possible to closely fit the energy to a quadratic function of the form $E = \frac{1}{2} k(\Delta \theta)^2$.

The force constants, $k$, computed for bending the two H-bonded systems, $\text{FH}\cdots\text{NH}_3$ and $\text{HOH}\cdots\text{NH}_3$, were 15.8 and 10.5 kcal mol$^{-1}$ rad$^{-2}$, respectively. These same quantities were several times greater, between 61 and 70 kcal mol$^{-1}$ rad$^{-2}$, for the pnicogen, chalcogen, and halogen bonded systems incorporating $\text{H}_2\text{FP}$, HFS, and FCl. From another perspective, the H-bond energy of $\text{FH}\cdots\text{NH}_3$ can withstand a bend of some 40º and still maintain half its optimal value, as listed as $\tau$ in the last column of Table 1; the $\text{HOH}\cdots\text{NH}_3$ system is even more flexible with a value of $\tau$ of 45º. These same quantities are greatly reduced in the pnicogen, chalcogen, and halogen-bonded systems, which lose half of their binding energy when bent by only 15-20º. One can conclude that any thresholds imposed on angular features of these types of bonds might be quite different than those applied to H-bonds, and should take into account their lesser flexibility.

CONCLUSIONS

Halogen, chalcogen, and pnicogen bonds all exhibit a reduction in binding energy upon stretching that is fairly similar to H-bonds, even though the systems considered covered a wide range of interaction energy at equilibrium. As a general rule, a stretch of 1 Å from equilibrium reduces the binding energy by a factor of one half for all systems. When the two molecules are separated by the sum of their van der Waals atomic radii, the binding energies of the halogen, chalcogen, and pnicogen bonds are all 4.6 ± 0.1 kcal/mol. In contrast to similarities in terms of stretching, the H-bonds are considerably less sensitive to angular distortions than are the other bond types.
REFERENCES


Table 1. Distortions that result in reduction of maximal binding energy, BE, by a factor of one half

<table>
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$^a\rho =$ stretch required to reduce the interaction energy to half its maximal value.

$^b\tau =$ bend required to reduce the interaction energy to half its maximal value.
Fig 1. Optimized geometries of various complexes, all involving NH$_3$ as electron donor. Acceptors are a) HOH, b) FH, c) H$_2$FP, d) HFS, and e) FCl. Distance in Å and angles in degs. Large blue numbers indicate counterpoise-corrected binding energies in kcal/mol.
Fig 2. Weakening of binding energy of various complexes, all involving NH₃ as electron donor, as intermolecular distance is stretched. HF and HOH form H-bonds with NH₃. P label indicates H₂FP···NH₃ complex, S refers to HFS···NH₃, and Cl to FCl···NH₃. The zero of energy in each case refers to fully separated monomers. Optimized equilibrium distance in each complex (see Fig 2) is taken as ΔR=0.