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Research paper

# Critical comparison of R—X···Y and R—H···Y directionality in halogen and hydrogen bonds using modern computational chemistry methods

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## HIGHLIGHTS

- Halogen bond.
- Hydrogen bond.
- Noncovalent interactions.
- Computational Chemistry.

## ABSTRACT

Symmetry adapted perturbation theory anlysis and intermolecular overlap volume calculations are used to investigate the origins of halogen- and hydrogen bond directionality. The central finding is that exchange-repulsion is primarily responsible for destabilizing both types of interaction as the R-x···Y (x = H, Cl, Br) angle deviates from linearity. The particular shape of the electron density envelope on the halogen/hydrogen bond donor plays a large role in dictating the degree to which a complex is destabilized upon R-x···Y rotation, with halogen bonds exhibiting a roughly linear destabilization and hydrogen bonds exhibiting destabilization that is approximately quadratic.

## 1. Introduction

One of the main reasons that halogen bonds of the type C—X···Y (X = Cl, Br, I; Y = O, N, S, π) have received such a large amount of attention in recent years is that these noncovalent interactions have been shown to be very directional in nature, with the positive region (σ-hole) of the halogen, located on the extension of the C—X bond, tending to point directly toward the negative halogen bond acceptor, Y (ie. a (C—X···Y) = 180°) [1–5]. Largely owing to this directionality, halogen bonds are often seen as being closely related to their more ubiquitous counterparts, hydrogen bonds, which also exhibit linear R-H···Y directionality [5,6]. Halogen bonds and hydrogen bonds have similar binding energies and hold several physical properties in common, both being strongly directional interactions whose attraction is largely attributable to electrostatic forces [7]. Many studies aimed at replacing hydrogen bonds with halogen bonds [8–10] or (rarely) vice versa [11], in material structures have been conducted in recent years, taking advantage of the similarity between these two interaction types. It should be noted that there are physical attributes that set halogen- and hydrogen bonds apart. Notably, because halogens are large atoms having high polarizabilities, dispersion forces generally play a larger role in stabilizing halogen bonds [12].

Perhaps surprisingly, the results of several studies indicate that halogen bonds actually tend to favor linear configurations more strongly than do hydrogen bonds [5,13,14]. It had long been taken for granted that the directionality of halogen bonds is electrostatically driven, as would seem most intuitively apparent, given the strong role that electrostatics plays in stabilizing these interactions. In a study incorporating symmetry adapted perturbation theory (SAPT), Stone showed that exchange-repulsion, not electrostatics, is responsible for halogen bond directionality [4]. In this study, which considers several halogen bonding pairs, a halogen bond distance is held fixed while the C—X···Y angle is modified, generally to 40° from linearity. It is clearly seen that the electrostatic, dispersion, and induction terms are very weak functions of this rotation, while the exchange term becomes substantially larger, destabilizing the complex, as the halogen bond deviates from linearity. The magnitude of the exchange destabilization is roughly equal to the total destabilization energy of the complex, meaning that the exchange term, not electrostatics, plays the principal role in halogen bond directionality. The reason for this lies in the oblate shape of the halogen, often described as polar flattening [15]. Our laboratory has found similar results for systems involving a cation [16] as the halogen bond donor and for systems involving the π-system of a benzene ring [17] as the halogen bond acceptor.

The halogen σ-hole is a region of relative electron deficiency located along the extension of a C—X bond [18]. The most commonly noted characteristic of a σ-hole is the corresponding region of positive charge clearly seen in electrostatic potential maps of halogen-containing molecules. The electron deficiency associated with a σ-hole also impacts the shape of the halogen, resulting in an oblate electron density

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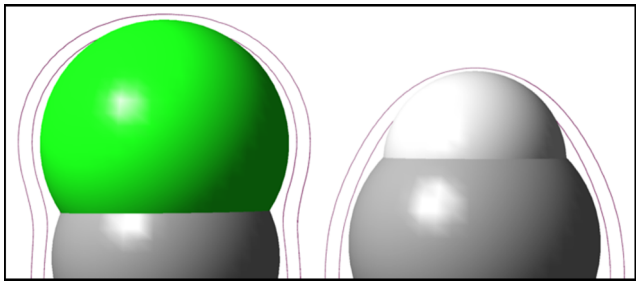

**Fig. 1.** 0.001 and 0.002 e-/Å$^3$ isosurfaces for ClCN (left) and HCN (right). Here the polar flattening associated with covalently bound halogens can be seen. The shape of the electron density envelope on hydrogen is roughly parabolic.

envelope. The establishment of this oblate shape upon bonding (σ-hole formation) is often referred to as polar flattening (Fig. 1) [15]. Owing to the particular shape of the electron density envelope in a covalently bound halogen, a decrease of the C—X···Y angle results in an increase in the overlap between the Y and halogen electron densities, thus increasing the repulsion energy and, to a smaller extent, augmenting dispersion attraction [4].

It is also seen in Fig. 1 that the electron density envelope of a covalently bound hydrogen also deviates from sphericity significantly. The shape of the electron density envelope here is not oblate but approximately parabolic, owing to the small size of hydrogen relative to its bonding partner. Although the electron density envelope of a bound hydrogen does not deviate from sphericity to the same extent as does that of a bound halogen, being approximately spherical along the extension of the C—H bond, the parabolic shape has strong potential to increase overlap (and repulsion) because hydrogen bond distances (~2–2.5 Å) are substantially shorter than halogen bond distances (~3–3.5 Å). Several studies exploring the nature of halogen bond [4,19–23] and hydrogen bond [5,6,22–27] directionality have been undertaken in the past several years. Here we use modern quantum chemical methods to investigate halogen- and hydrogen bonding systems to augment our understanding concerning the directionalities of these interactions.

## 2. Computational methods

In this study R-X···Y and R-H···Y directionalities of halogen- and hydrogen bonds are investigated using the SAPT2 + 3δMP2/aug-c C—pVTZ [28] method (PSI4[29]) as well as intermolecular overlap volume calculations. Here complexes containing linear molecules are investigated, as the electron density envelopes of these molecules are the least complex and as using these types of complexes minimizes the potential for secondary interactions. Here four halogen bonding complexes, NCCl···NCH, HCCCl···NCH, HCCCl···N2, and NCBr···NCH, and three hydrogen bonding complexes, NCH···NCH, HCCH···NCH, and HCCH···N2, are considered. The complexes were chosen to represent a range of interaction strengths, with NCx···NCH (x = Cl,H) being strong, HCCx···NCH intermediate, and NCCx···N2 weak interactions. NCBr···NCH is also considered in order to verify that results found for chlorine-containing halogen bonding systems also apply to systems containing larger halogens.The geometry for each of the complexes was generated in a two-stage process. First, optimization was carried out at the counterpoise-corrected MP2/def2-TZVP level of theory, next a five-point potential energy curve was generated for modification of the Cl···Y, Br···Y, or H···Y distance, within the fixed monomer approximation, using SAPT2 + 3δMP2/aug-c C—pVTZ. The minimum of this potential energy curve was taken to represent the equilibrium geometry of the complex.

To further investigate the effects of molecular shape on directionality in halogen- and hydrogen bonds the density overlap volumes between monomers are computed as a function of θ (the C—x···N angle, x = Cl,H) for several dimers. These calculations were performed using the MULTIWFN [30] program with densities generated at the B3LYP/6-311G* level using Gaussian 16 software [31]. It should be noted that, as the overlap densities computed are between two non-interacting monomers, induction effects are not accounted for here. This is not problematic, as induction plays a negligible role in each of these complexes.

## 3. Results

Fig. 2 gives SAPT components as a function of C—Cl···Y tilting for the three halogen bonding complexes considered here. Focusing on the bottom graphs in this figure, giving unscaled SAPT terms, it is seen that both electrostatics and dispersion play large roles in stabilizing these halogen bonds, with the relative contribution from electrostatics increasing for stronger halogen bonds. This is consistent with previous results in which it is found that the magnitude of the electrostatic term

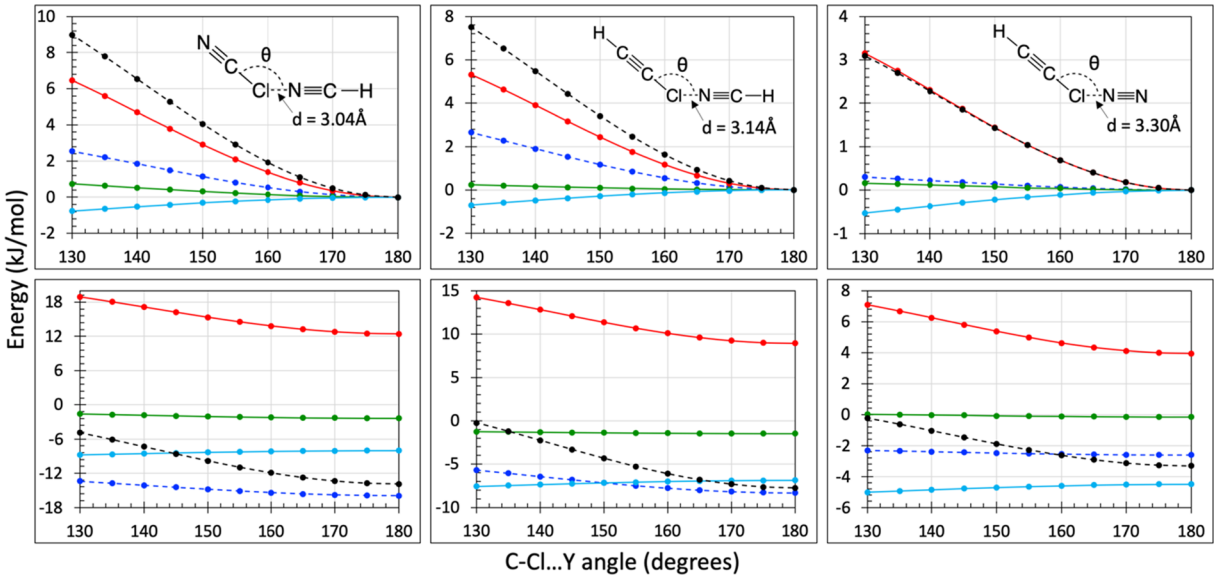


**Fig. 2.** Deviation of SAPT components from their θ = 180° values (top) and absolute SAPT component values (bottom) as a function of C—Cl···N halogen bond donor molecule rotation (θ) in halogen bonding complexes: electrostatics, exchange, induction, dispersion, interaction energy (black).

increases significantly with increasing halogen bond strength, while contributions from dispersion and exchange also become larger (in magnitude), but to much smaller extents [12]. The weakest halogen bond here, HCCCl···$N_2$ ($\triangle E_{int}$[180°] = 3.32 kJ/mol), is dominated by dispersion attraction while the strongest, NCCl···NCH ($\triangle E_{int}$[180°] = 13.88 kJ/mol), is primarily stabilized by electrostatics.

It can also clearly be seen in these graphs, and even more so in the upper graphs showing the deviation of the SAPT terms from their values at 180°, that it is the exchange term that varies most strongly as a function of C—Cl···Y rotation. In the case of HCCCl···$N_2$ the electrostatic and induction terms are essentially flat, varying insignificantly as a function of θ, while the dispersion term becomes slightly more attractive and the exchange term significantly more repulsive as the C—Cl···N angle deviates from linearity. The curves generated for this system are very similar to those for the F-Cl···$N_2$ complex generated by Stone. Here exchange can clearly be seen to dominate the directional behavior of this halogen bond. For the HCCCl···NCH and NCCl···NCH complexes, it is seen that an increase in exchange-repulsion is again dominant in terms of the directionality of the interactions, although the electrostatic term increases non-negligibly as a function of halogen bond rotation for both complexes. For both these complexes, the magnitude of destabilization attributable to exchange is about 2 – 2.5 times larger than that attributable to electrostatics for all angles between 130° and 170°. It should also be noted that deviations in the exchange term, and thus the total interaction energy, become larger with increasing

halogen bond strength. The reason for this is that stronger halogen bonds have shorter Cl···Y distances, resulting in higher degrees of density overlap upon C—Cl···Y rotation. These results confirm the findings of Stone, indicating that exchange, not electrostatics, plays the dominant role in mediating halogen bond directionality.

In Fig. 3 it is seen that the NCBr···NCH complex exhibits the same general directional behavior, in terms of SAPT interaction energy

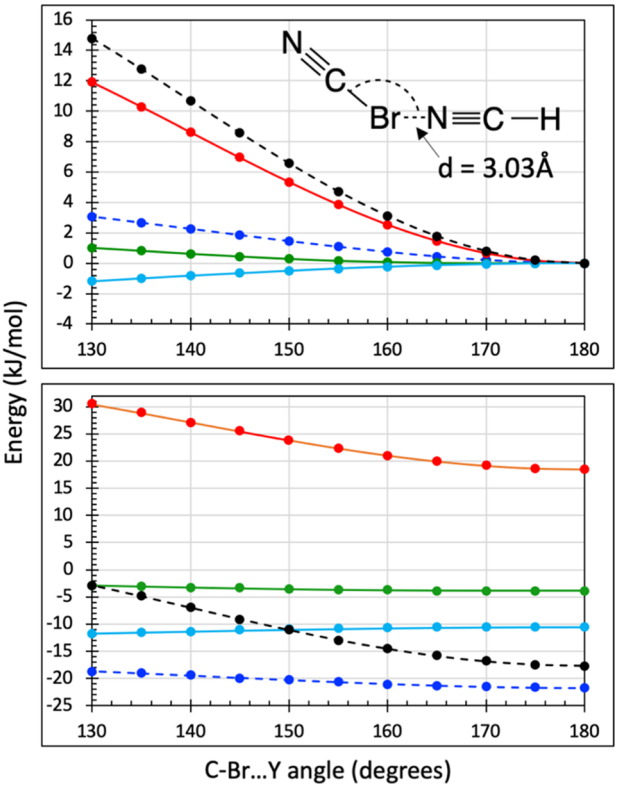


**Fig. 3.** Deviation of SAPT components from their θ = 180° values (top) and absolute SAPT component values (bottom) as a function of C—Br···N halogen bond donor molecule rotation (θ) in NCBr···NCH: electrostatics, exchange, induction, dispersion, interaction energy (black).

contributions, as do the three chlorine-containing halogen bonding systems. Here C—X···N rotation results in a significantly higher degree of destabilization in NCBr···NCH than in NCCl···NCH; at an angle of 140° NCBr···NCH is destabilized by 10.7 kJ/mol while NCCl···NCH is destabilized by 6.5 kJ/mol. There are two factors that contribute to this enhanced directional behavior, both of which are related to the fact that the halogen σ-hole is larger in NCBr than in NCCl. The presence of a larger σ-hole implies a greater degree of polar flattening, leading to an enhanced degree of electron density overlap upon C—Br···N rotation. Bromine's larger σ-hole also results in enhanced electrostatic attraction, which results in a significantly shorter distance between donor and acceptor electron density envelopes [32]. Here it is seen that the Br···N distance (between atomic centers) in NCBr···NCH is slightly smaller than the Cl···N distance in NCCl···NCH despite the fact that the bromine van der Waals radius is significantly larger than that of chlorine ($r_{vdw}$(Br) = 1.85 Å, $r_{vdw}$(Cl) = 1.75 Å). This higher degree of overlap between donor and acceptor molecules in NCBr···NCH, relative to NCCl···NCl, is reflected in exchange and dispersion terms that have substantially larger magnitudes at 180° ($E_{disp}$(NCBr···NCH) = -10.51 kJ/mol, $E_{disp}$(NCCl···NCH) = -8.03 kJ/mol, $E_{exch}$(NCBr···NCH) = 18.49 kJ/mol, $E_{exch}$(NCCl···NCH) = 12.44 kJ/mol. The closer proximity of the electron density envelopes in NCBr···NCH leads to a larger degree of destabilization upon halogen bond tilting.

Fig. 4 gives SAPT components for the three hydrogen bonding complexes considered here as a function of C—H···N tilting. Here it is seen that the two stronger hydrogen bonds, those in HCCH···NCH and NCH···NCH, are stronger than their halogen bonding counterparts and are more strongly stabilized by electrostatics than by dispersion (eg. $E_{elec}/E_{disp}$[NCH···NCH,180°] = 3.19, $E_{elec}/E_{disp}$[NCCl···NCH,180°] = 1.99). The interaction energy for the HCCH···$N_2$ complex is similar to that of HCCCl···$N_2$, with electrostatics playing a larger role in stabilization.

Focusing on the upper curves in Fig. 4, showing deviations in SAPT terms from their values at 180°, it can be seen that, as in the case of halogen bonds, exchange, not electrostatics, plays the largest role in destabilizing these hydrogen bonds as they rotate away from linearity. The electrostatic and induction terms are relatively insensitive to C—H···N tilting, although the electrostatic term does increase slightly with decreasing θ for the HCCH···NCH complex. As in the case of the halogen bonding systems, here stronger interactions exhibit larger destabilizations as their structures deviate from linearity. Again, this is attributable to the fact that stronger hydrogen bonds have shorter intermolecular distances, which result in more electron density overlap upon C—H···Y rotation.

Comparison of these curves with those shown for halogen bonds in Fig. 2 shows that deviations from linearity result in larger degrees of destabilization for the halogen bonds than for the hydrogen bonds, in agreement with previous studies indicating that halogen bonds exhibit stronger directionality than do hydrogen bonds. It is also seen that the shape of the curve for the total interaction energy is distinct for these two types of interactions. In halogen bonds, these curves are approximately linear from 130° to 165°, while for hydrogen bonds these curves are roughly quadratic through all angles. Interestingly, for each type of interaction, the exchange and dispersion terms behave similarly to the total interaction energy, meaning that these terms are also roughly linear from 130° to 165° for halogen bonds and roughly quadratic for hydrogen bonds. As both dispersion and exchange depend strongly on intermolecular overlap effects, this behavior implies that the difference in the directionality of these interaction types lies in the differences in shape of the halogen- and hydrogen bond donor electron density envelopes.

Fig. 5 shows monomer density overlap volume deviations from their values at θ = 180°, as a function of C—x···Y tilting, for all complexes considered here (with isovalue 0.0015, the unscaled curves are given in SI Fig. 1). Here it is seen that rotation of the C—x···Y angle away from linearity results in monomer density overlap volume increases for all complexes. Notably, these overlap volume deviations behave similarly

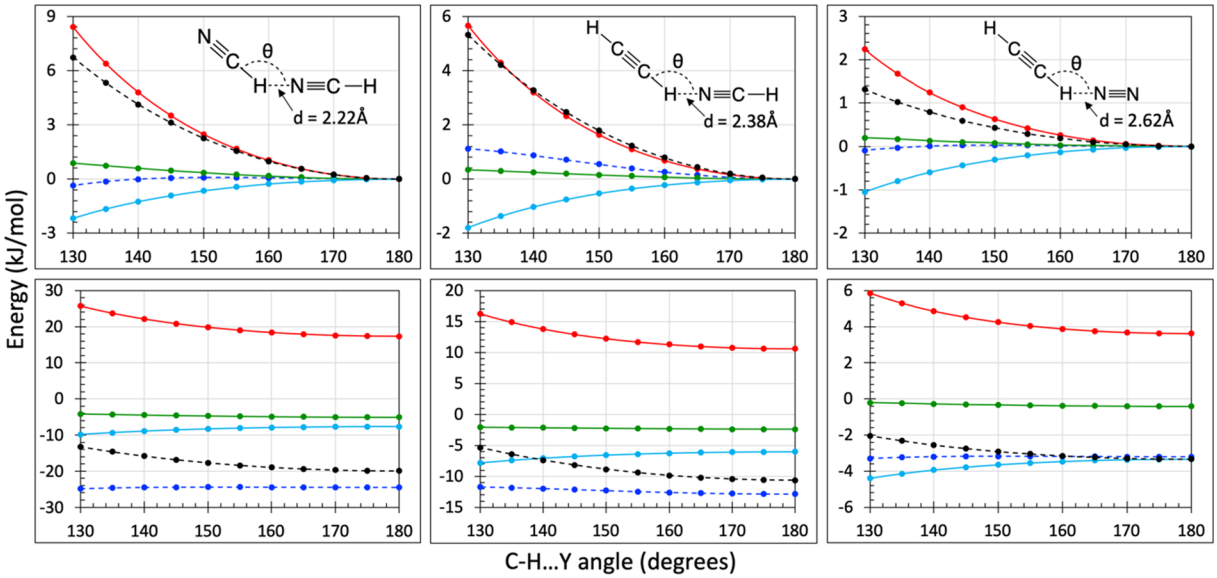


**Fig. 4.** Deviation of SAPT components from their θ = 180° values (top) and absolute SAPT component values (bottom) as a function of hydrogen bond donor molecule rotation (θ) in hydrogen bonding complexes: electrostatics, exchange, induction, dispersion, interaction energy (black).

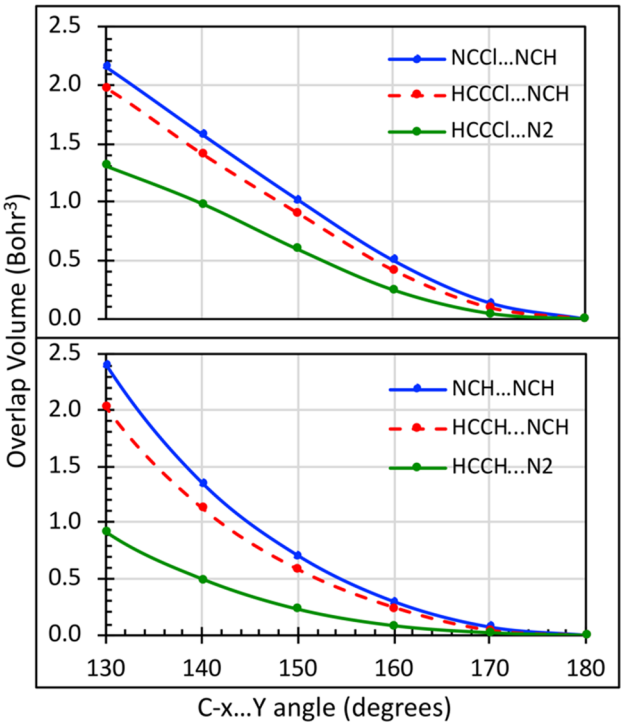


**Fig. 5.** Deviation in density overlap volumes for all complexes as a function of θ for C—Cl···Y interactions (top) and C—H···Y interactions (bottom).

to the deviations in the exchange and interaction energy curves for each complex, with halogen bonds exhibiting approximate linearity between θ values of 130° and 165° and hydrogen bonds being roughly quadratic through all angles. This result further supports the idea that it is the enhanced overlap between the electron density envelopes of the interacting molecules, with the associated increase in exchange repulsion, that is responsible for destabilizing these complexes upon C—x···Y rotation away from linearity.

## 4. Conclusions

Here it has been shown that exchange forces play the dominant role in the R-x···Y directional behavior of both halogen- and hydrogen bonds. These studies utilize complexes composed of linear structures, as the simple structures of these systems allowed for interpretation of results to be much more straightforward. The particular shape of the electron density envelope on the halogen/hydrogen bond donor plays a large role in dictating the degree to which a complex is destabilized upon R-x···Y rotation, with halogen bonds exhibiting a roughly linear destabilization and hydrogen bonds exhibiting destabilization that is approximately quadratic.

In terms of halogen bonding, the results presented here are in good agreement with those of Stone, as has been indicated above. To put these results into a wider context, it should be noted that Adhikari and Scheiner have conducted a study, based on SAPT analyses, indicating that exchange plays the dominant role in the directionality of not only halogen bonds, but also pnicogen and chalcogen bonds [22]. Hydrogen bonds are also investigated here, however dependence of the interaction energy on the R-H···Y angle is not directly considered. It is found that halogen-, pnicogen-, and chalcogen bonds all exhibit angular dependencies that are roughly quadratic functions of the R-x···Y angle (x = P, S, Cl). Shields et. al. performed an investigation of halogen- and hydrogen bond directionality, based on interaction energy calculations and careful evaluation of electrostatic potentials computed at the B3PW91/6- 311G(3d,2p) level. Here it is indicated that electrostatics, not exchange, are primarily responsible for halogen- and hydrogen bond directionality. This conclusion is largely based on the very good correlation between interaction energies at varying C—x···N angles (x = Cl, H, acceptor molecules here are $NH_3$ and NCH) and the value of the electrostatic potential at the site of the halogen/hydrogen bond acceptor nitrogen atom. It should be noted, however, that in these studies the intermolecular distance is optimized at each angle, resulting x···N (x = Cl, H) distances that increase with increasing C—x···N angles. Both the interaction energy (compare results presented here with, for example, results from reference 32) and the electrostatic potential are stronger functions of the distance than of angular deviations, thus the modulations in distance, rather than angle, likely play larger roles in determining the values of both the interaction energies and the electrostatic potentials that are compared. Based on the results of the current study, it would be argued that the increase of the intermolecular distance upon increase of C—x···N angle is attributable to enhanced exchange-repulsion upon deviation of the C—x···N angle from linearity.

Clearly, the shape of the electron density envelope, and thus the

directional behavior of an intermolecular interaction, can be much more complicated than the model systems investigated here, even for the simplest non-linear molecules. Thus, further investigations of directionality in halogen- and hydrogen bonds are called for.

## CRediT authorship contribution statement

**Kevin E. Riley:** Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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