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# Geometrical Analysis to Understand the Ability of Halogen Atoms to Act as Hydrogen-Bond Acceptors: A Structural Database Study

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Non-covalent interactions involving halogen atoms play a major role in supramolecular chemistry, biochemistry, coordination and organometallic chemistry and also act as conformation-determining factors. Therefore, the hydrogen-bonding nature of the halogen acceptors in solid state are analyzed statistically, and the geometrical characteristics of weak hydrogen-bonded interactions are studied for the oxygen, nitrogen, and carbon atom donors. The hybridization states of the donor atoms and the different coordination environment of the halogen acceptors were also considered. The distance and the directionality characteristics that dictate the hydrogen bonds are given importance. Oxygen and nitrogen donors both showed the ability to form a strong hydrogen bond whereas carbon donors formed weak hydrogen bonds. The hydrogen-bonding nature of the carbon donor with a halogen acceptor was proven with this analysis; however, it had a hydrogen···acceptor distance cutoff of 2.7 Å for chlorine. Different hybridization states of the donor atoms did not significantly change the nature of the interaction; however, various coordination environments had some effect.

Intermolecular interactions in the crystals of organic compounds are of two types: isotropic medium-range forces that define the shape, size, and close packing, and anisotropic long-range forces which are electrostatic and include hydrogen bonds and heteroatom interactions. In the crystals, the observed architecture is the result of interplay between the isotropic van der Waals forces and the anisotropic hydrogen-bond interactions wherein the distinction lies in their orientational and angular attributes.[1] The nature of intermolecular interactions that mediate molecular recognition are: strong O–H···O, N–H···O, O–H···N hydrogen bonds; weak C–H···O, C–H···N hydrogen bonds; heteroatom interactions X···X, X···O (X = Br and I); $\pi$–$\pi$ interactions; and van der Waals forces.[2] Hydrogen bonds, which are regarded as the strongest and most directional of intermolecular interactions, have been widely exploited in many fields.[3] These molecular interactions are influenced by dispersion, polarization, electrostatic, charge-transfer, and exchange forces.[4] Depending on the particular chemical donor–acceptor combination and the detailed contact geometry, all of these terms contribute with different weights.[5] For strong donors like O–H or N–H, the electrostatic component is dominant, whereas for weakly polarized donor groups like C–H, the magnitude of electrostatic component is due to van der Waals forces.[5,6]

Hydrogen bonding is a well-known classical structural phenomenon,[7] whereas the topic of weak intermolecular interactions is still contentious. These interactions enable one to design and manipulate the molecular systems and applied to the fields of rational drug design, crystal engineering, supramolecular chemistry, and physical organic chemistry.[8] Also, these secondary interactions have ramifications in the systematic design of new materials possessing novel chemical, magnetic, optical, or electronic properties.[9] Critical assessment of the weak intermolecular interactions is a must because they may exert a substantial effect when added together. In this context, the acceptor capabilities of halogen atoms are controversial and noteworthy.[10] The geometric characteristics of these interactions are essential since they form the basis for theoretical calculations of molecular electronic structure in molecular mechanics and molecular dynamics, in modeling studies, in protein structure determination, and in the derivation of new potential energy functions.[11] Geometric characterization of hydrogen bonding using computation involves statistical analysis of structural data (information obtained from a large number of crystal structures), which is very important for a correct interpretation of several chemical phenomena,[12,13] as well as to understand better the nature of hydrogen bonds and intermolecular interactions. An advantage with this database approach is that any distortion in individual interaction geometry can be averaged out in the diverse sample of X-ray crystal structures determined for a variety of reasons.[2]

Intermolecular interactions involving halogen atoms, namely halogen···halogen and X–H···halogen (Hal), continue to attract significant attention in chemical, crystallographic, and crystal engineering literature.[14] Similarly the hydrogen-bond acceptor capability of halogens has attracted attention from the fields of supramolecular chemistry, biochemistry, coordination and organometallic chemistry.[15] C–H···Cl interactions act as conformation-determining factors in metal complexes as do other non-conventional hydrogen bonds,[16] and a C–H···F–C interaction is a necessary in transition-metal-catalyzed alkene polymerization, ligand–enzyme binding, and molecular conformation.[10] Recent studies revealed both the ability and inability of specific halogens to form strong hydrogen bonds depending upon the coordination environment of the halogen.[7,10,14–20] This study is a statistical analysis of X–H···Hal interactions observed in the crystal structure of small molecules in order to establish the acceptor capability of halogen atoms. Hydrogen bonds are typically described in terms of various parameters (lengths and angles) obtained from actual crystal

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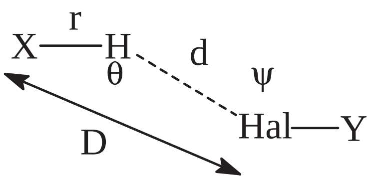


Fig. 1. Description of the geometric parameters. X: oxygen, nitrogen, or carbon atom and Y: either transition metals (TM) or elements other than ions and metals (organic).

structure determinations.[13] The explanation of the various parameters used for the study of hydrogen-bonding interactions of halogen acceptor are depicted in Fig. 1. The geometrical parameters donor···acceptor distance ($D$), hydrogen···acceptor distance ($d$), donor angle [X–H···Hal] ($\theta$), and the acceptor angle [H···Hal–Y] ($\psi$) are calculated for all of the structures using the Cambridge Structural Database (CSD) as explained in the Materials and Method section.

## Results and Discussion

The capability of halogen atoms to act as hydrogen-bond acceptor was studied using geometrical parameters. For this analysis, two datasets were created. The first dataset, named General dataset, involved a search of the CSD for all unique X–H···Hal interactions (Hal = F, Cl, Br, and I) for the three different donor atoms (oxygen, nitrogen, and carbon), and the second dataset involved more specific searches in which the hybridization state of the donor atoms and the atomic species attached to acceptor groups were varied. The second dataset was further classified into three sub-datasets based on the halogen acceptor moiety: Hal$^-$ (ion), Hal–TM (transition-metal-bound halogen) and Hal–Organic (all other elements except metal; only organic compounds were considered) interacting with four different donor moieties at various hybridization states {O (sp$^2$ and sp$^3$), N [sp, sp$^2$, sp$^2$(+), sp$^3$, and sp$^3$(+)], C (sp, sp$^2$, sp$^3$), and S(no distinctions)}. Mean and standard deviation ($\sigma$) values were calculated for all of the geometric parameters for each screen. Cone correction was done for angular distribution, and normalization for d and $\theta$ parameters were made in order to compare the different X–H···Hal systems which are described in the Materials and Method section.

**General Dataset.** The mean H···Hal ($d$) and X···Hal ($D$) distances are compiled in Table 1 for hydrogen bonds from the donors O–H, N–H, and C–H to the acceptors F, Cl, Br, and I. Comparatively the data volume is larger for chlorine acceptors than all of the other acceptors. The typical donor···acceptor and H···acceptor distances for a strong hydrogen bond like O–H···O are 2.5–3.2 and 1.5–2.2 Å, respectively, and they have nearly linear angles (170–180°). For the weaker bonds, the values are 3.0–4.0 and 2.0–3.0 Å, and the donor angle is 90–180°. From the table, fluorine falls in the strong bond category, and all of other halogen species fall in the weak hydrogen-bond category.[21] The normalized mean values (Table 1) indicate that the values fall near the van der Waals radii for both distances, $D$ and $d$. In addition, the mean values of the donor···acceptor distance in C–H donor group for bromine and iodine acceptors are less when compared to their O–H and N–H donor counterparts. However, analyses of the mean

Table 1. Mean Values and the Normalized Mean Values for Donor···Acceptor and H···Acceptor Distances for the General Dataset[a)]

| | Mean values for donor···acceptor distance/Å | | | | | | | | Mean values for H···acceptor/Å | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | | Cl | | Br | | I | | F | | Cl | | Br | | I | |
| | Actual | Norm. | Actual | Norm. | Actual | Norm. | Actual | Norm. | Actual | Norm. | Actual | Norm. | Actual | Norm. | Actual | Norm. |
| O–H | 2.8(1)[c)] | 0.95(4) | 3.12(9)[f)] | 0.95(3) | 3.3(2)[i)] | 0.96(4) | 3.4(2)[l)] | 0.98(5) | 2.2(3) | 0.87(11) | 2.3(2) | 0.80(6) | 2.4(2) | 0.83(6) | 2.6(2) | 0.85(6) |
| N–H | 2.92(6)[d)] | 0.97(2) | 3.15(8)[g)] | 0.96(2) | 3.28(9)[j)] | 0.97(3) | 3.5(1)[m)] | 0.98(4) | 2.2(2) | 0.88(8) | 2.3(2) | 0.81(6) | 2.4(2) | 0.83(6) | 2.7(2) | 0.87(6) |
| C–H | 3.09(9)[e)] | 0.98(3) | 3.3(2)[h)] | 0.96(6) | 3.3(4)[k)] | 0.92(11) | 3.3(4)[n)] | 0.89(11) | 2.5(1) | 0.99(4) | 2.7(2) | 0.95(8) | 2.7(3) | 0.93(11) | 2.8(4) | 0.92(12) |

a) The standard errors of the mean values are given in parentheses. b) Norm.: Normalized mean values. Number of observations c) 25; d) 39; e) 150; f) 1025; g) 1938; h) 332; i) 301; j) 419; k) 118; l) 43; m) 32; n) 39.

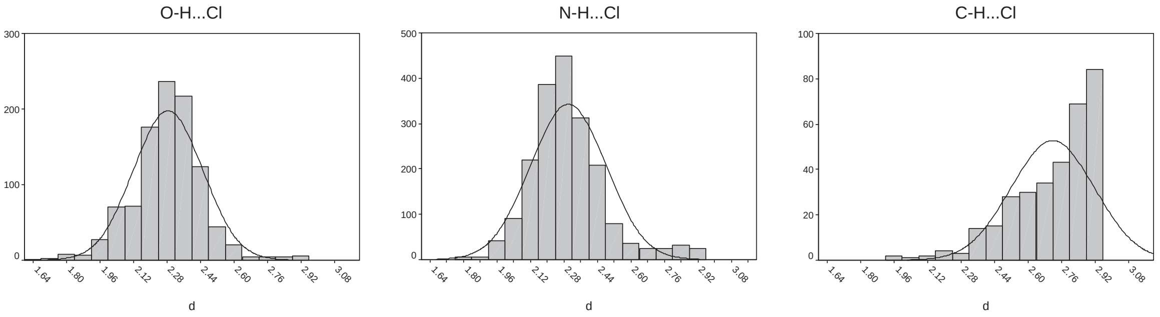


Fig. 2. Frequency distribution of H···acceptor distance (*d*) for the general dataset of X–H···Cl interactions (the distribution for all the dataset is shown in Supporting Section S1). The solid line indicates the normal curve of the distribution.

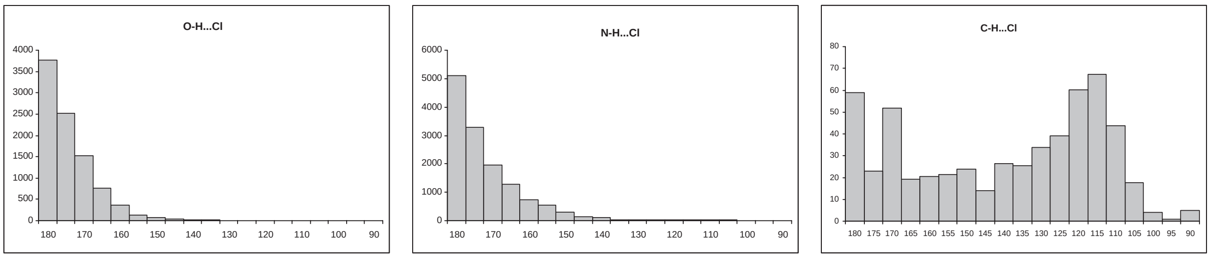


Fig. 3. Normalized frequency distribution of donor angle ($\theta$) for the general dataset of X–H···Cl interaction (the distribution for all the dataset is shown in Supporting Section S2).

values for H···acceptor distance show similar tendency for all the halogen categories and on average the C–H donor distance is 0.10 Å longer than O–H and N–H donors, whereas no difference is observed between the O–H and N–H donors. Elongation of the H···acceptor distance is observed for the fluorine acceptor in all of the donor categories. Since bond H···Y in a X–H···Y hydrogen is chemically more relevant than X···Y,[19] discussion will be focused mainly on the H···Hal distances.

The standard deviation of the values for O–H and N–H donors in Cl, Br, and I acceptor categories is $\sigma = 0.06$ Å, and for C–H donors, it is around 0.10 Å. For fluorine acceptors, large variations are noted. The $\sigma$ values indicate that roughly 95% of the data fall into ranges of approximately ±0.12 Å around the mean value for O–H and N–H donors and ±0.20 Å for C–H donor in Cl, Br, and I acceptors. As expected, this clearly demonstrates narrower distribution among strong donors and broader distribution among the weaker donors.[19] A normal frequency distribution is observed for H···acceptor distances (d) for "conventional" hydrogen bonds like O–H···O. Whereas for weaker donors, the maximum is shifted to longer distances and is less pronounced. For the weakest C–H donor species, there is no maximum, and the number of contacts increases with increasing distance.[6] The typical shape and location of the H···Hal distributions for the present study are shown in Fig. 2. The frequency distribution of H···Hal interactions for O–H and N–H donors have a well-defined maximum, which may correspond to an optimal value, and fall off for longer distances. The C–H donor groups show the characteristics of weak bonds for all acceptor categories except for fluorine of which the distribution resembles that of a strong bond. The normalized frequency distribution of donor angle ($\theta$) is shown in Fig. 3. It is interesting to note that the strong donors (O–H and N–H) prefer linear angles, i.e., 180 to 150°, whereas the weakest donor (C–H) has a maximum angle around 120°. C–H groups are less acidic and have weaker energy which lead to easy bending if steric hindrance or competition with other hydrogen bonding comes into play in the crystal.[6]

To investigate the distance and directionality characteristics of the interactions under study, normalized scatter plots were drawn for all subgroups, between $R^3$ and $1 - \cos(180 - \theta)$ and are shown in Fig. 4. Although the number of data points are low for fluorine and iodine acceptors, similar features are observed for each category. For the O–H and N–H donor groups, there is a well-defined cluster of hydrogen bonds with donor angle ($\theta$) between 150 and 180°, and the H···acceptor distances (*d*) are around half of the van der Waals radii. All other regions are almost unpopulated supporting the strong hydrogen-bond concept of "linear and short interactions." This concept is followed for all the halogen-acceptor groups with O–H and N–H donor atoms. In the C–H donor subset concentration of data points are minimal but show a characteristic relationship, namely a positive correlation between *d* and $\theta$. In other words, as the H···acceptor distance becomes longer, the donor angle bends accordingly. The data points are scattered over regions of the plot, which is different from the fluorine acceptor. The reason for this may be two fold: (i) weak polar donors, such as C–H groups, span a wide range of polarities[5,7] and (ii) the weaker energy scale of these interactions (roughly an order of magnitude weaker than covalent bonds), which can easily be deformed by packing forces and can easily be bent, elongated, or compressed.[2,5] The elongation of these hydrogen bonds from optimal geometry also establishes its electrostatic nature.[5]

Because the data points in the C–H scatter plot are not scattered in all directions but follow a linear relationship, van der Waals interaction are not involved, which needs the distribution to be isotropic. This establishes that the C–H···Hal interactions to be an attractive, electrostatic interaction commonly

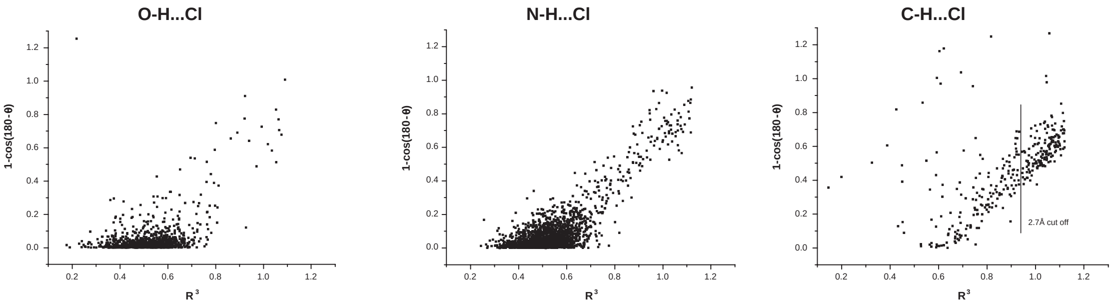
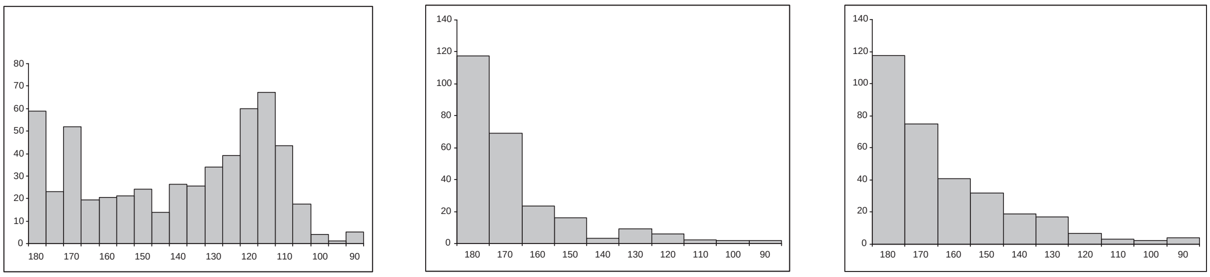
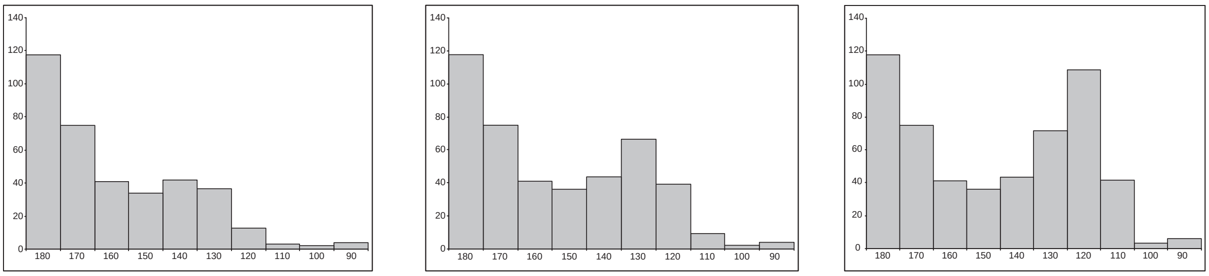


Fig. 4. Normalized scatterplots for H···acceptor distance ($R^3$) vs donor angle $[1 - \cos(180 - \theta)]$ for the general dataset of X–H···Cl interaction (Some useful points of reference are: $R^3 = 1$ corresponds to $d(\text{H}\cdots\text{Hal}) = \sum(r_\text{H} + r_\text{Hal})$; $1 - \cos(180 - \theta) = 0.0$ corresponds to $\theta = 180°$, $1 - \cos(180 - \theta) = 0.5$ corresponds to $\theta = 120°$, $1 - \cos(180 - \theta) = 0.75$ corresponds to $\theta = 104.5°$, and $1 - \cos(180 - \theta) = 1.0$ corresponds to $\theta = 90°$). The plots for all the dataset is shown in Supporting Section S3.



**Overall** **< 2.5 Å** **< 2.6 Å**



**< 2.7 Å** **< 2.8 Å** **< 2.9 Å**

Fig. 5. Frequency distribution of the donor angle ($\theta$) with various H···acceptor distance ($d$) cutoff for the C–H···Cl interaction in the general dataset.

displayed at distances greater than the conventional van der Waals limit as reported by Aakeroy and co-workers[20] for chlorine ions. Many researchers[5,10,14,20] have stated that the conceptual van der Waals cut-off criterion be dropped when determining the presence of intermolecular and intramolecular hydrogen-bonding interactions and be replaced by a distance/angle criterion determined by using the empirical approach.

In order to establish the concept of hydrogen bond in C–H···Hal interactions, the frequency distribution for the donor angle was reexamined. Taylor and Kennard[22] showed that the C–H···O interaction is indeed a hydrogen bond by observing the frequency distribution of the donor angle at various H···acceptor distance ($d$) cut-offs. The same procedure is adopted here for only the chlorine acceptor groups because the number of observations for this group is large and the conclusions obtained can be generalized for all the acceptor groups since they all show similar tendency. Frequency distribution (as histograms) for the donor angle is plotted for various d cut-offs starting from 2.5 to 2.9 Å, since the sum of the van der Waals radii for H and Cl is 2.84 Å (Fig. 5). From the distribution, it is clear that values of $d$ less than 2.7 Å corresponds to a strong hydrogen bond, i.e., linear angles are preferred over the bent ones. Therefore, C–H···Cl behaves like a hydrogen bond within a H···acceptor ($d$) cut-off distance of 2.7 Å and then gradually weakens in strength. The C–H donor group within the fluorine acceptor dataset is different in the sense that the points are not spread over all regions in the plot but present only in defined areas. The frequency distribution of $d$ also represents a similar trend, wherein the distribution looks similar to O–H or N–H donor groups. This may be attributed to the electronic nature of the lighter fluorine atom whose potential energy minima is very low when compared to their heavier counterparts.[15]

**Dataset of Various Hybridization States of the Donor Groups and Different Coordination Environment of the Halogen Acceptor.** In order to verify whether hybridization

Table 2. Mean Values for Donor···Acceptor (*D*) Distance (Å) for the Dataset with Various Hybridization States for the Donor Atoms and the Different Coordination Environment of the Halogen Atoms[a)]

| | Hal$^-$ | | | | Hal–TM | | | | Hal–Organic | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | Cl | Br | I | F | Cl | Br | I | F | Cl | Br | I |
| R-factor/% | 10 | 3 | 4 | 4 | 10 | 3 | 4 | 4 | 3 | 3 | 3 | 3 |
| O($sp^3$) | 2.8(3)[81] | 3.2(2)[779] | 3.3(2)[359] | 3.6(1)[148] | 2.9(3)[171] | 3.3(2)[340] | 3.5(2)[45] | 3.7(2)[25] | 3.1(2)[26] | 3.5(2)[47] | 3.6(2)[17] | 3.8(1)[10] |
| N($sp^2$)[+] | 3.0(3)[9] | 3.3(2)[61] | 3.4(1)[50] | 3.7(1)[7] | 3.1(2)[31] | 3.4(2)[71] | 3.6(1)[34] | na[b)] | 3.2(2)[6] | 3.4(2)[11] | na[b)] | na[b)] |
| N($sp^2$) | na[b)] | 3.2(2)[11] | 3.5(2)[11] | 3.8(1)[8] | na[b)] | 3.4(2)[15] | 3.5(2)[8] | na[b)] | na[b)] | na[b)] | na[b)] | na[b)] |
| N($sp^3$)[+] | 2.9(2)[90] | 3.2(2)[584] | 3.3(1)[241] | 3.6(1)[71] | 2.9(2)[297] | 3.4(2)[281] | 3.5(1)[67] | 3.8(1)[15] | 3.0(1)[35] | 3.5(2)[34] | 3.74(8)[4] | 3.8(1)[11] |
| N($sp^3$) | 2.9(3)[53] | 3.3(2)[783] | 3.5(2)[470] | 3.7(1)[432] | 3.0(2)[114] | 3.4(1)[806] | 3.6(1)[214] | 3.8(1)[82] | 3.2(2)[24] | 3.5(2)[47] | 3.6(2)[14] | 3.8(1)[32] |
| C($sp^2$) | 3.4(2)[7] | 3.6(1)[133] | 3.7(1)[128] | 4.0(2)[165] | 3.3(2)[14] | 3.7(1)[620] | 3.8(2)[149] | 4.0(1)[152] | 3.4(2)[49] | 3.7(1)[70] | 3.9(1)[34] | 4.0(1)[38] |
| C($sp^3$) | 3.3(2)[388] | 3.7(1)[2667] | 3.8(1)[2324] | 4.0(1)[2461] | 3.4(2)[1282] | 3.7(1)[8277] | 3.9(1)[1973] | 4.0(1)[1554] | 3.4(2)[903] | 3.7(1)[1651] | 3.9(1)[461] | 4.0(1)[724] |

a) The standard errors of the mean values are given in parentheses and the number of hydrogen bonds [*n*] is represented in bracket. b) na represents either the no. of data is less than 5 or no data is available for this particular screen.

states of the donor atoms and/or the coordination environment around the halogen acceptors influence the strength of the hydrogen bond, the following study was carried out. The idea was invoked by the following statement: "It has been qualitatively concluded from vibrational spectroscopic experiments that the ability of a C–H group to donate hydrogen bonds depends on the C hybridization, as C(sp)–H > C($sp^2$)–H > C($sp^3$)–H, and increases with the number of adjacent electron-withdrawing groups."[23]

Thirty-three datasets (11 × 3) were constructed for each acceptor group, accordingly for oxygen ($sp^2$ and $sp^3$), nitrogen (sp, $sp^2$, $sp^2(+)$ [positively charged], $sp^3$, and $sp^3(+)$), carbon (sp, $sp^2$, and $sp^3$), and sulphur (no distinctions) donor atoms of varying hybridization states with halogen acceptor existing as ions (−), bound to transition metals (TM) and bound to elements other than ions and metals (organic). Since the number of observations for sulphur donors and the Osp$^2$, Nsp, and Csp hybridization states of the atoms were very low (number of data points was less than 5), they were not considered for further analysis. Therefore, the number of datasets was reduced to twenty-one (7 × 3) for each halogen acceptor. In addition, for the Nsp$^2$ and Nsp$^2$(+) groups, there are a few missing categories presented in Table 2.

From the analysis of the donor···acceptor (*D*) and H···acceptor distance (*d*) for various hybridization states of the donor atoms, there were not any marked variations in their mean values; however, in the acceptor groupings, there are some differences (Tables 2 and 3). It has been reported that, as the acidity of the donor and/or the basicity of the acceptor increases, the H···acceptor distance decreases. The ability of the donor strength generally depends on the hybridization and whether the donor atom is bonded to electron-withdrawing atoms or groups. Since the analysis on the nature of the atoms or groups attached to the donor atom has not been done, the results obtained here may be an average in which the effect of electron-withdrawing groups are countered by the electron-donating groups and, therefore, there is no net result. In addition, acidity effects in the solid state depend on both electronic and steric factors. For sterically unhindered donor atoms, the *D* values correlate with the p$K_a$ values whereas, for donor atoms with bulkier substituents the *D* values are longer. Also, the crystal packing forces play an important role for these weak interactions.[21] Therefore, in order to get a clear picture for the influence on the hybridization of the donor atom, the nature of chemical group attached to it, the steric factor and the crystal environment are to be analyzed in detail. Comparison of the H···acceptor distances (*d*) for the oxygen donor with the three acceptor grouping (ion, TM, and organic) results in an average deviation of 0.2 Å between ion and metal but 0.4 Å between metal and organic groupings. The deviations are similar for nitrogen and carbon groupings (0.2 and 0.1 Å, respectively). All these differences fall within the standard deviation and should not be considered reliable. However, the analyses produce some interesting results; the overall strength of hydrogen bond with respect to the acceptor grouping can be given as Hal(−) > Hal–TM > Hal–Organic. The strength of the halogen ions is attributed to their spherical shape which are highly mobile and can move more easily to positions of lowest energy than any other hydrogen-bonding moiety.[24]

Table 3. Mean Values for H···Acceptor ($d$) Distance (Å) for the Dataset with Various Hybridization States for the Donor Atoms and the Different Coordination Environment of the Halogen Atoms[a]

| | Hal$^-$ | | | | Hal–TM | | | | Hal–Organic | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | Cl | Br | I | F | Cl | Br | I | F | Cl | Br | I |
| O(sp$^3$) | 1.9(4) | 2.3(3) | 2.4(3) | 2.7(2) | 2.1(5) | 2.6(4) | 2.8(4) | 3.1(4) | 2.5(5) | 3.0(3) | 3.1(2) | 3.2(3) |
| N(sp$^2$)[+] | 2.1(4) | 2.4(3) | 2.5(3) | 2.9(3) | 2.4(4) | 2.7(4) | 2.8(3) | na[b] | 2.4(3) | 2.8(3) | na[b] | na[b] |
| N(sp$^2$) | na[b] | 2.3(3) | 2.7(2) | 3.0(1) | na[b] | 2.5(2) | 2.8(3) | na[b] | na[b] | na[b] | na[b] | na[b] |
| N(sp$^3$)[+] | 2.1(4) | 2.5(4) | 2.5(3) | 2.9(3) | 2.2(4) | 2.7(3) | 2.8(3) | 3.2(4) | 2.4(4) | 2.9(4) | 3.46(3) | 3.1(3) |
| N(sp$^3$) | 2.1(4) | 2.5(3) | 2.7(3) | 2.9(3) | 2.2(4) | 2.7(3) | 2.8(3) | 3.0(3) | 2.5(4) | 3.0(4) | 2.8(4) | 3.1(3) |
| C(sp$^2$) | 2.65(9) | 2.9(3) | 2.9(2) | 3.2(2) | 2.6(3) | 2.9(2) | 3.1(2) | 3.2(2) | 2.7(2) | 3.0(2) | 3.2(2) | 3.3(2) |
| C(sp$^3$) | 2.6(3) | 3.0(2) | 3.1(2) | 3.2(2) | 2.6(3) | 3.0(2) | 3.1(2) | 3.3(2) | 2.7(2) | 3.1(2) | 3.2(2) | 3.3(2) |

a) The standard errors of the mean values are given in parentheses. b) na represents either the no. of data is less than 5 or no data is available for this particular screen.

Table 4. Mean Values for Acceptor Angle ($\psi$) for the Dataset with Various Hybridization States for the Donor Atoms and the Different Coordination Environment of the Halogen Atoms[a]

| | Hal–TM/° | | | | Hal–Organic/° | | | |
|---|---|---|---|---|---|---|---|---|
| | F | Cl | Br | I | F | Cl | Br | I |
| O(sp$^3$) | 118(24) | 109(23) | 102(23) | 102(26) | 121(23) | 109(26) | 106(26) | 86(13) |
| N(sp$^2$)[+] | 112(25) | 102(22) | 95(23) | na[b] | 107(31) | 108(19) | na[b] | na[b] |
| N(sp$^2$) | na[b] | 100(16) | 107(16) | na[b] | na[b] | na[b] | na[b] | na[b] |
| N(sp$^3$)[+] | 109(20) | 97(21) | 96(21) | 100(21) | 110(21) | 111(22) | 117(21) | 105(14) |
| N(sp$^3$) | 118(19) | 109(23) | 106(24) | 105(21) | 119(23) | 106(26) | 101(20) | 102(20) |
| C(sp$^2$) | 137(16) | 116(25) | 113(27) | 115(27) | 123(20) | 117(23) | 105(23) | 111(25) |
| C(sp$^3$) | 123(23) | 121(25) | 119(25) | 118(27) | 124(23) | 116(25) | 117(27) | 102(28) |

a) The standard errors of the mean values are given in parentheses. b) na represents either the no. of data is less than 5 or no data is available for this particular screen.

The shapes and widths of the H···Hal distributions are similar for the different acceptor types (Fig. S4 of Supporting Information Section). As expected they are narrow for strong donors, like oxygen and nitrogen, and broader for the weak donor, i.e., carbon. The ionic distribution is comparatively narrow for the oxygen and nitrogen donors interacting with the metal and organic bound halogen, whereas they show little variation for the carbon donors. In the nitrogen subdivision, the positively charged groups Nsp$^2$(+) and Nsp$^3$(+) show bimodal distribution. This may be due to the three-center hydrogen-bonding phenomenon for this type of charged donors.[19] The Csp$^3$ distribution for various acceptor subdivisions (Fig. S5 of Supporting Information Section) clearly show that all distributions are characteristic of weak donors, except for the fluorine ion and metal bound fluorine acceptor categories which tend to fall into the strong donor group due to its smaller size and electronic nature.[15] Examination of the molecular orbitals for the model systems to halogens indicates that its p-orbitals are involved in $\sigma$-bonding which will deplete the charge density in the direction of the spherical halide. This effect is more pronounced for Cl, Br, and I than for F, due to smaller p-orbitals, and therefore, strong hydrogen bonding is formed.[15]

Hydrogen bonds are directional at the acceptor site,[5] and to analyze this concept, the acceptor angle ($\psi$) was calculated for two datasets, i.e., metal bound and organic, and the results are summarized in Table 4. It is reported that metal chloride acceptor group shows anisotropy with a strong preference for H···Cl–M angles of 90–130°.[3] As expected, the mean values fall between 90–140°. As well, chlorine and bromine acceptors show a similar tendency, iodine acceptors are relatively bent, and fluorine acceptors are relatively linear as observed by Brammer and co-workers.[15]

## Conclusion

The ability of halogen atoms to act as hydrogen-bond acceptors were analyzed statistically using geometrical characteristics for the oxygen, nitrogen, and carbon atom donors with and without different hybridization and for the various coordination environment of the acceptor atoms. Strong hydrogen-bond characteristics were observed for oxygen and nitrogen donors whereas carbon atoms showed weaker nature. Carbon donor groups form weaker interactions because of attractive electrostatic interactions and not van der Waals interactions. As well, it was determined that the hydrogen-bonding ability for chlorine acceptors was found to have a H···Cl distance cutoff of 2.7 Å. The different hybridization states of the donor atoms did not produce significant deviation in the nature of interaction; however, deviations were noted for the various coordination environments.

## Materials and Methods

For this analysis, two different datasets were retrieved from the Cambridge Structural Database (CSD),[25] update 5.24 (November 2002):

1) General Dataset: The CSD was searched for all unique X–H···Hal (Hal = F, Cl, Br, and I) interactions for three different subsets of the donor atoms (oxygen, nitrogen, and carbon) with halogen acceptors. The secondary search criteria used were: (a)

R-values (crystallographic error factor) $\leq 0.05$, (b) ordered and error-free crystal structures, (c) no crystallographic disorder, (d) no polymeric structures, (e) X–H bond lengths normalized to the neutron diffraction values,[2] and (f) distance criteria for H⋯Hal and X⋯Hal being within sum of the respective van der Waals radii ($r_F = 1.47$ Å; $r_{Cl} = 1.75$ Å; $r_{Br} = 1.85$ Å; $r_I = 1.98$ Å; $r_N = 1.55$ Å; $r_O = 1.52$ Å; $r_C = 1.70$ Å; $r_S = 1.80$ Å, and for hydrogen $r_H = 1.09$ Å) so as to produce a normalized plot[8] and angular criteria X–H⋯Hal ($\theta$), being in the range 90 to 180°.

2) The second dataset included three different sub-datasets of the Halogen acceptor moiety: $\mathrm{Hal}^-$ (ion), Hal–TM (transition-metal-bound halogen), and Hal–Organic (all other elements except metal; only organic compounds were considered) with four different donor moieties with various hybridization states {O ($sp^2$ and $sp^3$), N [sp, $sp^2$, $sp^2(+)$, $sp^3$, and $sp^3(+)$], C (sp, $sp^2$, $sp^3$), and S(no distinctions)}. In order for the number of observations to be similar and also statistically significant in the different distributions, the R-factor was varied, and the cut-off was used for each search (Table 3).[14] The secondary search criteria used were: (a) ordered and error-free crystal structures, (b) no crystallographic disorder, (c) no polymeric structures, (d) X–H bond lengths normalized to the neutron diffraction value, and (e) distance criteria for $d$ and $D$ being sum of the appropriate van der Waals radii plus 0.5 Å and angular criteria for donor, $\theta$, in the range 90 to 180° and acceptor, H⋯Hal–Y ($\psi$) from 0 to 180°.

Mean and standard deviation ($\sigma$) values were calculated for all geometric parameters for each screen. All data falling outside $\pm 4\sigma$ cut-off of the mean values were excluded from further analysis.[26] Angular distributions of X–H⋯Hal were plotted as histograms in 5° intervals and are corrected for the geometric error in the frequency of observations (cone correction), because there is a greater probability of finding the interactions on the rims of cones in increasing solid angles and the use of $N/\sin\theta$ instead of $N$, where $N$ is the number of hydrogen bonds in the interval $\theta$ to $\theta + \mathrm{d}\theta$, in the histograms effectively resolves this contradiction.[2,13,15,27]

Distance and directionality characteristics of hydrogen bonds can be conveniently studied in scatter plots of hydrogen-bond angles versus the $d$ and/or $D$ distances.[28] In order to compare the different X–H⋯Hal systems, the distances $d$ were normalized according to the sum of the van der Waals radii:

$$\mathrm{R} = \frac{d(\mathrm{H}\cdots\mathrm{Hal})}{\sum(\mathrm{r_{Hal}} + \mathrm{r_H})}. \tag{1}$$

Furthermore, a change of variables $\mathrm{x} = \mathrm{R}^3$ and $\mathrm{y} = 1 - \cos(180 - \theta)$, was used to obtain better insight into the spatial distribution of short contacts, so that a uniform distribution of the data points in three-dimensional space transforms into a uniform distribution in the two-dimensional scattergram.[8] This normalization allows a qualitative assessment of the relative strengths of the different hydrogen-bond types.[15]

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## Supporting Information

The frequency distribution plots for the H⋯acceptor distance and the donor angle for the general dataset and the different hybridization dataset are given. In addition, the normalized scatterplots for H⋯acceptor distance ($\mathrm{R}^3$) vs donor angle for the general dataset and the frequency distribution of H⋯acceptor distance ($d$) for the carbon donor in $sp^3$ hybridization states with various coordination environment of the halogen acceptor are presented. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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