

THE HALOGEN BOND – THAT INTERACTION SIMILAR TO THE HYDROGEN BOND

It seems to be useful to begin this short article with the following quote:

*“with courageous simplification, one might assert that the chemistry of the last century was largely the chemistry of covalent bonding, whereas that of the present century is more likely to be the chemistry of noncovalent binding”*¹.

There are different terms for the inter-atomic interactions which play an important role in various chemical processes and reactions and which are not classified as typical covalent bonds. One can mention non-covalent or non-binding interaction, Lewis acid – Lewis base interaction, inter-atomic contact etc. The common feature of a part of them is the meaningful electron charge shift from the Lewis base unit to the Lewis acid one which often leads to further processes, among them to particular chemical reactions.

The hydrogen bond is the most often analyzed non-covalent interaction since it plays a key role in chemical, physical and bio-chemical processes^{2,3}. One can mention numerous examples such as the role of hydrogen bond in enzymatic catalysis, arrangement of molecules in crystals, crystal engineering, proton transfer reactions, and also its important role in life processes⁴. This interaction is often designated as A-H...B where the A and B atoms are usually negatively charged while the H-atom is characterized by the positive charge. For example, the O-H...O hydrogen bond which links water molecules is analyzed in numerous studies. The hydrogen bond, because of the opposite charges of the B and H centers being in a contact (the O and H centers in a case of water), is usually classified as the electrostatic in nature interaction. However the mentioned above electron charge transfer processes are very important for the hydrogen bond and this is why also the covalent nature of this interaction is often the subject of disputes and debates. These processes, in a case of the hydrogen bond, often lead to the proton transfer reaction⁵.

The halogen bond often designated as A-X...B (X is the halogen atom) is another non-covalent interaction which is the subject of numerous analyses, especially in recent years⁶. This is surprising that this interaction possesses numerous characteristics typical for the hydrogen bond⁷ where usually negatively charged X-atom, commonly known as an electronegative element, acts as the Lewis acid center interacting with B, the negatively charged Lewis base center! Various concepts were proposed to explain this phenomenon, for example it was stated that the X halogen atom is characterized by the anisotropy of the electron charge distribution what results in the excess of the electron charge ($-\delta$) in the direction perpendicular to the A-X bond and the depletion of this charge ($+\delta$) in the elongation of this bond (Figure 1)⁸. However it seems that the reason of such anisotropy of the electron charge distribution may be explained in terms of a very simple σ -hole concept⁹.

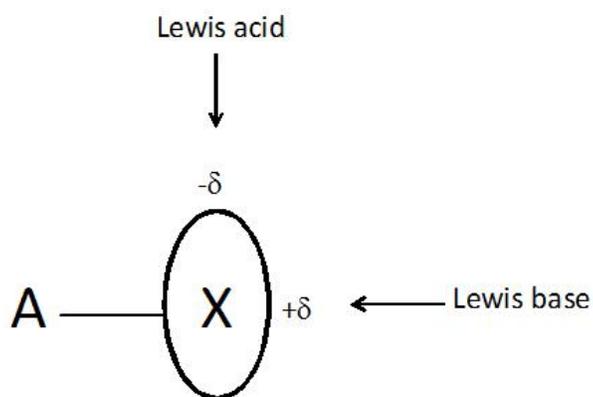


Figure 1. The anisotropy of the electron charge distribution of the halogen (X) atom.

For example, one may consider the $s^2p_x^2p_y^2p_z^1$ valence electronic structure of the chlorine atom to understand the formation of the σ -hole in CF_3Cl . The half-occupied p_z orbital interacts with a carbon orbital forming the σ molecular orbital. The electron density of the single occupied p_z orbital of chlorine is shifted to the σ -bond region what results in the depletion of this density in the outer lobe of the p_z orbital. This depletion is named as the σ -hole and if it is sufficient enough it is characterized by a positive electrostatic potential. This is why the halogen atom, even if it is negatively charged, may be characterized by the area of the positive electrostatic potential and may interact with the electron rich Lewis base centers. An example of the CF_3Cl molecule is given in Figure 2. The σ -hole is formed in the elongation of the A-X bond (C-Cl bond

in a case of CF_3Cl molecule) thus the A-X...B arrangements corresponding to the interactions with the Lewis bases, i.e. halogen bonds, are usually linear or close to the linearity. It was found that the σ -hole is more positive if the more electron attracting is the remainder of the molecule, and the heavier (more polarizable) the halogen ($\text{I} > \text{Br} > \text{Cl} > \text{F}$).

On the other hand the p_x and p_y double occupied orbitals of the halogen atom (see Figure 2) form the belt of the negative electrostatic potential around the X-atom, in the direction perpendicular to the A-X bond. One can see that in such a way the halogen atom possesses the dual character since it may act simultaneously with the Lewis bases and with the Lewis acids (see Figure 1).

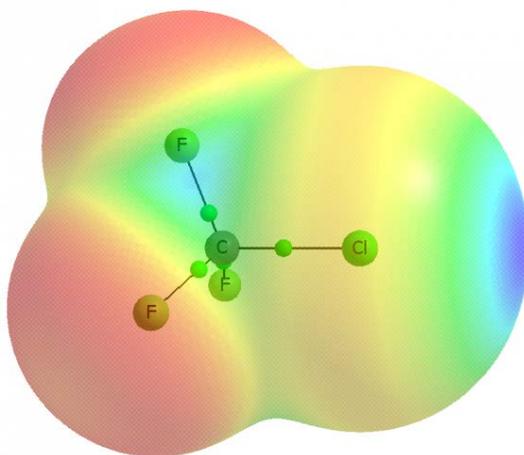


Figure 2. Computed (MP2/6-311++G** level of calculations) electrostatic potential on the 0.001 au molecular surface of CF_3Cl . Blue color, in the elongation of C-Cl bond, corresponds to the maximum (+0.0367 au) and red one to the minimum (-0.0070 au) electrostatic potential. The belt of negative electrostatic potential around Cl-atom is observed (orange color, -0.0045 au).

The halogen bonds steered by the distribution of the electrostatic potential in the species being in contact do really exist and they are observed in solids and liquids. For example, in the numerous crystal structures the halogen bonds compete with the more common hydrogen bonds to influence on the arrangement of molecules or ions. Figure 3 presents the fragment of the crystal structure of trichloroacetic acid (TCA). It is commonly known that the TCA molecules are linked by two equivalent O-H...O hydrogen bonds. However there are also the interactions of the CCl_3 groups, i.e. C-Cl...O halogen bonds.

It was pointed out earlier here that the halogen atom, owing to the specific electrostatic potential distribution, may act simultaneously. This σ -hole concept prediction has also the experimental confirmation since numerous crystal structures exist where such a situation is observed. Figure 4 presents an example where the Br-atom has the closest contacts with O and H atoms what corresponds to the C-Br...O halogen bond and the N-H...Br hydrogen bond, respectively.

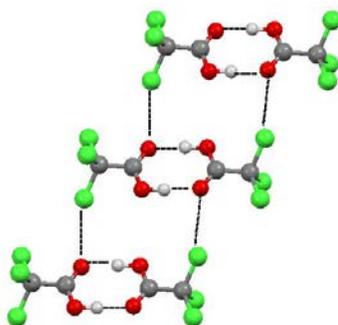


Figure 3. The fragment of the crystal structure of trichloroacetic acid (Cl, O, C and H atoms are designated by green, red, grey and bright grey colors, respectively). Broken lines correspond to H...O and Cl...O contacts (hydrogen and halogen bonds, respectively). | Credit: Cambridge Structural Database (CSD) Allen, F.H. *Acta Cryst.* 2002, B58, 380-388.

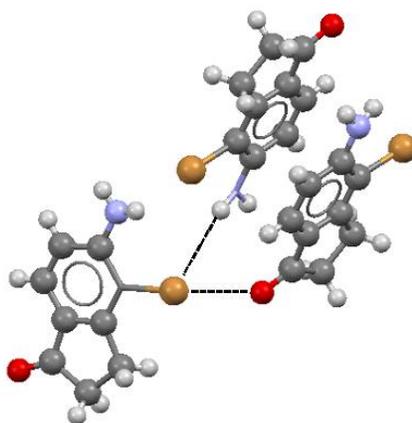


Figure 4. The fragment of the crystal structure of 5-Amino-4-bromo-2,3-dihydro-1H-inden-1-one (Br, O, N, C and H atoms are designated by brown, red, blue, grey and bright grey colors,

respectively). Broken lines correspond to Br...O and Br...H contacts (halogen and hydrogen bonds, respectively). | Credit: Cambridge Structural Database (CSD) Allen, F.H. Acta Cryst. 2002, B58, 380-388.

Thus halogen bonds, similarly as hydrogen bonds, are responsible for the arrangement of molecules in crystals. However there are other numerous studies on halogen bonds as for example in biological systems and drug discovery¹⁰. One can also mention that halogen bonds are important in ligand recognition by proteins, and that halogen bonds can be engineered to direct the conformation of DNA junctions.

Source : <http://mappingignorance.org/2014/03/07/the-halogen-bond-that-interaction-similar-to-the-hydrogen-bond/>