Theoretical study on O...Br and O...Cl halogen bonds in some small model molecular systems

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MS received 15 January 2014; revised 8 April 2014; accepted 26 April 2014

Abstract. Halogen bonding interactions of type X...O=C are important in various fields including biological systems. In this work, theoretical calculations were carried out using B3LYP/6-31++G**, MP2/6-31++G** and MP2/aug-cc-pVDZ methods on a series of O...X halogen bonds between CH₂O and CH₃CHO as halogen bond acceptor with X-Y (X = Cl, Br; Y = CF₃, CF₂H, CFH₂, CN, CCH, CCCN) as halogen bond donors. The strength of interaction energy for O...Br halogen-bonded complexes varies from –2.16 to –5.26 kcal/mol while for O...Cl complexes, it is between –1.65 to –3.67 kcal/mol, which indicate the O...Br bond to be stronger in comparison to O...Cl bond. SAPT analysis suggests that the strength of halogen bonding arises from the electrostatic and induction forces while dispersion is playing a comparatively smaller role. The halogen-bonded interaction energies were found to correlate well with positive electrostatic potential $V_{S,max}$, halogen bonded distances, and the change in s-character of C-X bond. The halogen-bonded interaction energies were also evaluated for O...I bonded complexes and thus these complexes were found to be stronger than O...Br and O...Cl bonded complexes.

Keywords. Halogen bonding; σ -hole; electrostatic potential; AIM; SAPT; NBO.

1. Introduction

Halogen bonding^{1,2} is referred to as the non-covalent interactions between the electron deficient halogen atoms and the electronegative sites, for instance, a lone pair present on the oxygen,³ nitrogen,⁴ sulphur,⁵ etc., of lewis bases. It has been a subject of study in many fascinating fields,^{6–9} such as drugs discovery,^{10–12} materials chemistry,¹³ and crystal engineering¹⁴ with a recent focus of this research into the field of solid state synthesis of organic molecules¹⁵ and supramolecular chemistry as well.^{16–18} Halogen bonding can be depicted as R-X...D, where X is the halogen atom, R is remaining group and D is halogen bond acceptor,¹⁹ which is lewis base. According to the theoretical studies carried out on the halogen bonding, the outermost portion of the halogen surface has a positive electrostatic potential and this positive region is referred to “ σ -hole”.^{20–24} It is this region that gives rise to favourable directional interaction with an electronegative atom, such as oxygen. Moreover, the studies^{20,25} also predicted that the size of halogen’s σ -hole becomes larger as a function of the mass number of the halogen atom forming halogen bond with the tendency of halogen bond to become stronger in the order of F < Cl < Br < I. The other

factor which affects the size and charge of σ -hole is the electron-withdrawing power of R, which is covalently bonded with X. It has been observed that fluorine possesses least polarizability amongst the halogens and as a result, it displays negative electrostatic potential over its surface which implies that it cannot form halogen bond. But it has been shown to form halogen bond with the presence of strongly electronegative substituents in the studies carried out by Legon²⁶ and other recent communications.^{27,28}

There have been several theoretical^{29–33} and experimental^{34–36} studies that describe the geometries and energetic properties of the halogen bonds. For example, Silvana C. Pamies *et al.* carried out a systematic study of halogen bond complexes between Lewis bases (NH₃, H₂O and H₂S) and Lewis acids (X-Y = ClF, BrF, IF, BrCl, ICl and IBr) using atoms in molecules (AIM) theory and natural bond orbital (NBO) analysis and inferred that halogen bonding results from interaction between the lone pair of donor atom of lewis base (N, O and S atoms) and the σ -hole.³⁷ Halogen bonds with oxygen, as halogen bond acceptors are especially important due to their relevance in biochemistry. These are found to be important class of interactions in protein ligand interactions.^{38–41}

In a study based on a data set of 66 protein structures and 6 nucleic acid structures from protein data bank,

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Auffinger *et al.* observed that 81 out of 113 $X \cdots O$ interactions involve carbonyl oxygen.⁴² In a study on the nature of halogen bonding including ‘Symmetry Adapted Perturbation Theory Analysis’ on halomethane-formaldehyde complexes, Riley and Hobza concluded that the halogen bonds in the systems studied are principally dispersive, augmented by electrostatic contributions.⁴³ To study halogen bonded complexes of bromobenzenes and bromopyridines with acetone further, Riley *et al.* involved the study of σ -hole and its electrostatic potential of Br affected by the presence of substituents on aromatic ring.⁴⁴ In a recent report, Pavel Hobza and co-workers studied the structures and binding energies of the halogen bonded complexes of anaesthetics (chloroform, haloethane, enflurane and isoflurane) with formaldehyde using *ab initio* MP2 and CCSD(T) methods and concluded that all anaesthetics make stable complexes with formaldehyde through the $Cl \cdots O$ halogen bonding. The report also inferred that calculated binding energies varied between 2.83 and 4.21 kcal mol⁻¹ at CCSD(T) level and contributed to 95% of interactions arising from electrostatic and dispersion forces.⁴⁵ $X \cdots O$ halogen bonding has also been studied by Qingzhong Li and his co-workers for the complexes of formaldehyde with hypohalous acids (HOX, X=F, Cl and Br) at MP2/aug-cc-pVTZ computational level.⁴⁶ Keeping in view the importance of $X \cdots O=C$ halogen bonding interactions in biological systems, our present study is focused on the halogen bonding interactions with formaldehyde and acetaldehyde as halogen bond acceptors.

In this work, the complexes formed by X-Y (X = Cl, Br; Y = CF₃, CF₂H, CFH₂, CN, CCH, CCCN) halogen bond donors with CH₂O and CH₃CHO as halogen acceptors were studied to inquire the nature of these halogen bonds and investigated the electrostatic potential, interaction energies components (SAPT), charge transfer delocalizations (NBO), etc.

2. Computational Details

The geometries of the monomers and the complexes were optimized using *ab-initio* molecular orbital (MO) and density functional methods using 6-31++G** basis set. For the exchange correlation, Dunning’s correlation consistent augmented polarized double zeta basis (aug-cc-pVDZ) set was employed at MP2 level of theory. The harmonic vibrational frequencies were then computed at the same level to confirm that these geometries were local minima on their potential energy surfaces. To correct the inherent basis set superposition error (BSSE), the counterpoise procedure proposed

by Boys and Bernadi⁴⁷ was adopted to obtain the counterpoise corrected interaction energies (ΔE_{Corr}). The calculations given above for the monomers and the complexes were carried out using Gaussian 09 program package.⁴⁸

The electrostatic potential $V(\mathbf{r})$ that electrons and nuclei of a molecule create at any point $\mathbf{r}$ in the surrounding space is given by equation 1.

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}') d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|} \quad (1)$$

Z is charge on nucleus A , located at $\mathbf{R}_A$ and $\rho(\mathbf{r})$ is the electronic density function of the molecule. $V(\mathbf{r})$ is positive in regions in which dominant contribution is that of nuclei and negative where it is of electrons. The molecular electrostatic potential were computed on the halogen donors with WFA surface analysis suite,⁴⁹ calculated on 0.001 au contour of the molecule’s electron density.⁵⁰

NBO analysis was performed at MP2 level via the procedure contained within the Gaussian 09.⁵¹ The electron densities (ρ) and Laplacian (∇^2_ρ) at the bond critical points of the halogen-bonded complexes were evaluated employing atoms in molecules (AIM) methodology^{52–54} with AIM2000 program.⁵⁵ The Symmetry Adapted Perturbation Theory Analysis (SAPT) was performed with the use of GAMESS package that was interfaced to the SAPT2008.2 code.^{56–58} The SAPT expansion was truncated and took account of the energy correction terms up to second order with respect to the intermolecular interaction operator.

$$\begin{aligned} E^{\text{SAPT}} = & E_{\text{elst}}^{(10)} + E_{\text{exch}}^{(10)} + E_{\text{ind,resp}}^{(20)} + E_{\text{exch-ind,resp}}^{(20)} + E_{\text{elst,resp}}^{(12)} \\ & + {}^tE_{\text{ind}}^{(22)} + {}^tE_{\text{exch-ind}}^{(22)} + E_{\text{disp}}^{(20)} + E_{\text{exch-disp}}^{(20)} + E_{\text{elst}}^{(13)} \\ & + \varepsilon_{\text{exch}}^{(1)}(\text{CCSD}) + \varepsilon_{\text{disp}}^{(2)}(2) + \delta\text{HF}_{\text{resp}}^{\text{HF}} \quad (2) \end{aligned}$$

The right side of the above equation is a sum of perturbative energy correction terms that are the consequences of various physical interaction forces.^{56,57} These energy correction terms, except for the very last one, were collected into four fundamental physical components: electrostatic (E_{elst}), induction (E_{ind}), dispersion (E_{disp}) and exchange (E_{exch}) as follows:

$$E_{\text{elst}} = E_{\text{elst}}^{(10)} + E_{\text{elst,resp}}^{(12)} + E_{\text{elst}}^{(13)}$$

$$E_{\text{ind}} = E_{\text{ind,resp}}^{(20)} + {}^tE_{\text{ind}}^{(22)}$$

$$E_{\text{disp}} = E_{\text{disp}}^{(20)} + \varepsilon_{\text{disp}}^{(2)}(2)$$

$$E_{\text{exch}} = E_{\text{exch-ind,resp}}^{(10)} + {}^tE_{\text{exch-ind}}^{(22)} + E_{\text{exch-disp}}^{(20)} + \varepsilon_{\text{exch}}^{(1)}(\text{CCSD})$$

The values obtained at the MP2/aug-cc-pVDZ level are used for the discussion except in case of SAPT analysis wherein results at MP2/6-31++G** are reported.

3. Results and Discussion

3.1 Molecular electrostatic potentials, geometries and halogen-bonded interaction energies

3.1a *Molecular electrostatic potentials (MEPs) of halogen bond donors:* The molecular electrostatic potential has been found to be an effective tool for

Figure 1. Calculated electrostatic potential on the 0.001 electrons/bohr³ surfaces of X-Y molecules at MP2/aug-cc-pVDZ level (halogen atoms are towards the viewer).

Figure 1. (cont.)

analyzing and predicting non-covalent interactions.^{59–61} The 0.001 au contours of the electron density have been utilized to obtain MEP (figure 1) at the halogen surface, as suggested by Bader *et al.*⁶² Figure 1 clearly depicts that the positive electrostatic potential region (i.e., σ -hole) is on the outer surface of the X (X = Cl, Br) atom, along the extension of the C-X bond.⁶³ As

mentioned in the introduction of this paper, three factors determine the magnitude of positive electrostatic potential: a) polarizability of the halogen X, b) its electronegativity, and c) the electron-withdrawing power of the remainder group attached to X. It can be seen in figure 1 that positive halogen's σ -hole is surrounded by negative electrostatic region which indicates that the same atom

Table 1. Most positive electrostatic potential, $V_{S,max}$ (kcal/mol) associated with halogen atoms X (Br, Cl) in X-Y molecules at the MP2/aug-cc-pVDZ level.

Molecules	Atom	$V_{S,max}$	Molecules	Atom	$V_{S,max}$
F_3C-Br	Br	32.09	F_3C-Cl	Cl	27.06
HF_2C-Br	Br	21.97	HF_2C-Cl	Cl	17.10
H_2FC-Br	Br	13.54	H_2FC-Cl	Cl	7.99
$N \equiv C-Br$	Br	48.61	$N \equiv C-Cl$	Cl	41.19
$H-C \equiv C-Br$	Br	31.49	$H-C \equiv C-Cl$	Cl	24.01
$NC-C \equiv C-Br$	Br	45.19	$NC-C \equiv C-Cl$	Cl	39.34

Figure 2. Optimized complexes of CH_2O with X-Y molecules at MP2/aug-cc-pVDZ level.

Figure 2. (cont.)

can interact electrostatically with both electrophiles and nucleophiles, which has been observed in some studies on crystals.^{64–66}

The most positive electrostatic potential of the σ -hole ($V_{S,max}$) associated with halogen atoms of X-Y are listed in table 1. It can be seen from the data in

table 1 that the $V_{S,max}$ values are larger for bromine than for the chlorine for the same substituent Y ($Y = CF_3$, CF_2H , CFH_2 , CN , CCH , $CCCN$). For instance, the $V_{S,max}$ values of F_3C-Br and F_3C-Cl are 32.09 and

27.06 kcal/mol respectively. Figure 1 shows that the electron-withdrawing substituent can produce an enhancement on the size of σ -hole and it is also apparent from the comparison of the values of $V_{S,max}$

Figure 3. Optimized complexes of CH_3CHO with $X-Y$ molecules at MP2/aug-cc-pVDZ level.

Figure 3. (cont.)

for the fluorinated halomethanes. The magnitude of $V_{S,\text{max}}$ increases with increasing number of F to the halomethane substituent. For example, the $V_{S,\text{max}}$ values for $\text{H}_2\text{FC-Br}$, $\text{HF}_2\text{C-Br}$ and $\text{F}_3\text{C-Br}$ are 13.16, 21.43 and 31.59 kcal/mol respectively. The highest $V_{S,\text{max}}$ for BrCN and ClCN with respect to their remaining halogen bond donors suggests more electron-withdrawing

power of $-\text{CN}$ with respect to remaining substituents on Y. It is due to the fact that the $-\text{CN}$ group withdraws electron density from X atoms in XCN ($\text{X} = \text{Br}, \text{Cl}$) both through resonance and inductive effects while $-\text{CF}_3$ acts through inductive effect only. Also, the inductive effect of CF_3 is lower than that of $-\text{CN}$. Though the $-\text{CN}$ group in $\text{NC-C}\equiv\text{C-X}$ withdraws electron density

via inductive and resonance effect, but the presence of triple bond reduces the electron-withdrawing effect of $-CN$ substituent on the X atom.

3.1b Geometries and interaction energies of halogen bonded complexes: The optimized geometries of halogen bonded complexes $CH_2O \cdots X-Y$ and $CH_3CHO \cdots X-Y$ are displayed in figures 2 and 3 at MP2/aug-cc-pVDZ level. Table 2 presents the optimized equilibrium $O \cdots X$ ($X = -Br, -Cl$) distances and angles for the complexes under study. The σ -hole of $X-Y$ points towards the negative electrostatic potential of CH_2O and CH_3CHO , the angle of $O \cdots X-C$ fall in the range of 156.8 – 180.0° . From the data in table 2, it can be seen that the intermolecular distances are significantly affected by the chemical environment of the halogen atoms forming halogen bonds. For the same halogen bond donor, all the respective complexes have $O \cdots Cl$ distances longer than $O \cdots Br$ distances. The complexes can be placed into two groups, the one with substituted fluoromethyls (XCF_3 , XCF_2H and $XCFH_2$) and other with linear halogen donors (XCN ,

$XCCH$ and $XCCCN$). The halogen bond formation is accompanied by the contraction of $C-X$ bond in the former complexes while it elongates in the latter complexes (table S1). For the halogen bond donors XCF_3 , XCF_2H and $XCFH_2$, the contraction of $C-Br$ bond in the complexes with CH_2O as halogen bond acceptor lies in the range of 0.005 – $0.011 \text{ \AA}$ while for the adducts involving CH_3CHO as halogen bond acceptor lies in the range 0.002 – $0.009 \text{ \AA}$. Similar contraction of $C-Cl$ bond for respective adducts with CH_2O and CH_3CHO lies in the range 0.001 – $0.004 \text{ \AA}$ and 0.005 – $0.006 \text{ \AA}$ respectively. On the other hand, the complexes of XCN , $XCCH$ and $XCCCN$ undergo the elongation of $C-X$ bond on complexation with exception of $CH_2O \cdots ClCN$. The elongation of $C-Br$ bond ranges between 0.004 – $0.008 \text{ \AA}$ for both CH_2O and CH_3CHO complexes. As can be seen from figures 2 and 3 and supporting information, angle $Cl \cdots O=C$ is much smaller in comparison to $Br \cdots O=C$ angle. Further analysis reflects that secondary weak interactions of $Cl \cdots H-C$ type are responsible for it.

Table 2. Halogen-bonded distances, angles obtained at MP2/aug-cc-pVDZ and interaction energies (ΔE_{Corr})[#] at B3LYP/6-31++G** level (L1), MP2/6-31++G** (L2) and MP2/aug-cc-pVDZ level (L3). (The distances are in $\text{\AA}$, angles in degrees and interaction energies in kcal/mol).

Complexes	$d(O \cdots X)$		$O \cdots X-C (\theta)$		$\Delta E_{\text{Corr}} (-ve)$		
					L1	L2	L3
$CH_2O \cdots BrCF_3$	$O6 \cdots Br5$	2.952	$O6-Br5-C1$	172.7	1.69	2.11	2.74
$CH_3CHO \cdots BrCF_3$		2.910		172.2	1.96	2.69	3.61
$CH_2O \cdots ClCF_3$	$O6 \cdots Cl5$	3.029	$O6-Cl5-C1$	168.5	1.11	1.50	2.09
$CH_3CHO \cdots ClCF_3$		3.010		177.9	1.29	2.25	2.84
$CH_2O \cdots BrCF_2H$	$O6 \cdots Br5$	3.040	$O6-Br5-C1$	169.8	1.05	1.45	2.34
$CH_3CHO \cdots BrCF_2H$		3.018		170.5	1.11	2.04	3.23
$CH_2O \cdots ClCF_2H$	$O6 \cdots Cl5$	3.125	$O6-Cl5-C1$	164.0	0.70	1.16	1.80
$CH_3CHO \cdots ClCF_2H$		3.124		175.7	0.70	1.81	2.30
$CH_2O \cdots BrCFH_2$	$O6 \cdots Br5$	3.113	$O6-Br5-C1$	170.6	0.41	0.95	2.16
$CH_3CHO \cdots BrCFH_2$		3.097		170.0	0.39	1.43	2.53
$CH_2O \cdots ClCFH_2$	$O6 \cdots Cl5$	3.117	$O6-Cl5-C1$	156.8	0.35	0.76	1.65
$CH_3CHO \cdots ClCFH_2$		3.165		172.5	0.29	0.62	2.27
$CH_2O \cdots BrCN$	$O4 \cdots Br1$	2.864	$O4-Br1-C2$	175.0	3.16	3.37	4.27
$CH_3CHO \cdots BrCN$		2.811		176.0	3.92	4.60	5.26
$CH_2O \cdots ClCN$	$O4 \cdots Cl1$	2.936	$O4-Cl1-C2$	180.0	2.30	2.52	3.07
$CH_3CHO \cdots ClCN$		2.899		180.0	2.81	3.62	3.67
$CH_2O \cdots BrCCH$	$O5 \cdots Br1$	2.952	$O5-Br1-C2$	180.0	1.46	1.90	2.35
$CH_3CHO \cdots BrCCH$		2.918		179.7	2.97	2.20	3.21
$CH_2O \cdots ClCCH$	$O5 \cdots Cl1$	3.044	$O5-Cl1-C2$	166.9	1.03	1.30	2.08
$CH_3CHO \cdots ClCCH$		3.023		176.1	1.16	1.53	2.58
$CH_2O \cdots BrCCCN$	$O6 \cdots Br1$	2.860	$O6-Br1-C2$	179.9	2.80	3.08	4.07
$CH_3CHO \cdots BrCCCN$		2.824		179.9	3.32	4.40	5.01
$CH_2O \cdots ClCCCN$	$O6 \cdots Cl1$	2.943	$O6-Cl1-C2$	179.1	2.21	2.45	2.96
$CH_3CHO \cdots ClCCCN$		2.908		179.1	2.71	3.86	3.56

* $\Delta r = r_{\text{VW}} - r$; r_{VW} (sum of van der Waals radii) = $r_O + r_{Br} = 3.35$, $r_O + r_{Cl} = 3.21$ [#] $\Delta E_{\text{Corr}} = E_{\text{(Complex)}} - [E_{\text{(Carbonyl compound)}} + E_{\text{(X-Y)}}] + \text{BSSE correction}$

Figure 4. Variation of halogen-bonded interaction energies as a function of O...X distances of the complexes at MP2/aug-cc-pVDZ level.

The halogen bond interaction energies of the complexes which were corrected for BSSE are listed in table 2 and it is clearly evident that interaction energies computed at the MP2/aug-cc-pVDZ level are higher than those obtained at B3LYP/6-31++G** and MP2/6-31++G** levels. From table 2, it is seen that interaction energies at MP2/aug-cc-pVDZ are computed to be in a range of -1.65 to -4.27 kcal/mol for the complexes with CH_2O and -2.27 to -5.26 kcal/mol with CH_3CHO . For the same substituent group Y of X-Y, the ΔE_{Corr} are higher for X = Br than for X = Cl for both CH_2O and CH_3CHO . For example, the ΔE_{Corr} values of $\text{CH}_2\text{O} \cdots \text{BrCF}_3$ and $\text{CH}_2\text{O} \cdots \text{ClCF}_3$ are -2.74 and -2.09 kcal/mol respectively. Also, higher interaction energies are indicated for complexes with substituents Y = CN, CCH and CCCN in comparison to substituents CF_3 , CF_2H and CFH_2 , with an exception of XCF_3 halogen bond donor, which display somewhat higher ΔE_{Corr} than XCCH donor. The interaction energy of $\text{CH}_2\text{O} \cdots \text{BrCN}$ is -4.27 kcal/mol which is highest and that of $\text{CH}_2\text{O} \cdots \text{ClCFH}_2$ is least (-1.65 kcal/mol) amongst the various complexes of CH_2O under study.

The complexes with CH_3CHO have smaller halogen bond distances and higher interaction energies relative to the values in complexes with CH_2O highlighting the role of $-\text{CH}_3$ substituent on the halogen bond acceptor ability. Compared to -4.27 kcal of $\text{CH}_2\text{O} \cdots \text{BrCN}$, the ΔE_{Corr} for $\text{CH}_3\text{CHO} \cdots \text{BrCN}$ becomes -5.26 kcal/mol and the O...Br distance is decreased by 0.053 Å. Similar trend is observed with other halogen bonded complexes of CH_3CHO when compared to their respective analogues of CH_2O . From the discussion above, one can infer that the strength of halogen bond is affected by the presence of substituents at the carbonyl carbon as well as at the halogen. It is evident from figure 4 that there exists a linear relationship between halogen-bonded interaction energies and halogen bonded distances for both CH_2O and CH_3CHO complexes with R^2 (square of correlation coefficient) 0.887 and 0.871 respectively. The relatively lower correlation coefficient in CH_3CHO complexes arises due to the existence of weak intermolecular interactions between the hydrogen atom of CH_3CHO and X of X-Y halogen donors, which are confirmed from AIM analysis (table 3). AIM topological parameters support the presence of H-bond interaction with small ρ values though the atomic separations are slightly longer than the sum of van der Waals radii. In order to evaluate the contribution of additional stabilization resulting from interactions other than halogen bonding, the energy of stabilization ΔE_{B} (without any corrections) has been calculated with linear geometry and compared with that ΔE_{A} (without any corrections) for the optimized complex. The differences in ΔE_{A} and ΔE_{B} (table 3) suggest that significant stabilization of the order 24–50% results from such interactions.

The interaction energies for the complexes $\text{CH}_2\text{O} \cdots \text{X-Y}$ and $\text{CH}_3\text{CHO} \cdots \text{X-Y}$ correlate with the respective $V_{\text{S,max}}$ values at the σ -holes of X-Y molecules. The linear correlation coefficient is 0.876

Table 3. Uncorrected interaction energies ΔE_{A} for the complexes with CH_3CHO under study and ΔE_{B} evaluated for the complexes with single point calculations with X...O=C angle of 180° along with AIM parameters computed at MP2/aug-cc-pVDZ level.

Adducts	ΔE_{A} (kcal/mol)	* ΔE_{B} (kcal/mol)	$\rho_{\text{O} \cdots \text{X}}$	$\nabla^2_{\rho_{\text{O} \cdots \text{X}}}$
$\text{CH}_3\text{CHO} \cdots \text{BrCF}_2\text{H}$	4.12	2.92	0.003	0.012
$\text{CH}_3\text{CHO} \cdots \text{ClCF}_2\text{H}$	3.21	1.84	0.003	0.012
$\text{CH}_3\text{CHO} \cdots \text{BrCFH}_2$	3.83	2.19	0.004	0.012
$\text{CH}_3\text{CHO} \cdots \text{ClCFH}_2$	3.11	1.55	0.003	0.012
$\text{CH}_3\text{CHO} \cdots \text{ClCCH}$	3.48	2.64	0.003	0.012

* ΔE_{B} are absolute energy differences for the adducts obtained by keeping $\text{C}=\text{O} \cdots \text{X}$ (X=Cl, Br) = 180.0°

Figure 5. Variation of halogen-bonded interaction energies of the complexes with electrostatic potential of the halogen bond donors at MP2/aug-cc-pVDZ level.

in former complexes, as shown in figure 5 whereas the correlation coefficient in latter complexes drops to the value of 0.863, which again suggests the involvement of secondary interactions. These figures reflect that higher is the $V_{s,max}$, higher is the interaction energy, and hence stronger the halogen bonds which has demonstrated in the earlier studies as well.^{67,68}

3.2 Electronic properties of the halogen-bonded complexes

NBO and AIM methodologies have been used to study the electronic properties of the complexes. The information about the charge transfer between the vacant and filled orbitals is reflected by the second order stabilization energy $E^{(2)}$ for the relevant orbital interactions from NBO analysis. The data supplied in table 4 corresponds to the second-order stabilization energies resulting from the delocalization of lone pair of oxygen atom to the σ_{C-X}^* orbital in the molecule X-Y. In all the complexes under study, the $E^{(2)}$ values are larger when bromine is an interacting atom than those obtained in similar complexes with Cl as interacting atom. Also, it is interesting to note that methyl group enhances the electron donor ability of carbonyl oxygen for the same X-Y molecule, as apparent from the $E^{(2)}$ values of $CH_2O \cdots BrCN$ (3.60 kcal/mol) and $CH_3CHO \cdots BrCN$ (4.62 kcal/mol). The $E^{(2)}$ values in the CH_3CHO complexes follow the same trend as that observed for CH_2O complexes as a function of the X-Y molecule. Though the values are smaller in comparison to the usual range seen in the case of hydrogen bonded adducts,^{69–73} but the order of second order stabilization

Table 4. The second order perturbation stabilization energies $E^{(2)}$ (kcal/mol) for the orbital interactions important for halogen bond and Δs , the increase in s-character (kcal/mol) of C of C-X bond from NBO analysis kcal/mol, and AIM parameters for the complexes under study at MP2/aug-cc-pVDZ theoretical level.

Complexes	Donor Acceptor	$E^{(2)}$	Δs	$\rho_{O \cdots X}$	$\nabla^2_{\rho_{O \cdots X}}$
$CH_2O \cdots BrCF_3$	$n_{O6} \rightarrow \sigma_{C1-Br5}^*$	2.68	0.88	0.012	0.048
$CH_3CHO \cdots BrCF_3$		3.04	1.06	0.012	0.052
$CH_2O \cdots ClCF_3$	$n_{O6} \rightarrow \sigma_{C1-Cl5}^*$	1.07	0.50	0.010	0.040
$CH_3CHO \cdots ClCF_3$		1.10	0.63	0.009	0.040
$CH_2O \cdots BrCF_2H$	$n_{O6} \rightarrow \sigma_{C1-Br5}^*$	1.90	0.46	0.010	0.040
$CH_3CHO \cdots BrCF_2H$		2.19	0.58	0.011	0.044
$CH_2O \cdots ClCF_2H$	$n_{O6} \rightarrow \sigma_{C1-Cl5}^*$	0.64	0.64	0.008	0.032
$CH_3CHO \cdots ClCF_2H$		0.69	0.75	0.008	0.032
$CH_2O \cdots BrCFH_2$	$n_{O6} \rightarrow \sigma_{C1-Br5}^*$	1.46	0.50	0.009	0.036
$CH_3CHO \cdots BrCFH_2$		1.61	0.62	0.010	0.036
$CH_2O \cdots ClCFH_2$	$n_{O6} \rightarrow \sigma_{C1-Cl5}^*$	0.39	0.44	0.007	0.032
$CH_3CHO \cdots ClCFH_2$		0.60	0.56	0.007	0.032
$CH_2O \cdots BrCN$	$n_{O4} \rightarrow \sigma_{Br1-C2}^*$	3.60	1.35	0.013	0.056
$CH_3CHO \cdots BrCN$		4.62	1.64	0.015	0.064
$CH_2O \cdots ClCN$	$n_{O4} \rightarrow \sigma_{Cl1-C2}^*$	1.41	0.94	0.010	0.044
$CH_3CHO \cdots ClCN$		1.76	1.11	0.011	0.048
$CH_2O \cdots BrCCH$	$n_{O5} \rightarrow \sigma_{Br1-C2}^*$	2.08	1.05	0.010	0.044
$CH_3CHO \cdots BrCCH$		2.34	1.18	0.011	0.048
$CH_2O \cdots ClCCH$	$n_{O5} \rightarrow \sigma_{Cl1-C2}^*$	1.06	0.76	0.009	0.040
$CH_3CHO \cdots ClCCH$		1.21	0.95	0.009	0.040
$CH_2O \cdots BrCCCN$	$n_{O6} \rightarrow \sigma_{Br1-C2}^*$	2.88	1.12	0.012	0.056
$CH_3CHO \cdots BrCCCN$		3.27	1.26	0.013	0.048
$CH_2O \cdots ClCCCN$	$n_{O6} \rightarrow \sigma_{Cl1-C2}^*$	1.29	0.96	0.010	0.044
$CH_3CHO \cdots ClCCCN$		1.68	1.14	0.011	0.048

Figure 6. Relationship between the interaction energy (kcal/mol) and the change in s-character of the C hybrid orbital of C-X bond (%) as result of complex formation at MP2/aug-cc-pVDZ level.

energies for the complexes are consistent with trends in the interaction energies. The electron charge transfer from the Lewis base to the Lewis acid is followed by repolarization in which there is an increase in negative charge of the C atom and an increase in positive charge at the X atom. If X acts as Lewis acid, there is an increase in s-character in the C hybrid orbital of the C-X bond. On the other hand, a decrease in s-character is indicated in the C orbital if X acting as Lewis base

centre. In the present study, it is evident that X atoms of X-Y halogen donor are acting as Lewis acids, thus the increase in s-character of the C hybrid orbital is observed. The Δs values for such an increase are listed in table 4. Figure 6 presents the correlation between the interaction energies and the change in s-character in the complexes involving CH_2O and CH_3CHO . It is clear from the figure 6 that the s-character is a good descriptor of the strength of the halogen bonding interactions.

Several scientists have studied the non-covalent interactions including halogen bonding^{74–77} using AIM theory. The AIM parameters like electron density ρ_b and laplacian ∇_ρ^2 , have been suggested to give information about the presence of bonding interactions and their nature. The presence of intermolecular $\text{O} \cdots \text{X}$ bond critical points (BCPs) is observed in all the complexes under study. According to Koch and Popelier,⁷⁸ for the closed shell interactions, both ρ_b and ∇_ρ^2 should be positive and fall within the range 0.002–0.0035 a.u. and 0.024–0.139 a.u. respectively. From table 4, it is seen that the electron density (ρ_b) at BCP for the $\text{O} \cdots \text{Br}$ and $\text{O} \cdots \text{Cl}$ halogen bonded complexes under study lies in the range 0.009–0.015 au and 0.007–0.011 au respectively, thereby suggesting $\text{O} \cdots \text{Br}$ bond to be stronger than $\text{O} \cdots \text{Cl}$ bond. ∇_ρ^2 indicates whether the electron density is locally concentrated ($\nabla_\rho^2 < 0$)

Table 5. SAPT components (kcal/mol) of the interaction energies for the complexes at MP2/6-31++G** theoretical level.

Complexes	E_{els}	E_{ind}	E_{disp}	E_{exc}	E_{int}
$\text{CH}_2\text{O} \cdots \text{BrCF}_3$	−4.62	−4.65	−1.84	9.44	−2.18
$\text{CH}_3\text{CHO} \cdots \text{BrCF}_3$	−5.34	−5.55	−2.27	11.18	−2.61
$\text{CH}_2\text{O} \cdots \text{ClCF}_3$	−3.01	−2.13	−1.33	5.19	−1.56
$\text{CH}_3\text{CHO} \cdots \text{ClCF}_3$	−3.24	−2.25	−1.52	5.36	−1.94
$\text{CH}_2\text{O} \cdots \text{BrCF}_2\text{H}$	−3.46	−3.68	−1.62	7.69	−1.45
$\text{CH}_3\text{CHO} \cdots \text{BrCF}_2\text{H}$	−4.26	−5.15	−2.23	10.38	−1.75
$\text{CH}_2\text{O} \cdots \text{ClCF}_2\text{H}$	−2.31	−1.46	−1.27	4.08	−1.18
$\text{CH}_3\text{CHO} \cdots \text{ClCF}_2\text{H}$	−2.42	−1.77	−1.46	4.51	−1.36
$\text{CH}_2\text{O} \cdots \text{BrCFH}_2$	−2.56	−3.14	−1.48	6.61	−0.87
$\text{CH}_3\text{CHO} \cdots \text{BrCFH}_2$	−3.11	−4.33	−2.15	9.12	−0.88
$\text{CH}_2\text{O} \cdots \text{ClCFH}_2$	−2.19	−1.30	−1.41	4.33	−0.81
$\text{CH}_3\text{CHO} \cdots \text{ClCFH}_2$	−2.22	−1.94	−1.68	5.44	−0.66
$\text{CH}_2\text{O} \cdots \text{BrCN}$	−6.12	−5.17	−1.99	10.38	−3.51
$\text{CH}_3\text{CHO} \cdots \text{BrCN}$	−7.61	−7.48	−2.40	14.12	−4.16
$\text{CH}_2\text{O} \cdots \text{ClCN}$	−3.89	−2.04	−1.29	4.87	−2.66
$\text{CH}_3\text{CHO} \cdots \text{ClCN}$	−4.70	−2.90	−1.52	6.43	−3.09
$\text{CH}_2\text{O} \cdots \text{BrCCH}$	−3.39	−2.24	−1.66	5.71	−1.92
$\text{CH}_3\text{CHO} \cdots \text{BrCCH}$	−3.93	−2.78	−1.92	6.75	−2.29
$\text{CH}_2\text{O} \cdots \text{ClCCH}$	−2.66	−1.98	−1.34	4.99	−1.24
$\text{CH}_3\text{CHO} \cdots \text{ClCCH}$	−2.92	−2.31	−1.56	5.53	−1.53
$\text{CH}_2\text{O} \cdots \text{BrCCCN}$	−5.28	−3.38	−2.02	7.92	−3.28
$\text{CH}_3\text{CHO} \cdots \text{BrCCCN}$	−6.15	−4.23	−2.33	9.48	−3.87
$\text{CH}_2\text{O} \cdots \text{ClCCCN}$	−3.64	−1.91	−1.34	4.60	−2.57
$\text{CH}_3\text{CHO} \cdots \text{ClCCCN}$	−4.50	−2.92	−1.60	6.44	−2.96

or depleted ($\nabla_{\rho}^2 > 0$). The laplacians for all the halogen bonded complexes range from 0.032 to 0.056 au. The values for ∇_{ρ}^2 are clearly positive, as expected for the intermolecular interaction. Similarly, one can compare the strength of $CH_2O \cdots X-Y$ complexes with those of $CH_3CHO \cdots X-Y$ complexes from AIM analysis. For example, for the strongest complex $CH_3CHO \cdots BrCN$ the ρ_b and ∇_{ρ}^2 are 0.015 and 0.064 au while for the similar complex with CH_2O as halogen bond acceptor, the values are 0.013 and 0.056 au respectively. There exists exponential relationship between

the value of electron densities at BCP and interatomic distances between the halogen bonding atoms and is in agreement with the results found previously for other weak interactions.^{79,80}

3.3 SAPT analyses

The decomposition by means of SAPT technique is quite useful to investigate the nature of halogen bond. For instance, Jablonski *et al.* investigated the nature of

Figure 7. Optimized structures of $O \cdots I$ halogen bonded complexes at MP2/aug-cc-pVDZ-PP level.

Figure 7. (cont.)

hydride-halogen bond between either LiH or HBeH and XCF_3 or XCCH ($\text{X} = \text{F}, \text{Cl}, \text{Br}, \text{I}$). Their studies demonstrate the dominant role of inductive energy while electrostatic interactions play a minor role in stabilizing hydride-halogen complexes.⁸¹ In order to examine the nature of halogen bonded complexes studied in this article, the symmetry adapted perturbation theory (SAPT) analysis has been performed at MP2/6-31++G** level. The brief description of all energy components have been gathered in table 5. It can be seen that the sum of all attractive terms (E_{els} , E_{ind} and E_{disp}) overcompensates repulsion exchange energy (E_{exc}), thus indicating the stability of complexes. The comparison of all SAPT terms of CH_2O complexes with those of CH_3CHO complexes clearly reveals the enhancement of all terms in the latter complexes relative to the former ones.

It is clearly seen that E_{ind} dominates over E_{elst} in the complexes of CH_2O and CH_3CHO with $\text{O} \cdots \text{Br}$ halogen bond involving fluoromethyls as halogen bond donors while dispersive interactions are indicated to be much lower in magnitude. However, in the similar complexes with $\text{O} \cdots \text{Cl}$ halogen bond, E_{elst} dominates over E_{ind} . The studies by Riley and Hobza⁴³ concluded that in the halogen-bonded complexes of type $\text{H}_3\text{CX} \cdots \text{OCH}_2$ ($\text{X} = \text{Br}, \text{Cl}$), the dispersive interactions are dominating over other terms in the interaction energy. The least stabilized $\text{CH}_2\text{O} \cdots \text{ClCFH}_2$ complex with $\text{O} \cdots \text{Cl}$ halogen bond has the strongest E_{elst} component out of all three components and the E_{disp} component is higher than E_{ind} ; suggesting the role of dispersion forces over induction forces. Thus, the decomposition analysis indicates the difference in

the nature of interactions strengthening $O\cdots Br$ and $O\cdots Cl$ halogen-bonded complexes. On the other hand, the complexes involving linear halocompounds; both $O\cdots Br$ and $O\cdots Cl$ halogen bond have E_{elst} component higher than E_{ind} with E_{disp} playing least role in stabilizing these complexes.

3.4 Comparison of interaction energies of $O\cdots I$ with $O\cdots Br$ and $O\cdots Cl$ halogen bonds

In order to investigate the nature of halogen atom on the strength of the halogen bond, the $O\cdots I$ halogen bonded complexes with similar substituents and CH_2O and CH_3CHO as halogen bond acceptors have also been optimized at MP2/aug-cc-pVDZ-PP level. In order to account for relativistic effects,⁸² the aug-cc-pVDZ-PP basis set which uses small-core pseudopotentials was used for iodine, whereas for all other remaining atoms the aug-cc-pVDZ^{83–85} basis set was used. The optimized structures for both the CH_2O and CH_3CHO complexes are depicted in figure 7. As can be seen from tables given in supporting information, the $O\cdots I$ halogen bond distances are shorter than $O\cdots Cl$ and $O\cdots Br$ distances with a few exceptions ($r_O + r_I = 3.55 \text{ \AA}$). The presence of weak secondary interactions are also indicated for the $O\cdots I$ bonded complexes.

The computed interaction energies with BSSE correction, ΔE_{Corr} for the complexes with $O\cdots I$ halogen bonds at the above mentioned level are listed in table 6. It was already pointed out by the studies carried out by Politzer *et al.*^{20,25} that a halogen's σ -hole tends to become larger and more positive with increasing size of halogen atom, thus follows the order $Cl < Br < I$. Thus, halogen bonding becomes stronger in the same order with $O\cdots I$ bonded complexes exhibit higher

interaction energies than $O\cdots Cl$ and $O\cdots Br$ complexes. The effect of nature of halogen atom on the interaction energies is clearly evident and one can compare the ΔE_{Corr} values (tables 2 and 6) of the $O\cdots Cl$, $O\cdots Br$ and $O\cdots I$ halogen bonded complexes for the same halogen bond donor i.e., X-Y molecule. For instance, consider XCF_3 as halogen bond donor, the ΔE_{Corr} for $CH_2O\cdots ClCF_3$, $CH_2O\cdots BrCF_3$ and $CH_2O\cdots ICF_3$ are -2.09 , -2.74 and -4.45 kcal/mol respectively, hence reflecting the highest stability of the $O\cdots I$ bonded complexes relative to those having $O\cdots Cl$ and $O\cdots Br$ bonds. The trends of the interaction energies for all three types of the $O\cdots X$ complexes are same, with XCN halogen donor displaying the highest stability relative to all remaining X-Y donors and halogen donor $XCFH_2$ exhibiting the lowest stability. The complexes $CH_2O\cdots ClCN$, $CH_2O\cdots BrCN$ and $CH_2O\cdots ICN$ are stabilized with ΔE_{Corr} values of -3.07 , -4.27 and -6.17 kcal/mol respectively. As apparent from the tables 2 and 6, the CH_3CHO complexes are adorned with somewhat higher ΔE_{Corr} values than CH_2O complexes, thus the ΔE_{Corr} values for the complexes $CH_3CHO\cdots ClCN$, $CH_3CHO\cdots BrCN$ and $CH_3CHO\cdots ICN$ are increased to -3.67 , -5.264 and -7.68 kcal/mol respectively. Similar comparison of ΔE_{Corr} values for the other halogen donors can be made for the $O\cdots Cl$, $O\cdots Br$ and $O\cdots I$ bonded complexes.

4. Conclusions

The present study analyzes the nature of $O\cdots Br$ and $O\cdots Cl$ halogen bonding in a series of $CH_2O\cdots X-Y$ and $CH_3CHO\cdots X-Y$ ($X = Cl, Br$; $Y = CF_3, CF_2H, CFH_2, CN, CCH, CCCN$) complexes at B3LYP/6-31++G** and MP2/aug-cc-pVDZ level of theory. The higher polarizability and lower electronegativity of Br results in high $V_{S,max}$ value than for Cl with the similar substituent. The positive electrostatic potential ($V_{S,max}$) on the halogen atom are linearly correlated with halogen-bonded interaction energies involving CH_2O and CH_3CHO as halogen bond acceptors which is also in line with the enhancement of size of σ -hole with increasing electron-withdrawing nature of the substituent. The analysis of halogen-bonding distances and interaction energies reveals that the order for the strength of halogen bonding is $O\cdots I > O\cdots Br > O\cdots Cl$. Also, the stabilization of complexes with CH_3CHO as halogen bond acceptor is higher relative to that of complexes of CH_2O . Thus, the strength of halogen bond is affected by the presence of substituents at the carbonyl carbon as well as at the halogen. The $O\cdots Br$ halogen bond with fluoromethyl substituents at

Table 6. The BSSE-corrected interaction Energies (kcal/mol) for the $O\cdots I$ bonded complexes at MP2/aug-cc-pVDZ-PP theoretical level.

Complexes	ΔE_{Corr} (-ve)
$CH_2O\cdots ICF_3$	4.45
$CH_3CHO\cdots ICF_3$	5.54
$CH_2O\cdots ICF_2H$	3.19
$CH_3CHO\cdots ICF_2H$	4.19
$CH_2O\cdots ICFH_2$	2.73
$CH_3CHO\cdots ICFH_2$	3.80
$CH_2O\cdots ICN$	6.17
$CH_3CHO\cdots ICN$	7.68
$CH_2O\cdots ICCH$	3.74
$CH_3CHO\cdots ICCH$	5.81
$CH_2O\cdots ICCCN$	5.16
$CH_3CHO\cdots ICCCN$	7.33

the Br, the inductive component from SAPT analysis is higher in comparison to electrostatic component, while for the $O \cdots Cl$ halogen bond with similar substituents, E_{els} dominates over E_{ind} . However, for the remaining substituents -CN, -CCH and -CCCN at the halogen both in case of $O \cdots Br$ and $O \cdots Cl$ bonds, E_{els} is found to be larger relative to E_{ind} .

Supplementary Information

The differences of the halogen bonding distances between the values in the complex and in the isolated molecule for C-X bond of X-Y molecules and for C=O bond of carbonyl molecules are given in table S1 at MP2/aug-cc-pVDZ level. Tables S2–S19 include the optimized parameters for the CH_2O and CH_3CHO along with their complexes with X-Y (X = Cl, Br; Y = CF_3 , CF_2H , CFH_2 , CN, CCH and CCCN) at B3LYP/6-31++G** and MP2/aug-cc-pVDZ theoretical levels. Table S21 lists the percentage s-character of C in C-X bond of the halogen donors for the monomers and the complexes at MP2/aug-cc-pVDZ level. The atomic charges on the halogen bonding atoms obtained using NBO analysis at MP2/aug-cc-pVDZ level are given in table S22. Figure S1 shows a correlation between SAPT-based interaction energies and interaction energies obtained at MP2/cc-pVDZ level for both CH_2O and CH_3CHO complexes under study. The optimized parameters for $O \cdots I$ bond complexes of CH_2O and CH_3CHO at MP2/cc-pVDZ-PP level are reported in tables S23–S28.

Acknowledgement

We are highly thankful to the Department of Science and Technology (DST) (INSPIRE Fellowship Programme) for the financial assistance.

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