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# Do resonance-assisted intramolecular halogen bonds exist without a charge transfer and a σ-hole?

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## Abstract

To analyze the properties and mechanisms of six types of intramolecular resonance-assisted halogen bonding (Br --- O, Cl --- O, F --- O, Br --- O, Cl --- S and F --- S), we have chosen the five-membered closed ring system X - $C_1R_1 = C_3R_2 - C_2R_3 = Y$ (X=Br, Cl & F; Y=O & S) of unsaturated compounds with the substituents $NO_2$, $CH_3$ and H. A total of 78 structures were investigated by quantum chemical calculations at the MP2/aug-cc-pVTZ level of theory. A molecular electrostatic potential (MESP) map reveals that the cusp point of the σ-hole was not utilized but the belt point was used for all these intramolecular halogen-bonding interactions, indicating that all are electrostatic interactions. The halogen-bonding angle is below $100^0$ with the strongest interactions. The value of the nucleus-independent chemical shift (NICS (1)) reflects the changes and efficiency of resonance in all structures with a long bond. The presence of all interactions was proved by the bond critical point (BCP) and analyzed through its electron density, Laplacian of electron density and ellipticity parameter. The linear-probability correlation between the difference of the sum of the van der Waals radius and the non-covalent bond length (ΣVDW-L) and the electron density of the BCP was reported. 2D and 3D-NCI (non covalent interactions) plots show that halogen-bonding interactions are a mixed type of interactions with an attractive term. Natural bond orbital (NBO) analysis clearly indicates that the halogen bond lacks charge transfer and orbital overlapping through non-interacting lobes.

**Key words**: Resonance-assisted interaction, MESP map, atoms in molecules, NBO, 2D & 3D NCI plots, NICS (1).

## Introduction

Electron-transfer non-covalent interactions (NCI) begin from hydrogen bonds, which are formed by an exotic interaction of Van der Waals interactions. Nowadays, the ideas, properties, classifications and applications of hydrogen bonding are extended over to other similar interactions of σ-hole bonds and slightly to π-hole bonds[1-6]. When one of the half-filled p orbitals of a group IV–VII atom is implicated in a covalent bond, then the outer lobe of that orbital has an electron deficiency. This charge-depletion zone is called a σ-hole, where the small amount of positive charge suffices for the interaction with the nucleophilic region. σ-hole bonds are divided into halogen, chalcogen, pnicogen and tetrahedral or carbon bonds based on the donor atoms of groups VII, VI, V and IV, respectively. It should be noted, however, that σ-holes do not always have to be positive; low charge anisotropy can result in a negative σ-hole. When going from lighter to heavier elements, the polarizability of the σ-hole size increases and electronegativity decreases. With increasing size, σ-holes thus become more positive and their interactions grow stronger[7-12]. Specifically in those σ-hole bonds, their strength, properties and applications, compete with hydrogen bonds. The halogens appearing on molecular surfaces actively participate in molecular-recognition processes. A halogen atom acts as a donor in halogen bonding and as an acceptor in hydrogen and σ-hole bonding, because these halogens are both nucleophilic and electrophilic in character [13, 14]. Therefore, without knowing the role of the halogens present in non-covalent interactions, it is impossible to understand clearly the self assembly of nanomaterials and biomolecules, the chemical interactions between proteins and drugs or catalysts.

The intramolecular bonds reported in the literature imply the complications of manipulating such systems. However, an intramolecular interaction is too complicated to compare with intermolecular interactions, where molecular orientation depends on intramolecular interactions. Furthermore, resonance-assisted intramolecular interactions cannot be properly described by the electrostatic model alone, since it is associated with π delocalization[15-17]. Moreover, these interactions are enhanced for unsaturated compounds through an increase of the charge delocalization within the system. Therefore, the aim of the present study is to explain the detailed mechanism of intra-molecular halogen-bonding interactions with the resonance concept in an unsaturated closed ring system.

Studies of intramolecular hydrogen bonds have been briefly reported in malonaldihyde and its derivatives through experimental and theoretical investigations[18-20]. In addition, an intramolecular dihydrogen bond is analyzed through (1Z)-2-borylethen-1-ol ($BH_2$–CH–CH–OH) and its derivatives[21, 22]. Grabowski et al.[23] have reported intramolecular Cl---O contacts in the five-membered ring structure of Cl – C = C – C = O, where the Cl --- O contact has been confirmed by the quantum theory of atoms in molecules (QTAIM) analysis and its strength and topological analysis have been calculated with fluorine substituted in the carbon-atom method. P. Bowling et al.[24] have experimentally reported the intramolecular halogen bonds between aryl halide donors and suitable acceptors, such as carbonyl or quinolinyl groups in triangular structures. P. Johansson et al.[25] have reported the exotic intramolecular halogen --- halogen interactions in $X_3C$–$CY_3$ systems, concluding that there are no bond critical points between the halogens and that the σ-holes of the halogens are not utilized for bonding. The nature of exotic intramolecular halogen bonding studied here thus appears to be of an unusually strong van der Waals type. A study on resonance-assisted intramolecular interactions in halogen bonding, their properties and mechanisms is still lacking. The present study hence analyzes the detailed mechanism of six intramolecular types of halogen-bonding interactions with the donor (Br, Cl and F) and acceptor (O, S).

We have compared and analyzed six types of halogen-bonding interactions, including Br --- O, Cl --- O, F --- O, Br --- S, Cl --- S, F --- S, with the insight into the geometrical parameters obtained by performing quantum mechanical calculations (QM). The presence of intramolecular bonds was checked and graphically visualized, and the strength was analyzed through the 2D- and 3D-NCI plots of an isosurface map for the regions of non-covalent interactions. The nature and directionality were analyzed by the σ-hole concept through a molecular electrostatic potential map (MESP). Furthermore, the BCP of the corresponding interactions and its parameters such as electron density, the Laplacian of electron density and ellipticity were performed using QTAIM. Intramolecular halogen-bonding donor and acceptor radii were also discussed. Charge-transfer mechanisms were analyzed through natural bonding orbital analysis.

## Computational details:

All the computations in the present study were performed using the Gaussian 09W program[26]. The calculations were carried out in the framework of the MP2/aug-cc-pVTZ level of theory. All the optimized model structures correspond to the minima in the potential energy surface, because no imaginary frequencies were observed. The nucleus independent chemical shift (NICS) was used to study aromaticity, where a ring current arises when a magnetic field perpendicular to the ring (delocalized $\pi$-electron) is applied. This induced ring current was used as a criterion for the study of magnetic aromaticity. This makes it possible to determine the efficiency of resonance in the closed ring structure. This value was calculated through gauge invariant atomic orbital (GIAO) analysis in the absolute shielding constant. The NMR shielding at ring centers (the non-weighted mean of heavy-atom coordinates) is a NICS (0); a NICS (1) is 1.0 A° above the ring center[27].

Bader's theory of atoms in molecules (AIM) was employed to find the critical points and to analyze the electron densities and their Laplacians. The properties of bond critical points (BCPs) were studied, including electron density (ρ), its Laplacian ($\Delta^2\rho$) and the ellipticity at a BCP. The AIM calculations were carried out using the AIM2000 package[28]. The NCI PLOT program, developed by Contreras-Garcia et al.,[29] was used to identify and visualize non-covalent interactions. It analyzes the reduced density gradient (**S)** of the electron density (**r**) obtained by single-point energy calculations at low densities that are related to the weakest interaction. Therefore, a density cutoff of $\rho < 0.1$ a.u. was chosen as it includes the region of interest. Natural bond orbital (NBO) analysis was used to examine stabilizing interactions in the ground state.

The electrostatic potential map has been generated for the five-membered close structures in order to gain insight into the nature and directionality of the halogen-bond interactions being considered here. The electrostatic potentials have been computed on molecular surfaces, with a surface being defined as the 0.001-a.u. (electrons/bohr3) outer contour of the electron density, as proposed by Bader et al. The most positive value of the potentials (the maximum value) is referred to as $V_{s,max}$. There may be several of each on a given molecular surface[14].

## Results and discussion:

The aim of the present study is to analyze and compare the strength and characteristic properties of strong intramolecular halogen bonding with different combinations of donors and acceptors. In order to make the study more precise, we restrict our survey to a five-membered closed ring system ($X - C_1R_1 = C_3R_2 - C_2R_3 = Y$) of unsaturated compounds. The preferred structures elucidate systems that contain intramolecular halogen bonding through the substitutions X = Br, Cl and F & Y= O and S. Six systems with the interactions Br --- O, Cl --- O, F --- O, Br --- O, Cl --- S and F --- S have been taken into account. The intramolecular halogen-bonding mechanism is rather similar to resonance-assisted hydrogen bonding (RAHB), whose interactions are enhanced for unsaturated compounds through an increase of charge delocalization within the system[30-32]. This type of interaction thus has conjugative resonance, where donor (Y) and acceptor (X) atoms are brought close together by the resonance of the structure associated with electrostatic interactions between them. This intramolecular halogen bonding is the reason behind a closed ring structure. This study can facilitate the understanding of the enhanced stability of intramolecular halogen bonding in five-membered close structures with resonance-assisted hydrogen bonds. Moreover, the intramolecular RAHB structure has been discussed with the intramolecular RAXB in order to understand the mechanism of the exotic interaction. In the preferred structures, the stabilization of the systems results from the charge delocalization triggered by the formation of an intramolecular halogen bond.

To confirm the responsible resonance effects in intramolecular halogen bonding for a neutral system, we decided to analyze the structure, stability and bonding characteristics of the considered systems along with other structures, whose delocalization effects are absent in systems such as $X - C_1H_2 - C_3H_2 - C_2H = Y$. Structures with and without resonance are shown in Fig. 1b and 1c. The bond-length interaction and stability can be modified through a substitution effect. In order to explain the mechanism of bonding characteristics, the preferred substituents for inductive electron-withdrawing groups (EWGs), resonance EWGs [$NO_2$] and inductive electron-donating groups (EDGs) [$CH_3$] are $R_1$, $R_2$, $R_3$, respectively. The substitution effects were handled in four ways: (i) a hydrogen atom only substituted for all Rs (Hs); (ii) an EWG only substituted for any R (EWGs); (iii) an EDG only substituted for any R (EDGs); (iv) both EWG and EDG are simultaneously substituted in two of Rs (EWDGs). Fig. 1a also clearly shows these substituted systems.

## Electrostatic Potential Map

All the 78 structures have been analyzed by molecular electrostatic potential maps (MESP) with $V_{S,max}$ values for the σ-hole bond at the MP2/aug-cc-pVTZ level of theory (see Table 1). Fig. 2 shows graphically visualized molecular electrostatic potential maps for selected interesting intramolecular halogen-bonding structures. The $V_{max}$ values (Table 1) of EWG and EWDG systems have been found to be similar with slight variations in the corresponding interactions. Similarly, H- and EDG-substituted systems also have similar $V_{S,max}$ values (Table 1). On the other hand, the $V_{S,max}$ values (Table 1) of EWG- and EWDG-substituted systems are higher than those of H- and EDG-substituted systems. Fig 2A depicts the σ-hole for chlorine atom with the $V_{s,max}$ value of 0.1604 a.u, whereas in Fig 2B, fluorine atom is observed with positive region along the C-F axis, but it's not a σ-hole. Further, Fig 2C (H, CH3, H order of Cl --- S) having $V_{s,max}$ value of 0.1325 a.u is lesser than σ-hole for chlorine atom (Fig 2a) in $NO_2$, $CH_3$, H order of Cl --- O interaction's. This indicates that $NO_2$ substitutions plays a major role in increasing the $V_{s,max}$ value. Fig 2D, 2E and 2F of same order of substitution ($CH_3$, $NO_2$, H) with the sulfur accepted systems clearly differentiates the σ-hole between chlorine, bromine and fluorine atom as Br > Cl, where fluorine atom has only less positive region. While comparing Br --- O and Br --- S interaction, bromine atom with oxygen acceptor has high $V_{s,max}$ (0.1413 a.u) value for σ-hole. The size of positive region for fluorine atom is higher in case of F --- S interaction which is shown in Fig.2I. For the halogen atoms in the EWGs of the $NO_2$-substituted (ii) and (iv) methods, the $V_{S,min}$ value ranging from 0.03–0.06 a.u clearly reveals the efficiency of the $NO_2$-substituted (ii) and (iv) methods. Fig. 2 shows the presence of the σ-hole in the bromine and chlorine atom, but the fluorine atom has a less positive region in the cusp point with a $V_{S,}$ value of 0.0297 a.u.

Specifically the σ-hole present in halogens occurs along the C-X axis and away from the interacting region, whose belt point interacts with the negative region of the electronegative atoms O and S. This can be visualized in Fig. 2A for the $NO_2$, $CH_3$, H order of substitutions, where the Cl --- O interaction was observed with a $V_{S,max}$ value of 0.065 a.u and the F --- O interaction utilized a positive belt point. A comparison of all the structures reveals that the halogen-atom σ-hole is affected by $R_1$, $R_2$ and $R_3$ substituents. Based on the ESP map, the cusp point of the σ-hole was not utilized in the intramolecular halogen bonding, but the belt point was utilized for all types of resonance-assisted intramolecular halogen-bonding interaction.

Electrostatic potential is very interesting for the sulfur atom, whose positive site of the σ-hole was along the C-X axis and the negative site was perpendicular to the C-X axis on both sides. Table 1 clearly indicates that the $V_{S,max}$ value of Br---O, Cl---O, F---O in NO2, H, H systems are 0.1995, 0.1699, 0.2003 and the corresponding values for the S substituted ones are 0.1781, 0.1562, 0.1883, which are almost nearer. The H, H, H order of substitutions has lower $V_{S,max}$ values for each corresponding interaction. Notably, Fig. 2D, 2E and 2F were considered as an exception of sulfur-accepted halogen-bonding interactions (Br---S, Cl---S and F---S) of the $CH_3$, $NO_2$, H order of substitutions. The structures lack strong halogen bonding and deviate from the closed planar five-membered ring structures. In these structures, when a sulfur-bonded carbon atom saturates with R ($NO_2$), it becomes more electronegative than in the case of $CH_3$ due to it's electropositive nature. Yet the $CH_3$, $NO_2$, H order of substitutions lacks the electrostatic interaction between the individual components (Fig. 2); its belt point of halogens faces the positive sites of the sulfur atom. The ESP map shows that all types of resonance-assisted halogen bonding have an electrostatic interaction.

## **Structural properties:**

The intramolecular interactions observed in 78 structures (system A) were referred to as intramolecular resonance-assisted halogen bonding (RAXB) because of the role of resonance in the halogen-bonding interaction. Notably, the intra-molecular halogen-bonding interactions do not occur without resonance. For example, Fig. 3A, considered as an icon of the intra-molecular RAHB structure belonging to the five-membered ring close structure has a strong hydrogen-bond (SHB) interaction (1.64Å). Similarly, Fig. 3B of the same five-membered ring close structure but without resonance, satisfying tetravalent properties through the carbon, has a moderate hydrogen-bonding interaction (2.21Å). It arises from this that the resonance within the system is responsible for the enhancement of the hydrogen-bonding interaction from a moderate to a strong bond. Fig. 3C, with the substitution of X= Br & Y = O, has intra-molecular Br --- O (3.09Å) interactions with a true conjugative resonance of unsaturated compounds. Fig. 3D has the same X and Y substitutions of Fig. 3C but without resonance in carbon atoms. These structures (between Br and O) are observed with the distance of 3.46Å, indicating a lack of an intra-molecular halogen bond. The absence of a BCP between Br and O also proves the lack of interaction between them. This is supported by the MESP map, where the σ-hole was not utilized in the intra-molecular halogen bonding. Nevertheless, electrostatic interactions are observed between the positive charges of the belt point of halogen and the negative charges of the acceptor atom (O/S). This small amount of positive charge is not sufficient to interact between them, so the interactions are formed only through a conjugative resonance effect. In the RAXB, two electronegative atoms hence come close together and interact strongly through a true conjugative resonance effect.

The bond lengths and angles of the 78 structures with halogen-bond interactions are included in supplementary Tables S1 and S2. Table 2 clearly expresses the intra-molecular-halogen-bond ranges and the changes in the halogen-bond length through EWG, EDG and EWDG substitutions and the sum of the Van Der Waals radius (VDW) for the corresponding atoms. For intra-molecular resonance-assisted halogen bonding, the $CH_3$, $NO_2$, H order of substitutions has the highest bond length as compared to other orders of substitutions for the corresponding interactions (Br---O=3.16Å, Cl---O=3.07Å, F---O=2.84Å, Br---S=3.73Å, Cl---S=3.87Å and F---S=3.31Å), respectively. Overall, H structures have the highest bond lengths of all three types of substitutions (EWGs, EDGs and EWDGs). Moreover, bond lengths were shorter in the order EWDGs < EDGs < EWGs, indicating stronger intramolecular halogen bonding in the EWDG than EDG and EWG substituted compounds.

Specifically the $CH_3$, $NO_2$, H order of substitutions of sulfur-accepted halogen bonds (Br---S, Cl---S and F---S) has a higher bond length than the sum of VDW radii for the corresponding atoms. Hence, these 3 out of 78 structures were found to lack halogen bonds according to the concept of the VDW radius. In oxygen-acceptor halogen bonds, however, the highest bond lengths were below the VDW radius. Likewise the reversed H, $NO_2$, $CH_3$ order of substitutions has shorter bond lengths associated with the strongest interaction than other substitutions in sulfur-accepted halogen bonds (Br---S=3.33Å, Cl---S=3.24Å and F---S=2.75Å). In the $CH_3$, $NO_2$, H order of substitutions, the smaller negative charges in the sulfur atom are not sufficient to interact with the belt point, resulting in the lack of interaction. On the other hand in the H, $NO_2$, $CH_3$ order of substitutions, the sulfur atom with high negative charges is responsible for the strongest bond among the substitutions. Yet in the oxygen-acceptor halogen bond, the H, $CH_3$, $NO_2$ order of substitutions has shorter bonds, associated with the strongest interaction of the substitutions (Br---O=3.00Å, Cl---O=2.93Å and F---O=2.67Å). The variation in the bond length observed for four type of substitutions is too small (of 0.06–0.07Å) in sulfur accepted halogen bonds (Br---S, Cl---S and F --- S interactions).

The bond lengths were modified through the substitutions of Br---O=3.00–3.16Å, Br---S=3.33–3.39Å, Cl---O=2.93–3.02Å, Cl---S=3.24–3.31Å, F---O=2.67–2.83Å and F---S=3.01–3.08Å, whose ranges are smaller than the sum of the VDW radii for the corresponding atoms. All the halogen-bond interactions are compared through relative-bond-length analysis, which is clearly shown in Fig. 4. Moreover, the strength of the H, $NO_2$, H order is in EWGs; the strength of the H, $CH_3$, H order is only in EDGs; and the strength of the H, $NO_2$, $CH_3$ and H, $CH_3$, $NO_2$ orders is in EWDGs. The increase and decrease of the bond length for the corresponding substitutions is almost the same for the six types of interactions. In order to compare the strength of all types of electron-transferred non-covalent interactions (hydrogen and σ-hole bonds) through the bond length, the ΣVDW-L parameter is used. This value shows that intramolecular Br --- O interactions are stronger than other intramolecular halogen-bonding interactions. Specifically the H, $NO_2$, $CH_3$ order of substitutions for the Br --- O interaction is stronger than in all the other halogen-bonding interactions. The H, H, H order of the F --- O interaction (0.16Å) is the weakest interaction, where all the other interactions are between 0.16Å and 0.35Å. From ΣVDW-L values, it is clear that the F---O halogen-bonding interaction below the 0.20Å value is associated with the weakest interaction. Nevertheless, the H, $NO_2$, $CH_3$ order of the F --- O interaction (0.28Å) is stronger than the H, H, H order of the Br --- O, Br --- S, Cl --- O, Cl --- S, F --- S interactions, respectively.

In comparison with hydrogen bonds, halogen bonds show a much higher directionality. The angle for a reasonably strong halogen-bond adduct is thus always close to $180^0$. Yet these types of strong intramolecular halogen bonding have directionality opposite to strong halogen bonding, since the resonance-assisted intramolecular halogen-bonding range is $67^0$–$94^0$. The fluorine atom contains a halogen-bonding angle of more than $80^0$ and the others are low. In all halogen-bond interactions, the H, $NO_2$, $CH_3$ order of substitutions has the highest bond length among all the substitutions, whose angles are: Br --- O=$73.28^0$, Cl --- O=$76.69^0$, Br --- S=$77.21^0$, Cl --- S=$81.02^0$, F --- O=$87.85^0$ and F --- S=$93.29^0$. It has been found that the strength of intramolecular halogen-bonding angles is not very dominant. When compared with the bond angle of halogen bonds in all substitutions such as Br --- O < Cl --- O < Br --- S < Cl --- S < F --- O < F --- S, the lack of halogen-bonded structures (the $CH_3$, $NO_2$, H order of Cl---S, Br---S and F---S interactions) results in a low bond angle ($65.02^0$, $68.25^0$, $80.39^0$, respectively) as compared to other substitutions.

Overall we had compared our existing results with the previous results. Grobowski et al.,[23] performed the Cambridge structural database (CSD) search for intramolecular interactions and found the range of bond lengths in Cl---O contacts as 2.75 - 3.20Å, which coincides well with our Cl---O contacts (3.02Å). Further, they performed MP2/6-311++G(d,p) calculations for system $Cl - CR_1 = CR_2 - CR_3 = O$ with fluorine atom derivatives in $R_1$, $R_2$, $R_3$ (similar to the present study) and reported the range as 3.03-3.07Å . Whereas in the present study the Cl---O contact obtained through the substitution's ((i), (ii), (iii) and (iv) type method) for the same $Cl - CR_1 = CR_2 - CR_3 = O$ system has similar range as 2.93 - 3.07 Å. Moreover, the intramolecular bond angle in the present study is observed to be less than $95^0$. But P. Bowling et al.,[33] reported experimentally, the intra molecular contacts

(Br --- O and Cl --- O) between aryl halide donors and acceptors such as carbonyl or quinolinyl groups, held in proximity by 1, 2-aryldiyne linkers, provide triangular structures in the solid state. Interestingly the bond angles observed for halogen atoms are approximately $180^0$ and the bond length is 2.75-3.50 Å, which is contradictory to the present bond angle results.

## NICS analysis:

The presence of aromaticity due to resonance or anti-aromaticity and the changes of aromaticity during any external effort can be examined by NICS. NICS studies have been carried out to analyze the efficiency of resonance for 78 structures. Moreover, resonance is one of the parameters to compare the strength of intramolecular halogen-bond interactions, whose value is higher for NICS (1) than for NICS (0). This is because of the center of $\pi$-delocalization, which has the maximum of the diatropic ring current effect of the $\pi$-bond and is offset by a paratropic contribution of $\sigma$-bonds. This paratropic effect decreases with the distance from the center. Specifically 1.0Å above the center, the $\sigma$-bonds vanish. The NICS (1) value hence provides a more reliable indication of resonance. In our previous study, we have reported[34] the value of resonance (NICS (0) & NICS (1)) for six-membered and five-membered closed ring systems through an intramolecular hydrogen bond. The reference values for NICS (0) & NICS (1) were taken as 2.82 and -1.55, respectively, for the malonaldehyde molecule. The low negative and very low positive values thus indicate the resonance of five-membered closed ring systems through non-covalent interactions. The resonance of X - $C_1R_1$ = $C_3R_2$ - $C_2R_3$ = Y closed ring systems was affected by substitutions (X, Y, $R_1$, $R_2$ and $R_3$). The values in Table 3 report the changes of resonance capacity through substituents and the NICS (1) value of five-membered systems. Furthermore, the NICS (1) values seem to have good efficiency of resonance for all structures through the low negative values of NICS (1) except for the $CH_3$, $NO_2$, H order of substituted structures. The structures with the positive NICS (1) value represent less resonance and the corresponding bond lengths lack the VDW-radius concepts. This type of substitution hence reduces the resonance-associated interaction between two corresponding atoms. The H, H, $NO_2$ order of substituted structures has higher efficiency than other structures for each corresponding interaction. In all of these structures for all interactions, EDG-substituted structures have a high resonance value and EWDG-substituted structures have low resonance. The NICS (1) value, having the lowest bond length for the $NO_2$, $CH_3$, H and $NO_2$, H, $CH_3$ orders of substituted structures, competes with the NICS (1) value of EDG-substituted structures. This NICS (1) value does not exactly correlate with the bond length or any other parameter. Therefore, resonance is the only parameter reflecting the occurrence of interactions, and the donor–acceptor combination and its property role are vital for their strength.

## **Atoms-in-molecules theory:**

The presence of an intramolecular halogen bond was verified through the atoms-in-molecules (AIM) theory. The occurrence of the (3, -1) BCP (i.e. the point at which the electron density is minimum along the bond and maximum in the other two perpendicular directions) between the corresponding two electronegative atoms, the concomitant bond path and its electron density provide preliminary data for the occurrence of a non-covalent interaction by means of eight criteria, indicating the presence of non-covalent interactions. From the eight criteria, we have identified NCIs, covalent bonds, hydrogen bonds and weak dispersions. Three components of the electron-density distribution were used for the analysis of NCIs, including electron density and the Laplacian of the electron density of the bond critical point. Among the 78 structures, all the interactions have the BCP and the affiliated bond path except for the three interactions (Br---S, Cl---S and F---S) belonging to the $CH_3$, $NO_2$, H order of substitutions. Generally, the range of the electron density at the corresponding BCP for a hydrogen bond is 0.002–0.04 a.u. Similarly, here all the intramolecular halogen bonding is within the range of the electron density of a hydrogen bond (0.0090–0.0150a.u.). It seems that these intramolecular halogen bonds were stronger than a few hydrogen bonds. The resonance-assisted intramolecular halogen bonds are the inversely proportional to the bond length and electron density of BCP, shown separately for the corresponding interactions in Fig. 5. The electron density is directly proportional to the strength of interaction. Fig. 6 expresses the proportional relation between electron density and the Laplacian of electron density in individual correlations for all halogen-bonding interactions. The graph clearly indicates a similar range of bond length and electron density for Cl---O and F---S interactions. Nevertheless, the modified bond lengths were higher in Cl---O interactions than in F---S interactions. Likewise, sulfur-accepted halogen bonds have a small range of electron density for the corresponding bond lengths. Notably, F---O interactions are weak interactions, with the electron density of the BCP being below 0.0100a.u. Nevertheless, some of the F---O interactions are stronger than several intramolecular halogen-bond interactions. The ranges of electron density for Br---S and Cl---S interactions were almost the same.

The positive values of the Laplacian mostly indicate non-covalent interactions. Similarly, all the interactions have positive values between 0.0398–0.0725a.u. In our previous study[34], we reported the Laplacian of electron density in the range of 0.014–0.139a.u. for all types of hydrogen bonds with different classifications. On the other hand in the present study, the resonance-assisted intramolecular halogen-bonding interactions are found to be similar. The relation between electron density and the Laplacian of electron density for Cl---O and F---S interactions is not the same as the relation between electron density and bond length. The ΣVDW-L parameter was the common parameter to explain the strength of all interactions as well as the electron density of BCP[34]. The relation between the two parameters above (ΣVDW-L and electron density) and all interactions was compared. Fig. 7 confirms the linear-probability correlation between the ΣVDW-L and electron density of the BCP on the one hand and the equation of $\rho = 0.0044 + 0.0298\Sigma\text{VDW-L}$ (R=0.94) on the other. Interestingly enough, this relation is resonance-assisted intramolecular halogen bonding except for three cases of sulfur-accepted halogen bonding. Moreover, the ellipticity of the bond critical point (BCP) and the radius of the non-covalent interactions are the most important parameters to analyze the NCI. Through ellipticity, it is possible to determine the stability of the bond – the higher the ellipticity, the lower the stability (see Table 4 for all interactions). The bond strength is parallel to stability but not fully dependent on it, which is confirmed by the ellipticity values. The ellipticity value implies that the $CH_3$, $NO_2$, H order of substitutions for oxygen-acceptor halogen bonding is the weakest stable interaction (above 3.2a.u.). Furthermore, the H, H, $CH_3$ order of the Cl --- O interaction is the most stable interaction and the ellipticity value is 0.0004a.u. Also the Br --- O interaction is more stable than other interactions. Specifically, the ellipticity of the corresponding (Br --- O) BCP does not correlate with electron density and the Laplacian of electron density.

According to Koch and Popelier[35], the mutual penetration of electron density is used as the necessary and sufficient condition for the presence of non-covalent interactions. From this mutual-penetration condition, the halogen-bond radius of the donor and acceptor is used. The halogen-bond radius $R_{H---BCP}$ of the donor means the distance from the BCP to the halogen atom. The distance from the BCP to the O or S atom is referred to as the halogen-bond radius of the acceptor atom $R_{Y---BCP}$. The halogen-bond distance (X---Y) is the sum of the halogen-bond radii of the donor and acceptor atoms. Table 5 reports the halogen-bond radius of the donor and acceptor atoms for the corresponding intramolecular halogen bonding. The halogen-bond radii for the oxygen atom when bonded with Br, Cl and F are 1.37–1.44Å, 1.37–1.44Å and 1.40–1.47Å, respectively. The 1.44Å of the Br---O interaction is the weakest oxygen acceptor of the $CH_3$, $NO_2$, H order – without it, the $R_{Y---BCP}$ for the oxygen atom is 1.39Å on average when bonded with the bromine and chlorine atom. When bonded with the fluorine atom at 1.47Å, it has the same order of substitution. In F---O interactions, the $R_{Y---BCP}$ of the oxygen atom is greater than the $R_{X---BCP}$ of the fluorine atom (on average by 0.08Å) like the VDW radius

(0.05Å). The $R_{Y---BCP}$ for the sulfur atom when bonded with Br, Cl and F is 1.67–1.70Å, 1.66–1.70Å and 1.67–1.73Å, respectively. When the sulfur atom interacts with the fluorine atom, the $R_{Y---BCP}$ alters. The halogen-bond radii of the donor are 1.64–1.73Å, 1.57–1.64Å and 1.32–1.37Å for Br, Cl and F, respectively. In the Br --- S interaction, the halogen-bond radii of the donor and acceptor are almost equal. The halogen-bond donor and acceptor are below 0.21Å and 0.15Å

## ***2D and 3D-NCI plots***

The weak interactions are analyzed through 3D-NCI plots (NCI isosurfaces) and 2D-NCI plots (plotting the reduced gradient S as a function of the electron density r, oriented by the sign of $\lambda_2$) based on the presence of the BCP having three eigenvalues, $\lambda_1$, $\lambda_2$ and $\lambda_3$, of the Hessian. The Laplacian interaction is derived from the equations $4(2G\ (r\text{BCP}) + V\ (r\text{BCP}))$ and $\lambda_1 + \lambda_2 + \lambda_3$. Specifically the interaction is considered as bonding for $\lambda_2 < 0$ and as non-bonding for $\lambda_2 > 0$. The reduced density gradient (RDG) $s = |\Delta\rho| / (2(3\pi^2)^{1/3}\rho^{4/3})$, is one of the three components of electron-density distribution. The presence and type of interaction (hydrogen bonding, attraction, van der Waals, repulsive, steric clashes) and whether it is bonding or non-bonding can be identified from the eigenvalues. When a non-covalent interaction is present, it enables a graphical visualization of the regions for the interactions in real space. The NCI plot thus distinguishes between localized atom–atom contacts corresponding to strong directional attractions and weakly interacting molecular regions. The NCI isosurfaces are present not only in stabilizing interactions but also in the repulsive cases. Fig. 8 shows several selected 3D NCI plots from 78 structures for the evidence of the presence of weak interactions. First of all, the strongest interaction of intramolecular RAHB appears in the 3D NCI plot in Fig. 8A as a well-defined isosurface of dark-blue color associated with the strong hydrogen bonding existing between the oxygen and hydrogen atoms. The moderate intramolecular hydrogen bond without resonance (Fig. 8B) is marked in greenish color to show the lack of an intramolecular strong hydrogen bond. A strong intramolecular hydrogen-bonded system has two types of regions – a ring closure and RAHB, indicating that the red curve in the green-color region was established for the ring closure, where the same concept also exists for the Cl---O interaction.

The resonance structure with an intramolecular Cl---O interaction (Fig. 8C) is denoted by a bicolor region (the light blue/red curved in green), which is expressed as a mixed type of interaction (attraction/repulsion). This bicolor region is formed in the groove between the C-O and C-Cl groups within the intramolecular system. The external part of the light-blue color was established as the directional C-Cl---O attractive interaction, whereas the internal part of the green color indicates the repulsive interaction between the C-O and C-Cl groups, resulting from multicentric density in the inner region of five-membered ring structures. The intramolecular Cl---O interactions for structures without resonance (Fig. 8D) are marked in green, indicating the lack of halogen bond associated with a weak interaction. These figures clearly show the donor atoms from bromine to fluorine. The intensity of the light-blue color decreases for the interaction in isosurfaces, but all regions come under the attractive regions only, except for three sulfur-accepted halogen-bonded structures. It is clear from this that the donor-atom strength for fluorine to bromine increases for resonance-assisted intramolecular halogen-bonding systems. From the 78 structures, 75 structures have a bicolor region between the corresponding atoms. This is the evidence of the intramolecular RAXBs as a mixed type of interaction, indicating the dual characteristics of attraction/repulsion. The remaining three sulfur-accepted halogen-bond structures (in green) indicate the lack of halogen bonding between the donor and sulfur atom. Several structures have a hydrogen bond between the substituents ($NO_2$, $CH_3$, and H) in the five-membered rings, which is clearly expressed in Fig. 8E, 8F and 8H by the blue/red combination. Such a bicolored isosurface is thus assigned to the closure of an intramolecular ring, which results from stabilizing features (H bonds, NH–p bonds), indicated by the blue color. This is counterbalanced by destabilising interactions arising from steric crowding within the ring marked by the red color.

The 2D-NCI plot analysis makes it possible to understand the type of weak interaction between atoms and its strength. Fig. 9A shows the 2D-NCI plot of RAHB and non-RAHB structures. The light blue represents the RAHB structure and the light pink color represents non-RAHB structures and the violet (a combination of light blue and light pink) represents the common data between them. Each color has two troughs, one of which contains the positive sign $(\lambda_2)\rho$ and the other the negative sign $(\lambda_2)\rho$. The negative-sign $(\lambda_2)\rho$ region corresponds to QTAIM BCPs, whereas the positive region represents rings and cages (associated with s=0 points located inside the region). Hence the very low (nearly zero) RDG versus the negative sign$(\lambda_2)\rho$ with above -0.05 represents the strong hydrogen bond for RAHB structures and the negative sign$(\lambda_2)\rho$ with below -0.025 represents the moderate hydrogen bond. 2D-NCI plot analysis thus provides information on the weak interactions and compares them with strong interactions. The positive sign $(\lambda_2)\rho$ with two very low RDG troughs clearly explains that the RAHB-ring closure is stronger than the HB structure. Similarly, the RAXB structure (for the Br ---O interaction) and the non-RAXB structure are compared through the 2D-NCI plot in order to determine the resonance effect in the halogen bond as shown in Fig. 9B. The trough for the non-RAXB structure has values above 0.25 for S, which clearly shows the absence of a halogen bond. Without resonance in five-membered ring structures, an intramolecular halogen bond is lacking.

Notably, the dual character of halogen bonding (attractive/repulsive) in the RAXB structure is reflected in the simultaneous existence of two symmetric or nearly symmetric twin troughs of the opposite values of sign $(\lambda_2)$ $\rho$. Fig. 9C is another example of the 2D-NCI plot for Br --- O interactions with the $NO_2$, H, $CH_3$ order of substitutions. The graph indicates the dual characteristics of hydrogen and halogen bonding through double twin troughs. Also Fig. 9D is used to analyze the strength of interaction through the two plots of Cl---S interactions for the H, $NO_2$, H and H, $CH_3$, H orders of substitutions. The H, $CH_3$, H order of substitutions has only a halogen bond between the chlorine and sulfur atoms but the H, $NO_2$, H order of substitutions has a halogen bond between the chlorine and sulfur atoms and a hydrogen bond between the oxygen and hydrogen atoms as shown in Fig. 9D. For RDG, the end point of the trough of the H, $CH_3$, H order of substitutions is very close to zero when compared with the H, $NO_2$, H order of substitutions, indicating the strength of the H, $CH_3$, H order of substitutions. Similar results have been observed for all structures.

## NBO analysis

The donor–acceptor NBO interactions in hydrogen- and halogen-bond formation are well recognized in the literature[36] and provide valuable information. Also the charge-transfer mechanism and its stabilization energies have been performed through the second-order perturbation term by NBO analysis. In a hydrogen- and halogen-bond structure, a strong $n–\sigma^*$ interaction is dominant, which means that charge is transferred from a lone-pair acceptor to an anti-bonding orbital of the acceptor atom. As expected, the stabilization energy for the hydrogen bond is much higher than for the halogen bond. In a RAHB structure, the stabilization energy of $n–\sigma^*$ for the O – H --- O interaction is 31.80 kcal/mol, but the stabilization energy of the non-RAHB structure is only 1.64 kcal/mol. The high variation was also in agreement with all studies based on the resonance concept. Yet for all types of resonance-assisted intramolecular halogen bonds, there is a lack of an $n–\sigma^*$ charge-transfer mechanism. This indicates that charge transfer is below 0.5 kcal/mol, which confirms that the intramolecular interactions are not charge-transfer interactions, but there is attraction alone. This is confirmed by the blue-color region in the 3D-NCI plot. Fig. 10A is the NBO view for analyzing the overlap. It shows that the F --- O interaction, when it reaches the minimum or almost vanishes, indicates the presence of non-interacting lobes. Fig. 10B and 10C are examples of orbital-overlapping intramolecular interactions, indicating the hydrogen bond with and without resonance. The merging lobes, reflecting showing the strength of interaction, are present in such a way that they can overlap easily and clearly express the size. Fig. 10D is another example of the presence of two hydrogen bonds and one halogen bond, which are all resonance-assisted interactions. The merging lobes associated with strong interactions are clearly visible for the two hydrogen bonds and non-interacting lobes between the anti-bonding orbital of bromine and the lone-pair orbital of sulfur atoms. The above-mentioned phenomena of the charge-transfer mechanism exist for all the 78 structures. It is concluded from these results that there is no charge-transfer mechanism, but the interaction is attractive for all types of resonance-assisted halogen bonding.

## Conclusions:

In summary, the present study sheds light on the exotic interaction of six types of intramolecular resonance-assisted halogen bond (Br --- O, Cl --- O, F --- O, Br --- S, Cl --- S and F --- S). It also provides physical insight into the evidence of directional halogen bonds. The MESP map reveals that the cusp point of the σ-hole was not utilized, but the belt point was utilized for all types of resonance-assisted intramolecular halogen bonding interaction, indicating that all are electrostatic interactions. In the five-membered closed ring systems, resonance was used to enhance the strength of the hydrogen bond, and resonance is the reason behind the presence of halogen bonding. Electron-donating-group and electron-withdrawing-group substitutions enhance and reduce the strength of the exotic short strong halogen-bonding interaction. In the H, $NO_2$, $CH_3$ order of substitutions, sulfur-acceptor halogen bonding is more enhanced while for the H, $CH_3$, $NO_2$ order of substitutions, it is the oxygen-acceptor halogen bonding that is more enhanced. On the other hand in the $CH_3$, $NO_2$, H order of substitution, the oxygen-acceptor halogen boding is the weakest and sulfur-accepted halogen bonding lacks halogen-bonding interaction. This is proved by the VDW radius concept, the MESP map, the BCP and the 2D and 3D-NCI plots.

Overall stronger intramolecular halogen bonding is observed in the EWDG than in the EDG and EWG substituted compounds. The strongest halogen bonding has the halogen-bond angle below $100^0$. The value of the NICS (1) reflects the changes and efficiency of resonance in all structures with long halogen bond length. The AIM theory indicates the presence of all interactions, proven by the BCP and analyzed through its electron density, Laplacian of electron density and ellipticity parameter. The electron density ranges for all these interactions are 0.0090–0.0150 a.u. and the Laplacian of electron density is 0.0398–0.0725 a.u. Intramolecular halogen bond donor and acceptor radii were reported for all interactions. The H, H, $CH_3$ order of the Cl --- O interaction is the most stable of the interactions, because it has the ellipticity value of 0.0004a.u. The 3D-NCI plot confirms the intramolecular halogen bonding as attraction and a mixed type of interaction (attraction/repulsion). The region for halogen bonding is bicolor (the light blue/light red curved in green); for hydrogen bonding, it is in the blue/red color. 2D-NCI plots clearly indicate the strength of the interaction and show the mixed type of interaction through a similar twin trough with the opposite sign of ρ. NBO analysis clearly shows that the halogen bonding lacks charge transfer and orbital overlapping through non-interacting lobes.

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