

Theoretical study on cooperative effects between X \cdots N and X \cdots Carbene halogen bonds (X=F,Cl,Br and I)

Mehdi D. Esrafilı · Fariba Mohammdain-Sabet · Parvin Esmailpour

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Abstract Quantum chemical calculations are performed to study the interplay between halogen \cdots nitrogen and halogen \cdots carbene interactions in NCX \cdots NCX \cdots CH₂ complexes, where X=F, Cl, Br and I. Molecular geometries and interaction energies of dyads and triads are investigated at the MP2/aug-cc-pVTZ level of theory. It is found that the X \cdots N and X \cdots C_{carbene} interaction energies in the triads are larger than those in the dyads, indicating that both the halogen bonding interactions are enhanced. The estimated values of cooperative energy E_{coop} are all negative with much larger E_{coop} in absolute value for the systems including iodine. The nature of halogen bond interactions of the complexes is analyzed using parameters derived from the quantum theory atoms in molecules methodology and energy decomposition analysis.

Keywords Cooperative effects · Electrostatic potential · Energy decomposition · Halogen bond · QTAİM

Introduction

There is now a growing awareness of the importance of noncovalent interactions, due to their key role in areas ranging from crystal engineering to biological recognition processes [1–8]. Although research has traditionally focused on the most common hydrogen-bonded interactions, more recently interest has grown for another type of intermolecular interactions, such as dihydrogen bond [9–11], lithium bond [12, 13] and π - π stacking [14]. The term “halogen-bonding” is usually taken to mean the noncovalent RX \cdots YZ interaction, where

X is a halogen (typically chlorine, bromine, or iodine) that is part of the molecule RX and YZ is a Lewis base; Y is often an atom, such as oxygen, nitrogen, or sulfur, that has a lone pair [15–18]. A key feature of halogen-bonding is its highly directional character; the angle between the R–X and X–Y bonds is always close to 180°. Halogen bond interaction energies are fairly broad, with values varying from about -1.2 kcal mol⁻¹ (Cl \cdots Cl) to about -43.0 kcal mol⁻¹ (I₃⁻ \cdots I₂) [3].

Since covalently-bonded halogen atom X and the electron donor Y in RX \cdots YZ are themselves typically viewed as being negative in character, the stability of the halogen bond were puzzling, until Brinck et al. [19], and subsequently others [20, 21] showed that the halogen atoms X in some molecules RX have regions of positive electrostatic potential on their outer surfaces, on the extensions of the R–X bonds. According to Politzer’s viewpoint [22], when a half-filled *p* orbital participates in forming a covalent bond, its electron normally tends to be somewhat localized in internuclear region, thereby diminishing the electronic density in the outer lobe of that orbital. Through this positive region, which has been labeled a “ σ -hole”, the halogen atom can interact attractively with a negative site. This positive region is usually, but not always, surrounded by a belt of negative electrostatic potential, which accounts for the possibility of interacting laterally with a positive site. For a given R, the σ -hole potential on the halogen X in R–X becomes more positive in the order F \ll Cl<Br<I [23, 24]. The attractive electrostatic interactions between the positive charge on the σ -hole of halogen atom and negative charge of Lewis base are thus the sources of the attraction of the halogen bond. The origin of halogen bond has been studied with many methods including natural bond orbital (NBO) [25, 26], quantum theory of atoms in molecules (QTAİM) [27–29], and symmetry-adapted perturbation theory (SAPT) [30–32] analyses. Now, it is well-recognized that attractive nature of halogen bonds is mostly attributable to the electrostatic effect, polarization, charge-transfer, and dispersion contributions. The relative magnitudes of these terms are

M. D. Esrafilı (✉) · F. Mohammdain-Sabet · P. Esmailpour
Laboratory of Theoretical Chemistry, Department of Chemistry,
University of Maragheh, Maragheh, Iran
e-mail: esrafilı@maragheh.ac.ir

highly dependent upon the identity of the halogen X, with the relative contribution of the electrostatic term increasing for larger X [30]. Recently, Riley et al. [33] indicated that halogens with larger, more positive σ -holes tend to exhibit weaker dispersion interactions, which are attributable to the lower local polarizabilities of the larger σ -holes.

There are recent numerous theoretical [34–40] and experimental [41–43] studies seeking to characterize the geometrical and energetic properties of halogen bonds. With the progress in the study of halogen-bonding, different types of halogen bonds have been proposed in the recent years. Conventional halogen bonds of the sort where a halogen donor C–X group approaches an acceptor atom with lone pair like O or N, have been well studied over the years, and their fundamental nature is understood. There are also so-called unconventional halogen bonds such as halogen-hydride [44, 45], halogen- π [46], or even halogen-single electron bond [47]. Very recently, we reported the X \cdots C halogen bond with carbene as an electron donor in YCCX \cdots CH₂ complex where X=Cl, Br, I and Y=H, F, COF, COOH, CF₃, NO₂, CN, NH₂, CH₃, OH [48]. All interactions mentioned above may be classified as Lewis acid-Lewis base interactions, and there is an electron transfer from the Lewis base to the Lewis acid for all of them.

A number of studies have indicated that halogen bond shares some common characteristics in structure, strength, and nature with the hydrogen bond [49–51] and they can also coexist in chemical and biological processes. Recently, the cooperativity between the hydrogen and halogen bonds has been paid much attention [52, 53]. Li et al. [54] presented interesting cooperative effects between hydrogen bond and halogen bonds in H₃N–XY–HF complexes (X, Y=F, Cl, Br). The results show that the effect of a halogen bond on a hydrogen bond is more pronounced than that of a hydrogen bond on a halogen bond. However, to the best of our knowledge, neither a theoretical nor an experimental study has thus far been reported to examine the interplay between halogen \cdots nitrogen and halogen \cdots carbene interactions. Herein, we report our theoretical study on the cooperative effects in NCX \cdots NCX \cdots CH₂, where X=F, Cl, Br and I. Although carbene has two classes: singlet and triplet, we only consider the singlet one due to the presence of a free electron pair in singlet state. We believe that such a theoretical study may provide some valuable information of the mutual influence of the two interactions, which would be very important in halogen-based supra-molecular architectures and biological design.

Computational details

All molecular orbital calculations were carried out using the GAMESS suite of programs [55]. The geometries of all studied dyads and triads of NCX \cdots NCX \cdots CH₂ were fully optimized at the MP2 level. For complexes containing fluorine, chlorine and bromine the aug-cc-pVTZ basis [56] was used for optimization,

while for systems containing iodine a mixed basis set approach was used; here the iodine atom is described using the pseudopotential based aug-cc-pVTZ-PP basis [57] and the aug-cc-pVTZ is used for other atoms. Harmonic frequencies were calculated to confirm the equilibrium geometries that correspond to energy minima. The interaction energy was calculated as the difference of the total energy of the complexes and the sum of the isolated monomers in the complex geometry. The basis set superposition error (BSSE) calculated with the counterpoise method [58] was used to correct the interaction energies.

The cooperativity energy for the complexes studied here is defined as:

$$E_{coop} = E_{int}(ABC) - E_{int}(AB) - E_{int}(BC), \quad (1)$$

where $E_{int}(ABC)$ is the interaction energy of the triad, $E_{int}(AB)$ and $E_{int}(BC)$ are the interaction energies of the isolated dyads in their minima configuration. The nature of the halogen bond interactions have been explored using the following energy decomposition analysis [59]:

$$E_{int} = E_{elst} + E_{exch-rep} + E_{pol} + E_{disp}, \quad (2)$$

where E_{elst} , $E_{exch-rep}$, E_{pol} and E_{disp} correspond to electrostatic, exchange-repulsion, polarization and dispersion terms, respectively.

Electrostatic surface potentials were calculated at the MP2/aug-cc-pVTZ(-PP) level using WFA code [60]. The topological analysis of the electron charge density performed for all complexes was performed using Bader's QTAIM [61]. The QTAIM analysis was performed with the help of AIM 2000 software [62] using the wave functions generated at the MP2/aug-cc-pVTZ(-PP) level.

Results and discussion

Geometries Figure 1 shows a sketch of the NCX \cdots NCX \cdots CH₂ complexes, where X=F, Cl, Br and I. It should be noted that no symmetry constraints were introduced in the optimization of the complexes. All these species are true minima on the potential energy surface, as the vibrational analysis proved a posteriori. Two bond lengths (r_{X-N} and $r_{X-carbene}$) are marked explicitly in Fig. 1. Table 1 summarizes the optimized binding distance and the corresponding bond length change of the halogen bonds in

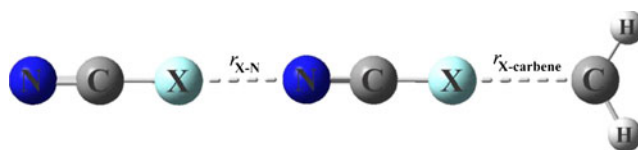


Fig. 1 The structure of NCX \cdots NCX \cdots CH₂ complexes (X=F, Cl, Br and I)

Table 1 Binding distances (in Å) of the studied triads and dyads. ΔR indicates the change of bond lengths relative to the dyads ^{a,b}

Triads (A–B–C)	R(AB)	R(AB,T)	$\Delta R(AB)$	R(BC)	R(BC,T)	$\Delta R(BC)$
NCF–NCF–CH ₂	2.971	2.955	–0.016	3.312	3.282	–0.030
NCF–NCCI–CH ₂	2.964	2.943	–0.022	3.094	3.081	–0.013
NCF–NCBr–CH ₂	2.947	2.935	–0.012	2.961	2.951	–0.010
NCF–NCI–CH ₂	2.930	2.912	–0.018	2.780	2.761	–0.019
NCCI–NCF–CH ₂	2.960	2.940	–0.019	3.312	3.249	–0.063
NCCI–NCCI–CH ₂	2.943	2.918	–0.025	3.094	3.066	–0.029
NCCI–NCBr–CH ₂	2.934	2.906	–0.028	2.961	2.935	–0.027
NCCI–NCI–CH ₂	2.918	2.883	–0.036	2.780	2.729	–0.051
NCBr–NCF–CH ₂	2.925	2.904	–0.022	3.312	3.236	–0.076
NCBr–NCCI–CH ₂	2.902	2.874	–0.028	3.094	3.056	–0.039
NCBr–NCBr–CH ₂	2.892	2.860	–0.033	2.961	2.924	–0.037
NCBr–NCI–CH ₂	2.876	2.833	–0.044	2.780	2.708	–0.072
NCI–NCF–CH ₂	2.937	2.912	–0.025	3.312	3.211	–0.101
NCI–NCCI–CH ₂	2.905	2.868	–0.036	3.094	3.041	–0.053
NCI–NCBr–CH ₂	2.894	2.852	–0.042	2.961	2.909	–0.052
NCI–NCI–CH ₂	2.876	2.818	–0.058	2.780	2.662	–0.118

^a R(AB) and R(BC) are interaction distances in isolated AB and BC dyads, respectively.

^b R(AB,T) and R(BC,T) correspond to bond distances in isolated AB and BC dimers using the geometry within the triads

the in the 16 triads and the respective dyads calculated at the MP2/aug-cc-pVTZ(–PP) level. The optimized C–X \cdots N contacts in NCX \cdots NCX dyads are highly directional, all of the predicted X \cdots N distances are significantly shorter than the sums of the van der Waals radii of the atoms involved [63], consistent with the structural features of strong halogen bonds that are predominantly electrostatic in nature. One can see that the halogen bond distances for the iodine bonded complexes are stronger than those from other lighter halogen atoms, which is consistent with the electrostatic potentials on the halogen atoms: 14 kcal mol^{–1} (NCF) < 41 kcal mol^{–1} (NCCI) < 48 kcal mol^{–1} (NCBr) < 56 kcal mol^{–1} (NCI). The $r_{X\text{-carbene}}$ in the NCX \cdots CH₂ dyads are calculated to be 3.312, 3.094, 2.961 and 2.781 Å for X = F, Cl, Br and I, respectively. These are comparable to halogen-carbene distances of halogen with acetylene and its derivatives [48]. Evidently, for a X = F, Cl and Br substitution, the $r_{X\text{-carbene}}$ in the NCX \cdots CH₂ complex is larger than that in the NCX \cdots NCX complex. In addition, a bigger contraction is observed when the fluorine atom in NCX \cdots CH₂ is replaced by heavier halogen atoms than NCX \cdots NCX (Table 1).

From Table 1, it is seen that the $r_{X\text{-N}}$ and $r_{X\text{-carbene}}$ distances in the triads are smaller than the corresponding values in the dyads. The differences in distances between triads and dyads are in the range between 0.015 to 0.058 Å and 0.010 to 0.0118 Å for $r_{X\text{-N}}$ and $r_{X\text{-carbene}}$, respectively (Table 1). That is, the two types of interaction have a cooperative effect on each other. Although both types of interactions are enhanced by each other in the triads, the shortening of the halogen bond distances is not equal. We noted, however, the shortening of the halogen bond distances in the triads is dependent on the strength of the other. For a given X substitution, the contraction of the $r_{X\text{-carbene}}$ halogen bond distance is quite larger than that of the $r_{X\text{-N}}$ distance in the triads. The shortening of the

X \cdots N binding distance in the NCX \cdots NCX \cdots CH₂ trimer is more than that in the F₃CX \cdots NCH \cdots HMgH trimer [64], in which a halogen bond and a dihydrogen bond coexist.

Interaction energies The interaction energy has been widely used in the study of the interplay between two kinds of non-covalent interactions. The interaction energies of the halogen bonds of the triads and dyads are listed in Table 2. The interaction energy, E_{int} , of the dyads was calculated by the formula $E_{\text{int}} = E(\text{AB}) - E(\text{A}) - E(\text{B})$. The E_{int} of the triads is calculated in a similar way. The interaction energies of NCX \cdots NCX dyads are

Table 2 Calculated BSSE-corrected interaction energies (in kcal mol^{–1}) of the studied triads and dyads

Triads (A–B–C)	$E_{\text{int}}(\text{AB})$	$E_{\text{int}}(\text{BC})$	$E_{\text{int}}(\text{ABC})$	E_{coop}
NCF–NCF–CH ₂	–1.18	–1.12	–2.49	–0.19
NCF–NCCI–CH ₂	–1.29	–3.88	–5.45	–0.28
NCF–NCBr–CH ₂	–1.31	–5.53	–7.19	–0.35
NCF–NCI–CH ₂	–1.37	–9.10	–10.98	–0.51
NCCI–NCF–CH ₂	–3.20	–1.12	–4.73	–0.41
NCCI–NCCI–CH ₂	–3.48	–3.87	–7.96	–0.61
NCCI–NCBr–CH ₂	–3.54	–5.50	–9.82	–0.78
NCCI–NCI–CH ₂	–3.66	–9.10	–13.99	–1.23
NCBr–NCF–CH ₂	–4.05	–1.11	–5.70	–0.54
NCBr–NCCI–CH ₂	–4.41	–3.86	–9.08	–0.81
NCBr–NCBr–CH ₂	–4.49	–5.48	–11.00	–1.03
NCBr–NCI–CH ₂	–4.62	–9.10	–15.42	–1.70
NCI–NCF–CH ₂	–5.31	–1.10	–7.14	–0.73
NCI–NCCI–CH ₂	–5.83	–3.83	–10.78	–1.12
NCI–NCBr–CH ₂	–5.94	–5.44	–12.83	–1.45
NCI–NCI–CH ₂	–6.13	–9.10	–17.78	–2.55

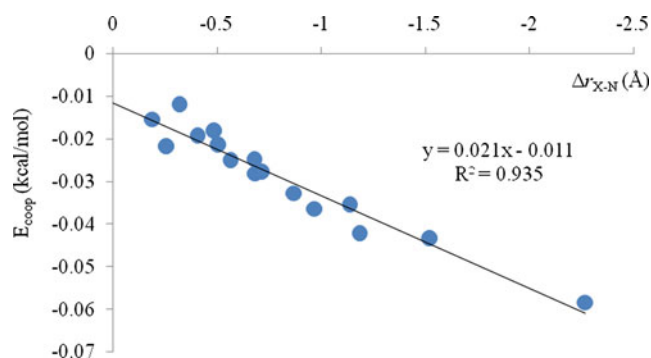


Fig. 2 Correlation between the magnitude of cooperative energy E_{coop} and $X \cdots N$ bond length change in $\text{NCX} \cdots \text{NCX} \cdots \text{CH}_2$ complexes

estimated to lie in the range from -1.18 to -6.13 kcal mol $^{-1}$ (Table 2), which compares favorably with the results of previous calculations [65]. As anticipated, heavier halogens form stronger $X \cdots N$ halogen bonds, in good agreement with the increased positive ESP cap on heavier X atoms. The calculated E_{int} of the $\text{NCX} \cdots \text{CH}_2$ dyads spans the range of -1.12 kcal mol $^{-1}$ in the $\text{NCF} \cdots \text{CH}_2$ up to -9.10 kcal mol $^{-1}$ in the $\text{NCI} \cdots \text{CH}_2$. As evident, the interaction strength increases in the order fluorine bond < chloride bond < bromide bond < iodide bond, which is consistent with the shorter intermolecular distance and as well as the greater amount of positive electrostatic potential on the halogen atom. The interaction energy is calculated to be -3.89 kcal mol $^{-1}$ in the $\text{NCCl} \cdots \text{CH}_2$ kcal mol $^{-1}$ dyad, which is close to that of $\text{NCC} \equiv \text{CCl} \cdots \text{CH}_2$ (-3.60 kcal mol $^{-1}$) at the same level of theory [48].

The cooperative energy (E_{coop}) is applied here to evaluate the interplay of the $X \cdots N$ and $X \cdots C_{\text{carbene}}$ halogen bonds in

their ternary systems. It is computed with formulas of $E_{\text{coop}} = E_{\text{int}}(\text{ABC}) - E_{\text{int}}(\text{AB}) - E_{\text{int}}(\text{BC})$, where $E_{\text{int}}(\text{ABC})$ is the total interaction of the triads and $E_{\text{int}}(\text{AB})$ and $E_{\text{int}}(\text{BC})$ are the interaction energies of the isolated dyads within their corresponding minima configurations. The results are also given in Table 2. The estimated values of E_{coop} are all negative with much larger E_{coop} in absolute value for the systems including iodine. As a consequence, the complexes in which strong halogen bond interactions are present exhibit strong cooperativity, while much weak cooperativity occurs in the complexes involving fluorine atom. For example, in the $\text{NCI} \cdots \text{NCI} \cdots \text{CH}_2$ trimer, the interaction energy of the $X \cdots N$ bond is increased by -1.80 kcal mol $^{-1}$, while the interaction energy of the $\text{NCF} \cdots \text{NCF} \cdots \text{CH}_2$ is increased by only -0.002 kcal mol $^{-1}$. The increased value of the $X \cdots C_{\text{carbene}}$ interaction energy varies in the order: $\text{F} < \text{Cl} < \text{Br} < \text{I}$. However, the increased percentage is more prominent for the interaction energy of the $X \cdots N$ halogen bond. Good linear correlations are found between the cooperative energy E_{coop} the $X \cdots N$ bond length change in $\text{NCX} \cdots \text{NCX} \cdots \text{CH}_2$ complexes (Fig. 2).

QTAIM analysis We applied the QTAIM to further analyze the characteristics of the $X \cdots N$ and $X \cdots C_{\text{carbene}}$ interactions in the $\text{NCX} \cdots \text{NCX} \cdots \text{CH}_2$ complexes. The electron densities (ρ_{BCP}) at the BCPs as well as their Laplacians ($\nabla^2 \rho_{\text{BCP}}$) were considered for complexes analyzed here since these topological parameters may characterize the type of interaction. Table 3 lists the values of ρ_{BCP} and the corresponding $\nabla^2 \rho_{\text{BCP}}$ values computed at the $X \cdots N$ and $X \cdots C_{\text{carbene}}$ critical

Table 3 QTAIM analysis results of the studied triads and dyads^a

Triads (A–B–C)	ρ_{BCP} (AB,T)	$\Delta\rho_{\text{BCP}}$ (AB,T)	ρ_{BCP} (BC,T)	$\Delta\rho_{\text{BCP}}$ (BC,T)	$\nabla^2\rho_{\text{BCP}}$ (AB,T)	$\Delta\nabla^2\rho_{\text{BCP}}$ (AB,T)	$\nabla^2\rho_{\text{BCP}}$ (BC,T)	$\Delta\nabla^2\rho_{\text{BCP}}$ (BC,T)
NCF–NCF–CH ₂	0.535	0.021	0.436	0.026	2.984	0.131	1.858	0.127
NCF–NCCl–CH ₂	0.561	0.032	1.226	0.034	3.131	0.193	4.547	0.096
NCF–NCBr–CH ₂	0.575	0.022	1.900	0.041	3.211	0.121	5.845	0.074
NCF–NCI–CH ₂	0.614	0.035	3.372	0.128	3.439	0.196	7.657	0.129
NCCl–NCF–CH ₂	1.077	0.051	0.467	0.057	5.363	0.227	2.007	0.276
NCCl–NCCl–CH ₂	1.152	0.071	1.270	0.077	5.677	0.307	4.673	0.222
NCCl–NCBr–CH ₂	1.190	0.084	1.968	0.109	5.840	0.353	5.978	0.207
NCCl–NCI–CH ₂	1.269	0.115	3.590	0.346	6.156	0.463	7.871	0.344
NCBr–NCF–CH ₂	1.407	0.069	0.480	0.070	6.275	0.267	2.072	0.341
NCBr–NCCl–CH ₂	1.523	0.098	1.298	0.105	6.698	0.360	4.754	0.303
NCBr–NCBr–CH ₂	1.581	0.120	2.011	0.152	6.903	0.431	6.065	0.294
NCBr–NCI–CH ₂	1.692	0.172	3.745	0.501	7.277	0.587	8.019	0.491
NCI–NCF–CH ₂	1.730	0.093	0.504	0.094	6.923	0.302	2.194	0.464
NCI–NCCl–CH ₂	1.921	0.150	1.339	0.147	7.518	0.463	4.870	0.419
NCI–NCBr–CH ₂	1.997	0.182	2.078	0.219	7.740	0.543	6.190	0.420
NCI–NCI–CH ₂	2.167	0.272	4.093	0.849	8.198	0.759	8.332	0.804

^a All ρ_{BCP} , $\nabla^2\rho_{\text{BCP}}$, $\Delta\rho_{\text{BCP}}$ and $\Delta\nabla^2\rho_{\text{BCP}}$ values in 10^2 au

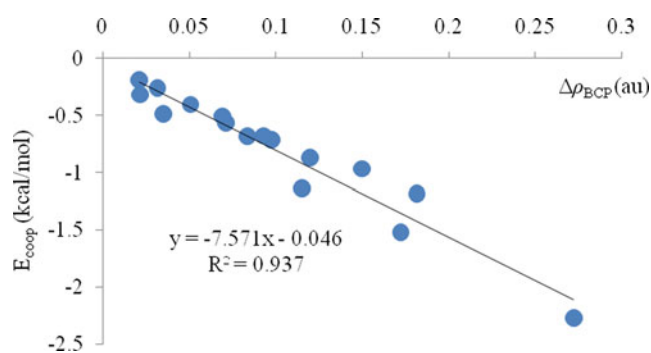


Fig. 3 Correlation between the magnitude of cooperative energy E_{coop} and electron density change at the $X \cdots N$ critical points in $NCX \cdots NCX \cdots CH_2$ complexes

points of the triad systems. In addition, we also give the variation of these values with respect to the values obtained for the binary systems. The calculated ρ_{BCP} values in $X \cdots N$ and $X \cdots C_{\text{carbene}}$ halogen bonds are predicted to be in the range 0.005–0.022 au and 0.004–0.0140 au, whereas the values of $\nabla^2 \rho_{\text{BCP}}$ are all positive, ranging from 0.030 to 0.082 and 0.019 to 0.083 au, respectively. These values are within the commonly accepted values for hydrogen bond interactions [66], thus indicating the closed-shell interactions in these systems. The results of Table 3 indicate that the ρ_{BCP} and $\nabla^2 \rho_{\text{BCP}}$ values at the $X \cdots N$ critical points in the triad are slightly greater than that in the corresponding dyad. This result confirms that the $X \cdots N$ interaction in the triad is reinforced with respect to the binary system. The same behavior is also evident for the ρ_{BCP} and $\nabla^2 \rho_{\text{BCP}}$ values at the $X \cdots C_{\text{carbene}}$ critical points in the triad. This reveals that the $X \cdots C_{\text{carbene}}$ interaction is also strengthened in the triad system. However,

comparison between $X \cdots N$ and $X \cdots C_{\text{carbene}}$ halogen bonds interactions indicates a more important electronic density redistribution in the latter one. The estimated amount of electron density change upon trimer formation ranges from 0.0002 to 0.0027 au for the $X \cdots N$ and 0.003 to 0.085 au for the $X \cdots C_{\text{carbene}}$ interactions. These results are in good agreement with the tendencies of shortening of intermolecular distances of these systems, as discussed above. In fact, a linear correlation between E_{coop} and $\Delta \rho_{\text{BCP}}$ at the $X \cdots N$ critical points is found in Fig. 3 ($R^2=0.937$).

Energy decomposition analysis To unveil the nature of the halogen bonds interactions and to determine the origins of cooperative effects in the $NCX \cdots NCX \cdots CH_2$ systems, the interaction energies were analyzed in terms of electrostatic, exchange-repulsion, polarization and dispersion energies (Eq. (2)). The results are given in Table 4. However it may be noted that there is no rigorous basis for defining such energy terms [67], since they are not physical observable quantities. The energy components are also not independent of each other, no matter what procedure is used. Even considering these limitations, however, it is possible to estimate the electrostatic and the dispersion portions of noncovalent interaction energies [33].

It is evident from Table 4 that for the $NCX \cdots NCX$ binary systems, the dominant attraction energy originates in the electrostatic term. This is consistent with the decomposition for other conventional halogen bonds, which are known to be electrostatic in nature [30–32]. The contribution of electrostatic energy in the $X \cdots N$ interaction increases in the order $F < Cl < Br < I$, which is consistent with the greater amount of positive electrostatic

Table 4 Calculated energy terms (in kcal mol⁻¹) of the studied triads and dyads

Triads (A–B–C)	$E_{\text{elst}}(\text{AB}:\text{BC})$	$E_{\text{exch-rep}}(\text{AB}:\text{BC})$	$E_{\text{pol}}(\text{AB}:\text{BC})$	$E_{\text{disp}}(\text{AB}:\text{BC})$	$E_{\text{elst}}(\text{ABC})$	$E_{\text{exch-rep}}(\text{ABC})$	$E_{\text{pol}}(\text{ABC})$	$E_{\text{disp}}(\text{ABC})$
NCF–NCF–CH ₂	–1.08:–1.39	0.80:1.10	–0.13:–0.20	–0.64:–0.51	–2.67	2.07	–0.43	–1.20
NCF–NCCI–CH ₂	–1.20:–7.04	0.85:6.07	–0.16:–1.73	–0.66:–1.05	–8.53	7.25	–2.11	–1.71
NCF–NCBr–CH ₂	–1.23:–12.18	0.84:12.30	–0.16:–2.84	–0.67:–1.82	–13.89	13.79	–8.22	–2.32
NCF–NCI–CH ₂	–1.35:–24.08	0.96:29.23	–0.19:–11.40	–0.69:–2.26	–26.63	32.07	–12.63	–3.03
NCCI–NCF–CH ₂	–3.94:–1.39	3.13:1.10	–0.90:–0.20	–1.29:–0.51	–5.79	4.71	–1.42	–1.86
NCCI–NCCI–CH ₂	–4.26:–7.04	3.30:6.07	–1.01:–1.73	–1.36:–1.05	–12.03	10.29	–3.40	–2.40
NCCI–NCBr–CH ₂	–4.38:–12.18	3.41:12.30	–1.05:–2.84	–1.39:–1.82	–17.73	17.38	–5.86	–3.07
NCCI–NCI–CH ₂	–4.64:–24.08	3.70:29.23	–1.13:–11.40	–1.42:–2.26	–32.07	38.39	–15.52	–3.85
NCBr–NCF–CH ₂	–5.45:–1.39	4.88:1.10	–1.51:–0.20	–1.70:–0.51	–7.45	6.65	–2.15	–2.31
NCBr–NCCI–CH ₂	–5.98:–7.04	5.31:6.07	–1.72:–1.73	–1.78:–1.05	–14.01	12.72	–4.37	–2.92
NCBr–NCBr–CH ₂	–6.54:–12.18	5.48:12.30	–1.80:–2.84	–1.86:–1.82	–19.93	20.17	–6.99	–3.62
NCBr–NCI–CH ₂	–9.07:–24.08	9.14:29.23	–3.48:–11.40	–2.31:–2.26	–35.57	43.25	–17.73	–4.44
NCI–NCF–CH ₂	–7.82:–1.39	7.65:1.10	–2.77:–0.20	–2.02:–0.51	–10.17	9.97	–3.72	–2.68
NCI–NCCI–CH ₂	–8.79:–7.04	8.78:6.07	–3.30:–1.73	–2.22:–1.05	–32.84	38.62	–10.31	–5.17
NCI–NCBr–CH ₂	–9.07:–12.18	9.14:12.30	–3.48:–2.84	–2.31:–1.82	–23.81	25.45	–9.57	–4.16
NCI–NCI–CH ₂	–9.74:–24.08	9.88:29.23	–3.82:–11.40	–2.36:–2.26	–42.12	53.20	–22.63	–5.08

potential on the halogen atom. On the other hand, for the $\text{NCX}\cdots\text{CH}_2$ dyads considered here, the electrostatic term (E_{elst}) is significantly larger (i.e., more negative) than the polarization (E_{pol}) and dispersion (E_{disp}) terms and the changes in the electrostatic interactions are mainly responsible for the enhancement of the halogen bond. It is also that halogens with larger, more positive σ -holes tend to exhibit weaker dispersion interactions, which is attributed to the lower local polarizabilities of the larger σ -holes [33].

As evident from Table 4, the attractive electrostatic and polarization components make the major contribution to the interaction energy of the triads. The former term can be interpreted mainly with the dipole–dipole interaction, while the latter one accounts for the mutual polarization effect between the monomers in the triads. Our results indicate that for the $\text{NCX}\cdots\text{NCX}\cdots\text{CH}_2$ systems, all E_{elst} , E_{pol} and E_{disp} terms have an increase in magnitude for both types of interactions, showing the additional stability of the ternary complexes relative to the corresponding binary complexes. However, the cooperative effect of the $\text{X}\cdots\text{C}_{\text{carbene}}$ is more evident than that of the $\text{X}\cdots\text{N}$ one. The increase of polarization energy can be attributed to the distortion of the electron clouds of electron donor by the electric field of the electron acceptor in the complex. This reveals that the polarization caused by the NCX unit on the $\text{NCX}\cdots\text{CH}_2$ molecule is of major importance in the enhancement of the $\text{X}\cdots\text{C}_{\text{carbene}}$ bond.

Conclusions

Ab initio calculations were performed to study the interplay between halogen \cdots nitrogen and halogen \cdots carbene interactions in $\text{NCX}\cdots\text{NCX}\cdots\text{CH}_2$ complexes, where X=F, Cl, Br and I. The following conclusions are found:

- (1) The halogen bond distances for the iodine bonded complexes are shorter than those from other lighter halogen atoms, which is consistent with the electrostatic potentials on the halogen atoms: 14 kcal mol^{-1} (NCF) < 41 kcal mol^{-1} (NCCI) < 48 kcal mol^{-1} (NCBr) < 56 kcal mol^{-1} (NCI).
- (2) Although both types of interactions are enhanced by each other in the triads, the shortening of the halogen bond distances is not equal. We noted, however, the shortening of the halogen bond distances in the triads is dependent on the strength of the other.
- (3) The complexes in which strong halogen bond interactions are present exhibit strong cooperativity, while much weaker cooperativity occurs in the complexes involving fluorine atom.
- (4) The ρ_{BCP} and $\nabla^2\rho_{\text{BCP}}$ values at the $\text{X}\cdots\text{N}$ as well as $\text{X}\cdots\text{C}_{\text{carbene}}$ critical points in the triad are slightly greater than that in the corresponding dyad. This result confirms

that the halogen bonds interaction in the triad is reinforced with respect to the binary system.

- (5) For the $\text{NCX}\cdots\text{NCX}\cdots\text{CH}_2$ systems, all E_{elst} , E_{pol} and E_{disp} terms have an increase in magnitude for both types of interactions, showing the additional stability of the ternary complexes relative to the corresponding binary ones. These are consistent with the σ -hole concept that the electrostatic contribution increases with the increase of positive electrostatic potential on the halogen atom.

References

1. Scheiner S (1997) Hydrogen bonding: A theoretical perspective. Oxford University Press, Oxford
2. Guardigli C, Liantonio R, Mele ML, Metrangolo P, Resnati G, Pilati T (2003) Design and synthesis of new tectons for halogen bonding-driven crystal engineering. *Supramol Chem* 15:177–188
3. Metrangolo P, Neukirch H, Pilati T, Resnati G (2005) Halogen bonding based recognition processes: A world parallel to hydrogen bonding. *Acc Chem Res* 38:386–395
4. Berka K, Laskowski R, Riley KE, Hobza P, Vondrášek J (2009) Representative amino acid side chain interactions in proteins. A comparison of highly accurate correlated ab initio quantum chemical and empirical potential procedures. *J Chem Theory Comput* 5:982–992
5. Kerdawy AE, Murray JS, Politzer P, Bleiziffer P, Heßelmann A, Görling A, Clark T (2013) Directional noncovalent interactions: Repulsion and dispersion. *J Chem Theory Comput* 9:2264–2275
6. Esrafil MD, Behzadi H, Hadipour NL (2008) Density functional theory study of $\text{N-H}\cdots\text{O}$, $\text{O-H}\cdots\text{O}$ and $\text{C-H}\cdots\text{O}$ hydrogen-bonding effects on the ^{14}N and ^2H nuclear quadrupole coupling tensors of N-acetyl-valine. *Biophys Chem* 133:11–18
7. Esrafil MD, Behzadi H, Beheshtian J, Hadipour NL (2008) Theoretical ^{14}N nuclear quadrupole resonance parameters for sulfa drugs: Sulfamerazine and sulfathiazole. *J Mol Graph Model* 27:326–331
8. Esrafil MD (2012) Characteristics and nature of the intermolecular interactions in boron-bonded complexes with carbene as electron donor: An ab initio, SAPT and QTAIM study. *J Mol Model* 18:2003–2011
9. Crabtree RH, Siegbahn PEM, Eisenstein O, Rheingold AL (1996) A new intermolecular interaction: Unconventional hydrogen bonds with element–hydride bonds as proton acceptor. *Acc Chem Res* 29:348–354
10. Alkorta I, Zborowski K, Elguero J, Solimannejad M (2006) Theoretical study of dihydrogen bonds between $(\text{XH})_2$, X=Li, Na, BeH, and MgH, and weak hydrogen bond donors (HCN, HNC, and HCCN). *J Phys Chem A* 110:10279–10286
11. Alkorta I, Elguero J, Solimannejad M, Grabowski SJ (2011) Dihydrogen bonding vs metal– σ interaction in complexes between H_2 and metal hydride. *J Phys Chem A* 115:201–210
12. Y. Feng, L. Liu, J. Wang, X. Li, Q. Guo, Blue-shifted lithium bonds. *Chem. Commun.* (2004) 88–89.
13. Li Y, Wu D (2006) Do single-electron lithium bonds exist? Prediction and characterization of the $\text{H}_3\text{C}\cdots\text{Li}-\text{Y}$ (Y=H, F, OH, CN, NC, and CCH) complexes. *J Chem Phys* 125:084317
14. Wang W, Zhang Y, Wang Y (2012) The $\pi\cdots\pi$ stacking interactions between homogeneous dimers of $\text{C}_6\text{F}_x\text{I}_{(6-x)}$ (x=0, 1, 2, 3, 4, and 5): A comparative study with the halogen bond. *J Phys Chem A* 116:12486–12491
15. Grabowski SJ, Bilewicz E (2006) Cooperativity halogen bonding effect—Ab initio calculations on $\text{H}_2\text{CO}\cdots(\text{CIF})_n$ complexes. *Chem Phys Lett* 427:51–55

16. Riley KE, Merz KM Jr (2007) Insights into the strength and origin of halogen bonding: The halobenzene-formaldehyde dimer. *J Phys Chem A* 111:1688–1694
17. Alkorta I, Blanco F, Elguero J (2009) A computational study of the cooperativity in clusters of interhalogen derivatives. *Struct Chem* 20: 63–71
18. Parker AJ, Stewart J, Donald KJ, Parish CA (2012) Halogen bonding in DNA base pairs. *J Am Chem Soc* 134:5165–5172
19. Brinck T, Murray JS, Politzer P (1992) Surface electrostatic potentials of halogenated methanes as indicators of directional intermolecular interactions. *Int J Quantum Chem Quantum Biol Symp* 19:57–64
20. Murray JS, Paulsen K, Politzer P (1994) Molecular surface electrostatic potentials in the analysis of non-hydrogen-bonding noncovalent interactions. *Proc Indiana Acad Sci* 106:267–275
21. Auffinger P, Hays FA, Westhof E, Shing PS (2004) Halogen bonds in biological molecules. *Proc Natl Acad Sci U S A* 101:16789–16794
22. Politzer P, Lane P, Concha MC, Ma YG, Murray JS (2007) An overview of halogen bonding. *J Mol Model* 13:305–311
23. Politzer P, Murray JS, Concha MC (2008) σ -hole bonding between like atoms; a fallacy of atomic charges. *J Mol Model* 14:659–665
24. Murray JS, Lane P, Clark T, Riley KE, Politzer P (2012) σ -Holes, π -holes and electrostatically-driven interactions. *J Mol Model* 18:541–548
25. Mohajeri A, Pakiari AH, Bagheri N (2009) Theoretical studies on the nature of bonding in σ -hole complexes. *Chem Phys Lett* 467:393–397
26. Wang ZX, Zheng BS, Yu XY, Yi PG (2008) Characteristics and nature of the intermolecular interactions between thiophene and XY (X, Y=F, Cl, Br): A theoretical study. *J Mol Struct (THEOCHEM)* 857:13–19
27. Esrafil MD, Ahmadi B (2012) A theoretical investigation on the nature of Cl \cdots N and Br \cdots N halogen bonds in F-Ar-X \cdots NCY complexes (X=Cl, Br and Y=H, F, Cl, Br, OH, NH₂, CH₃ and CN). *Comput Theor Chem* 997:77–82
28. Li Q, Dong X, Jing B, Li W, Cheng J, Gong B, Yua Z (2010) A new unconventional halogen bond C–X \cdots H–M between HCCX (X=Cl and Br) and HMH (M=Be and Mg): An ab initio study. *J Comput Chem* 31:1662–1669
29. Alkorta I, Blanco F, Solimannejad M, Elguero J (2008) Competition of hydrogen bonds and halogen bonds in complexes of hypohalous acids with nitrogenated bases. *J Phys Chem A* 112:10856–10863
30. Riley KE, Hobza P (2008) Investigations into the nature of halogen bonding including symmetry adapted perturbation theory analyses. *J Chem Theory Comput* 4:232–242
31. Esrafil MD (2013) A theoretical investigation of the characteristics of hydrogen/halogen bonding interactions in dibromo-nitroaniline. *J Mol Model* 19:1417–1427
32. Jabłoński M, Palusiak M (2012) Nature of a hydride–halogen bond. A SAPT-, QTAIM-, and NBO-based study. *J Phys Chem A* 116: 2322–2332
33. Riley KE, Murray JS, Fanfrlík J, Řezáč J, Solá RJ, Concha MC, Ramos FM, Politzer P (2013) Halogen bond tunability II: The varying roles of electrostatic and dispersion contributions to attraction in halogen bonds. *J Mol Model*. doi:10.1007/s00894-012-1428-x
34. Esrafil MD (2012) Investigation of H-bonding and halogen-bonding effects in dichloroacetic acid: DFT calculations of NQR parameters and QTAIM analysis. *J Mol Model* 18:5005–5016
35. Grabowski SJ (2012) QTAIM characteristics of halogen bond and related interactions. *J Phys Chem A* 116:1838–1845
36. Politzer P, Riley KE, Bulat FA, Murray JS (2012) Perspectives on halogen bonding and other σ -hole interactions: Lex parsimoniae (Occam's Razor). *Comput Theor Chem* 998:2–8
37. Metrangolo P, Murray JS, Pilati T, Politzer P, Resnati G (2011) The fluorine atom as a halogen bond donor, viz. a positive site. *Cryst Eng Comm* 13:6593–6596
38. Riley KE, Murray JS, Fanfrlík J, Řezáč J, Solá RJ, Concha MC, Ramos FM, Politzer P (2011) Halogen bond tunability I: The effects of aromatic fluorine substitution on the strengths of halogen-bonding interactions involving chlorine, bromine, and iodine. *J Mol Model* 17:3309–3318
39. Politzer P, Murray JS, Clark T (2013) Halogen bonding and other σ -hole interactions: A perspective. *Phys Chem Chem Phys* 15:11178–11189
40. Politzer P, Murray JS (2013) Halogen bonding: An interim discussion. *Chem Phys Chem* 14:278–294
41. Awwadi FF, Willett RD, Peterson KA, Twamley B (2006) The nature of halogen \cdots halogen synthons: Crystallographic and theoretical studies. *Chem Eur J* 12:8952–8960
42. Jiang Y, Alcaraz AA, Chen JM, Kobayashi H, Lu YJ, Snyder JP (2006) Diastereomers of dibromo-7-epi-10-deacetylcephalomannine: Crowded and cytotoxic taxanes exhibit halogen bonds. *J Med Chem* 49:1891–1899
43. Wang F, Ma N, Chen Q, Wang W, Wang L (2007) Halogen bonding as a new driving force for layer-by-layer assembly. *Langmuir* 23: 9540–9542
44. Li Q, Yuan H, Jing B, Liu Z, Li W, Cheng J, Gong B, Sun J (2010) Theoretical study of halogen–hydride halogen bonds in F₃CL \cdots HM (L=Cl, Br; M=Li, BeH, MgH) complexes. *Mol Phys* 108:611–617
45. Mohajeri A, Alipour M, Mousaee M (2011) Halogen–hydride interaction between Z–X (Z=CN, NC; X=F, Cl, Br) and H–Mg–Y (Y=H, F, Cl, Br, CH₃). *J Phys Chem A* 115:4457–4466
46. Li RY, Li ZR, Wu Y, Li Y, Chen W, Sun CC (2005) Study of π –halogen bonds in complexes C₂H_{4-n}F_n–ClF (n=0–2). *J Phys Chem A* 109:2608–2613
47. Wang YH, Zou JW, Lu YX, Lu QS, Xu HY (2007) Single-electron halogen bond: Ab initio study. *Int J Quantum Chem* 107:501–506
48. Esrafil MD, Mohammadirad N (2013) Insights into the strength and nature of carbene \cdots halogen bond interactions: A theoretical perspective. *J Mol Model* 19:2559–2566
49. Metrangolo P, Carcenac Y, Lahtinen M, Pilati T, Rissanen K, Vij A, Resnati G (2009) Nonporous organic solids capable of dynamically resolving mixtures of diiodoperfluoroalkanes. *Science* 323:1461–1464
50. Aakeröy CB, Fasulo M, Schultheiss N, Desper J, Moore C (2007) Structural competition between hydrogen bonds and halogen bonds. *J Am Chem Soc* 129:13772–13773
51. Esrafil MD, Solimannejad M (2013) Revealing substitution effects on the strength and nature of halogen–hydride interactions: A theoretical study. *J Mol Model* 19:3767–3777
52. Zhao Q, Feng D, Hao J (2011) The cooperativity between hydrogen and halogen bond in the XY \cdots HNC \cdots XY (X, Y=F, Cl, Br) complexes. *J Mol Model* 17:2817–2823
53. Li QZ, Sun L, Liu XF, Li WZ, Cheng J, Zeng YL (2012) Enhancement of iodine–hydride interaction by substitution and cooperative effects in NCX–NCI–HMY complexes. *Chem Phys Chem* 13(2012):3997–4002
54. Li Q, Lin Q, Li W, Cheng J, Gong B, Sun J (2008) Cooperativity between the halogen bond and the hydrogen bond in H3N \cdots XY \cdots HF complexes (X, Y=F, Cl, Br). *Chem Phys Chem* 9:2265–2269
55. Schmidt MW, Baldrige KK, Boatz JA, Elbert ST, Gordon MS, Jensen JH, Koseki S, Matsunaga N, Nguyen KA, Su SJ, Windus TL, Dupuis M, Montgomery JA (1993) General atomic and molecular electronic structure system. *J Comput Chem* 14:1347–1363
56. Dunning TH (1989) Gaussian basis sets for use in correlated molecular calculations. I. The atoms boron through neon and hydrogen. *J Chem Phys* 90:1007–1023
57. Peterson KA, Figgen D, Goll E, Stoll H, Dolg M (2003) Systematically convergent basis sets with relativistic pseudopotentials. II. Small-core pseudopotentials and correlation consistent basis sets for the post-d group 16–18 elements. *J Chem Phys* 119:11113–11123
58. Boys SF, Bernardi F (1970) The calculation of small molecular interactions by the differences of separate total energies. Some procedures with reduced errors. *Mol Phys* 19:553–566
59. Su P, Li H (2009) Energy decomposition analysis of covalent bonds and intermolecular interactions. *J Chem Phys* 131:014102

60. Bulat FA, Toro-Labbe A, Brinck T, Murray JS, Politzer P (2010) Quantitative analysis of molecular surfaces: areas, volumes, electrostatic potentials and average local ionization energies. *J Mol Model* 16:1679–1691
61. Bader RFW (1990) *Atoms in molecules—a quantum theory*. Oxford University Press, New York
62. Biegler-Konig F, Schonbohm J, Bayles D (2001) AIM 2000. *J Comput Chem* 22:545–559
63. Bondi A (1964) van der Waals volumes and radii. *J Phys Chem* 68:441–451
64. Solimannejad M, Malekani M, Alkorta I (2010) Cooperative and diminutive unusual weak bonding in $F_3CX \cdots HMgH \cdots Y$ and $F_3CX \cdots Y \cdots HMgH$ trimers ($X=Cl, Br$; $Y=HCN$, and HNC). *J Phys Chem A* 114:12106–12111
65. Esrafil MD, Hadipour NL (2011) Characteristics and nature of halogen bonds in linear clusters of NCX ($X=Cl$, and Br): an ab initio, NBO and QTAIM study. *Mol Phys* 109:2451–2460
66. Koch U, Popelier PLA (1995) Characterization of $C-H \cdots O$ hydrogen bonds on the basis of the charge density. *J Phys Chem* 99:9747–9754
67. Hobza P, Zahradnik R, Muller-Dethlefs K (2006) The world of non-covalent interactions. *Coll Czech Chem Commun* 71: 443–531