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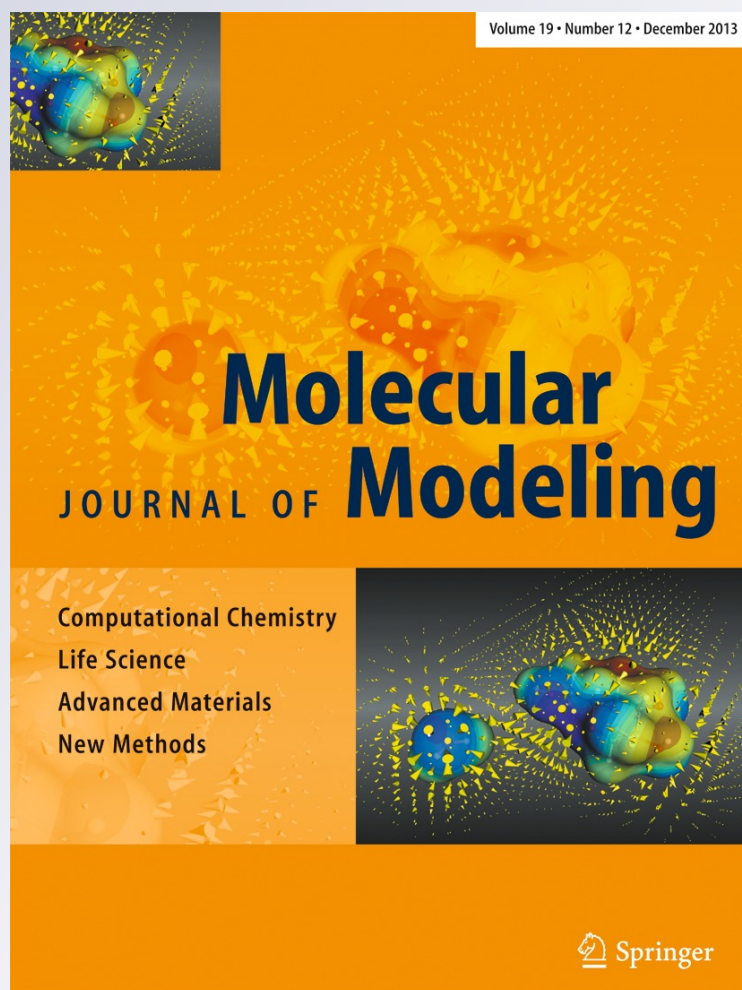
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Cooperativity between fluorine-centered halogen bonds: investigation of substituent effects

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Abstract This article analyzes the substitution effects on cooperativity between fluorine-centered halogen bonds in $\text{NCF} \cdots \text{NCF} \cdots \text{NCX}$ and $\text{CNF} \cdots \text{CNF} \cdots \text{CNX}$ complexes, where $\text{X} = \text{H}, \text{F}, \text{Cl}, \text{CN}, \text{OH},$ and NH_2 . These effects are investigated theoretically in terms of geometric and energetic features of the complexes, which are computed by *ab initio* methods. The topological analysis, based on the quantum theory of atoms in molecules (QTAIM), is used to characterize the interactions and analyze their enhancement with varying electron density at bond critical points. It is found that the complexes with electron-donating groups exhibit a strong cooperativity, while a much weaker cooperativity occurs in the $\text{NCF} \cdots \text{NCF} \cdots \text{NCCN}$ and $\text{CNF} \cdots \text{CNF} \cdots \text{CNCN}$ trimers. An excellent correlation is found between the cooperative energy in the ternary complexes and the calculated three-body interaction energies. The energy decomposition analysis (EDA) indicates that the electrostatic and dispersion effects play a main role in the cooperativity of fluorine-centered halogen bonding.

Keywords Cooperativity · Electrostatic potential · Halogen bond · QTAIM · σ -hole

Introduction

In recent years, halogen bond interaction has received considerable attention in many fields of chemistry and

biochemistry [1–4]. Halogen bonds interactions play a critical role in a wide variety of biochemical and chemical processes ranging from crystal engineering [5, 6] to biological recognition processes [7, 8]. The term “halogen-bonding” describes a $\text{R-X} \cdots \text{B}$ interaction, where a covalently bonded halogen atom X approaches a Lewis base B. This is typically characterized by unusually short $\text{X} \cdots \text{B}$ internuclear separations that are less than or equal to the sums of the van der Waals (vdW) radii of X and B, and a closely linear $\text{R-X} \cdots \text{B}$ bond angle. Halogen-bonding interaction shares some common characteristics in structure, physical properties, strength, and nature with the more commonly encountered hydrogen-bonding [9–12] and it was exciting to see that halogen-bonding prevailed over hydrogen-bonding in a competitive recognition process [13]. Several excellent reviews [14, 15] on halogen bonding are now available as well as a recent book [16].

The reason why a covalently bonded halogen atom can have attractive interaction with a negatively charged halogen bond acceptor B is a significantly anisotropic distribution of electrons in the halogen atom, with less electron densities in the R-X bond direction. According to Politzer’s viewpoint [17–20], 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. For a given R, the σ -hole potential on the halogen X in R-X becomes more positive in the order $\text{F} < \text{Cl} < \text{Br} < \text{I}$. As a result of a combination of extreme electronegativity and limited polarizability, the F atom is frequently deemed to not participate in halogen-bonding. The electron density distribution around F is nearly spherical rather than anisotropic and, consequently, F is most likely to behave as a halogen bond donor. However, it has recently been shown

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that the fluorine atom has the capability of forming halogen bond interactions and can also affect recognition and self assembly processes, but only under specific circumstances [21–24]. Thus, in FCN molecule, the electron-withdrawing CN group is sufficient to create a positive electrostatic potential on the fluorine atom [21]. 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 (QTAIM) [27–29], and symmetry-adapted perturbation theory (SAPT) [10, 30, 31] 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 highly dependent upon the identity of the halogen X, with the relative contribution of the electrostatic term increasing for larger X [27]. Recently, Riley et al. [32] 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.

The cooperativity is one of the most important characteristics of non-covalent interactions [33, 34]. Due to the similarity between halogen and hydrogen bonds, the halogen bond also exhibits cooperative effects with itself and other types of interactions [3, 33, 35–37]. More recently, the cooperative effects in the 4-Z-Py \cdots XCN \cdots XCN system (Z=H, F, OH, OCH₃, CH₃, NH₂, NO₂, and CN; Py=pyridine; and X=Cl and Br) was reported [38]. The results indicated that the cooperativity between the halogen bonds interactions strongly depends on the nature of the substituents (Z) as well as the type of halogen atom involved.

Careful studies in simple models are of interest in order to extend their conclusion to larger ones. To the best of our knowledge, neither a theoretical nor an experimental study has thus far been reported to examine the substituent effects in cooperativity between fluorine-centered halogen bonds interactions. Herein, we report our quantum chemical study on the cooperative effects in NCF \cdots NCF \cdots NCX and CNF \cdots CNF \cdots CNX, where X=H, F, Cl, CN, OH, and NH₂. For comparison, the respective dimers were also studied. These systems look like simple molecular models to investigate the F \cdots N(C) halogen bonds cooperativity in gas phase. To further analyze the origin of F \cdots N and F \cdots C bond interactions and to determine the origins of cooperative effects in the title complexes, we turn to quantum theory of atoms in molecules (QTAIM) [39] and energy decomposition analysis. This work could be very helpful in crystal engineering and molecular recognition, because fluorine-centered halogen bonds have been recently applied in the design and synthesis of novel functional materials and effective molecular receptors [21–24].

Computational details

All calculations were carried out using the GAMESS suite of programs [40]. Geometries were optimized at the MP2 level with the aug-cc-pVTZ basis set. Recent studies [41, 42] suggest that these methods are reliable for estimating the interaction energy of the halogen bonds. The harmonic vibrational frequencies calculations at the same level were carried out to confirm that the structures obtained corresponded to energy minima. The interaction energies were calculated at the MP2/aug-cc-pVTZ and CCSD(T)/aug-cc-pVTZ levels of theory with correction for the basis set superposition error (BSSE) by the Boys–Bernardi method [43]. The topological analysis of the electron charge density performed for all complexes was performed using QTAIM [39]. The QTAIM analysis was performed with the help of AIM 2000 software [44] using the wave functions generated at the MP2/aug-cc-pVTZ level. The interaction energy was decomposed with the So and Li scheme [45]:

$$E_{\text{int}} = E_{\text{elst}} + E_{\text{exch-rep}} + E_{\text{pol}} + E_{\text{disp}}, \quad (1)$$

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

Results and discussion

Geometries Figure 1 illustrates a sketch of the NCF \cdots NCF \cdots NCX and CNF \cdots CNF \cdots CNX complexes, where X=H, F, Cl, CN, OH and NH₂. 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_{AB} and r_{BC}) are marked explicitly in Fig. 1. Table 1 lists the optimized binding distance and the corresponding bond length change of the halogen bonds in the 12 triads and the respective dyads calculated at the MP2/aug-cc-pVTZ level. Some interesting points can be extracted from the geometrical results. The equilibrium distance r_{AB} in the binary (NCF)₂ and (CNF)₂ systems are calculated to be 2.984 and 3.009 Å, respectively. These are shorter than the sums of the vdW radii of the atoms involved [46], which implies that there is an attractive force between the two subunits. The binding distances r_{BC} in the binary NCF \cdots NCX and CNF \cdots CNX complexes are in the range of 2.937–3.000 Å and 2.972–3.035 Å, respectively. The presence of the electron-donating groups (OH and NH₂) in the NCX or CNX molecule causes a decrease of the binding distance, whereas the electron-withdrawing groups (F and CN) lead to a lengthening of the binding distance. In addition, for a given X substitution,

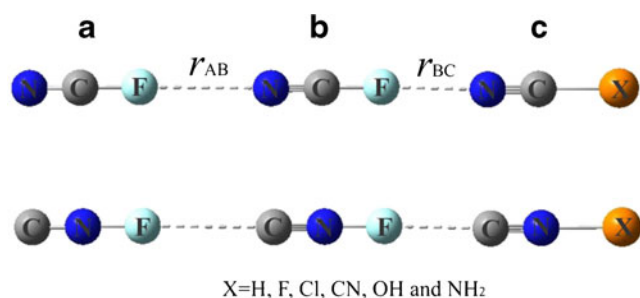


Fig. 1 Structure of NCF...NCF...NCX and CNF...CNF...CNX complexes

the r_{BC} distances in the NCF...NCX complex is slightly shorter compared to the complex CNF...CNX.

The equilibrium binding distances r_{AB} and r_{BC} in the trimer are always shorter than that in the respective dimer. The shortening of the r_{AB} distance varies from 0.031 Å in the NCF...NCF...NCCN trimer to 0.041 Å in the NCF...NCF...NCNH₂ trimer, while the shortening of the F...C distance is in a range of 0.004–0.018 Å. Evidently, the effect is larger in those complexes with shorter intermolecular distances than in those with the longest ones. The shortening of the r_{BC} binding distance in the CNF...CNF...CNX trimer is slightly less than corresponding interaction in the NCF...NCF...NCX trimer. It is worthy of note that for a given X substitution, the variation of the r_{AB} bond length is much more dramatic than that of the r_{BC} bond length. The shortening of the halogen bond distances is increased in the order: NH₂>OH>Cl>H>F>CN. We note that, however, the shortening of the binding distance in the title complexes is much less than that in the 4-Z-Py...XCN...XCN system (Z=H, F, OH, OCH₃, CH₃, NH₂, NO₂, and CN; Py=pyridine; and X=Cl and Br) [38] in which two X...N halogen bonds coexist. This indicates the interaction is enhanced in the former but the enhancement is not as large as for the latter.

Interaction energies The interaction energy in the binary and ternary complexes is obtained as the energy difference between the complex and sum of the isolated monomers. All MP2 and CCSD(T) evaluated interaction energies have been corrected for the BSSE using the counterpoise method (Table 2). From Table 2 results, it is seen that the MP2 interaction energies overestimate the attraction slightly in comparison with the more reliable CCSD(T) ones. The interaction energy is calculated to be $-1.12 \text{ kcal mol}^{-1}$ in the (NCF)₂ dimer, which is smaller than those of (NCCl)₂ and (NCBr)₂ at the same level of theory [36]. This is consistent with the shorter intermolecular distance and as well as the greater amount of positive electrostatic potential on the halogen atom. The calculated CCSD(T) interaction energies of NCF...NCX and CNF...CNX dyads are estimated to lie in the range from -0.74 to $-1.64 \text{ kcal mol}^{-1}$ and from -0.72 to $-1.54 \text{ kcal mol}^{-1}$, respectively, which compare favorably with the results of previous calculations [20]. The data in Table 2 reveals that the NCF...NCX and CNF...CNX interactions become stronger when the electron-donating ability of the X group increases. For example, the computed interaction energy of the complex NCF...NCNH₂ is larger in absolute value than NCF...NCH (-1.64 vs $-1.24 \text{ kcal mol}^{-1}$).

Table 2 also summarizes the computed value of cooperativity energy E_{coop} which is intended to provide an estimation of the “extra” energetic stabilization obtained in a multicomponent complex as a consequence of the coexistence of both interactions. 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. From the E_{coop} values listed in Table 2 several general conclusions can be extracted. The estimated values of E_{coop} are all negative which indicate a positive cooperativity between both of the interactions

Table 1 Calculated intermolecular bond distances (in Å) of the NCF...NCF...NCX and CNF...CNF...CNX ternary systems and their corresponding dimers. ΔR indicates the change of bond distances

| Complex (A...B...C) | R_{AB} | $R_{AB}(\text{T})$ | ΔR_{AB} | R_{BC} | $R_{BC}(\text{T})$ | ΔR_{BC} |
|--------------------------------|----------|--------------------|-----------------|----------|--------------------|-----------------|
| NCF...NCF...NCH | 2.984 | 2.948 | −0.036 | 2.953 | 2.966 | −0.018 |
| NCF...NCF...NCF | 2.984 | 2.949 | −0.035 | 2.984 | 2.946 | −0.007 |
| NCF...NCF...NCCl | 2.984 | 2.948 | −0.036 | 2.947 | 2.941 | −0.007 |
| NCF...NCF...NCCN | 2.984 | 2.954 | −0.031 | 3.000 | 2.988 | −0.012 |
| NCF...NCF...NCNH ₂ | 2.984 | 2.943 | −0.041 | 2.937 | 2.917 | −0.020 |
| NCF...NCF...NCOH | 2.984 | 2.945 | −0.040 | 2.944 | 2.925 | −0.019 |
| CNF...CNF...CNH | 3.009 | 2.995 | −0.014 | 3.001 | 2.993 | −0.007 |
| CNF...CNF...CNF | 3.009 | 2.998 | −0.011 | 3.009 | 2.995 | −0.014 |
| CNF...CNF...CNCl | 3.009 | 2.994 | −0.015 | 2.992 | 2.984 | −0.008 |
| CNF...CNF...CNCN | 3.009 | 3.005 | −0.004 | 3.035 | 3.032 | −0.003 |
| CNF...CNF...CNCNH ₂ | 3.009 | 2.992 | −0.018 | 2.972 | 2.955 | −0.017 |
| CNF...CNF...CNOH | 3.009 | 2.994 | −0.015 | 2.985 | 2.969 | −0.016 |

Table 2 Calculated interaction energies of trimers and related dimers, cooperative energy (E_{coop}), three-body energy ($E_{int}^{(3-body)}$) and deformation energy (df) for studied complexes

| Complex ($A \cdots B \cdots C$) | MP2 | | | | | | CCSD(T) | | | | | |
|---|--------------|--------------|---------------|------------|----------------------|------|--------------|--------------|---------------|------------|----------------------|------|
| | $E_{int,AB}$ | $E_{int,BC}$ | $E_{int,ABC}$ | E_{coop} | $E_{int}^{(3-body)}$ | df | $E_{int,AB}$ | $E_{int,BC}$ | $E_{int,ABC}$ | E_{coop} | $E_{int}^{(3-body)}$ | df |
| NCF \cdots NCF \cdots NCH | -1.18 | -1.29 | -2.69 | -0.23 | -0.20 | 0.03 | -1.12 | -1.24 | -2.58 | -0.22 | -0.19 | 0.02 |
| NCF \cdots NCF \cdots NCF | -1.18 | -1.18 | -2.55 | -0.20 | -0.18 | 0.01 | -1.12 | -1.12 | -2.43 | -0.19 | -0.16 | 0.01 |
| NCF \cdots NCF \cdots NCCl | -1.18 | -1.29 | -2.69 | -0.22 | -0.21 | 0.03 | -1.12 | -1.23 | -2.58 | -0.23 | -0.20 | 0.02 |
| NCF \cdots NCF \cdots NCCN | -1.18 | -0.81 | -2.08 | -0.10 | -0.09 | 0.01 | -1.12 | -0.74 | -1.98 | -0.12 | -0.10 | 0.01 |
| NCF \cdots NCF \cdots CNNH ₂ | -1.18 | -1.69 | -3.17 | -0.31 | -0.30 | 0.03 | -1.12 | -1.64 | -3.08 | -0.32 | -0.30 | 0.03 |
| NCF \cdots NCF \cdots NCOH | -1.18 | -1.51 | -2.96 | -0.27 | -0.26 | 0.02 | -1.12 | -1.46 | -2.84 | -0.26 | -0.23 | 0.02 |
| CNF \cdots CNF \cdots CNH | -1.11 | -1.39 | -2.68 | -0.18 | -0.10 | 0.02 | -1.01 | -1.28 | -2.44 | -0.15 | -0.09 | 0.02 |
| CNF \cdots CNF \cdots CNF | -1.11 | -1.11 | -2.36 | -0.14 | -0.07 | 0.01 | -1.01 | -1.01 | -2.16 | -0.14 | -0.08 | 0.01 |
| CNF \cdots CNF \cdots CNCl | -1.11 | -1.29 | -2.58 | -0.18 | -0.09 | 0.03 | -1.01 | -1.19 | -2.36 | -0.16 | -0.09 | 0.02 |
| CNF \cdots CNF \cdots CNCN | -1.11 | -0.70 | -1.86 | -0.05 | -0.04 | 0.01 | -1.01 | -0.72 | -1.8 | -0.07 | -0.03 | 0.01 |
| CNF \cdots CNF \cdots CNNH ₂ | -1.11 | -1.67 | -3.04 | -0.26 | -0.17 | 0.03 | -1.01 | -1.54 | -2.75 | -0.20 | -0.15 | 0.03 |
| CNF \cdots CNF \cdots CNOH | -1.11 | -1.48 | -2.81 | -0.22 | -0.13 | 0.02 | -1.01 | -1.35 | -2.54 | -0.18 | -0.13 | 0.02 |

^a All energies in kcal mol⁻¹

and is in agreement with shortening of the binding distances. It is evident that the complexes with electron-donating groups exhibit a strong cooperativity, while a much weaker cooperativity occurs in the NCF \cdots NCF \cdots NCCN and CNF \cdots CNF \cdots CNCN trimers. These are in good agreement with the tendencies of the shortening of binding distances of these systems. In Fig. 2, we represented the calculated values of E_{coop} against the corresponding Δr_{AB} values. An acceptable linear correlation is found for both interactions ($R^2=0.983$ and 0.946 for FCN and FNC comolplexes, respectively).

Many-body analysis To further understand the cooperativity between fluorine-centered halogen bonds in the NCF \cdots NCF \cdots NCF and CNF \cdots CNF \cdots CNF complexes, we performed an analysis of many-body decomposition of the interaction energy. The two- and three-body contributions to the total interaction energy were obtained using Xantheas scheme [47]. The calculated results are summarized in Table 2. The total energy equals to the sum of many-body terms and relaxation energy. It is found that for all the ternary complexes, the two-body and three-body interaction energies E_{AB} , E_{BC} , E_{AC} and $E^{(3-body)}$ are attractive, indicating a positive contribution to the

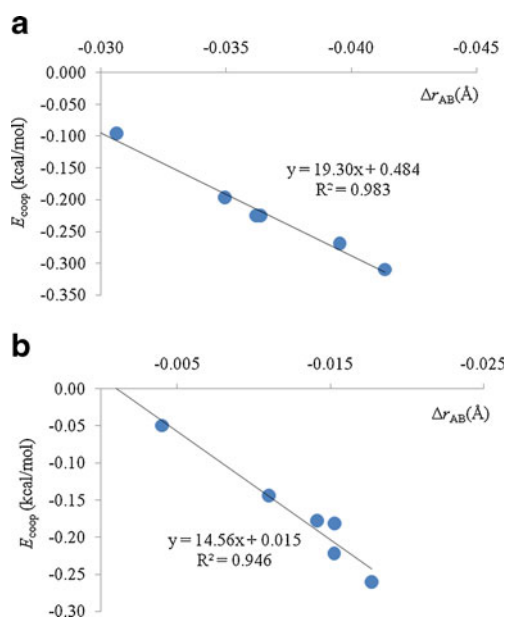


Fig. 2 Correlation between MP2 cooperative energy and intermolecular bond distance change in **a** NCF \cdots NCF \cdots NCX and **b** CNF \cdots CNF \cdots CNX

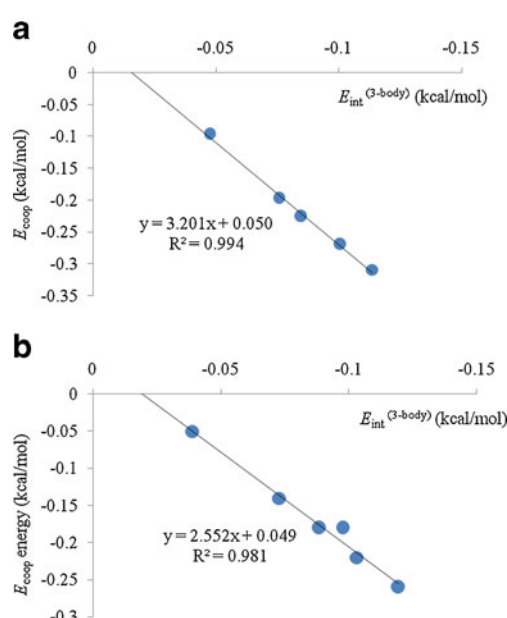


Fig. 3 Correlation between cooperative energy and three-body energy **a** NCF \cdots NCF \cdots NCX and **b** CNF \cdots CNF \cdots CNX

stabilization energy of complexes. For all triads E_{AC} is the smallest two-body interaction term which is consistent with the largest distance between them. In all complexes studied, two-body energy is largest and equals to about 95% of the total energy. The contribution of the three-body energy decreases with the electron-withdrawing ability of the substitution. An excellent correlation is found between the cooperative energy in the ternary complexes and the calculated three-body interaction energies with $R^2=0.994$ and 0.981 for the FCN and FNC complexes, respectively (Fig. 3).

The deformation energy (df) can be taken as a measure of the degree of strain that drives the distortion of the ternary system. As evident in Table 3, the deformation energy is positive, so it makes a destabilizing contribution to the total stabilization energy of the triads. The deformation energy is larger for complexes of NCF than complexes with CNF which is in line with order of interaction energies in these triads. In all cases studied, the estimated deformation energy corresponds to less than 1% of the total energy. It means that the geometry of molecules in the complexes have little change upon the complexation.

Electron density analysis To further analyze the cooperativity effects between fluorine-centered halogen bonds, we performed an analysis of atoms in molecules. Table 3 presents the electron densities (ρ_{BCP}) at the bond critical points as well as their Laplacians ($\nabla^2\rho_{BCP}$). It has been manifested in numerous studies that the ρ_{BCP} gives valuable information about the strength and origin of the halogen bond interactions [48]. Therefore, the variation in the ρ_{BCP} value at the BCP in the trimer with respect to the corresponding dimer can be used to analyze the mutual influence of the two interactions. From

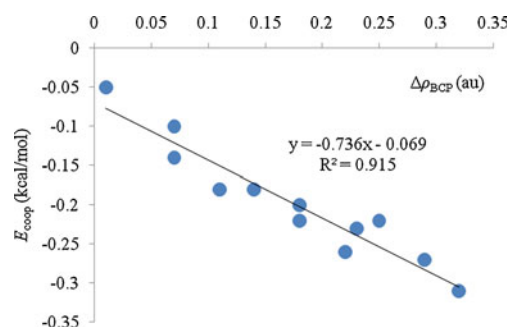


Fig. 4 Relationship between the calculated MP2 cooperative energy E_{coop} and $\Delta\rho_{BCP}$ values at A···B critical points

Table 3, it is seen that all electron densities at the $F\cdots N(C)$ critical points and their Laplacians of dyads are small and positive since the corresponding interactions belong to weak ones. The values of ρ_{BCP} at the $B\cdots C$ critical points are in the range of 0.0056–0.0067 au (for $F\cdots N$) and 0.0048–0.0057 au (for $F\cdots C$). These values fall in the generally accepted range of a hydrogen bond, which is in the range of 0.002–0.035 au [49]. In addition, their corresponding Laplacian $\nabla^2\rho_{BCP}$ values fall in the proposed range (0.024–0.139 au) of a hydrogen bond. However, the positive $\nabla^2\rho_{BCP}$ values indicate that the $F\cdots N$ and $F\cdots C$ interactions in all complexes are the closed-shell interactions. The results of Table 3 also indicate that the ρ_{BCP} and $\nabla^2\rho_{BCP}$ values at the $F\cdots N$ critical points in the triad are slightly greater than that in the corresponding dyad. This result confirms that the $F\cdots N$ interaction in the triad is reinforced with respect to the binary system. The same behavior is also evident for the ρ_{BCP} and $\nabla^2\rho_{BCP}$ values at the $F\cdots C$ critical points in the triad. The increase of the ρ_{BCP} value at the $F\cdots N$ and $F\cdots C$ critical points is the

Table 3 Calculated electron density (ρ_{BCP}), the corresponding Laplacian ($\nabla^2\rho_{BCP}$) values and their changes relative to binary systems at the $F\cdots N$ and $F\cdots C$ critical points

| Triads (A···B···C) | ρ_{BCP} (AB,T) | $\Delta\rho_{BCP}$ (AB,T) | ρ_{BCP} (BC,T) | $\Delta\rho_{BCP}$ (BC,T) | $\nabla^2\rho_{BCP}$ (AB,T) | $\Delta\nabla^2\rho_{BCP}$ (AB,T) | $\nabla^2\rho_{BCP}$ (BC,T) | $\Delta\nabla^2\rho_{BCP}$ (BC,T) |
|-------------------------------|------------------------|------------------------------|------------------------|------------------------------|--------------------------------|--------------------------------------|--------------------------------|--------------------------------------|
| NCF···NCF···NCH | 6.14 | 0.23 | 6.38 | 0.11 | 31.58 | 1.16 | 32.58 | 0.72 |
| NCF···NCF···NCF | 6.09 | 0.18 | 6.11 | 0.20 | 31.24 | 0.83 | 31.42 | 0.57 |
| NCF···NCF···NCCl | 6.16 | 0.25 | 6.40 | 0.13 | 31.69 | 1.28 | 32.93 | 0.96 |
| NCF···NCF···NCCN | 5.98 | 0.07 | 5.59 | 0.04 | 30.73 | 0.32 | 28.98 | 0.17 |
| NCF···NCF···NCNH ₂ | 6.23 | 0.32 | 6.95 | 0.27 | 32.13 | 1.72 | 35.69 | 1.76 |
| NCF···NCF···NCOH | 6.10 | 0.29 | 6.64 | 0.24 | 31.90 | 1.49 | 34.13 | 1.43 |
| CNF···CNF···CNH | 5.45 | 0.11 | 5.34 | 0.12 | 30.45 | 0.48 | 29.48 | 0.56 |
| CNF···CNF···CNF | 5.43 | 0.07 | 5.45 | 0.09 | 30.33 | 0.36 | 30.54 | 0.41 |
| CNF···CNF···CNCl | 5.44 | 0.14 | 5.60 | 0.15 | 30.44 | 0.47 | 31.34 | 0.69 |
| CNF···CNF···CNCN | 5.36 | 0.01 | 4.93 | 0.04 | 29.95 | 0.13 | 27.39 | 0.20 |
| CNF···CNF···CNNH ₂ | 5.52 | 0.22 | 6.02 | 0.24 | 30.90 | 0.93 | 33.68 | 1.49 |
| CNF···CNF···CNOH | 5.49 | 0.18 | 5.83 | 0.20 | 30.73 | 0.76 | 32.69 | 1.14 |

All ρ_{BCP} , $\nabla^2\rho_{BCP}$, $\Delta\rho_{BCP}$ and $\Delta\nabla^2\rho_{BCP}$ values are in 10^3 au

Table 4 Energy decomposition analysis for dimeric complexes

| Complexes | E_{elst} | $E_{\text{exch-rep}}$ | E_{pol} | E_{disp} | % E_{elst} | % E_{pol} | % E_{disp} |
|-----------------------|-------------------|-----------------------|------------------|-------------------|---------------------|--------------------|---------------------|
| NCF⋯NCH | −1.08 | 1.86 | −0.15 | −0.38 | 67 | 9 | 24 |
| NCF⋯NCF | −0.91 | 1.80 | −0.12 | −0.43 | 62 | 8 | 29 |
| NCF⋯NCCI | −1.02 | 1.90 | −0.14 | −0.45 | 63 | 9 | 28 |
| NCF⋯NCCN | −0.53 | 1.51 | −0.07 | −0.50 | 48 | 6 | 45 |
| NCF⋯NCNH ₂ | −1.43 | 2.34 | −0.23 | −0.41 | 69 | 11 | 20 |
| NCF⋯NCOH | −1.26 | 2.17 | −0.19 | −0.42 | 67 | 10 | 22 |
| CNF⋯CNH | −1.05 | 1.59 | −0.26 | −1.05 | 44 | 11 | 44 |
| CNF⋯CNF | −0.78 | 1.37 | −0.18 | −0.93 | 41 | 10 | 49 |
| CNF⋯CNCl | −1.03 | 1.60 | −0.23 | −1.07 | 44 | 10 | 46 |
| CNF⋯CNCN | −0.52 | 1.18 | −0.12 | −0.79 | 36 | 8 | 55 |
| CNF⋯CNNH ₂ | −1.23 | 1.81 | −0.33 | −1.21 | 44 | 12 | 44 |
| CNF⋯CNOH | −1.07 | 1.64 | −0.27 | −1.11 | 44 | 11 | 45 |

All energy terms in kcal mol^{−1}

largest in the NCF⋯NCF⋯NCNH₂ and CNF⋯CNF⋯CNNH₂ trimers, respectively, which shows a strong cooperativity as demonstrated above. In Fig. 4, we represented the calculated cooperative energies E_{coop} values against the electron density shift $\Delta\rho_{\text{BCP}}$ in these complexes. A linear relationship is found for each interaction. This reveals that the electron density at the F⋯N and F⋯C critical points can be regarded as a good description to quantify the degree of cooperative effects in these systems.

Energy decomposition analysis To investigate the role of different energy terms in cooperativity of F⋯N(C) interactions, an energy decomposition analysis has been performed (Eq. 1). This methodology divides the interaction energy into several components including electrostatic energy (E_{elst}), exchange-repulsion ($E_{\text{exch-rep}}$), polarization (E_{pol}) and dispersion (E_{disp}) terms. The results are collected in Tables 4 and 5. It is seen that, for all of the NCF⋯NCX dyads, the most important stabilizing component is electrostatic, which corresponds between 48 and 69% of all of the attraction energies. On the other hand, our

results indicate that the dispersion and electrostatic forces are the major source of the attraction in the CNF⋯CNX complexes. It should be noted that dipole–dipole interaction forms a part of the electrostatic energy component. The relatively larger dipole moment of NCF (2.32 D) compared to CNF (1.39 D) can be a logical reason for the different electrostatic energy contribution for these complexes. The second most important attraction term in the NCF⋯NCX dyads is the dispersion, which is closely followed by the polarization interaction. The E_{elst} is largest in the complexes with electron-donating groups and smallest in the complexes with electron-withdrawing substituents. It can be also seen that the exchange-repulsion energy ($E_{\text{exch-rep}}$) is larger than the absolute value of the electrostatic energy for all halogen-bonded complexes. What is notable, however, are the relative orders of the interaction energy terms are consistent with the results mentioned above.

One can see from Table 5 that the attractive electrostatic and dispersion components make the major contribution to the interaction energy of the ternary complexes. We found a

Table 5 Energy decomposition analysis for ternary complexes

| Complexes | E_{elst} | $E_{\text{exch-rep}}$ | E_{pol} | E_{disp} | % E_{elst} | % E_{pol} | % E_{disp} |
|---------------------------|-------------------|-----------------------|------------------|-------------------|---------------------|--------------------|---------------------|
| NCF⋯NCF⋯NCH | −2.20 | 1.75 | −0.36 | −0.82 | 65 | 11 | 24 |
| NCF⋯NCF⋯NCF | −2.00 | 1.73 | −0.32 | −0.90 | 62 | 10 | 28 |
| NCF⋯NCF⋯NCCI | −2.14 | 1.79 | −0.35 | −0.92 | 63 | 10 | 27 |
| NCF⋯NCF⋯NCCN | −1.52 | 1.55 | −0.24 | −0.97 | 56 | 9 | 36 |
| NCF⋯NCF⋯NCNH ₂ | −2.61 | 1.97 | −0.47 | −0.86 | 66 | 12 | 22 |
| NCF⋯NCF⋯NCOH | −2.40 | 1.88 | −0.41 | −0.87 | 65 | 11 | 24 |
| CNF⋯CNF⋯CNH | −1.94 | 3.09 | −0.49 | −2.10 | 43 | 11 | 46 |
| CNF⋯CNF⋯CNF | −1.67 | 2.91 | −0.40 | −1.96 | 41 | 10 | 49 |
| CNF⋯CNF⋯CNCl | −1.84 | 3.07 | −0.45 | −2.10 | 42 | 10 | 48 |
| CNF⋯CNF⋯CNCN | −1.34 | 2.67 | −0.32 | −1.79 | 39 | 9 | 52 |
| CNF⋯CNF⋯CNNH ₂ | −2.18 | 3.42 | −0.58 | −2.30 | 43 | 11 | 45 |
| CNF⋯CNF⋯CNOH | −1.99 | 3.22 | −0.51 | −2.18 | 43 | 11 | 47 |

All energy terms in kcal mol^{−1}

slightly larger substitution effect on the calculated energy terms of the $\text{NCF}\cdots\text{NCF}\cdots\text{NCX}$ than those of the $\text{CNF}\cdots\text{CNF}\cdots\text{CNX}$. Our results indicate that for the ternary complexes, 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 systems. On the other hand, the substituents do not largely change the dispersion and polarization contributions. Hence, it can be concluded that the electrostatic interactions are essentially responsible for the substituent effects on the cooperativity between fluorine-centered halogen bonds.

Conclusions

Ab initio calculations at the MP2 level of theory with the aug-cc-pVTZ basis set have been carried out to study the substituent effects on cooperativity between fluorine-centered halogen bonds in $\text{NCF}\cdots\text{NCF}\cdots\text{NCX}$ and $\text{CNF}\cdots\text{CNF}\cdots\text{CNX}$ complexes, where $\text{X}=\text{H}$, F , Cl , CN , OH and NH_2 . The equilibrium binding distances r_{AB} and r_{BC} in the ternary complexes are always shorter than that in the respective dimers. The shortening of the r_{AB} distance varies from 0.031 Å in the $\text{NCF}\cdots\text{NCF}\cdots\text{NCCN}$ trimer to 0.041 Å in the $\text{NCF}\cdots\text{NCF}\cdots\text{NCCNH}_2$ trimer, while the shortening of the $\text{F}\cdots\text{C}$ distance is in a range of 0.004–0.018 Å. The cooperative effect is stronger in those complexes with electron-donating substitution than in those with the electron-withdrawing ones. The estimated values of cooperative energy E_{coop} are all negative which indicates a positive cooperativity between both of the interactions and is in agreement with shortening of the binding distances. It is evident that the complexes with electron-donating groups exhibit a strong cooperativity, while a much weaker cooperativity occurs in the $\text{NCF}\cdots\text{NCF}\cdots\text{NCCN}$ and $\text{CNF}\cdots\text{CNF}\cdots\text{CNCN}$ trimers. These are in good agreement with the tendencies of the shortening of binding distances of these systems. According to the many-body analysis, two-body energy is largest and equals to about 95% of the total energy of the title complexes. The contribution of the two-body energy decreases with the electron-withdrawing ability of the substitution. The electron density analysis indicates that the ρ_{BCP} and $\nabla^2\rho_{\text{BCP}}$ values at the BCPs in the triads are slightly greater than that in the corresponding dyads. This result confirms that the $\text{F}\cdots\text{N}$ and $\text{F}\cdots\text{C}$ interactions in the triad is reinforced with respect to the binary system. The change in the interaction energy components indicates that the cooperative effects in the $\text{NCF}\cdots\text{NCF}\cdots\text{NCX}$ complexes are more significant than $\text{CNF}\cdots\text{CNF}\cdots\text{CNX}$ ones. Hopefully, the present findings are expected to be helpful for understanding the mutual influence and cooperativity of the

fluorine-centered halogen bonds interactions in molecular recognition, crystal engineering and biological systems.

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