

A theoretical investigation into the cooperativity effect between the H \cdots O and H \cdots F $^-$ interactions and electrostatic potential upon 1:2 (F $^-$:N-(Hydroxymethyl)acetamide) ternary-system formation

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Received: 28 June 2013 / Accepted: 11 September 2013 / Published online: 11 October 2013
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Abstract The cooperativity effects between the O/N–H \cdots F $^-$ anionic hydrogen-bonding and O/N–H \cdots O hydrogen-bonding interactions and electrostatic potentials in the 1:2 (F $^-$:N-(Hydroxymethyl)acetamide (signed as “ha $^-$ ”)) ternary systems are investigated at the B3LYP/6-311++G** and MP2/6-311++G** levels. A comparison of the cooperativity effect in the “F \cdots ha \cdots ha $^-$ ” and “FH \cdots ha \cdots ha $^-$ ” systems is also carried out. The result shows that the increase of the H \cdots O interaction energy in the O–H \cdots O–H, N–H \cdots O–H or N–H \cdots O=C link is more notable than that in the O–H \cdots O=C contact upon ternary-system formation. The cooperativity effect is found in the complex formed by the O/N–H \cdots F $^-$ and O/N–H \cdots O interactions, while the anti-cooperativity effect is present in the system with only the O/N–H \cdots F $^-$ H-bond or the “FH \cdots ha \cdots ha $^-$ ” complex by the N \cdots H–F contact. Atoms in molecules (AIM) analysis and shift of electron density confirm the existence of cooperativity. The most negative surface electrostatic potential ($V_{S,min}$) correlates well with the interaction energy $E'_{int.(ha\cdots F^-)}$ and synergetic energy

E_{syn} , respectively. The relationship between the change of $V_{S,min}$ (i.e., $\Delta V_{S,min}$) and E_{syn} is also found.

Keywords Anionic hydrogen bond · Cooperativity effect · MP2 · Surface electrostatic potential

Introduction

When the noncovalent interactions operate simultaneously and mutually enhance each others' strength, they are termed as acting cooperatively [1]. Cooperativity effect between the noncovalent interactions is currently a topic of wide ranging interest due to their extremely important role in chemical reaction, molecular recognition and regulation of biochemical process [2–6]. Mignon et al. stated that the π – π interaction had a significant influence on the hydrogen bonding capacity of stacked DNA/RNA bases [3]. Vijay's group studied the cooperativity effects between π – π and hydrogen-bonding interactions [7]. Deyà's group also reported experimental [8] and theoretical [9, 10] evidences of the cooperativity effects involving hydrogen bonds.

In general, the stronger the noncovalent interaction, the more notable the cooperativity effect is. Due to the favorable binding energies of charged complexes since there are electrostatic effects, the cooperativity effects in the anionic systems might be notable [6], and thus might remarkably influence their physical and chemical properties [8, 11]. Recently there have been many works devoted to the cooperativity effects involving anion– π interactions in the anionic complexes [12, 13]. Experimental findings observed in crystal structures supported the presence of cooperativity effect in anion– π – π complex [14]. Zaccheddu et al. explored the cooperativity effect between the anion– π and π – π interactions

Electronic supplementary material The online version of this article (doi:10.1007/s00894-013-2011-9) contains supplementary material, which is available to authorized users.

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[15]. Quiñero, Frontera and Deyà et al. reported the strong cooperativity effect between anion– π and hydrogen-bonding [16–18] or halogen-bonding interactions [19]. In 2010, a review on the cooperativity effect in multiple unusual weak bonds was published, in which several kinds of cooperativity effects involving anion-molecule interactions were mentioned [20]. In 2012, the cooperativity effect was found when anion– π and Ar/π Van der Waals interactions coexisted [21].

The $\text{H}\cdots\text{X}^-$ ($\text{X}=\text{F}, \text{Cl}, \text{Br}$, etc.) anionic hydrogen bond is one kind of the typical and strong interactions [22–24]. There are a great number of the $\text{H}\cdots\text{X}^-$ anionic hydrogen-bonding interactions in biological systems [25–28]. Properly characterizing the cooperativity effect involving the $\text{H}\cdots\text{X}^-$ anionic hydrogen-bonding interaction is crucial to understanding some biological processes [29]. However, to our knowledge, no theoretical investigation into the cooperativity effect involving the $\text{H}\cdots\text{X}^-$ anionic hydrogen-bonding interaction has been presented.

In this paper, we present a theoretical study on the cooperativity effect involving the $\text{H}\cdots\text{F}^-$ anionic hydrogen-bonding interaction in the ternary complex formed by the initial dimer of N-(Hydroxymethyl)acetamide, model molecule of ceramide, followed by addition of F^- . Ceramide is one kind of the important biological molecules [30, 31]. The polar head group of ceramide, with its amide linkage and two hydroxyl groups located in close proximity, constitutes a tridentate hydrogen-bonding donor/acceptor center and is capable of generating an effective network of directed hydrogen bonding interactions. Thus, it can self-assemble in the mitochondrial outer membrane, forming large channels capable of translocating anions [32]. In this biological process of translocating anions, the anionic hydrogen-bonding interaction might form, and the cooperativity effect involving the anionic hydrogen bond might be found. N-(Hydroxymethyl)acetamide ($\text{H}_3\text{C}-\text{CO}-\text{NH}-\text{CH}_2-\text{OH}$) consists of the $-\text{C}=\text{O}$, $-\text{NH}-$, $-\text{OH}$, $-\text{CH}_2-$ and $-\text{CH}_3$ groups. In the N-(Hydroxymethyl)acetamide dimer, the conventional $\text{O}-\text{H}\cdots\text{O}$, $\text{N}-\text{H}\cdots\text{O}$ and $\text{C}-\text{H}\cdots\text{O}$ hydrogen bonds might be found in the $\text{O}-\text{H}\cdots\text{O}-\text{H}$, $\text{O}-\text{H}\cdots\text{O}=\text{C}$, $\text{N}-\text{H}\cdots\text{O}-\text{H}$, $\text{N}-\text{H}\cdots\text{O}=\text{C}$, $\text{C}-\text{H}\cdots\text{O}-\text{H}$ and $\text{C}-\text{H}\cdots\text{O}=\text{C}$ contacts, respectively. In the 1:2 (F^- :N-(Hydroxymethyl)acetamide) ternary-system, the anionic hydrogen-bonding ($\text{O}-\text{H}\cdots\text{F}^-$, $\text{N}-\text{H}\cdots\text{F}^-$ and $\text{C}-\text{H}\cdots\text{F}^-$) and the conventional hydrogen-bonding interactions mentioned above might coexist. Thus, the cooperativity effect between anionic H-bonding and conventional H-bonding interactions might arise in the model system. Therefore, the ternary-complex of N-(Hydroxymethyl)acetamide with F^- can serve as a model system to investigate the cooperativity effect in the ceramide network with anion. This investigation reveals the nature of the cooperativity effect involving the anionic hydrogen bond in the ceramide system with F^- , and it will be very useful to understand the biological processes involving the anionic hydrogen-bonding interaction.

The surface electrostatic potential (ESP) has been an effective tool for the investigation into intermolecular interactions [33]. In 1995, Murray et al. found that the local maxima of surface potential ($V_{S,\text{min}}$) around hydrogen and the most negative surface potential ($V_{S,\text{min}}$) of basic site correlated well with empirical measures of hydrogen-bond-donating and -accepting tendencies, respectively [34]. In 2010, Mohammad et al. analyzed the electronic properties of $\text{F}_3\text{CX}\cdots\text{HMgH}\cdots\text{Y}$ and $\text{F}_3\text{CX}\cdots\text{Y}\cdots\text{HMgH}$ triads ($\text{X}=\text{Cl}, \text{Br}$; $\text{Y}=\text{HCN}$ and HNC) using the molecular surface electrostatic potential [35]. In 2012, Politzer et al. published one overview, in which some noncovalent interactions were discussed using surface potentials [36]. Recently, surface potential has been used to explain the cooperativity effect in hydrogen bonded clusters by Alkorta et al. [37]. In this work, the cooperativity effect is discussed using the molecular surface electrostatic potential in the ternary system.

Methodology

All calculations were performed with Gaussian 03 programs [38]. The monomer and complex were fully optimized using the DFT-B3LYP method with the 6-311++G** basis set. The structures corresponding to the minimum energy points at the molecular energy hypersurface ($\text{NImag}=0$) were obtained. Single point energy calculations were carried out at the B3LYP/6-311++G** and MP2(full)/6-311++G** levels. The shifts of the electron density [39] that accompanies the formation of complex were analyzed at MP2(full)/6-311++G** level, and the topological charge density was displayed by the AIM method [40] using AIMPAC program [41] at the same level.

For the binary system, the interaction energy (E_{int}) was calculated by evaluating the difference between the total energies of complex and individual monomers (N-(Hydroxymethyl)acetamide (signed as “ha”) and F^-) as given in Eqs. (1) or (2)

$$E_{\text{int.}(ha\cdots F^-)} = E_{ha\cdots F^-} - E_{ha} - E_{F^-} \quad (1)$$

$$E_{\text{int.}(ha\cdots ha)} = E_{ha\cdots ha} - E_{ha} - E_{ha}, \quad (2)$$

where $E_{ha\cdots F^-}$ and $E_{ha\cdots ha}$ are the total energies of complex, and E_{ha} and E_{F^-} are the total energies of monomer. $E_{\text{int.}(ha\cdots F^-)}$ and $E_{\text{int.}(ha\cdots ha)}$ were corrected with the basis set superposition error (BSSE) [42, 43].

In the ternary system, $E'_{\text{int.}(ha\cdots F^-)}$ and $E'_{\text{int.}(ha\cdots ha)}$ represent the interaction energy between both the moieties which are directly interacting with. They were calculated using Eqs. (3) and (4), respectively.

$$E'_{\text{int.}(ha\cdots F^-)} = E_{ha\cdots ha\cdots F^-} - E_{ha\cdots ha} - E_{F^-} \quad (3)$$

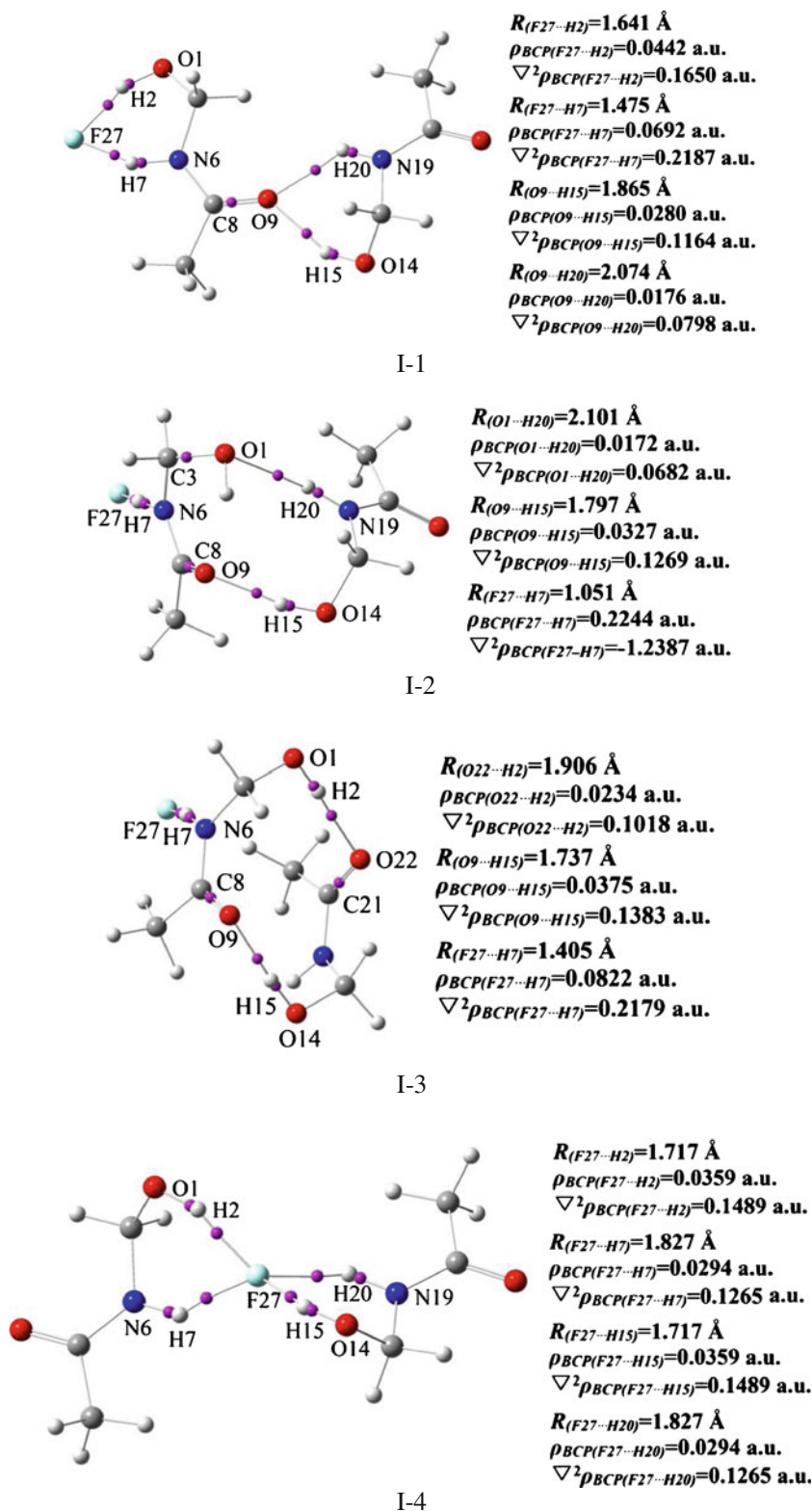


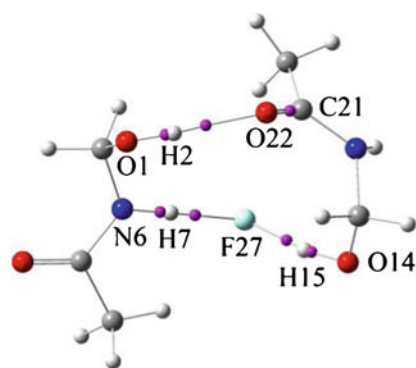
Fig. 1 The optimized geometries and AIM results of 17 ternary-system conformations at the B3LYP/6-311++G** level

$$E'_{int.(ha \cdots ha)} = E_{ha \cdots ha \cdots F} - E_{ha \cdots F} - E_{ha}, \quad (4)$$

where $E_{ha \cdots ha \cdots F}$, $E_{ha \cdots ha}$, $E_{ha \cdots F}$, E_{F} and E_{ha} are the total energies of the ternary, binary and monomeric systems,

respectively. $E'_{int.(ha \cdots F)}$ and $E'_{int.(ha \cdots ha)}$ were corrected with BSSE.

$E''_{int.(ha \cdots F)}$ and $E''_{int.(ha \cdots ha)}$ are defined as the through-space interaction energy between both the moieties with which



$$R_{(F27 \cdots H15)} = 1.485 \text{ \AA}$$

$$\rho_{BCP(F27 \cdots H15)} = 0.0634 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(F27 \cdots H15)} = 0.2198 \text{ a.u.}$$

$$R_{(F27 \cdots H7)} = 1.629 \text{ \AA}$$

$$\rho_{BCP(F27 \cdots H7)} = 0.0445 \text{ a.u.}$$

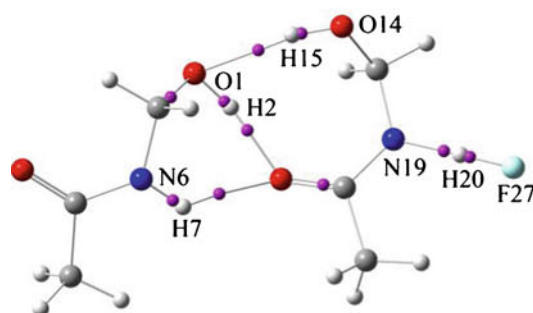
$$\nabla^2 \rho_{BCP(F27 \cdots H7)} = 0.1752 \text{ a.u.}$$

$$R_{(O22 \cdots H2)} = 1.934 \text{ \AA}$$

$$\rho_{BCP(O22 \cdots H2)} = 0.0211 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(O22 \cdots H2)} = 0.0960 \text{ a.u.}$$

II-1



$$R_{(O1 \cdots H15)} = 2.083 \text{ \AA}$$

$$\rho_{BCP(O1 \cdots H15)} = 0.0173 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(O1 \cdots H15)} = 0.0707 \text{ a.u.}$$

$$R_{(O22 \cdots H2)} = 1.684 \text{ \AA}$$

$$\rho_{BCP(O22 \cdots H2)} = 0.0439 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(O22 \cdots H2)} = 0.1584 \text{ a.u.}$$

$$R_{(O22 \cdots H7)} = 2.064 \text{ \AA}$$

$$\rho_{BCP(O22 \cdots H7)} = 0.0192 \text{ a.u.}$$

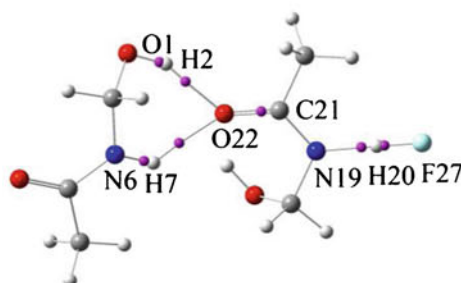
$$\nabla^2 \rho_{BCP(O22 \cdots H7)} = 0.0821 \text{ a.u.}$$

$$R_{(F27 \cdots H20)} = 1.076 \text{ \AA}$$

$$\rho_{BCP(F27 \cdots H20)} = 0.2071 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(F27 \cdots H20)} = -1.0018 \text{ a.u.}$$

II-2



$$R_{(F27 \cdots H20)} = 1.050 \text{ \AA}$$

$$\rho_{BCP(F27 \cdots H20)} = 0.2246 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(F27 \cdots H20)} = -1.2424 \text{ a.u.}$$

$$R_{(O22 \cdots H2)} = 1.829 \text{ \AA}$$

$$\rho_{BCP(O22 \cdots H2)} = 0.0309 \text{ a.u.}$$

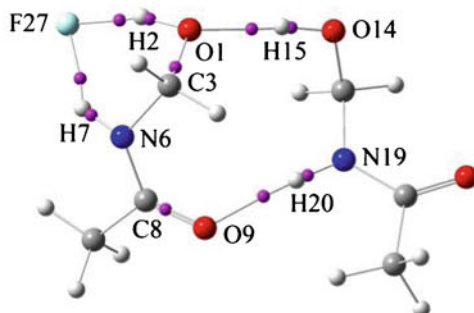
$$\nabla^2 \rho_{BCP(O22 \cdots H2)} = 0.1237 \text{ a.u.}$$

$$R_{(O22 \cdots H7)} = 2.073 \text{ \AA}$$

$$\rho_{BCP(O22 \cdots H7)} = 0.0183 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(O22 \cdots H7)} = 0.0793 \text{ a.u.}$$

II-3



$$R_{(O1 \cdots H15)} = 1.775 \text{ \AA}$$

$$\rho_{BCP(O1 \cdots H15)} = 0.0337 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(O1 \cdots H15)} = 0.1359 \text{ a.u.}$$

$$R_{(O9 \cdots H20)} = 1.976 \text{ \AA}$$

$$\rho_{BCP(O9 \cdots H20)} = 0.0213 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(O9 \cdots H20)} = 0.0889 \text{ a.u.}$$

$$R_{(F27 \cdots H2)} = 1.461 \text{ \AA}$$

$$\rho_{BCP(F27 \cdots H2)} = 0.0697 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(F27 \cdots H2)} = 0.2143 \text{ a.u.}$$

$$R_{(F27 \cdots H7)} = 1.713 \text{ \AA}$$

$$\rho_{BCP(F27 \cdots H7)} = 0.0394 \text{ a.u.}$$

$$\nabla^2 \rho_{BCP(F27 \cdots H7)} = 0.1578 \text{ a.u.}$$

II-4

Fig. 1 (continued)

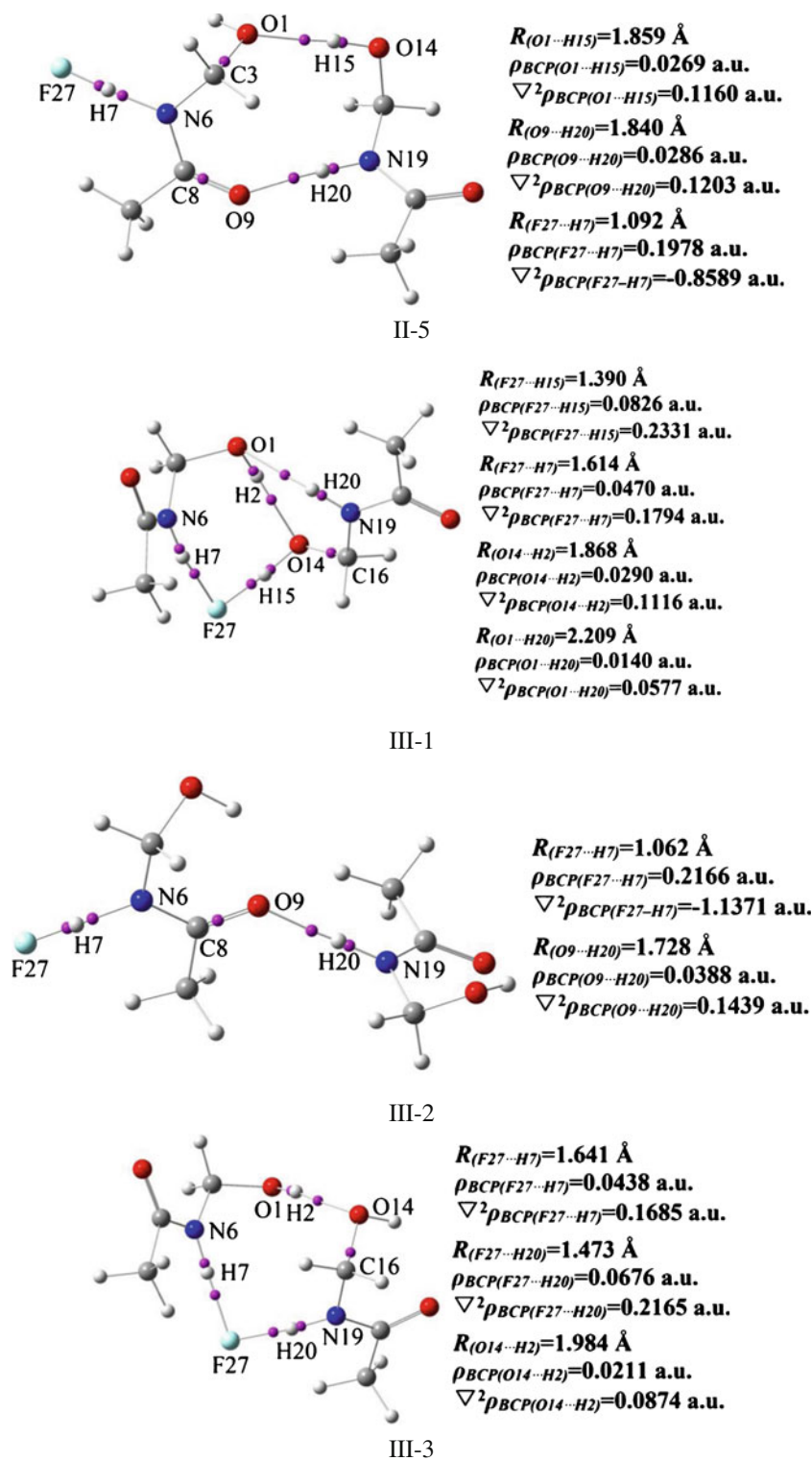


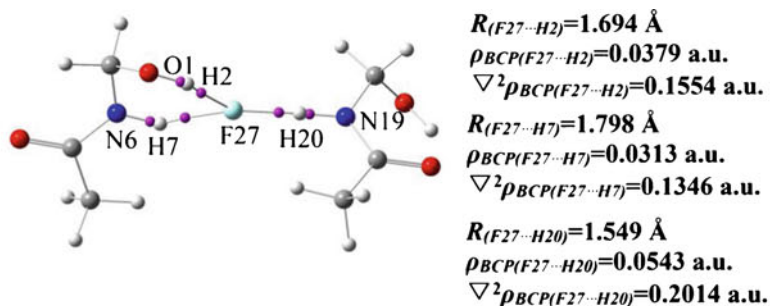
Fig. 1 (continued)

they are not directly interacting. They were calculated at the trimer geometry by employing Eqs. (5) and (6), respectively,

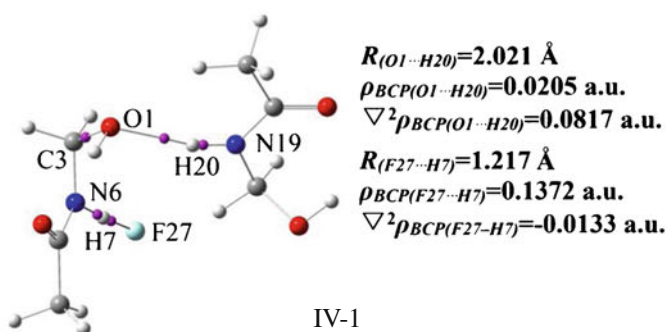
$$E''_{int.(ha \cdots F-)} = E'_{ha \cdots F-} - E_{ha} - E_{F-} \quad (5)$$

$$E''_{int.(ha \cdots ha)} = E'_{ha \cdots ha} - E_{ha} - E_{ha}, \quad (6)$$

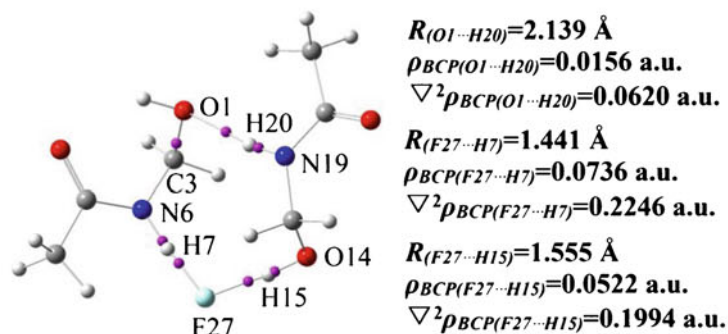
where $E'_{ha \cdots F-}$ and $E'_{ha \cdots ha}$ represent the total energies of the binary framework (not optimized) at the optimized trimer geometry.



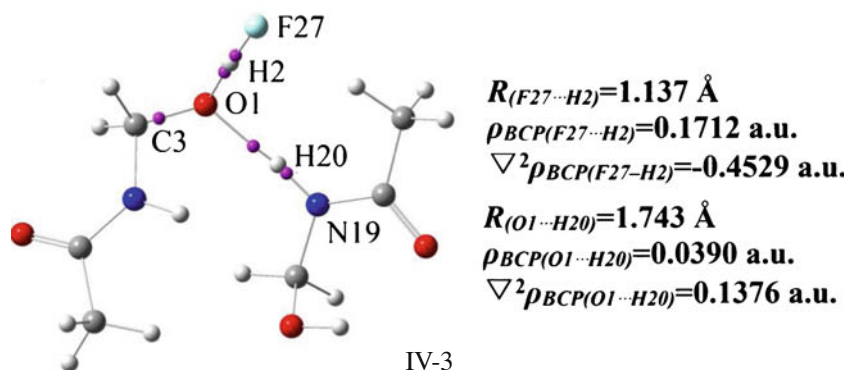
III-4



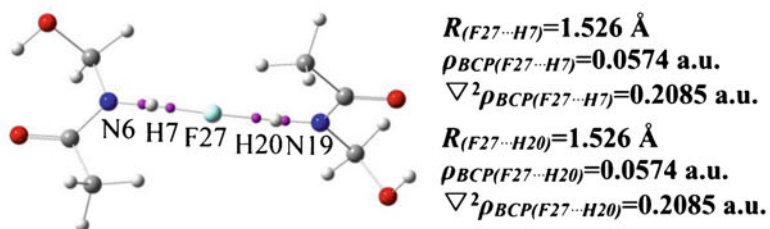
IV-1



IV-2



IV-3



IV-4

Fig. 1 (continued)

The synergetic energy ($E_{syn.}$) in the ternary complex was calculated using Eq. (7).

$$E_{syn.} = E_{int.(ha\cdots ha\cdots F^-)} - nE_{int.(ha\cdots F^-)} - mE_{int.(ha\cdots ha)} \quad (7)$$

$$(n = 1, 2; n + m = 2)$$

$E_{int.(ha\cdots F^-)}$ and $E_{int.(ha\cdots ha)}$ are the two-body terms. They were calculated using Eqs. (1) and (2), respectively. The complexation energy of the trimer, $E_{int.(ha\cdots ha\cdots F^-)}$, corresponds to the energy involved in the direct assembly of the ternary complex from its constituent monomers. It was calculated as follows:

$$E_{int.(ha\cdots ha\cdots F^-)} = E_{ha\cdots ha\cdots F^-} - E_{F^-} - E_{ha} - E_{ha} \quad (8)$$

The cooperativity ($E_{coop.}$) was calculated as the difference between the binding energy of the ternary complex and the binding energy of the sum of all pair interaction energies as given in Eqs. (9) or (10)

$$E_{coop.} = E_{int.(ha\cdots ha\cdots F^-)} - E_{int.(ha\cdots F^-)} - E_{int.(ha\cdots ha)} - E''_{int.(ha\cdots F^-)} \quad (9)$$

$$E_{coop.} = E_{int.(ha\cdots ha\cdots F^-)} - 2E_{int.(ha\cdots F^-)} - E''_{int.(ha\cdots ha)}, \quad (10)$$

where $E_{int.(ha\cdots F^-)}$ and $E_{int.(ha\cdots ha)}$ are corrected with BSSE.

Except for $E'_{ha\cdots F^-}$ in Eq. (5) and $E'_{ha\cdots ha}$ in Eq. (6), all the energies at the right side of equations correspond to the systems optimized separately.

Results and discussion

Binary system

Four conformations of N-(Hydroxymethyl)acetamide dimer (I, II, III and IV) were selected at the B3LYP/6-311++G** level (see Figs. 1S and 2S). Four kinds of hydrogen bonds are found in the N-(Hydroxymethyl)acetamide dimers. The first one is the hydrogen bond between the hydroxy groups (i.e., O–H \cdots O–H in II and III). The second is O–H \cdots O=C contacts in I and II. The other two kinds of hydrogen bonds, N–H \cdots O=C and N–H \cdots O–H, are confirmed in III and IV, respectively. The interaction energies are in the range between –44.0 and –55.1 kJ mol^{–1} at the MP2(full)/6-311++G** level (see Table 1S). The interaction energies obtained at two levels are in the same order of I>III>II>IV, which is almost in

accordance with the increase of the H \cdots O distance (see Fig. 2S). Furthermore, the conformation formed by the O–H \cdots O=C contacts is more stable than that with the N–H \cdots O–H links.

Due to the C–H \cdots F[–] anionic hydrogen bond turning into the N–H \cdots F[–] or O–H \cdots F[–] contact in the process of the optimization of complex, only one stable F[–] \cdots N-(Hydroxymethyl)acetamide binary conformation was obtained at the B3LYP/6-311++G** level. In this complex, F[–] points simultaneously toward the hydrogen atoms of the N–H and O–H groups (see Fig. 1S). The anionic H-bonding interaction is up to –162.1 kJ mol^{–1} at the MP2(full)/6-311++G** level (see Table 1S).

Ternary systems

Structure of ternary system

The optimization of the complex from F[–] and conformation I, II, III and IV has resulted in four (I-1~4), five (II-1~5), four (III-1~4) and four (IV-1~4) ternary complexes at the B3LYP/6-311++G** level, respectively. Their geometric results are shown in Figs. 1 and 3S. From Fig. 1, the O–H \cdots O=C hydrogen bond exists in the ternary complexes I-1, I-2, I-3, II-1, II-2 and II-3. The N–H \cdots O=C interaction is found in I-1, II-2, II-3, II-4, II-5 and III-2. The O–H \cdots O–H contact is suggested in II-2, II-4, II-5, III-1 and III-3, and the N–H \cdots O–H link is observed in I-2, III-1, IV-1, IV-2 and IV-3.

In the ternary complexes I-1, I-4, II-1, II-4, III-1, III-4 and IV-2, the H \cdots F distances in the O–H \cdots F[–] contact are in the range between 1.390 and 1.717 Å, and the H \cdots F distances of the N–H \cdots F[–] link in I-1, I-3, I-4, II-1, II-4, III-1, III-3, III-4, IV-2 and IV-4 are in the range of 1.405–1.828 Å at the B3LYP/6-311++G** level. These values are close to the accepted H \cdots F[–] anionic hydrogen-bond distance [44], suggesting the formation of the O–H \cdots F[–] and N–H \cdots F[–] anionic hydrogen-bonding interactions. However, in I-2, II-2, II-3, II-5 and III-2, the H \cdots F distances of the N–H \cdots F[–] moiety are in the range between 1.050 and 1.092 Å at the B3LYP/6-311++G** level. These values are very close to the sum of the covalent radii of the F and H atoms, suggesting the potential covalent interactions. Indeed, the F \cdots H distances in them are lower than that in [FHF][–] anion (1.134–1.164 Å at different levels of ab initio theory [44]).

As can be seen from Fig. 1, two or three O/N–H \cdots F[–] anionic hydrogen bonds coexist in I-4, III-4 and IV-4. In the other ternary complexes, the O/N–H \cdots F[–] anionic hydrogen bond and O/N–H \cdots O hydrogen bond coexist.

Some interesting points can be extracted from the geometrical results. Firstly, except for I-3, one or two O/N–H \cdots O hydrogen bonds are broken with the new O/N–H \cdots O H-bond formation upon the addition of F[–] into the dimers I, II, III and

IV. For example, from Figs. 2S and 1, in the N-(Hydroxymethyl)acetamide dimer I, there are two O–H \cdots O intermolecular hydrogen bonds. However, only one O–H \cdots O=C contact is found in I-1 and I-2, and the new N–H \cdots O hydrogen bond in N–H \cdots O=C or N–H \cdots O–H link is observed in I-1 or I-2, only the O–H \cdots F $^-$ and N–H \cdots F $^-$ anionic hydrogen bonds in I-4. These results suggest that, due to the addition of F $^-$, the structure of N-(Hydroxymethyl)acetamide complex changes greatly and the cooperativity effect in ternary complex might be notable.

Secondly, the H \cdots O distance in the ternary complex changes greatly in comparison with that in the corresponding N-(Hydroxymethyl)acetamide dimer. For example, in the dimer I, the O \cdots H distance is 1.829 Å, while in the ternary complexes I-1, I-2 and I-3, it turns into 1.865, 1.797 and 1.906 Å, respectively. The O \cdots H distance of the O–H \cdots O=C contact is increased greatly in II-1 and II-3 in comparison with that in the dimer II, while the O \cdots H distance of the O–H \cdots O–H contact is obviously decreased in II-4 and II-5. The notable change of the H \cdots O distance suggests that the presence of the H \cdots F $^-$ anionic H-bonding interaction might change the O–H \cdots O or N–H \cdots O H-bonding interaction, leading to the possible cooperativity effect.

Thirdly, when compared to the binary F $^-$ \cdots N-(Hydroxymethyl)acetamide, the equilibrium distance $R_{F\cdots H}$ of the O–H \cdots F $^-$ anionic hydrogen bond in the ternary complexes I-1, I-4 and III-4 is increased, while it is decreased in II-1, II-4, III-1, IV-2 and IV-3. Moreover, except for I-4, II-1 and II-4, the distance $R_{F\cdots H}$ in the N–H \cdots F $^-$ anionic hydrogen bond is also shortened in comparison with that in the binary complex F $^-$ \cdots N-(Hydroxymethyl)acetamide. In particular in I-2, II-2, II-3, II-5 and III-2, the H \cdots F distance of the N–H \cdots F $^-$ moiety is shortened greatly. These results suggest the change of the O–H \cdots F $^-$ and N–H \cdots F $^-$ anionic H-bonding interactions upon ternary-system formation, accompanied by the possible cooperativity effect.

To sum up, due to the addition of F $^-$, the structure of N-(Hydroxymethyl)acetamide dimer changes greatly. Simultaneously, the H \cdots F distance is also changed remarkably in comparison with that in the binary complex F $^-$ \cdots N-(Hydroxymethyl)acetamide. These results suggest that the O/N–H \cdots F $^-$ anionic hydrogen-bonding interaction might have important influence on the O/N–H \cdots O hydrogen-bonding interaction in ternary complex or vice versa.

Interaction energy and cooperativity effect

Tables 1 and 2 summarize the interaction energies in ternary complexes at the B3LYP/6-311++G** and MP2(full)/6-311++G** levels, respectively. From Tables 1 and 2, the interaction energies obtained at two levels are very close to each other.

From Tables 1, 2 and 1S, in I-4, II-1, III-4 and IV-4, the values of $E'_{int.(ha\cdots F^-)}$ are lower than in the F $^-$ \cdots N-(Hydroxymethyl)acetamide binary complex, showing that the H \cdots F $^-$ anionic H-bonding interaction is weakened upon the ternary-complex formation. However, in the other ternary complexes, the H \cdots F $^-$ anionic H-bonding interactions are strengthened greatly. In particular, in I-2, II-2, II-3, II-5, III-2 and IV-3, the value of $E'_{int.(ha\cdots F^-)}$ is up to –429.0, –383.2, –432.8, –388.1, –408.0 and –341.6 kJ mol $^{-1}$ at the MP2(full)/6-311++G** level, respectively. In [FHF] $^-$, H-bond energy is in the range 30–60 kcal mol $^{-1}$ (i.e., 120–240 kJ mol $^{-1}$) [45]. The H \cdots F $^-$ anionic H-bond energy in the above six systems is about three times that in [FHF] $^-$, suggesting the possible covalent interaction, as agrees with the analysis of structure. At the MP2(full)/6-311++G** level, for these six complexes, the proportion of the increment of the H \cdots F $^-$ interaction energy to the corresponding $E_{int.(ha\cdots F^-)}$ in binary system, defined as $[E'_{int.(ha\cdots F^-)} - E_{int.(ha\cdots F^-)}] / E_{int.(ha\cdots F^-)}$, is up to the range of 110.72 %–166.98 %.

From Table 2, the O/N–H \cdots O H-bonding interactions in ternary complexes are in the range between –84.6 and –149.7 kJ mol $^{-1}$ at the MP2(full)/6-311++G** level, about 2–3 times that of the corresponding N-(Hydroxymethyl)acetamide dimer. These results show that the O/N–H \cdots O interaction is strengthened greatly upon the formation of ternary complex, too. In other words, the presence of the O/N–H \cdots F $^-$ anionic H-bonding interaction strengthens the O/N–H \cdots O H-bonding interaction in all the ternary complexes.

The proportion of the increment in the O/N–H \cdots O interaction energy upon the formation of ternary complex to the value in the corresponding binary system, i.e., $[E'_{int.(ha\cdots ha)} - E_{int.(ha\cdots ha)}] / E_{int.(ha\cdots ha)}$, is up to 77.86 %, 82.24 %, 72.18 %, 136.23 %, 119.06 %, 121.44 %, 129.07 %, 189.16 %, 63.35 %, 136.73 %, 72.98 %, 208.10 % and 131.51 % for I-1, I-2, I-3, II-2, II-3, II-4, II-5, III-1, III-2, III-3, IV-1, IV-2 and IV-3 at the MP2(full)/6-311++G** level, respectively. The proportion in the ternary conformations formed by the initial formation of the N-(Hydroxymethyl)acetamide dimer I followed by addition of F $^-$ is moderate. However, except for III-2 and IV-1, the proportion in the conformations formed by the dimers II, III and IV with F $^-$ is very notable. In particular, in III-1 and IV-2, the proportion is close to 200.00 %. As mentioned above, there is only the O–H \cdots O hydrogen bond in the O–H \cdots O=C contact in I, while for the dimers II, III and IV, the O–H \cdots O and N–H \cdots O hydrogen bonds are found in the O–H \cdots O–H, N–H \cdots O–H and N–H \cdots O=C links, respectively. Thus, we can conclude that the H \cdots O H-bonding interaction in the O–H \cdots O–H, N–H \cdots O–H or N–H \cdots O=C link is strengthened more notable than that in the O–H \cdots O=C contact upon the formation of ternary complex.

The synergetic effects are investigated at B3LYP/6-311++G** and MP2(full)/6-311++G** levels. A negative synergetic effect would indicate that the two interactions work in concert with each other and enhance each other's strength while a

Table 1 Interaction energy (E'_{int} , or E_{int} , kJ mol^{-1}), synergetic energy (E_{syn} , kJ mol^{-1}) and cooperativity energy (E_{coop} , kJ mol^{-1}) in ternary system (sys.) at the B3LYP/6-311++G** level ^a

Sys.	$E'_{\text{int.}(ha\cdots F^-)}$	$E'_{\text{int.}(ha\cdots ha)}$	$E''_{\text{int.}(ha\cdots ha/F^-)}$ ^b	$E_{\text{int.}(ha\cdots ha\cdots F^-)}$	E_{syn}	E_{coop}
I-1	-302.0(-292.1)	-98.3 (-96.6)	-26.1	-341.3(-329.8)	-116.1	-90.0
I-2	-431.4(-422.4)	-96.2 (-93.3)	-30.4	-461.9(-449.4)	-235.7	-205.4
	<i>-145.7(-141.1)</i>	<i>-96.2 (-93.3)</i>	4.7	<i>-258.8(-251.5)</i>	17.4	12.7
I-3	-228.8(-217.0)	-88.8 (-83.3)	-64.6	-270.1(-255.2)	-41.5	23.1
I-4	-149.4(-146.3) ^c		15.3	-359.0(-345.9)	103.0	87.7
	<i>-149.4(-146.3)^c</i>					
II-1	-143.9(-139.3) ^c		-11.6	-313.6(-299.8)	24.7	36.3
	<i>-156.5(-165.3)^d</i>					
II-2	-384.3(-374.8)	-114.8(-112.5)	-24.9	-437.1(-425.1)	-217.9	-193.0
	<i>-161.8(-156.9)</i>	<i>-114.9(-112.6)</i>	2.7	<i>-295.4(-287.6)</i>	19.5	16.8
II-3	-434.9(-425.2)	-106.5(-104.6)	-26.7	-469.4(-458.6)	-251.4	-224.7
	<i>-145.9(-141.5)</i>	<i>-106.5(-104.7)</i>	3.1	<i>-269.5(-262.7)</i>	17.8	14.6
II-4	-305.1(-296.1)	-107.2(-103.8)	-47.5	-335.3(-332.5)	-53.0	-5.4
II-5	-392.3(-382.5)	-110.3(-107.5)	-28.7	-433.5(-420.5)	-213.3	-184.7
	<i>-170.4(-165.4)</i>	<i>-110.3(-107.6)</i>	4.9	<i>-300.1(-291.6)</i>	20.2	15.2
III-1	-328.1(-314.8)	-150.8(-145.5)	-176.0	-337.2(-322.7)	-113.0	60.0
III-2	-411.3(-401.9)	-83.0 (-81.4)	-22.2	-434.7(-423.9)	-214.5	-192.4
	<i>-153.9(-149.4)</i>	<i>-83.2(-81.6)</i>	2.9	<i>-251.2(-245.1)</i>	14.2	11.3
III-3	-290.2(-277.7)	-122.5(-117.9)	-157.4	-299.0(-285.4)	-76.0	81.5
III-4	-159.6(-156.3) ^d		11.2	-333.7(-321.5)	65.1	53.9
	<i>-121.0(-118.6)</i>					
IV-1	-292.6(-280.8)	-73.2 (-70.7)	-70.8	-311.7(-299.4)	-101.7	-30.9
IV-2	-308.9(-297.5)	-137.0(-133.6)	-162.6	-317.1(-304.3)	-106.6	56.0
IV-3	-353.2(-341.9)	-97.3 (-93.5)	-87.0	-366.5(-353.3)	-155.3	-68.3
IV-4	-128.6(-125.9) ^d		7.8	-305.7(-294.0)	30.3	22.5
	<i>-128.6(-125.9)^d</i>					

^a The values in parenthesis are corrected for BSSE, and those in italic are for “FH···ha···ha” system

^b It means $E''_{\text{int.}(ha\cdots ha)}$ in I-4, II-1, III-4 and IV-4. It means $E''_{\text{int.}(ha\cdots F^-)}$ in the other ternary systems

^c For O–H···F⁻ anionic hydrogen bond

^d For N–H···F⁻ anionic hydrogen bond

positive value indicates that the two interactions work anti-synergetically. From Tables 1 and 2, at two levels of theory, the value of synergetic effect is negative in I-1, I-2, I-3, II-2, II-3, II-4, II-5, III-1, III-2, III-3, IV-1, IV-2 and IV-3, while the ternary conformations I-4, II-1, III-4 and IV-4 have the positive synergetic effect. These results indicate that the synergetic effect is present in the former, while the anti-synergetic effect is confirmed in the latter. Indeed, as mentioned above, except for I-4, II-1, III-4 and IV-4, the O/N–H···O and O/N–H···F⁻ interactions are strengthened upon ternary-complex formation.

It is noted that, in I-1, I-2, I-3, II-2, II-3, II-4, II-5, III-1, III-2, III-3, IV-1, IV-2 and IV-3, there are the O/N–H···F⁻ anionic H-bond and O/N–H···O H-bond, while in I-4, II-1, III-4 and IV-4, there is only the O/N–H···F⁻ anionic H-bond (see Fig. 1). In general, the anionic H-bonding interaction is far stronger than the neutral H-bonding interaction. In going from a binary to a ternary complex by addition of the anion F⁻, the O/N–H···F⁻ anionic H-bonding interaction forming in this process might be so strong that the architecture of the certain “binary-system moiety” in the ternary complex is distorted badly in comparison with that of the corresponding stable binary conformation. Thus, some non-covalent interactions in ternary

system might become weak. In this case, two interactions will not enhance each other’s strength, leading to the anti-synergetic effect. Indeed, as mentioned above, in I-4, III-4 and IV-4, the O/N–H···O hydrogen bond disappears and the values of $E''_{\text{int.}(ha\cdots ha)}$ become positive. Furthermore, the O/N–H···F⁻ anionic H-bonding interactions are also weakened upon the formation of ternary complexes. Thus, in I-4, III-4 and IV-4, the anti-synergetic effect occurs. However, as aforementioned, in I-1, I-2, II-2, II-3, II-4, II-5, III-2, IV-1 and IV-3, the O/N–H···O hydrogen bonds are not broken and even the O/N–H···O interactions are strengthened due to the presence of the O/N–H···F⁻ interaction. Furthermore, the O/N–H···F⁻ anionic H-bonding interactions are also reinforced. Thus, the synergetic effects arise. A conclusion is drawn that, the synergetic effect might be observed in the conformations formed by the O/N–H···F⁻ anionic H-bonding interaction and the O/N–H···O interaction, while the anti-synergetic effect might be present in the complexes where only the O/N–H···F⁻ anionic H-bond is found and the O/N–H···O H-bond is broken in going from the binary to ternary complexes.

From Tables 1 and 2, the values of synergetic and anti-synergetic effect are large. For example, at MP2(full)/6-311++

Table 2 Interaction energy (E'_{int} , or E_{int} , kJ mol^{-1}), synergetic energy (E_{syn} , kJ mol^{-1}) and cooperativity energy (E_{coop} , kJ mol^{-1}) in ternary system (sys.) at the MP2(full)/6-311++G** level^a

Sys.	$E'_{\text{int}}(\text{ha}\cdots\text{F}^-)$	$E'_{\text{int}}(\text{ha}\cdots\text{ha})$	$E''_{\text{int}}(\text{ha}\cdots\text{ha}/\text{F}^-)$ ^b	$E_{\text{int}}(\text{ha}\cdots\text{ha}\cdots\text{F}^-)$	E_{syn}	E_{coop}
I-1	-287.6(-265.0)	-98.1 (-86.0)	-25.4	-328.8(-294.8)	-108.8	-83.5
I-2	-429.0(-401.9)	-100.5 (-81.8)	-29.4	-465.9(-421.2)	-235.3	-205.8
	<i>-133.4(-118.8)</i>	<i>-100.5 (-81.9)</i>	4.3	<i>-250.5(-217.5)</i>	17.6	13.2
I-3	-216.6(-191.5)	-94.9 (-65.9)	-56.5	-266.2(-217.7)	-31.7	24.8
I-4	-145.0(-129.7) ^c		14.0	-344.6(-311.9)	90.6	76.6
	-145.0(-129.7) ^c					
II-1	-141.5(-116.5) ^c		-14.8	-303.1(-262.7)	26.7	41.4
	-141.7(-121.2) ^d					
II-2	-383.2(-356.6)	-116.7 (-98.6)	-23.3	-436.2(-392.6)	-214.8	-191.6
	<i>-150.4(-134.6)</i>	<i>-116.8 (-98.6)</i>	3.5	<i>-284.6(-250.3)</i>	18.0	14.5
II-3	-432.8(-406.1)	-108.2 (-94.2)	-26.1	-470.7(-430.7)	-253.0	-226.9
	<i>-133.5(-119.3)</i>	<i>-108.3 (-94.3)</i>	3.9	<i>-259.1(-230.7)</i>	17.8	13.9
II-4	-289.4(-266.4)	-109.4 (-90.8)	-46.6	-324.3(-283.8)	-52.1	-5.5
II-5	-388.1(-361.9)	-113.2 (-95.3)	-29.8	-431.9(-388.2)	-210.5	-180.7
	<i>-159.5(-143.3)</i>	<i>-113.2 (-95.4)</i>	4.5	<i>-290.5(-256.1)</i>	18.4	13.9
III-1	-313.8(-285.2)	-149.7(-125.5)	-168.2	-325.8(-283.1)	-104.1	64.2
III-2	-408.0(-381.5)	-84.6 (-72.8)	-21.6	-434.6(-396.8)	-212.6	-191.0
	<i>-140.7(-126.1)</i>	<i>-84.8 (-72.9)</i>	2.8	<i>-234.0(-213.4)</i>	14.8	12.1
III-3	-276.5(-248.2)	-122.5(-100.7)	-147.4	-290.6(-251.1)	-66.9	80.5
III-4	-154.1(-139.3) ^d		9.7	-319.7(-288.2)	60.3	50.6
	-117.4(-103.6)					
IV-1	-284.2(-257.0)	-76.2 (-61.8)	-67.5	-307.1(-269.0)	-93.6	-26.1
IV-2	-293.9(-266.0)	-135.7(-115.3)	-158.9	-307.6(-269.1)	-93.7	65.2
IV-3	-341.6(-313.1)	-102.0 (-82.1)	-81.4	-360.9(-316.4)	-146.1	-64.7
IV-4	-124.5(-112.0) ^d		7.4	-292.8(-263.2)	31.3	23.9
	-124.5(-112.0) ^d					

^a The values in parenthesis are corrected for BSSE, and those in italic are for "FH \cdots ha \cdots ha" system

^b It means $E''_{\text{int}}(\text{ha}\cdots\text{ha})$ in I-4, II-1, III-4 and IV-4. It means $E''_{\text{int}}(\text{ha}\cdots\text{F}^-)$ in the other ternary systems

^c For O-H \cdots F $^-$ anionic hydrogen bond

^d For N-H \cdots F $^-$ anionic hydrogen bond

G** level, the value of E_{syn} in I-2, II-2, II-3, II-5 and III-2 is up to -235.3, -214.8, -253.0, -210.5 and -212.6 kJ mol^{-1} , respectively, and that of E_{syn} for anti-synergetic effect in I-4 and III-4 is up to 90.6 and 60.3 kJ mol^{-1} , respectively. Escudero et al. found that the values of synergetic effects between cation $\cdots\pi$ and hydrogen bonding interactions were only in the range of -4.76~ -6.64 kcal mol^{-1} (-19.91~-27.77 kJ mol^{-1}) in Na $^+$ /K $^+$ \cdots pyrrole/indole \cdots H $_2$ O at the MP2/6-31++G** level [46]. Estarellas et al. demonstrated that the values of synergetic effects between hydrogen bonding, cation $\cdots\pi$ and $\pi\cdots\pi$ interactions in Li $^+$ /Na $^+$ \cdots 1,4-diaminobenzene \cdots terephthaldehyde were only within the range between -0.64 and -7.45 kcal mol^{-1} (between -2.68 and -31.16 kJ mol^{-1}) at the RI-MP2/aug-cc-pVTZ//RI-MP2/aug-cc-pVDZ level [47]. It is noted that, in general, the cation/anion $\cdots\pi$ and $\pi\cdots\pi$ interactions are far weaker than the O/N-H \cdots F $^-$ anionic H-bonding interactions. As mentioned above, the stronger the noncovalent interactions, the more notable the synergetic effects are. Thus, the synergetic effect between the conventional H-bonding interaction and cation/anion $\cdots\pi$ or $\pi\cdots\pi$ interaction might be weaker than that involving the strong H \cdots F $^-$ anionic H-bond.

The cooperativity energies were also given in Tables 1 and 2. From Tables 1 and 2, the values of E_{coop} are large. For example, at MP2(full)/6-311++G** level, the value of E_{coop} in I-2, II-2,

II-3, II-5, III-2, I-4 and III-4 is up to -205.8, -191.6, -226.9, -180.7, -191.0, 76.6 and 50.6 kJ mol^{-1} , respectively. Escudero et al. have observed that the cooperativity energy is only -1.49 kcal mol^{-1} (-6.23 kJ mol^{-1}) in Na $^+$ -H $_2$ O-indole/pyrrole complex [46]. Vijay et al. have found that, in two aromatic benzene ring systems with the Na $^+$ cation, the largest value of the cooperativity of cation $\cdots\pi$ and $\pi\cdots\pi$ interactions is only -0.57 kcal mol^{-1} (-2.38 kJ mol^{-1}), and the greatest value of the anti-cooperativity is just 0.88 kcal mol^{-1} (3.68 kJ mol^{-1}) [1]. Recently, we have found that the cooperativity effect between cation-molecule and hydrogen-bonding interactions in the *O*-cresol complex with Na $^+$ is up to -34.55 kJ mol^{-1} and the anti-cooperativity effect is up to 40.96 kJ mol^{-1} [48]. These results suggest indirectly that the remarkable cooperativity or anti-cooperativity effect might lead to the notable structural distortion of the N-(Hydroxymethyl)acetamide complex upon the introduction of F $^-$. This might be one of the causes for the formation of the channels for translocating anions in ceramide network.

AIM analysis

The results of AIM analysis carried out for binary and ternary systems are presented in Figs. 2S and 1, respectively. The

small ρ_{BCP} and positive $\nabla^2\rho_{BCP}$ values confirm the O/N–H \cdots O/F $^-$ H-bonding interactions.

From Fig. 1, in I-4, III-4 and IV-4, the bond path linking the hydrogen atom of the H–O or H–N group with the oxygen atom of the C=O or O–H moiety is not found, showing that the O–H \cdots O and N–H \cdots O hydrogen bonds are broken. For the other ternary complexes, there are more than two distinct (3, –1) BCPs in the region showing the O/N–H \cdots O and O/N–H \cdots F $^-$ interactions. The values of $\rho_{BCP(O\cdots H)}$ in I-1, I-2, I-3, II-3, II-4, II-5, III-2, IV-1 and IV-3 increase in comparison with those in the corresponding binary systems. These results suggest that the O/N–H \cdots O interactions are strengthened upon the formation of the ternary complex. Furthermore, the values of $\rho_{BCP(F\cdots H)}$ in them are also larger than those in F $^-$ \cdots N-(Hydroxymethyl)acetamide, indicating the strengthened O/N–H \cdots F $^-$ anionic H-bonding interactions. Therefore, the cooperativity effect between the O/N–H \cdots F $^-$ and O/N–H \cdots O interactions is confirmed. In particular, in I-2, II-2, II-3, II-5 and III-2, a notable increase of $\rho_{BCP(F\cdots H-N)}$ is found upon the ternary-complex formation, showing the remarkably increased H \cdots F $^-$ interaction and notable cooperativity effect. Furthermore, the Laplacians $\nabla^2\rho_{BCP}$ turn negative, suggesting the covalent interaction of the H \cdots F $^-$ link.

Analysis of the electron density shifts

In order to obtain deeper insight into the origin of cooperativity effect, the electron density shifts were investigated. It was calculated by evaluating the difference between the total electron densities of ternary complex and individual monomers (the N-(Hydroxymethyl)acetamide dimer and F $^-$) as given in the following.

$$\rho_{\text{shift}} = \rho_{ha\cdots ha} : F^- - \rho_{ha\cdots ha} - \rho_{F^-} \quad (11)$$

The shifts of electron densities are illustrated in Fig. 2. Purple regions represent the accumulation of additional electron density; yellow regions indicate loss of density.

From Fig. 2, in the ternary conformations I-1, I-2, I-3, II-2, II-3, II-4, II-5, III-2, IV-1 and IV-3, most important for our present consideration is the region between two N-(Hydroxymethyl)acetamide units. It is apparent by the purple region that there is large charge buildup, indicating that many of the electron densities are shifted to this region. The increased density tends to the strengthened O/N–H \cdots O H-bonding interaction. Simultaneously, the O/N–H \cdots F $^-$ anionic H-bonding interaction is also enhanced shown by the large purple extending to the H \cdots F $^-$ region. Thus, the cooperativity effect is confirmed in these ten conformations.

For I-4, II-1, III-4 and IV-4, the O/N–H \cdots F $^-$ anionic H-bonding interaction is weakened indicated by the notable

yellow region between F $^-$ and N-(Hydroxymethyl)acetamide, accompanied by the anti-cooperativity effect.

Analysis of the surface electrostatic potential

The electrostatic potential (ESP) on the 0.001 au molecular surface of the complex is computed by the Multiwfn programs [49], utilizing the B3LYP/6-311++G** optimized geometries. Wave functions and electrostatic potential cube files come from Gaussian 03. The results are shown in Fig. 3 and Table 3.

For the isolated N-(Hydroxymethyl)acetamide monomer, the strongly positive ESP of the hydrogen atom of the –NH or –OH group, $V_{S,max}$ = 50.0 or 27.6 kcal mol $^{-1}$, and the notable negative ESP of the oxygen atom of the –C=O or –OH group ($V_{S,min}$ = –43.1 or –37.1 kcal mol $^{-1}$) indicate their propensities for noncovalent hydrogen bonding, as the donor and acceptor, respectively. The positive ESP of the hydrogen atom of the –CH $_3$ group is only 18.6 kcal mol $^{-1}$, weaker than that of the –NH or –OH group. Indeed, as mentioned above, the conformation formed by the O/N–H \cdots O hydrogen bond is more stable than that with the C–H \cdots O contact.

From Fig. 3 and Table 3, each of the ternary complexes has several surface minima, which are associated with the lone pairs of the O and N atom as well as F $^-$, and the strongest is that of F $^-$. The most negative values, i.e., the local minima ($V_{S,min}$), are in the range between –105.7 and –138.3 kcal mol $^{-1}$. There are also several surface maxima ($V_{S,max}$) with the hydrogen atom of the –CH $_3$, –CH $_2$ –, –OH and –NH groups for each of the ternary systems. The highest is around the hydrogen atom of the –CH $_3$ group (I-1, II-2, II-4, III-1, III-2, III-4, IV-1 and IV-4), –OH moiety (I-2, II-5, III-3, IV-2 and IV-3), –NH (I-3 and II-1) or –CH $_2$ – group (I-4 and II-3). These values are within the range of –19.2~–45.0 kcal mol $^{-1}$.

From Table 3, the order of the absolute of $V_{S,min}$ is I-3 > II-4 > I-1 > IV-1 > IV-2 > III-3 > III-1 > IV-3 > II-2 > III-2 > II-5 > I-2 > II-3. Except for I-1, III-2 and III-3, the order of $V_{S,min}$ is almost in accordance with that of the decrease of $E'_{int.(ha\cdots F^-)}$, $E_{int.(ha\cdots ha\cdots F^-)}$ and synergetic energy E_{syn} , respectively.

The correlation between the $V_{S,min}$ and $E'_{int.(ha\cdots F^-)}$ is given in Fig. 4. The correlation coefficient is up to 0.9622 and they fit the following equation:

$$V_{S,min} = 2.2836E'_{int.(ha\cdots F^-)} - 138.35$$

$V_{S,min}$ is in kcal mol $^{-1}$, and $E'_{int.(ha\cdots F^-)}$ is the interaction energy between N-(Hydroxymethyl)acetamide and F $^-$ in ternary system at MP2(full)/6-311++G** level (in kJ mol $^{-1}$).

The relationship between the $V_{S,min}$ and E_{syn} is shown in Fig. 5. The correlation coefficient is 0.9698 and they fit the following equation:

$$V_{S,min} = 2.7475E_{syn} - 138.69$$

The synergetic energy E_{syn} is in kJ mol $^{-1}$.

Fig. 2 Shifts of electron density as a result of the formation of the ternary complex at the MP2(full)/6-311++G** level. Purple regions denote gain, and yellow regions represent loss

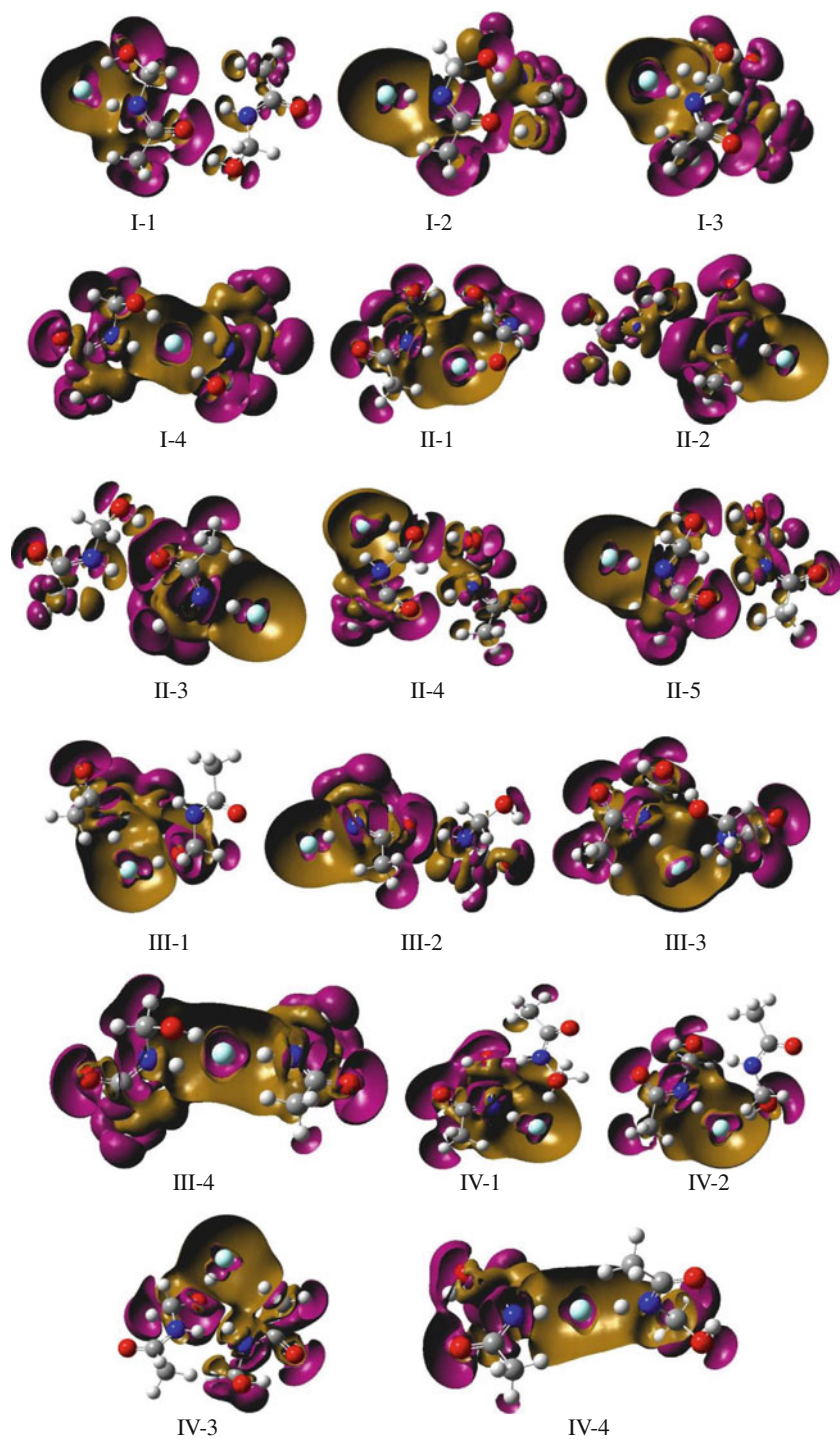


Fig. 3 Surface electrostatic potential on the 0.001 au molecular surface of the $F^- \cdots ha \cdots ha$ and $ha \cdots F^- \cdots ha$ ternary complexes. Red points mean surface maxima and blue points mean surface minima

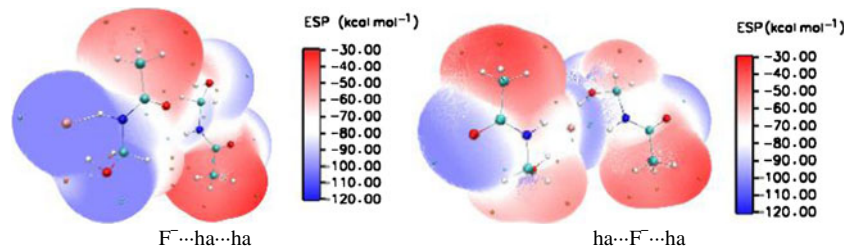


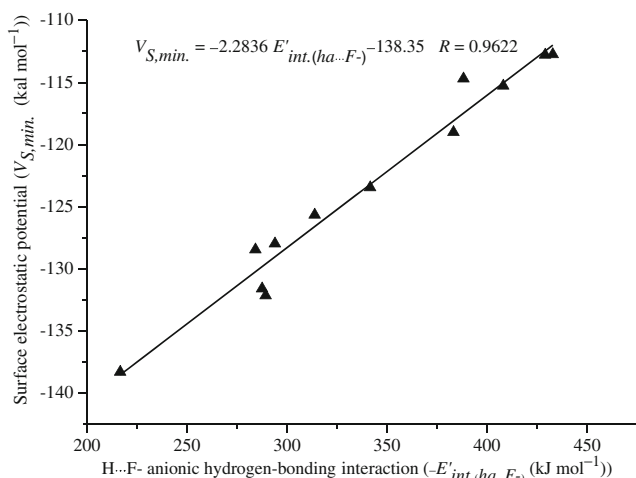
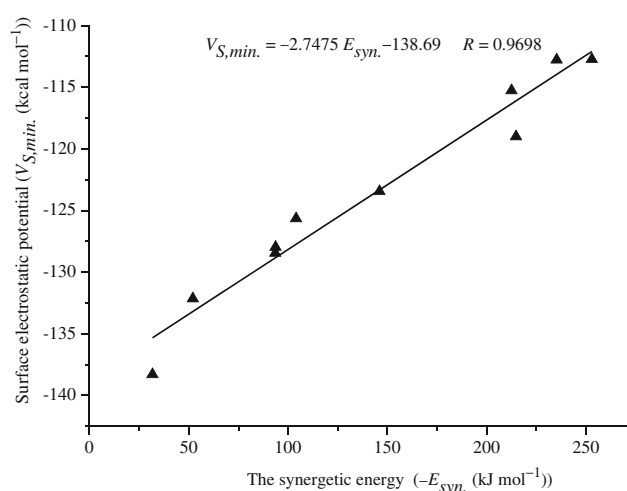
Table 3 The surface electrostatic potential (ESP) on the 0.001 au molecular surface (minimum $V_{S,min}$ and maximum $V_{S,max}$, kcal mol⁻¹) at the MP2(full)/6-311++G** level

	O1(O14)	H2(H15)	N6(N19)	H7(H20)	O9(O22)	Max.	Min. (F)
ha··F ⁻		-105.8		-43.2	-115.4	-48.5	-143.4
I	-43.7 (-43.8)	-19.1 (-19.7)	-5.0	45.5 (45.5)	45.5 (-36.8)	45.5	-43.8
II	-34.5 (-40.2)	2.6 (5.6)	-5.2 (-2.8)	45.2 (46.1)	46.1 (-37.5)	46.1	-40.2
III	-39.8 (-39.8)	0.1 (29.6)	17.4 (-7.8)	50.0 (16.4)	16.4 (-46.3)	50.0	-46.3
IV	7.9 (-23.2)	36.4 (36.4)	-6.9 (-6.9)	21.2 (22.9)	22.9 (-41.7)	36.4	-41.7
I-1	-106.2 (-95.7)	-87.7 (-54.0)	-87.4 (-66.3)	-54.2 (-39.0)	-79.9 (-96.7)	-33.4	-131.6
I-2	-95.0 (-106.0)	-71.2 (-51.5)	-125.8 (-68.9)	-61.4 (-71.2)	-104.7 (-104.8)	-39.8	-112.8
I-3	-123.5 (-96.0)	-87.5		-58.8 (-19.2)	-107.1	-19.2	-138.3
I-4	-105.6 (-105.6)	-78.8 (-78.7)	-105.7 (-105.7)		-103.4 (-103.4)	-38.0	-105.7
II-1	-114.4 (-108.2)	-101.6 (-99.5)	-79.0	-93.8 (-33.6)	-114.5 (-101.6)	-26.6	-122.5
II-2	-99.4 (-112.4)	(-64.2)	-67.3	-39.2	-97.7 (-97.6)	-31.1	-119.0
II-3	-99.6 (-59.8)	-64.4 (-44.0)	-68.7 (-102.8)	-50.7	-77.9 (-91.1)	-35.1	-112.7
II-4	-104.8 (-90.4)	-92.6 (-89.4)		-53.7 (-57.6)	-90.4 (-106.3)	-35.2	-132.2
II-5	-89.7 (-105.8)	-26.4	-82.0		-99.1 (-106.2)	-26.4	-114.7
III-1	-97.8 (-105.5)	-61.8 (-64.7)	(-78.2)	-57.0 (-50.0)	-106.4 (-103.6)	-38.1	-125.7
III-2	-105.6 (-91.8)	-55.3 (-36.1)	(-67.3)	(-42.9)	-98.1 (-103.6)	-36.1	-115.3
III-3	-94.8 (-108.5)	-66.0 (-42.2)		-51.7	-108.9 (-103.1)	-42.2	-125.8
III-4	-110.2 (-96.6)	-71.2 (-44.1)		-52.4 (-49.3)	-104.8 (-100.7)	-39.6	-124.7
IV-1	-86.2 (-105.5)	-48.3 (-42.7)		(-71.7)	-107.5 (-98.4)	-38.3	-128.5
IV-2	-83.3 (-116.2)	-38.2 (-105.0)	(-76.7)	(-66.7)	-100.2 (-108.5)	-38.2	-128.0
IV-3	-114.0 (-87.2)	-36.7 (-36.7)		-40.9	-106.5 (-99.4)	-36.7	-123.5
IV-4	-50.0 (-97.9)	-102.0 (-45.9)			-102.0 (-102.0)	-45.0	-110.5

From Table 3, the absolute values of the most negative $V_{S,min}$ and the highest $V_{S,max}$ in ternary complexes are all less than that in the corresponding F⁻··N-(Hydroxymethyl)acetamide binary system (-143.4 and -48.5 kcal mol⁻¹, respectively). These results indicate that, due to the introduction of the anion F⁻ into the N-(Hydroxymethyl)acetamide dimer,

both $V_{S,min}$ and $V_{S,max}$ in ternary complexes decrease. In particular, the highest $V_{S,max}$ in the N-(Hydroxymethyl)acetamide dimer is positive, while in the ternary system, it turns negative.

The change of the most negative $V_{S,min}$ in ternary complex in comparison with that in the corresponding binary system,

**Fig. 4** The surface electrostatic potential $V_{S,min}$ versus the H··F⁻ anionic hydrogen-bonding interaction $E'_{int.(ha··F^-)}$ (kJ mol⁻¹)**Fig. 5** The surface electrostatic potential $V_{S,min}$ versus the synergetic energy E_{syn} (kJ mol⁻¹)

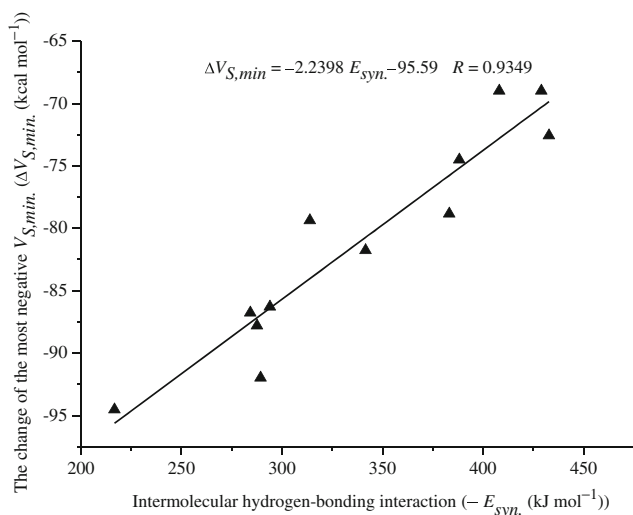


Fig. 6 The change of the most negative $\Delta V_{S,min}$ versus the synergetic energy E_{syn} (kJ mol^{-1})

$\Delta V_{S,min} = V_{S,min}(\text{ternary complex}) - V_{S,min}(\text{ha}\cdots\text{ha dimer})$, is up to $-87.8, -69.0, -94.5, -78.8, -72.6, -92.0, -74.5, -79.4, -69.0, -79.5, -86.8, -86.3$ and $-81.8 \text{ kcal mol}^{-1}$, respectively. The absolute values follow the order of I-3 > II-4 > I-1 > IV-1 > IV-2 > IV-3 > III-3 > III-1 > II-2 > II-5 > II-3 > III-2 > I-2. Except for I-1, II-3 and III-3, this order is in agreement with that of the synergetic effects.

The relationship between the $\Delta V_{S,min}$ and E_{syn} is shown in Fig. 6. The correlation coefficient is 0.9349 and they fit the following equation:

$$\Delta V_{S,min} = 2.2398 E_{syn} - 95.59$$

The synergetic energy E_{syn} is in kJ mol^{-1} .

FH \cdots ha \cdots ha system

As mentioned above, for I-2, II-2, II-3, II-5 and III-2, the H \cdots F distances of the N–H \cdots F $^-$ moiety are very close to the sum of the covalent radii of the F and H atoms, suggesting the potential covalent interactions. Furthermore, from Fig. 3S, the N \cdots H distances of the N–H \cdots F $^-$ moiety (1.408, 1.365, 1.409, 1.340 and 1.389 Å, respectively) are larger slightly than the sum of the covalent radii of the N and H atoms, showing the possible H \cdots N $^-$ H-bonding interactions. Thus, the N–H \cdots F $^-$ moiety might turn into the “N \cdots H–F” group, and the “F $^-$ \cdots ha \cdots ha” system might turn into the “FH \cdots ha \cdots ha” complex. Thus, the “FH \cdots ha \cdots ha” conformations were also designed and fully optimized at the B3LYP/6-311++G** level. The same geometry as I-2, II-2, II-3, II-5 or III-2 was obtained.

In “FH \cdots ha \cdots ha” system, $E'_{int.(\text{FH}\cdots\text{ha}^-)}$ and $E'_{int.(\text{ha}\cdots\text{ha})}$ were calculated as follows:

$$E'_{int.(\text{FH}\cdots\text{ha}^-)} = E_{\text{FH}\cdots\text{ha}\cdots\text{ha}} - E_{\text{ha}\cdots\text{ha}} - E_{\text{FH}}$$

$$E'_{int.(\text{ha}\cdots\text{ha})} = E_{\text{FH}\cdots\text{ha}\cdots\text{ha}} - E_{\text{FH}\cdots\text{ha}} - E_{\text{ha}}$$

The through-space interaction energy $E''_{int.(\text{FH}\cdots\text{ha})}$ was calculated at the trimer geometry.

$$E''_{int.(\text{FH}\cdots\text{ha})} = E'_{\text{FH}\cdots\text{ha}} - E_{\text{FH}} - E_{\text{ha}}$$

The synergetic energy (E_{syn}) and cooperativity (E_{coop}) in the “FH \cdots ha \cdots ha” ternary complex were calculated as following:

$$E_{syn} = E_{int.(\text{FH}\cdots\text{ha}\cdots\text{ha})} - E_{int.(\text{FH}\cdots\text{ha})} - E_{int.(\text{ha}\cdots\text{ha})}$$

$$E_{int.(\text{FH}\cdots\text{ha}\cdots\text{ha})} = E_{\text{FH}\cdots\text{ha}\cdots\text{ha}} - E_{\text{FH}} - E_{\text{ha}} - E_{\text{ha}}$$

$$E_{coop} = E_{int.(\text{FH}\cdots\text{ha}\cdots\text{ha})} - E_{int.(\text{FH}\cdots\text{ha})} - E_{int.(\text{ha}\cdots\text{ha})} - E''_{int.(\text{FH}\cdots\text{ha})}$$

The interaction energies at the B3LYP/6-311++G** and MP2(full)/6-311++G** levels are collected in Tables 1 and 2, respectively. From Tables 1 and 2, the values of $E'_{int.(\text{FH}\cdots\text{ha}^-)}$ are found to be $-133.4, -150.4, -133.5, -159.5$ and $-140.7 \text{ kJ mol}^{-1}$ for I-2, II-2, II-3, II-5 and III-2 at the MP2(full)/6-311++G** level, respectively. These values are lower than in the FH complex with the N-(Hydroxymethyl)acetamide anion ($-168.3 \text{ kJ mol}^{-1}$), showing that the H \cdots N $^-$ hydrogen-bonding interactions are weakened upon the formation of ternary complexes. Furthermore, the values of $E'_{int.(\text{ha}\cdots\text{ha})}$ in “FH \cdots ha \cdots ha” are also lower than in “ha \cdots ha”. These results indicate the possible anti-cooperativity effects upon ternary-system formation.

From Tables 1 and 2, at two levels of theory, the value of synergetic effect is positive in I-2, II-2, II-3, II-5 and III-2, confirming the anti-synergetic effect in the “FH \cdots ha \cdots ha” ternary complex. However, as mentioned above, in the “F $^-$ \cdots ha \cdots ha” ternary complexes I-2, II-2, II-3, II-5 and III-2, the values of synergetic effect are negative and synergetic effects are suggested.

The cooperativity energy obtained considering that it comes either from “F $^-$ \cdots ha \cdots ha” or “FH \cdots ha \cdots ha” was also different for the same geometry. At two levels of theory, the values of the cooperativity effects are positive in I-2, II-2, II-3, II-5 and III-2, indicating the anti-cooperativity effects in the “FH \cdots ha \cdots ha” complex. However, as mentioned above, in the “F $^-$ \cdots ha \cdots ha” complexes I-2, II-2, II-3, II-5 and III-2, the cooperativity effects are found.

Conclusions

The cooperativity effects between the O/N–H \cdots F $^-$ anionic H-bonding and O/N–H \cdots O H-bonding interactions and electrostatic potentials in the 1:2 (F $^-$:N-(Hydroxymethyl)acetamide) ternary systems are investigated using the B3LYP and MP2 methods.

The result shows that, the increase of the H···O interaction energy in the O–H···O–H, N–H···O–H or N–H···O=C link is more notable than that in the O–H···O=C contact. For the complex with the N–H···F[−] contact, the cooperativity energy obtained considering that it comes from “F[−]···ha[−]···ha” is negative, while it is positive when considering that it comes from “FH[−]···ha[−]···ha” for the same geometry. The cooperativity effect is found in the conformation formed by the O/N–H···F[−] and O/N–H···O interactions, while the anti-cooperativity effect is present in the complex where only the O/N–H···F[−] H-bond is found, as well as the “FH[−]···ha[−]···ha” system with the N[−]···H–F contact. The most negative surface electrostatic potential ($V_{S,min}$) and the change of the most negative $V_{S,min}$ ($\Delta V_{S,min}$) correlate well with the interaction energy $E'_{int.(ha\cdots F^-)}$ and synergetic energy E_{syn} , respectively.

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