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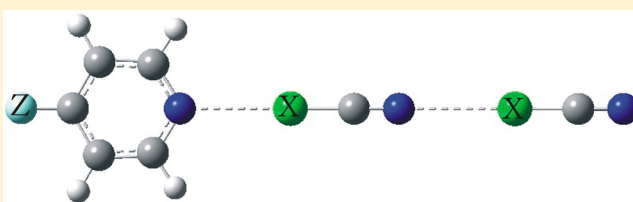
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ABSTRACT: DFT calculations (B97-1) with the 6-31+G-(d,p)-LanL2DZdp basis set were used to analyze the intermolecular interactions in 4-Z-Py...XCN...XCN triads (Z = H, F, OH, OCH₃, CH₃, NH₂, NO₂, and CN; Py = pyridine; and X = Cl and Br) that are connected by halogen-bond interactions. To understand the properties of the systems better, the corresponding dyads are also studied. Particular attention is given to parameters such as cooperative energy. All complexes show cooperative energy ranging from -1.39 to -3.46 kJ mol⁻¹ and -2.61 to -5.84 kJ mol⁻¹ for X = Cl and Br, respectively. We show that the effect of the substituents on the title interactions strongly depends on the nature of the substituents (Z). Thus, the electron-donor and electron-acceptor substituents increase and decrease the stability of complexes, respectively. The electronic properties of the complexes have been analyzed using molecular electrostatic potential (MEP) and minimum average local ionization energy, and the parameters were derived from the atoms in molecules (AIM) and natural bond orbital (NBO) methodologies.

Z=H, F, OH, OCH₃, CH₃, NH₂, NO₂, CN X=Cl, Br

1. INTRODUCTION

Noncovalent interactions between molecules play a very important role in supramolecular chemistry, molecular biology, and materials science.¹ Although research has traditionally focused on the more common hydrogen-bond (HB) interactions, interest has recently grown in another type of intermolecular interactions, namely, halogen bonding. Halogen bonding describes a directional interaction between covalently bound halogen atoms (X) and Lewis bases (A). Several excellent reviews on halogen bonding are now available^{2–4} as well as a recent book on halogen bonding.⁵

A σ hole is a region of positive electrostatic potential on the extension of a covalent bond.⁶ Halogen bonding is a subset of σ -hole bonding. It is increasingly recognized that σ -hole bonding, especially involving group VII, occurs widely in biological systems.^{7,8} There is also considerable interest and activity in applying it to crystal engineering.^{9,10} The presence of halogen bonding in biology was mostly ignored because there were few known crystal structures of halogen-containing biological molecules. Thus, a lot of the characteristics of halogen bonding have been discovered through computational studies. Cooperativity is an important feature of halogen bonding, as reported by other researchers.^{11–15}

The effects of the substituents on the binding energies of the 4-Z-Py...XCN...XCN triads (Z = H, F, OH, OCH₃, CH₃, NH₂, NO₂, and CN; Py = pyridine; and X = Cl and Br) and the cooperativity of the halogen-bond interactions have been investigated in the present study. The relationship between the binding energies and the Hammett constants have been

studied for binary and ternary complexes. In addition, the cooperativity of two halogen-bond interactions and the strength of the interactions have been investigated from the results of atoms in molecules (AIMs),¹⁶ natural bond orbital (NBO),¹⁷ and molecular electrostatic potential (MEP) analysis. The natural energy-decomposition analysis (NEDA)^{18,19} within the NBO methodology has been employed to determine the physically significant components of the total interaction energies for the studied complexes. To the best of our knowledge, the study of cooperativity in triads with halogen bonding involving aromatic rings is reported here for the first time.

2. COMPUTATIONAL DETAILS

Structures of the monomers, dimers, and trimers were optimized with the B97-1 DFT functional²⁰ and 6-31+G(d,p) basis set²¹ for all of the atoms with the exception of bromine, for which the LanL2DZdp basis set²² was used. Frequency calculations at the same level were carried out to confirm that the structures obtained corresponded to energy minima. Very recently, Chudzinski and Taylor pointed out that a certain DFT functional, specifically B97-1, provided outstanding linear correlations using the experimental thermodynamic data from halogen-bonded complexes, which was assessed by a variety of

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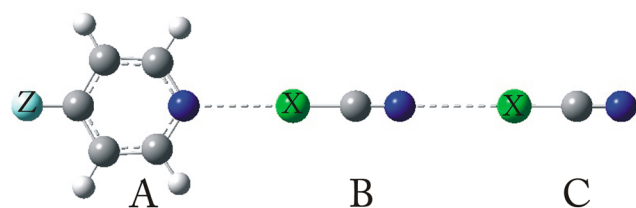
statistical methods.²³ Calculations were performed using the Gaussian 03 system of codes.²⁴

The stabilization energy has been calculated as the difference between the total energy of the complex and the sum of the isolated monomers in its minima configuration. The full counterpoise (CP) method²⁵ was used to correct the stabilization energy from the inherent basis-set superposition error (BSSE).

The natural charge (q) was derived using natural population analysis (NPA). The topological analysis was carried out with the AIMAll program.²⁶ The most negative-value of the MEP point (V_{\min})²⁷ for the lone-pair region of the nitrogen atoms in pyridine and the minimum average local ionization energy ($I_{S,\min}$)^{28,29} on the molecular surface of the 0.001 au contour of $\rho(r)$ have been calculated with the multiwfn package.³⁰ Among the different energy-decomposition procedures, the NEDA method implemented in the GAMESS program³¹ has been used in this Article. Although all of the energy-partition methods are arbitrary, they can provide chemical insights into energetic differences when they are applied to an analogous series of complexes, as in this case.

3. RESULTS AND DISCUSSION

3.1. Geometry. The systems studied form stable binary and ternary complexes (the general structure of a ternary complex is given in Figure 1). The binary and ternary complexes with Z =



Z = H, F, OH, OCH₃, CH₃, NH₂, NO₂, CN; X = Cl, Br.

Figure 1. Disposition of the monomers within the ternary complexes.

H, F, NO₂ and CN show C_{2v} symmetry, whereas in the rest of the cases C_s symmetry is found. The NCX molecules are aligned with the nitrogen atom of the pyridine, bisecting the aromatic-ring molecule. The intermolecular distances between the A and B molecules in the binary complexes are between 2.86–2.96 and 2.74–2.85 Å for X = Cl and Br, respectively (Table 1). In the ternary complexes, the intermolecular distances between the A and B molecules are always shorter than the ones in the corresponding binary complexes, ranging between 2.81–2.92 and 2.68–2.80 Å for X = Cl and Br, respectively. For a given X, the shorter A···B distances are found in the 4-NH₂ binary and ternary complexes, and the longest distance is obtained in the 4-NO₂ complexes. Good linear correlations are found between the A···B intermolecular distances in the binary and corresponding ternary complexes (R^2 values are 0.98 and 0.996 for the chlorine and bromine complexes, respectively).

The B···C intermolecular distances in the ternary complexes are always shorter than those in the corresponding (XCN)₂ dimers. The effect of the pyridine substituents not only affect the A···B intermolecular distances but also the B···C intermolecular distances. Thus, the shorter B···C distances are found in the 4-amino derivatives (2.997 and 2.949 Å for X = Cl and Br, respectively), whereas the longest are found in the 4-

Table 1. Intermolecular Distances, R (Å), in the Investigated Trimers (T) and Dimers at the B97-1/6-31+G(d,p)-LanL2DZdp Level^a

Z	X	$R(AB, T)$	$R(AB)$	ΔR_{AB}	$R(BC, T)$	$R(BC)$	ΔR_{BC}
NH ₂	Cl	2.812	2.856	−0.044	2.997	3.057	−0.060
CH ₃ O	Cl	2.835	2.872	−0.038	3.002	3.057	−0.056
CH ₃	Cl	2.842	2.877	−0.035	3.005	3.057	−0.053
OH	Cl	2.846	2.879	−0.033	3.006	3.057	−0.051
H	Cl	2.855	2.886	−0.031	3.011	3.057	−0.047
F	Cl	2.874	2.902	−0.028	3.017	3.057	−0.041
CN	Cl	2.906	2.940	−0.034	3.026	3.057	−0.031
NO ₂	Cl	2.918	2.955	−0.036	3.030	3.057	−0.028
NH ₂	Br	2.683	2.735	−0.052	2.949	3.020	−0.071
CH ₃ O	Br	2.701	2.749	−0.048	2.955	3.020	−0.065
CH ₃	Br	2.707	2.755	−0.048	2.958	3.020	−0.062
OH	Br	2.716	2.766	−0.050	2.960	3.020	−0.060
H	Br	2.726	2.777	−0.051	2.963	3.020	−0.057
F	Br	2.748	2.801	−0.052	2.970	3.020	−0.050
CN	Br	2.783	2.830	−0.047	2.978	3.020	−0.042
NO ₂	Br	2.801	2.846	−0.045	2.980	3.020	−0.040

^a ΔR indicates the changes relative to the respective dimers.

nitro derivatives (3.030 and 2.980 Å for X = Cl and Br, respectively). Linear relationships are found between the A···B and B···C distances for each ternary complex, with squared correlation coefficient, R^2 , values of 0.99 and 0.98 for X = Cl and Br, respectively

The shorter intermolecular distances found in the ternary complexes compared to those in the corresponding binary ones can be interpreted as a cooperative effect of the halogen bonds in these systems. The shortening effect is larger in the N···Br halogen bonds than in the corresponding N···Cl ones. In addition, the effect is larger in those complexes with shorter intermolecular distances than in those with the longest ones.

3.2. Energy. The stabilization energy in the binary and ternary complexes is obtained as the energy difference between the complex and sum of the isolated monomers (eqs 1 and 2). All results have been corrected for the inherent BSSE using the counterpoise method. As shown in Table 2, the binding energy of the AB binary complexes ranges from −12.7 to −20.8 kJ mol^{−1} when chlorine is the interacting halogen atom, whereas when the halogen is bromine, from −4.1 to −19.7 kJ mol^{−1}. In all of the cases studied here, the AB complexes in which the interacting halogen atom is chlorine show a larger stabilization energy (absolute value) than that of the corresponding complexes with bromine. The larger differences between the chlorine and the corresponding bromine complexes are found in the weaker complexes.

$$\Delta E(AB) = E_{AB} - (E_A + E_B) + BSSE_{AB} \quad (1)$$

$$\Delta E(ABC) = E_{ABC} - (E_A + E_B + E_C) + BSSE_{ABC} \quad (2)$$

In the case of the ternary complexes, the stabilization energy of the chlorine complexes ranges from −25.5 to −35.6 kJ/mol and in the bromine complexes, from −21.8 to −40.6 kJ/mol. In contrast to the results obtained for the AB binary complexes, the bromine derivatives are always more stable than their corresponding chlorine counterparts with the exception of the two weaker complexes, Z = CN and NO₂, where the opposite occurs. The different behavior observed between the AB binary and ABC ternary complexes can be explained on the basis of

Table 2. Stabilization Energies, ΔE , Corrected by BSSE (Dimers and Trimers), Cooperative Energies, E_{coop} , and Three-Body Terms, $\Delta^3 E(\text{ABC})$, in the Investigated Dimers and Trimers at the B97-1/6-31+G(d,p)-LanL2DZdp Level^a

Z	X	$\Delta E(\text{AB})$	$\Delta E(\text{BC})$	$\Delta E(\text{ABC})$	E_{coop}	$\Delta^3 E(\text{ABC})$
NH ₂	Cl	-20.78	-11.38	-35.63	-3.46	-2.92
CH ₃ O	Cl	-19.35	-11.38	-33.84	-3.10	-2.67
CH ₃	Cl	-18.91	-11.38	-33.29	-3.00	-2.60
OH	Cl	-18.58	-11.38	-32.85	-2.88	-2.53
H	Cl	-17.98	-11.38	-32.12	-2.76	-2.41
F	Cl	-16.29	-11.38	-29.93	-2.26	-2.15
CN	Cl	-13.43	-11.38	-26.37	-1.56	-1.74
NO ₂	Cl	-12.70	-11.38	-25.47	-1.39	-1.62
NH ₂	Br	-19.73	-15.02	-40.59	-5.84	-6.93
CH ₃ O	Br	-16.81	-15.02	-37.09	-5.26	-6.25
CH ₃	Br	-17.72	-15.02	-37.81	-5.07	-6.08
OH	Br	-16.74	-15.02	-36.66	-4.90	-5.84
H	Br	-17.42	-15.02	-37.10	-4.66	-5.6
F	Br	-13.41	-15.02	-32.39	-3.95	-4.82
CN	Br	-6.95	-15.02	-24.85	-2.87	-3.57
NO ₂	Br	-4.10	-15.02	-21.73	-2.61	-3.32

^aAll energies are given in kJ mol⁻¹.

the stabilization energy of the (ClCN)₂ and (BrCN)₂ dimers that shows the latter is more stable than the former (-11.4 vs -15.0 kJ/mol, respectively).

With respect to the stabilization-energy variation of the pyridine ring substituents, a parallel tendency to that of the intermolecular distances is observed. Thus, the shortest intermolecular distance, Z = NH₂, corresponds to the most stable complex in each series, whereas the longest distance, Z = NO₂, is the least stable complex. Good linear correlations are found between the N...X intermolecular distance in the AB dimers within the ABC ternary complex and the stabilization energy (Figure 2). Similar correlations are obtained when the intermolecular distances in the AB complexes are compared to the corresponding stabilization energies.

The natural energy-decomposition analysis (NEDA) within the natural bond orbital (NBO) methodology has been

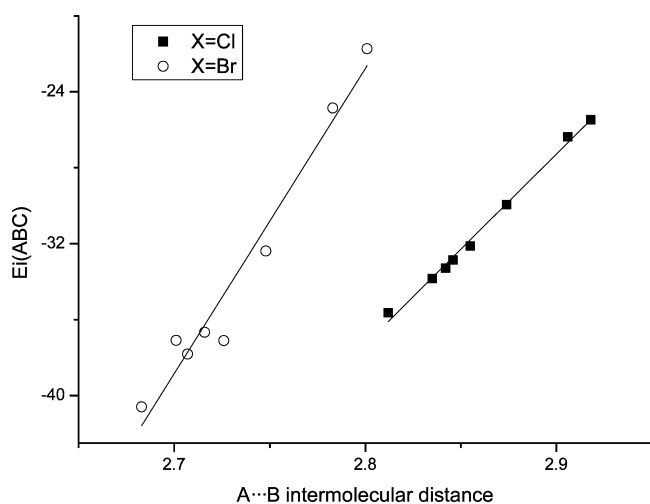


Figure 2. N...X intermolecular distance in the A...B molecules within the ternary complexes versus the stabilization energy (kJ/mol). The linear correlations show R^2 values of 0.99 and 0.95 for X = Cl and Br, respectively.

performed to obtain insight into the source of the interaction energy (Tables 3 and 4). This methodology divides the

Table 3. Natural Energy Decomposition Analysis (kcal mol⁻¹) of the Binary Complexes at the M05-2X/6-31+G(d,p)-LanL2DZdp Computational Level

Z	X	CT ^a	ES ^a	POL ^a	XC ^a	DEF ^a	TOT ^a
NH ₂	Cl	-8.62	-8.72	-18.54	-6.66	37.11	-5.43
CH ₃ O	Cl	-8.16	-8.12	-17.83	-6.59	35.64	-5.06
CH ₃	Cl	-8.03	-7.97	-17.81	-6.40	35.25	-4.96
OH	Cl	-7.98	-7.86	-17.34	-6.31	34.61	-4.88
H	Cl	-7.78	-7.62	-17.28	-6.26	34.19	-4.75
F	Cl	-7.38	-6.97	-16.24	-5.95	32.23	-4.31
CN	Cl	-6.59	-5.83	-14.83	-5.42	29.06	-3.61
NO ₂	Cl	-6.26	-5.45	-14.25	-5.26	27.83	-3.39
NH ₂	Br	-16.72	-15.80	-35.57	-10.07	69.64	-8.52
CH ₃ O	Br	-15.82	-14.81	-34.44	-10.73	67.85	-7.95
CH ₃	Br	-15.57	-14.49	-34.19	-9.76	66.25	-7.76
OH	Br	-15.07	-14.05	-33.12	-9.61	64.24	-7.61
H	Br	-14.57	-13.52	-32.54	-9.77	63.00	-7.40
F	Br	-13.46	-12.27	-30.59	-9.54	59.14	-6.72
CN	Br	-12.15	-10.60	-28.68	-9.00	54.75	-5.68
NO ₂	Br	-11.12	-9.94	-27.68	-8.69	52.07	-5.36

^aCharge-transfer (CT), electrostatic (ES), polarization (POL), exchange-correlation (EX), and deformational (DEF) components and the total interaction energy (TOT).

Table 4. Natural Energy Decomposition Analysis (kcal mol⁻¹) of the Ternary Complexes at the M05-2X/6-31+G(d,p)-LanL2DZdp Computational Level

Z	X	CT ^a	ES ^a	POL ^a	XC ^a	DEF ^a	TOT ^a
NH ₂	Cl	-14.49	-13.58	-35.13	-11.64	65.76	-9.08
CH ₃ O	Cl	-13.75	-12.76	-33.68	-11.26	62.82	-8.63
CH ₃	Cl	-13.53	-12.49	-33.43	-11.12	62.06	-8.51
OH	Cl	-13.41	-12.34	-32.71	-10.97	61.04	-8.39
H	Cl	-13.07	-11.99	-32.33	-10.86	60.00	-8.25
F	Cl	-12.50	-11.18	-30.78	-10.44	57.21	-7.69
CN	Cl	-11.60	-9.94	-28.99	-9.85	53.55	-6.83
NO ₂	Cl	-11.25	-9.52	-28.25	-9.60	52.05	-6.57
NH ₂	Br	-27.63	-23.59	-65.22	-16.63	119.20	-13.87
CH ₃ O	Br	-26.27	-22.33	-63.06	-17.91	116.49	-13.08
CH ₃	Br	-25.74	-21.90	-62.61	-16.96	114.33	-12.88
OH	Br	-25.33	-21.44	-61.33	-16.89	112.31	-12.68
H	Br	-24.66	-20.79	-60.55	-16.22	109.81	-12.41
F	Br	-23.24	-19.37	-57.84	-16.13	105.00	-11.58
CN	Br	-21.31	-17.20	-54.69	-15.24	98.20	-10.24
NO ₂	Br	-20.52	-16.37	-53.29	-14.69	95.04	-9.83

^aCharge-transfer (CT), electrostatic (ES), polarization (POL), exchange-correlation (EX), and deformational (DEF) components and the total interaction energy (TOT).

interaction energy into several attraction components. These include the orbital-charge transfer that arises from the delocalization of an electron from one monomer to another, the electrostatic interaction of the monomers, the polarization, and the exchange-correlation terms. Finally, a repulsion component is considered that takes into account the electronic deformation resulting from the complex formation in each monomer. In all of the dyads and triads, the most important stabilizing component is polarization, which corresponds between 44 and 51% of all of the attraction terms. The second

most important attraction term in the ternary complexes is the charge transfer, which is closely followed by the electrostatic interaction, leaving the exchange correlation as being the least important. The average contribution of these three terms in the ternary complexes is 20, 17 and 15%, respectively. In the case of the binary complexes, the contribution of the attraction terms follows the same ranking, with average values of 45, 20, 19 and 15% for the polarization, charge transfer, electrostatic, and exchange-correlation terms, respectively.

3.3. Cooperativity. Two methods to compute the cooperativity (nonpairwise-interaction energy) (Table 2) have been considered in this Article. In the first, the cooperativity was calculated using eq 3.^{32,33}

$$E_{\text{coop}} = \Delta E(\text{ABC}) - \Delta E(\text{AB}) - \Delta E(\text{BC}) - \Delta^2 E(\text{AC}) \quad (3)$$

where $\Delta E(\text{ABC})$ is the stabilization energy of the trimer, $\Delta E(\text{AB})$ and $\Delta E(\text{BC})$ are the stabilization energy of the isolated dimers within their corresponding minima configuration, and $\Delta^2 E(\text{AC})$ is the interaction energy of molecules A and C in the geometry that they possess in the trimer.

In the second approach, the many-body interaction-energy methodology was used.³⁴ In this methodology, the stabilization energy, $\Delta E(\text{ABC})$, of a ternary complex is defined as the difference between the energy of the complex at its equilibrium geometry and either the sum of the isolated molecules or the sum of the one, two, and three body terms (eqs 4–7).

$$\begin{aligned} E_{\text{r}}(\text{ABC}) &= E(\text{ABC}) - [E_{\text{iso}}(\text{A}) + E_{\text{iso}}(\text{B}) + E_{\text{iso}}(\text{C})] \\ &= [E_{\text{r}}(\text{A}) + E_{\text{r}}(\text{B}) + E_{\text{r}}(\text{C})] \\ &\quad + [\Delta^2 E(\text{AB}) + \Delta^2 E(\text{AC}) + \Delta^2 E(\text{BC})] \\ &\quad + \Delta^3 E(\text{ABC}) \end{aligned} \quad (4)$$

$$E_{\text{r}}(\text{A}) = E(\text{A}) - E_{\text{iso}}(\text{A}) \quad (5)$$

$$\Delta^2 E(\text{AB}) = E(\text{AB}) - [E(\text{A}) + E(\text{B})] \quad (6)$$

$$\begin{aligned} \Delta^3 E(\text{ABC}) &= E(\text{ABC}) - [E(\text{A}) + E(\text{B}) + E(\text{C})] \\ &\quad - [\Delta^2 E(\text{AB}) + \Delta^2 E(\text{AC}) + \Delta^2 E(\text{BC})] \end{aligned} \quad (7)$$

where $E(\text{A})$, $E(\text{AB})$, and $E(\text{ABC})$ are the energy of monomer A, the binary AB complex, and the ternary ABC complex, respectively, within the geometry of the complexes. $E_{\text{iso}}(\text{A})$ is the minimum energy of the isolated monomer. The first term of the equation is known as relaxation, the second is associated with the two-body interaction, and the third, with the three body. The three-body term within this methodology is considered the nonpairwise term (cooperativity).

Excellent linear correlations are found between E_{coop} and $\Delta^3 E(\text{ABC})$ for the chlorine and bromine complexes (R^2 of 0.997 and 0.999, respectively). In all cases studied, a favorable cooperativity is observed. This cooperative energy is much larger in complexes associated with bromine halogen bonds than it is in the ones with chlorine. A clear relationship is obtained between the total stabilization energy in the ternary complexes and the calculated cooperativity (R^2 of 0.999 and 0.96 for the chlorine and bromine complexes, respectively).

3.4. Electronic Properties of the Complexes. The electronic properties of the complexes have been analyzed using two methodologies: NBO and AIMs. The NBO analysis provides complementary information about the direction and

magnitude of the charge transfer between empty and occupied orbitals. The data supplied in Table 5 corresponds to the

Table 5. Second-Order Perturbation Stabilization Energy, E^2 $\text{LP}(\text{N}) \rightarrow \sigma^*(\text{X}-\text{C})$ (kcal mol⁻¹), in the Investigated Dimers and Trimers (T) at the B97-1/6-31+G(d,p)-LanL2DZdp Level

Z	X	$E^2_{\text{AB}}(\text{T})$	E^2_{AB}	$E^2_{\text{BC}}(\text{T})$	E^2_{BC}
NH ₂	Cl	3.79	3.24	1.41	1.09
CH ₃ O	Cl	3.48	3.03	1.38	1.09
CH ₃	Cl	3.38	2.97	1.36	1.09
OH	Cl	3.34	2.95	1.35	1.09
H	Cl	3.2	2.86	1.33	1.09
F	Cl	2.98	2.68	1.3	1.09
CN	Cl	2.61	2.3	1.24	1.09
NO ₂	Cl	2.48	2.17	1.23	1.09
NH ₂	Br	11.45	9.59	3.49	2.61
CH ₃ O	Br	10.65	9.03	3.41	2.61
CH ₃	Br	10.36	8.8	3.37	2.61
OH	Br	10.12	8.54	3.35	2.61
H	Br	9.71	8.18	3.31	2.61
F	Br	8.95	7.51	3.21	2.61
CN	Br	7.75	6.61	3.11	2.61
NO ₂	Br	7.29	6.26	3.08	2.61

second-order perturbation stabilization energy ($E^{(2)}$) resulting from the charge transfer from the lone pair of the halogen-accepting N atom to the σ^* orbital of the X–C covalent bond. In all of the cases, the $E^{(2)}$ values are larger in the trimers than they are in the dimers both in the A···B interaction as well as in the B···C. These results are another indication of the cooperative effect in the studied ternary complexes.

It is interesting to note that when bromine is the interacting halogen atom the $E^{(2)}$ values are much larger (up to 3 times) than those obtained in similar complexes in which the interacting atom is chlorine. In addition, the A···B interactions show larger values than those of the B···C interactions for each halogen atom, which is an indication that the nitrogen atom of the pyridine is a better electron donor than the nitrogen atom of the NCX molecule.

The values of the $E^{(2)}$ in the different complexes follow the same tendencies as those observed for the dimers and trimers as a function of the pyridine substituents. Thus, the stronger and weaker interactions correspond to the NH₂ and NO₂ substituents, respectively.

The electron density at the critical points of the halogen bond follows an exponential relationship in which the interatomic distance between the interacting atoms is in agreement with the results previously reported for a variety of weak interactions.^{35–37} In agreement with the relationship previously mentioned, a larger electron density is found in the BCP of the ternary complexes than that of the corresponding binary complexes (Table 6). The cooperative effect in the topological parameters is clearly due to the enhancement of the values in the ternary complexes when compared to those in the corresponding binary complexes. As expected, the enhancement is larger in the bromine complexes than it is in the chlorine complexes.

3.5. Quantum Chemical Parameters and Hammett Constants Relationships. A number of parameters have been used in the literature to correlate the properties of the isolated molecules with other properties in the complexes. Among the properties used to characterize the monomers, the effect of the

Table 6. Changes in Electron Density, ρ (au), and Laplacian, $\nabla^2\rho$ (au), at the N–X Bond Critical Points in the 4-Z-Py \cdots XCN \cdots XCN Ternary Complexes Relative to the Respective Binary Complex Calculated at the B97-1/6-31+G(d,p)-LanL2DZdp 1 Level

Z	X	$\Delta\rho_{AB}$	$\Delta\nabla^2\rho_{AB}$	$\Delta\rho_{BC}$	$\Delta\nabla^2\rho_{BC}$
NH ₂	Cl	0.0016	0.0053	0.0013	0.0053
CH ₃ O	Cl	0.0013	0.0043	0.0012	0.0048
CH ₃	Cl	0.0012	0.0039	0.0011	0.0046
OH	Cl	0.0011	0.0037	0.0011	0.0044
H	Cl	0.0010	0.0034	0.0010	0.0040
F	Cl	0.0009	0.0030	0.0009	0.0035
CN	Cl	0.0010	0.0035	0.0007	0.0027
NO ₂	Cl	0.0011	0.0036	0.0006	0.0023
NH ₂	Br	0.0027	0.0082	0.0019	0.0076
CH ₃ O	Br	0.0025	0.0075	0.0017	0.0069
CH ₃	Br	0.0024	0.0075	0.0017	0.0066
OH	Br	0.0025	0.0076	0.0016	0.0064
H	Br	0.0024	0.0077	0.0015	0.0060
F	Br	0.0024	0.0077	0.0013	0.0052
CN	Br	0.0020	0.0065	0.0011	0.0043
NO ₂	Br	0.0019	0.0061	0.0011	0.0042

substituents on the properties of aromatic systems, known as Hammett constants, are the most extensively used.³⁸ The values of the Hammett constants for the substituents studied here are presented in Table 7. The linear relationships established

Table 7. Hammett Constants, NPA Charges (q , e) on the N Atom, Minimum Electrostatic Potentials, $V_{S,min}$ (kcal mol⁻¹), and Minimum Average Local Ionization Energies, $\bar{I}_{S,min}$ (eV), on the 0.001 au Electron Density Isosurface of the Isolated Pyridine Derivatives at the B97-1/6-31+G(d,p)-LanL2DZdp Level

Z	σ_p	q	$V_{S,min}$	$\bar{I}_{S,min}$
NH ₂	-0.66	-0.494	-42.624	7.564
CH ₃ O	-0.27	-0.482	-40.111	7.742
CH ₃	-0.17	-0.464	-39.354	7.782
OH	-0.37	-0.481	-38.631	7.837
H	0	-0.457	-37.623	7.883
F	0.06	-0.467	-34.187	8.149
CN	0.66	-0.435	-27.982	8.588
NO ₂	0.78	-0.428	-26.560	8.696

between the A \cdots B interatomic distances for the binary and ternary complexes and the σ_p constants have R^2 values between 0.96 and 0.93. In the same way, the correlations between the stabilization energy of the binary and ternary complexes and the σ_p constants have R^2 values between 0.96 and 0.91. Finally, good linear relationships between E_{coop} and σ_p ($R^2 = 0.95$ and 0.95 for X = Cl and Br, respectively) are depicted in Figure 3. Similar results are obtained when $\Delta^3E(ABC)$ is considered as the cooperativity parameter ($R^2 = 0.96$ and 0.95, respectively).

Among the different atomic descriptors used in correlations with the stabilization energies, the NBO atomic charges of the nitrogen atom of the pyridine, the electrostatic-potential minima,²⁷ and the minima of the ionization energy, I ,^{28,29} on an 0.001 au electron-density isosurface of the isolated monomer are considered. These three parameters show linear correlations with the corresponding σ_p , with R^2 values of 0.95 in all cases.

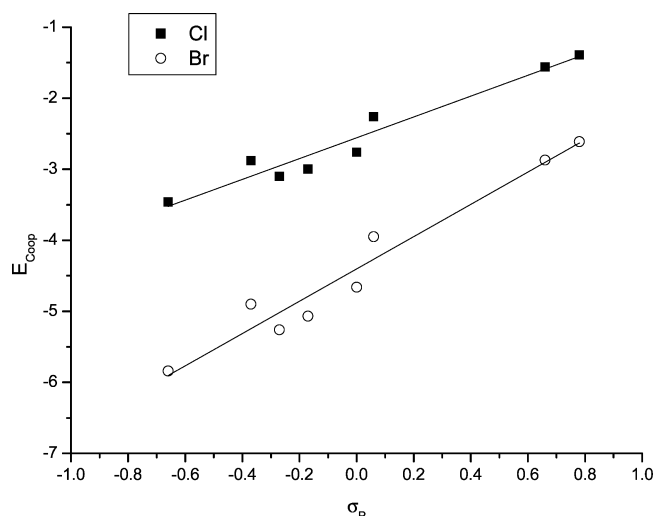


Figure 3. E_{coop} (kJ mol⁻¹) versus Hammett constants σ_p . The linear relationships show R^2 values of 0.95 for both X = Cl and Br.

Excellent linear relationships between the electrostatic-potential minima values of the isolated pyridines and the stabilization energies are obtained ($R^2 = 0.998$, 0.998, 0.97, and 0.98 for the binary and ternary complexes of X = Cl and Br, respectively). These results are in agreement with recent reports for several series of halogen-bonded complexes.³⁹ Similarly, the use of $\bar{I}_{S,min}$ provides excellent linear correlations with the stabilization energies.

Finally, both $V_{S,min}$ and $\bar{I}_{S,min}$ are excellent descriptors of the cooperativity, with R^2 values above 0.99 in their relationships with E_{coop} (Figure 4) and $\Delta^3E(ABC)$.

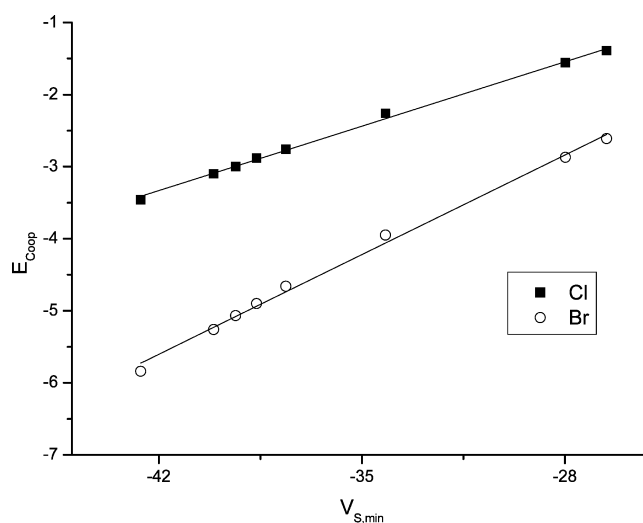


Figure 4. E_{coop} (kJ mol⁻¹) versus the surface minima around the nitrogen atom of the substituted pyridine, $V_{S,min}(N)$ (kcal mol⁻¹). The linear relationships show R^2 values of 0.998 and 0.996 for X = Cl and Br, respectively.

4. CONCLUSIONS

Density functional calculations at the B97-1/6-31+G(d,p)-LanL2DZdp computational level were used to explore the cooperativity in 4-Z-Py \cdots XCN \cdots XCN (Z = H, F, OH, OCH₃, CH₃, NH₂, NO₂, and CN; Py = pyridine; and X = Cl and Br) ternary complexes.

The equilibrium structures, energetics, and cooperative effects on the properties of the complexes were analyzed. Linear correlations between the stabilization energy and the intermolecular distances have been obtained. In all of the ternary complexes studied, the values of the cooperativity obtained are negative, which indicates that the ternary complex is more stable than the sum of the two isolated binary complexes. In addition, a linear relationship is found between the cooperativity and the total stabilization energy in the ternary complexes. The most stable complexes are the ones showing the larger absolute values for cooperativity.

Very good linear correlations are established between the cooperativity energies and the molecular parameters of the isolated pyridine derivatives, such as the Hammett constant, $V_{S,min}$, and $I_{S,min}$ surrounding the N atom of the aromatic ring. The most stable complexes are formed by the electron-donating substituents, whereas the least stable ones, by electron-withdrawing substituents.

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Notes

The authors declare no competing financial interest.

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