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Ab Initio Investigation of the Complexes between Bromobenzene and Several Electron Donors: Some Insights into the Magnitude and Nature of Halogen Bonding Interactions

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Halogen bonding, a specific intermolecular noncovalent interaction, plays crucial roles in fields as diverse as molecular recognition, crystal engineering, and biological systems. This paper presents an ab initio investigation of a series of dimeric complexes formed between bromobenzene and several electron donors. Such small model systems are selected to mimic halogen bonding interactions found within crystal structures as well as within biological molecules. In all cases, the intermolecular distances are shown to be equal to or below sums of van der Waals radii of the atoms involved. Halogen bonding energies, calculated at the MP2/aug-cc-pVDZ level, span over a wide range, from −1.52 to −15.53 kcal/mol. The interactions become comparable to, or even prevail over, classical hydrogen bonding. For charge-assisted halogen bonds, calculations have shown that the strength decreases in the order $OH^- > F^- > HCO_2^- > Cl^- > Br^-$, while for neutral systems, their relative strengths attenuate in the order $H_2CS > H_2CO > NH_3 > H_2S > H_2O$. These results agree with those of the quantum theory of atoms in molecules (QTAIM) since bond critical points (BCPs) are identified for these halogen bonds. The QTAIM analysis also suggests that strong halogen bonds are more covalent in nature, while weak ones are mostly electrostatic interactions. The electron densities at the BCPs are recommended as a good measure of the halogen bond strength. Finally, natural bond orbital (NBO) analysis has been applied to gain more insights into the origin of halogen bonding interactions.

Introduction

Intermolecular forces have attracted increasing interest in diverse fields of chemistry due to their significance in determining the three-dimensional structure of a large number of important molecules, such as proteins, DNA, and enzyme−substrate complexes. Among them, hydrogen bonding is the most particularly noteworthy case and has been extensively studied from both theoretical and experimental viewpoints. In recent years, a specific intermolecular interaction involving halogen atoms as acceptors of electron density has been under active investigation. Such an interaction is now referred to as halogen bonding to emphasize its striking similarities with classical hydrogen bonding. Indeed, most of the energetic and structural features probed in hydrogen-bonded complexes are reproduced in halogen-bonded complexes as well. On account of its strength, selectivity, and directivity, halogen bonding has led to a great many applications in fields as various as molecular recognition, enantiomers's separation, crystal engineering, and supramolecular architectures.[1−25] Particularly, the utilization of this specific interaction in the context of drug design is nowadays coming to light clearly.[3,26−30]

The formation of halogen bonding interactions can be rationalized on the basis of two computational findings: (1) the presence of a small positive electrostatic potential end cap along the C−X bond vectors (except for fluorine) and, therefore, electronegative atoms/groups located in a position to meet this positive cap that results in a linear arrangement; and (2) the anisotropic distribution of electron density around halogen atoms, that is, there are two different radii of halogens, a shorter one along the C−X bond and a longer one perpendicular to it. Of peculiar interest is that halogens exhibit both electrophilic character along the axes of the C−X bonds and nucleophilic character along vectors perpendicular to these bonds. In other words, halogen atoms can form both a halogen bond with nucleophiles (lone-pair-possessing atoms, frequently N, O, and S), displaying a roughly linear arrangement, and a hydrogen bond with electrophiles (hydrogen bond donors), occurring in the side-on fashion. We have, in a very recent work, investigated this unique amphoteric character of covalently bonded halogen atoms by means of ab initio calculations.[31]

The potential of halogen bonding shown by useful applications in the fields of synthetic chemistry, material science, and bioorganic chemistry was overviewed by Resnati and co-workers.[3] They mainly focused on interactions involving halocarbons and on the supramolecular architectures that they produce. More recently, Metrangolo et al. have described the prime importance of halogen bonding in the design of new and high-value engineering functional materials.[10] Nonetheless, the implications of halogen bonding, or halogen to oxygen (nitrogen and sulfur) interactions that are equal to or below the van der Waals radius sums, in biological molecules are only now emerging. These short contacts have rarely been observed in biological systems, probably attributed to the scarcity of available crystal structures of halogenated biomolecules to date. Recently, Auffinger and co-workers have screened and assembled a data set of protein and nucleic acid structures to characterize the prevalence and geometry of halogen bonding in biological systems.[26] Their data set primarily includes short X···O interactions with carbonyl (C=O), hydroxyl (O−H), or

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negatively charged acid (−O−C/P/S) groups. They also pointed out that halogen bonding offers potent tools for the design of ligands as drugs and materials.

Halogen bonding has, undoubtedly, been the subject of tremendous theoretical studies.[32−48] The key geometrical and energetic aspects of this interaction are fairly well established. For example, Riley et. al recently yielded potential energy curves for halogen bonding in some halobenzene−formaldehyde complexes and found that interaction energies heighten as the size of the halogen atoms increases. With a view to understand the behavior of halogen bonding interactions in large systems (e.g., biologically relevant molecules), it becomes essential to perform high-order calculations on small model systems selected to mimic the interactions found within the real systems of interest since the enormous size of real systems render accurate calculations out of reach. The behavior of the small model systems can subsequently be traced back to the real systems. A detailed analysis of small model systems that contain halogen bonding elements commonly discovered in real systems should be of vital importance for our understanding of crystal packing and molecular recognition processes in biological systems.

In this work, we perform a theoretical study at a reliable level of ab initio calculations on a series of dimeric complexes formed between bromobenzene and several electron donors: H_2CO, H_2O, OH^-, HCO_2^-, NH_3, H_2S, H_2CS, F^-, Cl^-, and Br^-. These small model systems are selected to mimic halogen bonding found within crystal structures as well as within biological molecules. Such a theoretical study may provide some valuable information of the origin and strength of halogen bonding interactions, which would be very important for the design and synthesis of new materials and effective drugs containing halogenated compounds.

Computational Details

The geometries of all of the monomers and complexes were fully optimized by using the SCF and MP2 methods in combination with Dunning's correlation-consistent basis set, aug-cc-pVDZ. No symmetry assumption was made in the optimization of dimer structures. Core electrons were not included in the correlation treatment with MP2 calculations, namely, the MP2 frozen core (FC) method was adopted. Analytical computations of vibrational frequencies at the HF/aug-cc-pVDZ level were preformed to ensure that the optimized structures found corresponded to genuine minima on the potential energy surface and to determine the zero-point energy (ZPE) corrections, thermal corrections, and entropy values. All of these calculations were carried out with the aid of the Gaussian 03 suite of programs.[49]

The MP2/aug-cc-pVDZ method has been widely used to investigate various nonbonded interactions, such as hydrogen bonding,[50] bromine bonding,[40] C−H/π,[51] and C−Br/π[52] interactions, and can obtain fairly accurate geometries and interaction energies of numerous intermolecular complexes. We thus believe that this computational approach is adequate (and also viable) for describing the halogen-bonded dimers considered in this work. To check the energy convergence, single-point calculations on the MP2/aug-cc-pVDZ geometries were also carried out at the MP2/aug-cc-pVTZ level.

The interaction energy (ΔE_{int}) was calculated as the difference between the total energy of the complex and the sum of total energies of the two monomers. The basis set superposition error (BSSE) was eliminated in terms of the counterpoise method of Boys and Bernardi.[53] Here, we employed a 50% BSSE correction for the interaction energy. Unless otherwise noted, the interaction energies reported in this work were corrected by BSSE. Natural bond orbital (NBO)[54] analysis was employed by the use of the NBO program implemented in the Gaussian 03 package. The quantum theory of atoms in molecules (QTAIM)[55] analysis was preformed with the help of AIM 2000 software[56] using the wave functions generated at the MP2/aug-cc-pVDZ level.

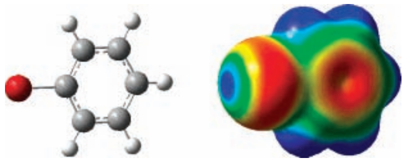


Figure 1. The electrostatic potential mapped on the surface of molecular electron density (0.002 e au^{-3}). The electrostatic potential varies between −0.020 (red) and +0.020 (blue) au.

Results and Discussion

Geometrical and Energetic Results. The graphical illustration of the electrostatic potential surface for bromobenzene is shown in Figure 1. It is clear that there exists a small positive electrostatic potential cap at the end region of the Br atom along the C−Br bond vector, which is surrounded by an electroneutral area and, next, a large electronegative domain. An electronegative atom/group prefers to approach the positive cap, thereby giving rise to a directional interaction. In a very recent article, the positive cap of halogen atoms was referred to as the "σ-hole" that intersects the C−X axis.[47]

The MP2/aug-cc-pVDZ-optimized molecular structures of the complexes under investigation are depicted in Figure 2. The majority of the systems examined here present multiple minima. In this work, however, we consider only the minimum associated with halogen bonding, albeit in some cases, it may not be the global minimum on the potential energy surface. From Figure 2, it can be seen that the intermolecular contacts are in a range from 2.333 to 3.670 Å. These separations are less than the sums of van der Waals (vdW) radii[57] of the atoms involved, with one exception. In the case of PhBr···SH_2, the Br···S distance is slightly longer than the vdW radius sum of the bromine and sulfur atoms (3.65 Å), implying a very weak halogen bond in this complex. The dimers PhBr···F^- and PhBr···OH^- exhibit the shortest halogen bonding distance (about 2.34 Å) among the systems considered. This is not surprising considering the strongest halogen bonds present in these two complexes (vide infra).

For the complexes PhBr···OCH_2 and PhBr···SCH_2, two stationary structures associated with halogen bonding, as shown in Figure 2, have been observed. In the A complexes, all of the atoms in the formaldehyde (or methanethione) and bromobenzene molecules are in the same plane, while in the B complexes, the H atoms in formaldehyde (or methanethione) are in a plane perpendicular to the benzene ring. In the latter perpendicular conformations, it is the π electron density, rather than the O/S nonbonding electron pairs, that serves as the electron donor. However, the A complexes are only about 0.05 kcal/mol less stable than the corresponding B complexes, and as a consequence, in the next discussions, we only focus on the results of the A complexes. In fact, the energetic preference of the π systems as electron donors cannot be neglected in protein structures because the O/S nonbonding electron pairs of the C═O/C═S are often involved in hydrogen bonds with adjacent groups (e.g., C═O/C═S···H−N).[26]

For most of the dimers studied, it has been shown that the optimized equilibrium C−Br···Y (Y represents atoms that

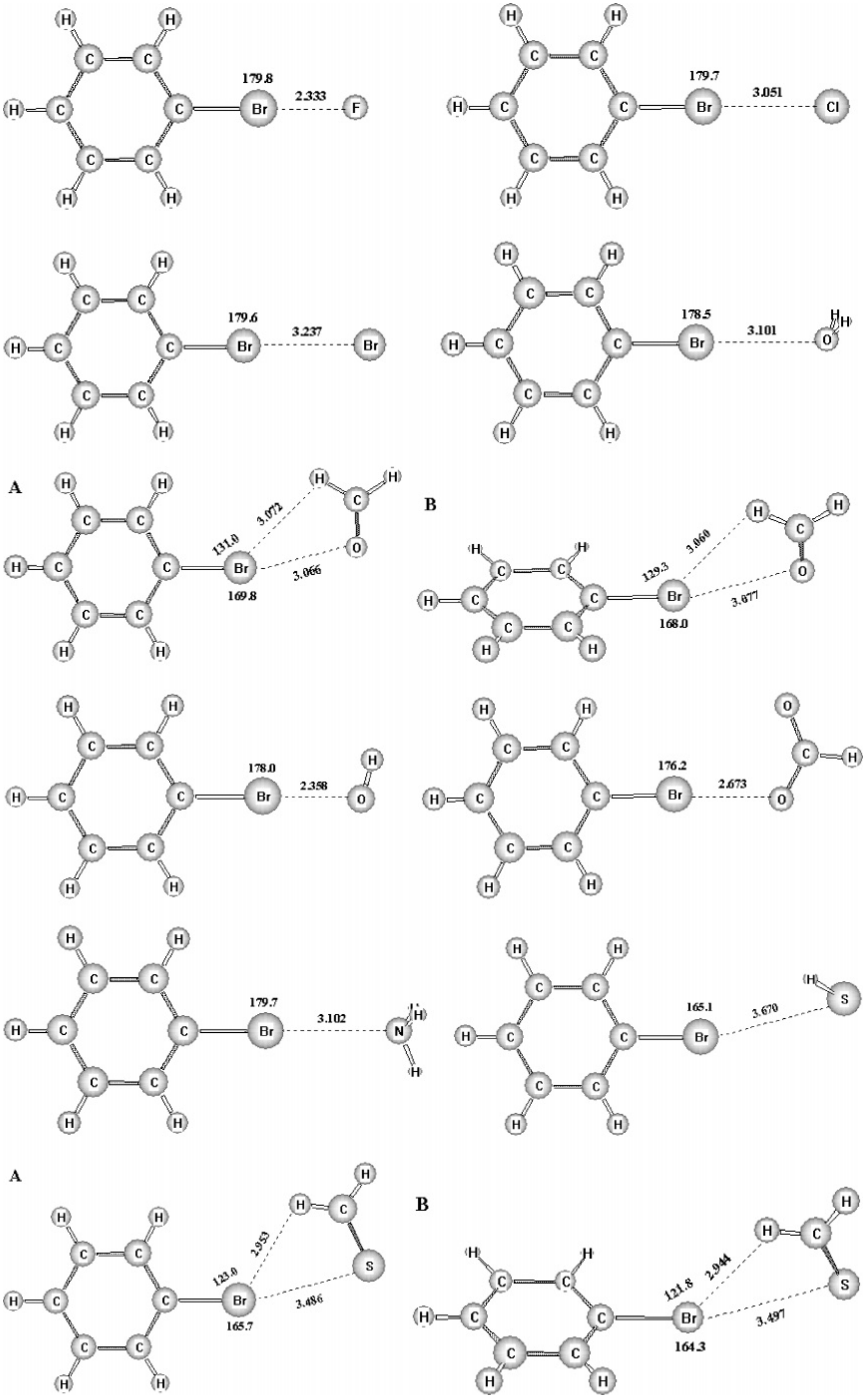


Figure 2. MP2/aug-cc-pVDZ-optimized geometries of the complexes. Bond lengths are in Å, and bond angles are in degrees.

possess lone-pair electrons) contacts are essentially linear. The C−Br···Y angles are all very close to 180°, except for the complexes PhBr···SH_2, PhBr···OCH_2, and PhBr···SCH_2, in which a significant departure from linearity occurs. The

TABLE 1: Calculated Interaction Energies (kcal/mol) and ΔS_{298} (eu)

complexes	ΔE_{int}	$\Delta E_{int}^{CP\ a}$	$\Delta E_0{}^b$	$\Delta E_{int,aVTZ}{}^c$	$\Delta E_{int,HF}{}^d$	ΔS_{298}
PhBr···F$^-$	−15.45	−14.64	−15.15	−15.40	−9.23	−23.53
PhBr···Cl$^-$	−7.01	−6.38	−6.81	−7.11	−0.46	−21.48
PhBr···Br$^-$	−6.62	−5.57	−6.47	−6.48	0.72	−21.72
PhBr···OCH$_2$	−2.98	−2.26	−1.13	−2.66	0.37	−33.05
PhBr···OH$_2$	−1.97	−1.52	0.93	−1.65	0.09	−28.42
PhBr···OH$^-$	−16.72	−15.53	−14.35	−16.33	−7.77	−29.71
PhBr···OOCH$^-$	−8.38	−7.45	−7.08	−7.89	−2.12	−37.36
PhBr···NH$_3$	−2.75	−2.15	−0.44	−2.21	0.14	−29.01
PhBr···SH$_2$	−2.12	−1.62	−0.67	−2.01	0.69	−27.30
PhBr···SCH$_2$	−3.48	−2.76	−2.06	−3.29	1.10	−32.53

[a] ΔE_{int}^{CP} are BSSE-corrected energies. [b] ΔE_0 are ZPE-corrected energies. [c] MP2/aug-cc-pVTZ energies. [d] HF/aug-cc-pVDZ energies.

C−Br···Y angles of these three dimers are predicted to be 165.1, 169.8, and 165.7°, respectively, which fall into the statistical scope of halogen bonding found in biological molecules (160−170°).[26] It should be pointed out that, for the systems involving H_2CO and H_2CS, there might exist a secondary interaction between the bromine atom and one of the hydrogen atoms of H_2CO or H_2CS. In fact, the Br···H (H_2CO or H_2CS) distances in the two cases, computed at the MP2/aug-cc-pVDZ level of theory, amount to about 3.07 and 2.95 Å, respectively, which are equal to or below the sum of the vdW radii of H and Br (3.05 Å). A topological analysis of the electron density reveals the presence of a bond critical point between the bromine atom and the hydrogen atom, that is to say, in the two complexes, there is a Br···H secondary hydrogen bond. On the other hand, calculations also show that the C−Br···H angles of the two dimers are 131.0 and 123.0°, respectively. In light of these computational findings, we are able to conclude that the bromine atom of bromobenzene is involved in a bifurcated interaction: a halogen bond in the “head-on” orientation and a hydrogen bond in the “side-on” fashion, which is in line with the amphoteric character of covalently bonded bromine atom (vide supra). In the same way, in the more complex biological systems, some deviations from the linearity for halogen bonding can be expected, ascribed to a double interaction of halogens involved. Interestingly, the C−Br···S angle in the dimer PhBr···SH$_2$ deviates from the linearity substantially as compared to the C−Br···O angle in PhBr···OH$_2$ (165 vs 178°). A simple rationale for this behavior may be that the sulfur atom shows an effect of polarity that is stronger than that of the oxygen atom, as also indicated by the larger C−Br···O angle in the dimer PhBr···OCH$_2$ relative to the C−Br···S angle in PhBr···SCH$_2$ (170 vs 166°). Additionally, in the three complexes involving H_2CS, H_2CO, and HCO_2^-, the C−O(S)···Br angles are in the 80−115° range, indicating that the Br atom interacts efficiently with the lone pairs of the O or S atom. Notice that all of the predicted Br···O distances (2.358−3.101 Å) are somewhat shorter than the average statistical value of those found in biological molecules (3.15 Å),[26] which is presumably a result of the steric effect in large systems (e.g., protein environment).

The interaction energies without (ΔE_{int}) and with BSSE corrections (ΔE_{int}^{CP}) for the complexes under study at various levels are summarized in Table 1. Also listed are the calculated values of ΔS at 298 K. From these data, it is apparent that MP2/aug-cc-pVDZ halogen bonding energies vary within a wide range, from −1.97 to −16.72 kcal/mol for ΔE_{int} and from −1.52 to −15.53 kcal/mol for ΔE_{int}^{CP}. The interactions become comparable to, or even prevail over, classical hydrogen bonding. By virtue of its strength and directionality, halogen bonding can be recognized as a driving force that influences the alignment of molecules in crystals so as to offer remarkable possibilities for designing and developing new materials as well as drugs involving halogenated compounds. A comparison of the ΔE_{int} values calculated at the MP2/aug-cc-pVDZ and MP2/aug-cc-pVTZ levels shows that the interaction energies are insensitive to the basis set. The mean absolute deviation of the MP2/aug-cc-pVDZ energies from the MP2/aug-cc-pVTZ ones is only 7.8%. Moreover, the values of ΔE_{int} and ΔE_{int}^{CP} calculated at the MP2/aug-cc-pVDZ level correlate very well with the ΔE_{int} values obtained with MP2/aug-cc-pVTZ (the correlation coefficients are both as high as 0.999). These results obviously indicate the reasonability of the MP2/aug-cc-pVDZ method applied in this work, especially in describing the relative halogen bond strengths. Note that the entropy term disfavors the formation of the complexes due to the negative ΔS values.

Inspection of Figure 2 and Table 1 reveals that the intermolecular distances increase in the order $F^- < Cl^- < Br^-$, which is the opposite trend shown in the interaction energies. The ΔE_{int}^{CP} values of the complexes of F^-, Cl^-, and Br^- with PhBr are −14.64, −6.37, and −5.57 kcal/mol, respectively. That is, upon complexation with PhBr, F^- forms the strongest halogen bond, followed by Cl^- and Br^-. For all charge-assisted systems, the halogen bond strength decreases in the following order: $OH^- > F^- > HCO_2^- > Cl^- > Br^-$. This tendency agrees with the basicity order of these five anions. As anticipated, charge-assisted halogen bonds are much stronger relative to neutral ones. For example, the halogen bonding energy of PhBr···OH$^-$ is almost 1 order of magnitude larger than that of PhBr···OH$_2$. By performing calculations at the MP2/aug-cc-pVDZ level of theory, we estimate the halogen bonding energy to be −1.52 kcal/mol for PhBr···OH$_2$ and −15.53 kcal/mol for PhBr···OH$^-$. In view of a number of C−X···O−Y (O−Y is carbonyl, hydroxyl, or negatively charged acid groups) interactions found in biological macromolecules,[26] we also take into account four electronegative groups containing the oxygen atom, H_2O, H_2CO, HCO_2^-, and OH^-. The present calculations have elucidated that the interaction energies increase in the order $H_2O < H_2CO < HCO_2^- < OH^-$, whereas the intermolecular Br···O separations vary in the reverse order. Upon going from H_2O to OH^-, the interaction energy is enhanced by 0.74−8.08 kcal/mol. Variations in the Br···O distances, which are shortened by 0.03−0.4 Å, are also observed. It is noteworthy that a large interaction energy is predicted for the complex PhBr···OCH$_2$ as compared to that for PhBr···OH$_2$ (−2.26 vs −1.52 kcal/mol), reflecting the stronger halogen bond in the former complex. This can be mainly ascribed to the greater basicity of the carbonyl oxygen relative to the hydroxyl one. The same tendency is also detected in the complexes PhBr···SCH$_2$ and PhBr···SH$_2$. For neutral systems studied in this work, their relative strengths attenuate in the order $H_2CS > H_2CO > NH_3 > H_2S > H_2O$.

HF/aug-cc-pVDZ calculation results obtained with the MP2/aug-cc-pVDZ geometries are also listed in Table 1. As can be seen, the HF method extremely underestimates the interaction energies of the complexes. In a previous publication, it was

TABLE 2: Calculated Charge Shifts of the Br Atom and Charges on the Molecular Unit PhBr in the Complexes[a]

complexes	q(Br)	Δq(Br)[b]	q(PhBr)
PhBr···F$^-$	0.2170	0.1616	−0.0773
PhBr···Cl$^-$	0.1671	0.1117	−0.0428
PhBr···Br$^-$	0.1560	0.1006	−0.0394
PhBr···OCH$_2$	0.0785	0.0217	−0.0033
PhBr···OH$_2$	0.0818	0.0026	−0.0038
PhBr···OH$^-$	0.1842	0.1288	−0.1310
PhBr···OOCH$^-$	0.1876	0.1322	−0.0322
PhBr···NH$_3$	0.0920	0.0366	−0.0079
PhBr···SH$_2$	0.0568	0.0014	−0.0029
PhBr···SCH$_2$	0.0685	0.0131	−0.0063

[a] Charges are given in au. [b] Difference in atomic charge between the complex and bromobenzene.

demonstrated that the difference between the MP2 and HF energies is mainly assigned to the effects of high-order electrostatic interaction such as a dispersion interaction.[58] Consequently, due to the large gain of the attraction by electron correlation (2.06−8.95 kcal/mol), dispersion force plays an important role in the stability of the complexes.

NBO and QTAIM Results. Charge distributions of the halogen-bonded complexes are examined in terms of the NBO analysis based on the HF/aug-cc-PVDZ wave functions using respective MP2/aug-cc-pVDZ geometries. In recent years, the use of the NBO analysis has been widespread. Unlike most other partitioning schemes, the presence of diffuse functions in the basis set has a marginal effect on this method. As follows from the data listed in Table 2, upon complexation, the positive charge on the Br atom increases in all cases. In general, the stronger the interaction in the complex, the more positive charge on the bromine atom in bromobenzene. The charge of the molecular unit PhBr can be viewed as the net charge transfer from the molecular unit electron donor to the unit PhBr because the charge for the isolated unit PhBr is zero. Obviously, upon complex formation, there is a magnitude of charge transfer, in a range of 3−130 me (see Table 2), from electron donors to bromobenzene. A close examination of the relationship between the amount of charge transfer and the interaction energies shows that there is a fairly good correlation, as displayed graphically in Figure 3. The correlation coefficient is as high as 0.95. These results explicitly demonstrate that a charge-transfer interaction plays an important role in the formation of these halogen-bonded complexes.

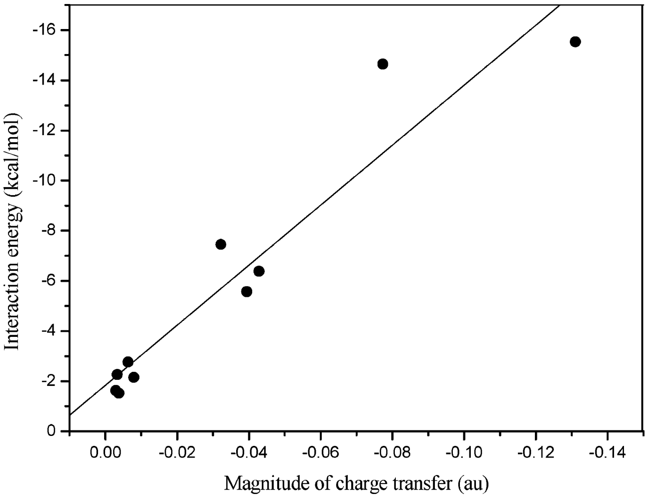


Figure 3. Correlation between the amount of charge transfer and the interaction energy.

TABLE 3: Some Significant Donor−Acceptor Natural Bond Orbital Interactions in the Complexes and Their Second-Order Perturbation Stabilization Energies[a]

orbital interactions	$\delta\epsilon$ (au)	F_{ij} (au)	E(2) (kcal/mol)
PhBr···F$^-$			
LP (1) F → BD*(1)C−Br	1.60	0.067	3.42
LP (4) F → BD*(1)C−Br	0.82	0.130	25.65
PhBr···Cl$^-$			
LP (1) Cl → BD*(1)C−Br	1.20	0.025	0.63
LP (4) Cl → BD*(1)C−Br	0.65	0.073	10.31
PhBr···Br$^-$			
LP (1) Br → BD*(1)C−Br	1.14	0.021	0.46
LP (4) Br → BD*(1)C−Br	0.62	0.066	8.79
PhBr···OCH$_2$			
LP (1) O → BD*(1)C−Br	13.0	0.020	0.39
LP (2) O → BD*(1)C−Br	0.79	0.029	1.28
LP (2) Br → BD*(1)C−H	1.05	0.020	0.46
PhBr···OH$_2$			
LP (1) O → BD*(1)C−Br	1.13	0.012	0.15
LP (2) O → BD*(1)C−Br	0.92	0.037	1.88
PhBr···OH$^-$			
LP (1) O → BD*(1)C−Br	1.13	0.054	3.07
LP (3) O → BD*(1)C−Br	0.70	0.148	38.70
PhBr···OOCH$^-$			
LP (1) O → BD*(1)C−Br	1.20	0.051	2.70
LP (2) O → BD*(1)C−Br	0.69	0.066	7.80
PhBr···NH$_3$			
LP (1) N → BD*(1)C−Br	0.85	0.049	3.48
PhBr···SH$_2$			
LP (2) S → BD*(1)C−Br	0.68	0.022	0.91
PhBr···SCH$_2$			
LP (1) S → BD*(1)C−Br	1.21	0.014	0.20
LP (2) S → BD*(1)C−Br	0.65	0.035	2.29
LP (2) Br → BD*(1)C−H	1.08	0.029	0.96

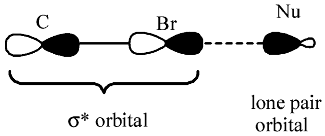
[a] LP denotes the occupied lone pair. BD* denotes the formally empty antibonding orbital.

Natural bond orbital (NBO) theory is also valuable for understanding molecular complex formation from the viewpoint of local orbital interactions. The formation of the complexes studied in this work can be viewed by NBO theory as a consequence of nucleophile interactions with the PhBr group's LUMO and electrophile interactions with the electron donor's HOMO. Note that the observed directional propensity of halogen bonding is also controlled by the orbital interaction. The second-order perturbation stabilization energies E(2) due to orbital interaction can be evaluated as

$$E(2) = \Delta E_{ij} = q_i \frac{F(i,j)^2}{\epsilon_j - \epsilon_i}$$

where q_i is the donor orbital occupancy, ϵ_i and ϵ_j are diagonal elements (orbital energies), and $F(i,j)$ is the off-diagonal NBO Fock matrix element. The NBO energy differences $\delta\epsilon$, the NBO wave function overlaps (Fock matrix) F_{ij}, and the second-order perturbation stabilization energies E(2) associated with the predominant orbital interactions are collected in Table 3. For all of the dimeric complexes under consideration, the present NBO data show that the main stabilization element, as graphically displayed in Scheme 1, arises from the second-order orbital interactions of the lone-pair donor orbital of the Y atom with the C−Br σ*-acceptor orbital. The total second-order perturbation NBO stabilization energies E(2) based on these orbital interactions, calculated at the HF/aug-cc-pVDZ level, are in the 0.91−41.77 kcal/mol range. These values are close to or even greater than the corresponding interaction energies. Furthermore, as shown in Figure 4, the second-order perturbation stabilization energies correlate with the interaction energies very well (the

SCHEME 1: Typical Orbital Interactions of Bromobenzene (C−Br) with Nucleophiles (Nu)



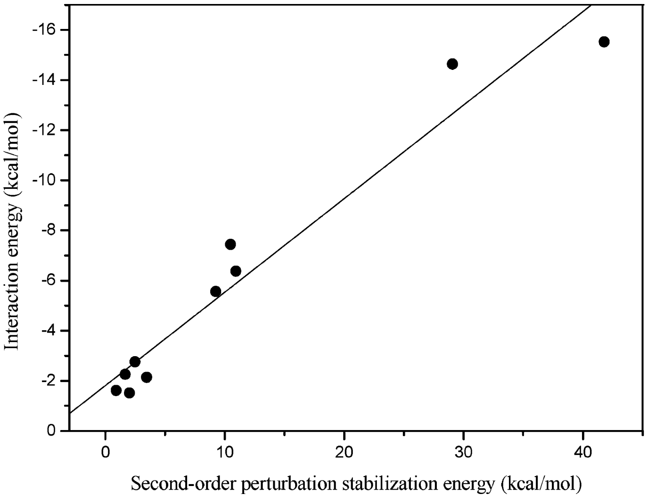


Figure 4. Relationship between the second-order perturbation stabilization energy and the interaction energy.

TABLE 4: AIM Parameters and Bond Orders for All of the Complexes[a]

complexes	ρ_b	$\nabla^2\rho_b$	G_b	V_b	H_b	BO
PhBr⋯F$^-$	0.0432	0.1527	0.0414	−0.0447	−0.0033	0.1002
PhBr⋯Cl$^-$	0.0178	0.0584	0.0126	−0.0107	0.0019	0.0523
PhBr⋯Br$^-$	0.0152	0.0450	0.0097	−0.0082	0.0015	0.0475
PhBr⋯OCH$_2$	0.0107	0.0398	0.0089	−0.0078	0.0011	0.0068
PhBr⋯OH$_2$	0.0096	0.0372	0.0080	−0.0068	0.0012	0.0066
PhBr⋯OH$^-$	0.0485	0.1398	0.0391	−0.0432	−0.0041	0.1646
PhBr⋯OOCH$^-$	0.0233	0.0848	0.0198	−0.0186	0.0012	0.0372
PhBr⋯NH$_3$	0.0118	0.0400	0.0086	−0.0073	0.0013	0.0128
PhBr⋯SH$_2$	0.0063	0.0191	0.0040	−0.0031	0.0009	0.0061
PhBr⋯SCH$_2$	0.0092	0.0274	0.0058	−0.0048	0.0011	0.0108

[a] Topological properties at the BCPs are in au. BO is bond order.

correlation coefficient amounts to 0.97). On the basis of these results, we suggest that the contribution from the n(Y) → σ*(C−Br) orbital interaction would be important for the stability of the halogen-bonded complexes. Here, it is worth mentioning that in the cases of PhBr⋯OCH$_2$ and PhBr⋯SH$_2$, the n(Br) → σ*(C−H) orbital interaction also makes contributions to the stability of the two dimers, albeit the values of $E(2)$ due to this orbital interaction are relatively small (0.46 kcal/mol for PhBr⋯OCH$_2$ and 0.96 kcal/mol for PhBr⋯SH$_2$). This is directly related to the fact that the Br atom in PhBr is involved into a bifurcated interaction in these two complexes, as mentioned above.

A topological analysis of the electron density further validates the existence of halogen bonds in all of the complexes. A bond critical point (BCP) is identified for Br⋯Y, accompanied by a bond path between the two corresponding atoms. The properties at the BCPs are analyzed in terms of the following parameters: the electron density (ρ_b), its Laplacian ($\nabla^2\rho_b$), and the electron energy density (H_b). The following components of H_b are also considered: the kinetic electron energy density (G_b) and the potential electron energy density (V_b).

Table 4 shows the AIM results for all of the complexes examined in this work. It can be seen that the values of ρ_b are calculated to be in a range of 0.0063−0.0485 au, whereas the values of $\nabla^2\rho_b$ are all positive, ranging from 0.0191 to 0.1527 au. These values are within the common accepted values for H bonding interactions, thus indicating the closed-shell interactions in these complexes. As pointed out previously, the electron energy density H_b is a more appropriate index to gain a deeper understanding of noncovalent interactions.[59] The sign of H_b at BCP determines whether the interaction is electrostatic dominant ($H_b > 0$) or covalent dominant ($H_b < 0$). From Table 4, it is evident that for the dimers PhBr⋯Cl$^-$, PhBr⋯Br$^-$, PhBr⋯OH$_2$, PhBr⋯OCH$_2$, PhBr⋯OOCH$^-$, PhBr⋯NH$_3$, PhBr⋯SH$_2$, and PhBr⋯SCH$_2$, the H_b values are all greater than zero, and therefore, halogen bonding interactions in these systems are basically electrostatic in nature. However, negative values of H_b are predicted for PhBr⋯F$^-$ and PhBr⋯OH$^-$, suggesting that the interactions in these two dimers have some degree of covalent character. On the other hand, the two complexes possess interaction energies that are significantly larger than those of the remaining systems. According to these results obtained, we can conclude that strong halogen bonds are more covalent in nature and weak halogen bonds are mainly electrostatic interactions, which follows the electrostatic−covalent model observed for H bonds (ECHBM).[60] As shown in Figure 5, plots of the electron densities and their Laplacians versus the interaction energies for the complexes are linear. The correlation coefficients amount to 0.99 and 0.97, respectively. That is to say, the electron densities and their Laplacians are good indications of the strength of halogen bonding interactions, which reproduces the well-documented properties of H bonds. We recommend here the electron densities at BCPs as an excellent description of halogen bond strengths.

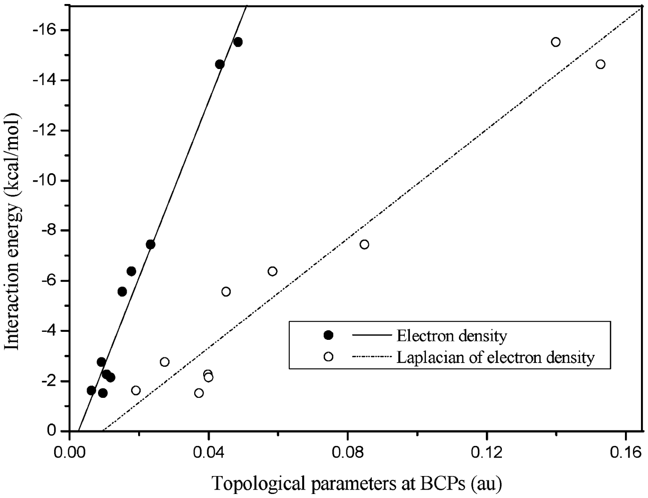


Figure 5. Relationships between the electron density and its Laplacian at BCPs and the interaction energy.

Bond order has proved to be a good measure of the number of bonding electron pairs between atoms. Here, the relevant quantity of interest is the bond order between the atoms involving intermolecular interactions. It can be seen from Table 4 that charge-assisted halogen bonding interactions have relatively higher bond orders, especially the interactions in the dimers PhBr⋯F$^-$ and PhBr⋯OH$^-$, indicating the covalent character of the interactions, to some extent. Moreover, we find that the bond orders are strongly related to the electron densities at the BCPs. Clearly, analysis of bond orders substantiates the findings derived from the QTAIM results.

Conclusions

In the present work, ab initio quantum chemical computations have been carried out on a series of dimeric complexes formed between bromobenzene and several electron donors. These small model systems contain halogen bonding elements commonly found within crystal structures and biological macromolecules. The quantum theory of atoms in molecules (QTAIM) and the second-order perturbation natural bond orbital (NBO) analyses have been applied to analyze the electron density distributions of these complexes and, in particular, to shed some light on the nature of halogen bonding interactions. The calculations described herein show that halogen bonding energies vary in a wide range between -1.52 and -15.53 kcal/mol. The interactions seem to be very significant as a driving force influencing the arrangement of molecules in crystals. As an NBO analysis suggested, both the charge-transfer force and the second-order orbital interaction play an important role in the formation of the complexes. The QTAIM analysis further validates the existence of halogen bonding interactions in the complexes, and the topological properties of halogen bond critical points (BCPs), such as the electron density (ρ_b) and its Laplacian ($\nabla^2\rho_b$), are shown to correlate well with the interaction energy. This analysis also reveals that weak halogen bonds are basically electrostatic in nature, while strong halogen bonds have some degree of covalent character. The electron densities at the BCPs can be considered as a good description of the strength of halogen bonding. In view of these conclusions reached, we can expect that the nature and magnitude of halogen bonding interactions described in this work would be very useful in the design and synthesis of new materials and effective drugs involving aromatic halogen compounds.

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