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A Computational Investigation of π-π Interactions in a Variety of Benzene Derivatives

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Abstract

A theoretical calculation into π-π interactions of several benzene derivatives, including aniline, benzonitrile, chlorobenzene, phenol, and toluene, was conducted and documented. All structures have been optimized using the MP2/aug-cc-pVDZ theoretical method. Homodimer of benzene derivatives with various geometrical configurations, including face-to-face, anti-face-to-face, slipped-parallel, and T-shape, have been explored. Variations have been made to the distance between two molecules of each dimer while conserving the geometry of each structure, as determined via geometry optimization. The potential energy curve has been drawn for each configuration, and all of the data for each configuration has been fitted to a polynomial equation. For each configuration, the minimal distance between two molecules at which the interaction energy is the lowest has been determined using a polynomial equation. At distances of 3.47 Å, the slipped parallel structure of aniline is the most stable, with interaction energies of -8.92 kcalmol^{-1}. At 3.41 Å, the anti-face-to-face structure of benzonitrile has the lowest interaction energy of -11.51 kcalmol^{-1}, making it the most stable configuration. At 3.65 Å, the most stable form of chlorobenzene is slipped parallel, which has an interaction energy of -11.14 kcalmol^{-1}. At distances of 3.81 Å and 3.69 Å, phenol and toluene exhibit interaction energies of -10.77 kcalmol^{-1} and -10.43 kcalmol^{-1}, respectively. The goal of π-π interactions is to provide a more comprehensive and more up-to-date understanding of the way this interaction works in fields like molecular biology.

Keywords: π-π interaction, ab-initio, MP2, Aug-cc-pVDZ, PES, Polynomial.

I. Introduction

π- π interactions are one of the most significant types of intermolecular interactions. This is non-covalent interaction that takes place between aromatic groups that contain π bonds[1,2]. This type of interaction can take place within the same molecule by producing a dimer, as well as between molecules of different types. However, they play a significant role in the chemical and biological processes despite their relative weak interactions[3]. A lot of research has been done on the stacking interaction between aromatic rings, especially for the typical benzene dimer[4-8]. Sinnokrot[9] claimed that the T-shaped and parallel displaced structures are most flexible and have almost the same amount of energy, while the co-faced parallel stacked structure is the one that is least likely to form. In contrast, the Sanders and Hunters model asserted that if two aromatic rings that interact are electron-rich, then their stacking geometry will resist one another. Computational investigations on monosubstituted benzene dimers in gaseous state, however, revealed that both electron-withdrawing and electron-donating substituents enhance the interaction between two benzenes with in sandwich configuration[10]. Whereas Sherril[11] came up with the idea that the London dispersion force is crucial to the stabilization of substituted benzene dimers after conducting an analysis based on a symmetry-adapted version of the perturbation theory. The π-π interaction in proteins can be more accurately portrayed by the toluene dimer[12]. Nitrobenzene dimer is an additional significant dimer for comprehending the characteristics of explosive substances[13-17]. According to Seiji[18], substantial stability may be achieved for the slipped-parallel orientation through dispersion interaction. They demonstrated that the interaction energies of the nitrobenzene–benzene complex as well as the nitrobenzene dimer are markedly higher than those of the benzene dimer. The side chains of many amino acids in proteins contain aromatic rings that enhance protein structure, and stability through π-π interactions. These aromatic side chains may participate in particular interactions that alter the structure and function of proteins[19-22]. Burley's[23] analysis of 34 proteins indicated that 60% of aromatic side chains are engaged in π-π interactions, where the T-shape geometry predominates. McGaughey[24] demonstrated that the dominant interactions in giant protein molecules had taken on a parallel-displaced shape. For sandwich configurations of substituted benzenes, the electron with drawing substituent strengthens the interaction, as demonstrated by the Hunter-Sanders model. In contrast, the electron-donating substituent reduced the electrostatic repulsion between the negatively charged - clouds, hence weakening the interaction[3,10]. Theoretical investigations at show that all substituted sandwich benzene dimers have a greater attraction than the unsubstituted benzene dimer, regardless of whether the substituent is electron-donating or electron-withdrawing. These effects are investigated in a variety of fields, including protein-DNA interactions and the development of stereoselectivity in organocatalyzed processes[25,26]. The π-π interaction is very much important for the base-base interactions that take place in DNA[27-30]. The interaction is essential for the formation of effective charge transport channels for both small molecules and polymeric semiconducting materials[31]. In nanomaterials, π-π interactions are the main force used to load drugs, make nanoparticles put themselves together, and connect three-dimensional networks[32-33]. π-π stacking interactions have the potential to be utilized in a vast range of biological and

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biotechnological sectors. π-π stacking interactions are utilized to deliver drugs since they don't change structural or functional characteristics[34-41]. Furthermore, π-π stacking interactions have been utilized to load delivery methods with anticancer chemical medicines, photosensitizers, polypeptide, and nucleic acids[38,42-48]. Despite this, the geometries and energy of π-π interactions in a number of benzene derivative molecules have still not been investigated.

In this work, high-level ab initio calculations have been employed to investigate the geometries and energy of π-π interactions in a number of benzene derivatives. Programming language software has been used in order to get an accurate position on the surface of potential energy. In addition to that, the roles that electrostatic and dispersion interactions play in the attraction and the directionality of it have been studied.

II. Methodology

Gauss View 6.016 program was used to construct the structures of benzene, aniline, benzonitrile, chlorobenzene, phenol, and toluene. Each structure was fully optimized using the Gaussian 16 program at the MP2 level of theory with the aug-cc-pVDZ basis set. These correlation-consistent polarization basis sets are widely used in post-Hartree-Fock computations to achieve high accuracy in theoretical calculations.

To investigate π-π interactions, benzene dimers and mono-substituted benzene homodimers with optimized structures for each monomer were constructed. For each dimer, the configurations of face-to-face (FF), anti-face-to-face (AFF), slipped-parallel (SP), and T-shape (TS) were considered. The separation distance between the two monomers was controlled based on the center-to-center distance of the aromatic rings. Specifically, the geometric centers of the benzene rings were used as reference points to ensure consistent measurement of intermonomer distances. This approach allowed for a systematic variation of the distance while keeping the relative orientation of the substituents fixed. The distance was varied in increments of 0.1 Å over the range of 1.00 to 5.00 Å.

Single-point energy calculations were performed at each distance using the same level of theory and basis set, ensuring that the geometry of each configuration remained constant. Potential Energy Surfaces (PES) were generated by plotting the distance (Å) on the x-axis and the interaction energy (kcal mol^{-1}) on the y-axis for each configuration. The interaction energy data was fitted to a polynomial equation using the MATLAB R2016a software package. From the polynomial equations, the minimum distance corresponding to the lowest (most negative) interaction energy was determined.

Additionally, MATLAB was employed to calculate the "norm of the residuals" coefficient, which quantifies the divergence between actual data and predicted values. A lower norm value indicates a better fit of the equation to the data. The formal definition of the norm of residuals is provided as follows:

$$\text{Norm of residuals} = \sqrt{\sum_{i=1}^{n} di^2}$$

Where di represents the residual, or the difference between the actual value and the anticipated value.

III. Results and Discussion

Benzene-benzene interaction energy for three fundamental configurations such as benzene-benzene FF, benzene-benzene SP, and benzene-benzene TS have been calculated in this work and compared with the literature value (Table 1). The minimum energies for benzene-benzene FF were found at r = 3.53 Å, benzene-benzene SP at r = 3.75 Å, and benzene-benzene TS at r = 2.47 Å with the energy values of -6.06 $kcalmol^{-1}$, -7.93 $kcalmol^{-1}$, and -4.48 $kcalmol^{-1}$ respectively. The most stable of these three configurations was benzene-benzene SP. Sinnokrot[48] found that the interaction energy between benzene in FF orientation was -2.90 $kcalmol^{-1}$, which is the half of the value obtained in this work. According to Tsuzuki[6], the interaction energy of benzene-benzene SP was estimated to be -3.98$kcalmol^{-1}$ using the MP2/cc-pvz level. Interaction energy value for all three orientations in benzene dimer obtained in this work is much more negative than the literature value. This is probably because of the lack of BSSE correction. But we have found that two benzene molecules interact most strongly in the SP orientation which is consistent with the published data (Table 1).

Fig. 1 illustrates four primary configurations for the aniline-aniline interaction: (a) face to face having parallel NH_2 groups (aniline-aniline FF), (b) face to face having NH_2 groups antiparallel position (aniline-aniline AFF), (c) slipped parallel (aniline-aniline SP), and (d) T-shaped (aniline-aniline TS). Fig. 1 depicts the computed interaction energy curves (in $kcalmol^{-1}$) between the two aniline dimers. Fig. 1 clearly demonstrate that aniline dimer interacts relatively strongly with the FF configuration. The aniline-aniline FF has energy minimum of -8.92 $kcalmol^{-1}$ at distance of 3.47 Å, whereas the aniline-aniline AFF has a minimum energy of approximately -7.96 $kcalmol^{-1}$ at distance of 3.44 Å. Energy emerges from the competition among H-π, NH_2-π, and π-π interactions. The aniline-aniline FF configuration has extra NH_2-NH_2 repulsion; hence the two stacked configurations are distinct. The slipped parallel (aniline-aniline SP) configuration depicted in Fig. (c) was the most stable configuration with a minimum energy of -9.87 $kcalmol^{-1}$ at r = 3.82 Å. The dispersion force of interaction enhances the stability of the aniline dimer's slipped parallel configuration. The T-shaped configuration (aniline-aniline TS) shown in Fig.(d) has a minimum energy of -5.39 $kcalmol^{-1}$ at r = 2.40 Å. This type of interaction energy arises due to H-π interaction. NH_2 is an electron-donating substituent, therefore its presence should enhance the π- π electrostatic repulsion and negativity of π charge.

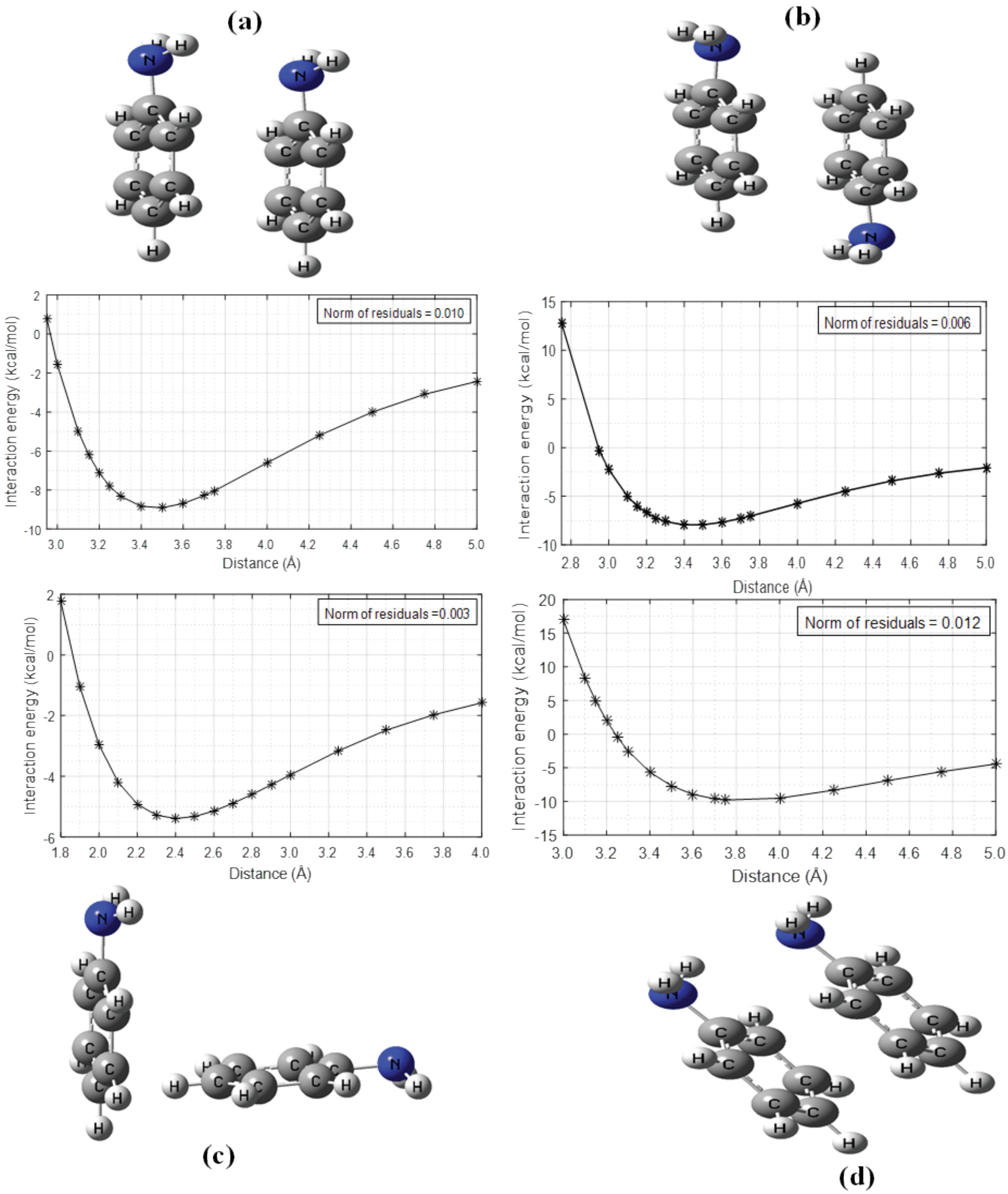

Fig. 1. Energy curve due to interaction of aniline dimer for its structural configurations:(a) face to face aniline-aniline (FF), (b) Anti face to face aniline-aniline (AFF), (c) T-shaped aniline-aniline (TS), and (d) slipped-parallel aniline-aniline (SP).

The interaction energy between two benzonitrile in benzonitrile homodimers of different configurations including FF, AFF, SP, and TS were computed.

Fig. 2. depicts the potential energy curves of benzonitrile dimers. The AFF configuration is the most stable as demonstrated in Fig. 2(b) and Table 1. The benzonitrile-benzonitrile AFF has a minimum energy of -11.51 kcalmol^{-1} at r = 3.41 Å, whereas the benzonitrile-benzonitrile FF has a minimum energy of approximately -8.15 kcalmol^{-1} at r = 3.48 Å. In this case, the energy is produced by the competition between the H-π, CN-π, and π-π interactions. The stability of the anti-face-to-face configuration of benzonitrile is due to the electron-withdrawing characteristics of the CN group, which reduces electrostatic repulsion between π-clouds, so stabilizing the configuration[50,51]. The interaction energy

values for AFF and T-shape configuration are highly over estimated compared to literature value. This is probably due to BSSE correction. The distinction between the two stacked arrangements was due to the presence of extra CN-CN repulsion in the benzonitrile-benzonitrile FF structure. The major contribution to the slipped parallel configuration depicted in Fig. 2(c) was dispersion interaction. The T-shaped (benzonitrile-benzonitrile TS) arrangement shown in Fig. 2(d) has a minimum distance of r = 2.45 Å and a minimum energy of 4.85 kcalmol^{-1}. This low energy resulted from H-π electrostatic interaction. Between the FF and SP forms of benzonitrile, the SP configuration was more stable. In this case, CN served as an electron-withdrawing substituent; hence, this substitution should lower the negative π charge and result in a reduction in π-π electrostatic repulsion.

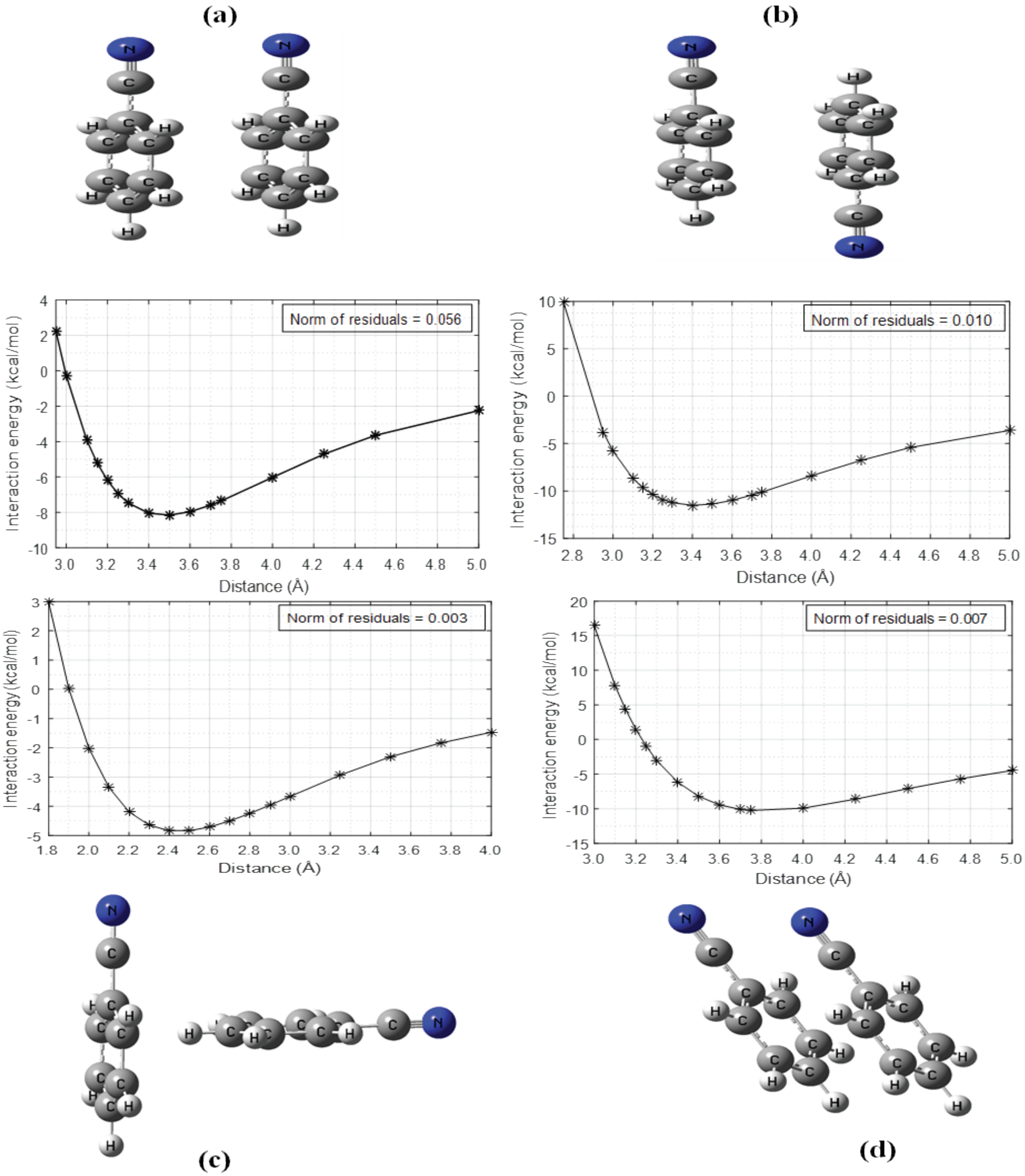

Fig. 2. Energy curve due to interaction of benzonitrile dimer for its structural configurations: (a) face to face benzonitrile-benzonitrile (FF), (b) anti face to face benzonitrile-benzonitrile (AFF), (c) T-shaped aniline-aniline (TS), and (d) slipped-parallel aniline-aniline (SP).

Fig. 3. depicts the chlorobenzene-chlorobenzene interaction energy computed for chlorobenzene dimers. The AFF structure was determined to be the more stable of the two stacked configurations of chlorobenzene dimer, FF and AFF, shown in Fig. 3(a) and 3(b). The chlorobenzene-chlorobenzene AFF has a minimum energy of -10.08 kcal mol^{-1} at r = 3.40 Å, whereas its FF counterpart has a minimum energy of -8.34 kcalmol^{-1} at r = 3.53 Å. This interaction energy was the result of competition between the H-π, Cl-π, and π-π interactions. Because of the Cl-Cl repulsion term, the interaction energy of the chlorobenzene-chlorobenzene FF configuration is different from that of the AFF configuration. Fig. 3(c) depicted chlorobenzene-chlorobenzene SP as the most stable form, with a minimum energy of -11.14 kcalmol^{-1} at r = 3.65 Å. The dispersion interaction strengthened the stability of the slipped parallel orientation of the chlorobenzene dimer. Due to the H-π interaction, the chlorobenzene-chlorobenzene TS configuration shown in Fig. 3(d) has a minimum energy of -5.39 kcal mol^{-1} at r = 2.42 Å. Gogfrey-Kittle[46] determined the interaction energy of the chlorobenzene-chlorobenzene AFF configuration using the MP2/cc-Pvdz theory to be 1.94 kcalmol^{-1}.

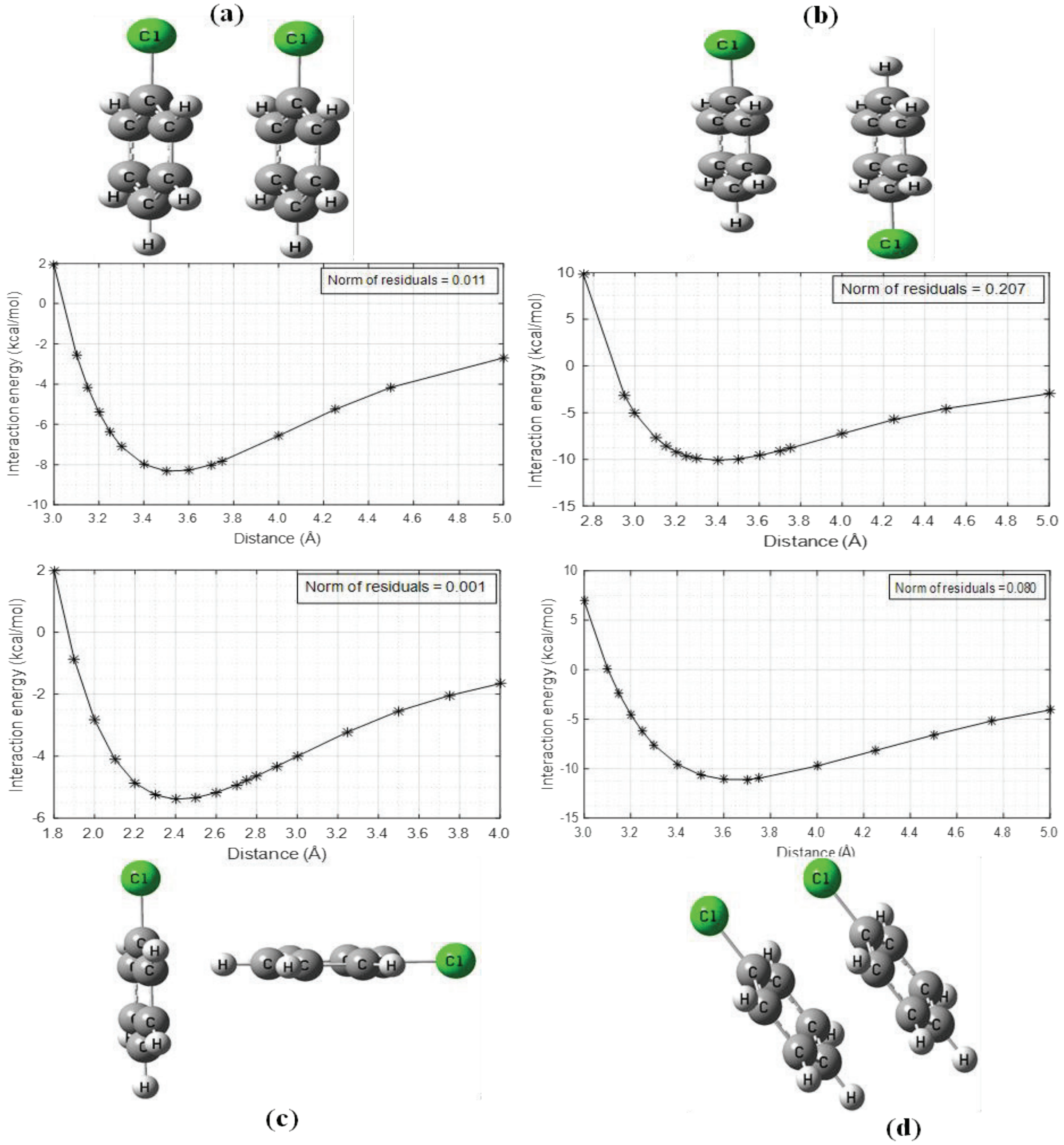

Fig. 3. Energy curve due to interaction of chlorobenzene dimer for its structural configurations: (a) face to face chlorobenzene-chlorobenzene (FF), (b) anti face to face chlorobenzene-chlorobenzene (AFF), (c) T-shaped chlorobenzene-chlorobenzene (TS), and (d) slipped-parallel chlorobenzene-chlorobenzene (SP).

Fig. 4. depicts interaction energy curves for phenol-phenol interactions for four fundamental configurations: FF, AFF, SP, and TS. Fig. 4(a) and 4(b) illustrate that the FF configuration of phenol was the more stable of the two stacked forms of phenol dimer, FF and AFF. The phenol-phenol FF configuration possessed a minimum energy of -10.77 kcalmol^{-1} at r = 3.81 Å, whereas the phenol-phenol AFF configuration possessed a minimum energy of -8.69 kcal mol^{-1} at r = 3.42 Å. The AFF configuration was different from the FF configuration due to OH-OH repulsion. De Moraes[47] reported that the phenol-phenol FF interaction energy was 0.78 kcal mol^{-1}. Figure 4(c) demonstrated that the phenol-phenol SP configuration was more stable than the phenol-phenol AFF configuration. The slipped-parallel showed in the Fig. 4(c) is the relatively more stable configuration than AFF configuration. This arrangement has a minimum energy of -9.45 kcal mol^{-1} at a distance of 3.71 Å due to the dispersion interaction. Due to the H-π interaction, phenol-phenol TS has a minimum energy of -3.74 kcalmol^{-1} at r = 2.46 Å, as shown in Fig. 4(d). De moraes[47] reported an interaction energy of -3.01 kcal mol^{-1} at r = 2.70 Å, which corresponds to the value determined in this study.

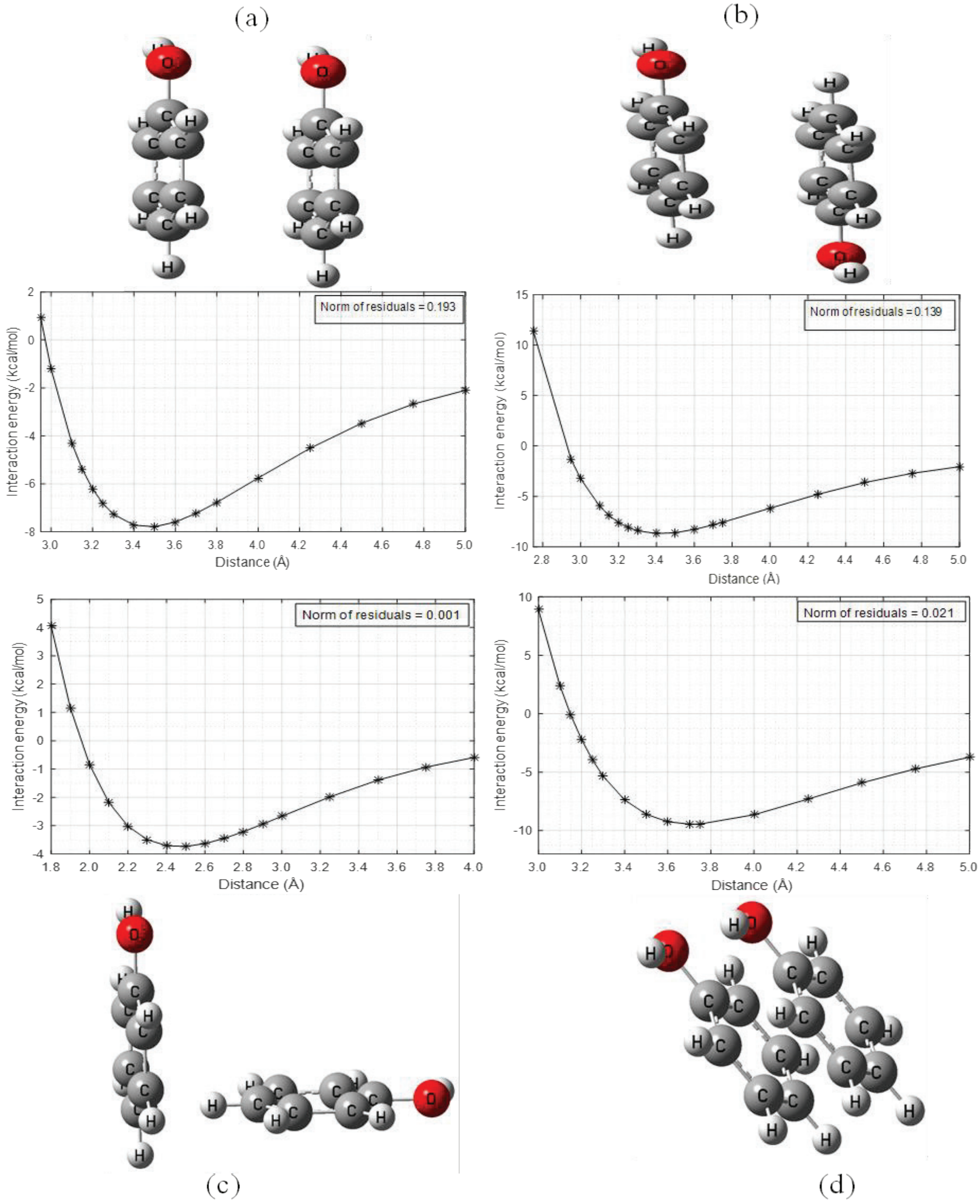

Fig. 4. Energy curve due to interaction of phenol dimer for its structural configurations: (a) face-to-face phenol-phenol (FF), (b) anti-face-to-face phenol-phenol (AFF), (c) T-shaped phenol-phenol (TS), and (d) slipped-parallel phenol-phenol (SP).

Fig. 5. illustrates the interaction energy curves that were calculated for toluene dimers with the four basic configurations (FF, AFF, SP, and TS). Among the two stacked configurations of toluene dimer, FF and AFF, shown in Fig. 5(a) and (b), toluene AFF was the more stable. The AFF configuration of toluene has a minimum energy of -9.78 kcalmol^{-1} at a distance of 3.45 Å, whereas the FF configuration has a minimum energy of -7.28 kcalmol^{-1} at a distance of 3.69 Å. These types of interaction energies were the result of H-π, CH_3 -π, and π-π interactions. Toluene SP, as shown in Fig. 5(c), has the most stable configuration with a interaction energy of -10.43 kcalmol^{-1} at r = 3.45 Å, which originated from the dispersion force of attraction. Toluene TS, as depicted in Fig. 5(d), has a minimum interaction energy of -5.29 kcalmol^{-1} at r = 2.46 due to the H-π interaction. The chlorobenzene SP configuration is more stable than the toluene SP configuration because the Cl group is an electron-withdrawing substituent that decreases the negative charge and π−π electrostatic repulsion, whereas the CH_3 group is a weak electron-donating substituent. According to Tsuzuki[18], the interaction energy of the toluene AFF configuration was calculated to be -4.52 kcalmol^{-1} at the MP2/aug(d)-6-311G* level of theory after BSSE correction. Whereas the CCSD(T)/aug(d)-6-311G* level estimated the interaction energy of toluene SP structure to be -5.93 kcal mol^{-1}.

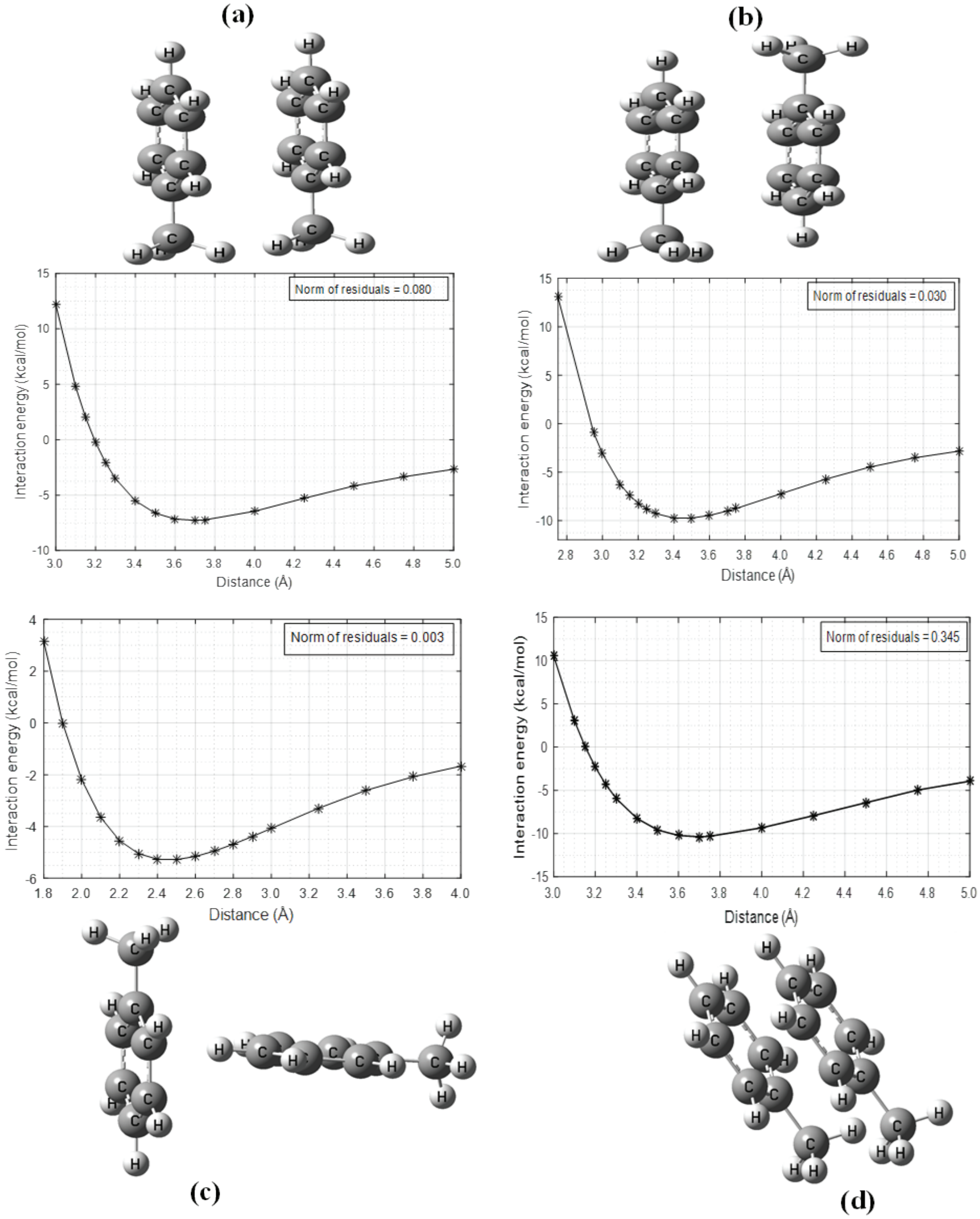

Fig. 5. Energy curve due to interaction of toluene dimer for its structural configurations: (a) face-to-face toluene-toluene (FF), (b) anti-face-to -face toluene-toluene (AFF), (c) T-shaped toluene-toluene (TS), and (d) slipped-parallel toluene-toluene (SP).

The most important results of this study were the discovery of π-π interactions in benzene derivatives like aniline, benzonitrile, chlorobenzene, phenol, and toluene that had never been explored before. The replication of several reported π-π interactions in a few benzene derivatives, including aniline, benzonitrile, chlorobenzene, phenol, and toluene, was another important result. In this computation, the aniline-aniline FF and SP configurations yielded interaction energies of -8.92 and -9.09 kcalmol^{-1}, respectively, which had not been studied previously. In the case of chlorobenzene-chlorobenzene FF and SP configurations, the calculated interaction energies of -8.34 and -11.14 kcalmol^{-1} have not before been explored. In this calculation, the interaction energies of FF and SP configurations for other benzene derivatives such as phenol, toluene, and benzonitrile have also been investigated. This research will aid in the comprehension of π-π interactions in benzene dimers due to the various orientations of the substituent group.

Table 1 shows the interaction energy and minimum distance between the homodimers for the FF, AFF, SP, and TS configurations.

Table 1. Configuration, interaction energies, and minimum distances for some benzene derivatives.

Molecule	Orientation	Obtained distance (Å)	Obtained Interaction energy (kcalmol^{-1})
Benzene-Benzene	Face-to-Face	3.53 (3.80)[48]	-6.06 (-2.90)[48]
	T-shape	2.47 (5.0)[48]	-4.48 (-3.16)[48]
	Slipped-Parallel	3.75 (3.50)[6]	-7.93 (-3.98)[6]
Phenol-Phenol	Face-to-Face	3.81 (3.80)[47]	-10.77 (-3.28)[47]
	Anti-Face-to-Face	3.42 (2.75)[47]	-8.69 (-5.35)[47]
	T-shape	2.46 (2.70)[47]	-3.74 (-12.58)[47]
	Slipped-Parallel	3.71 (2.75)[47]	-9.45 (-5.35)[47]
Aniline-Aniline	Face-to-Face	3.47	-8.92
	Anti-Face-to-Face	3.44 (4.0)[46]	-7.96 (0.82)[46]
	T-shape	2.40 (5.0)[46]	-5.39 (1.80)[46]
	Slipped-Parallel	3.82	-9.87
Toluene-Toluene	Face-to-Face	3.69	-7.28
	Anti-Face-to-Face	3.45 (3.6)[12]	-9.78 (-4.52)[12]
	T-shape	2.46 (5.0)[12]	-5.29 (-3.59)[12]
	Slipped-Parallel	3.69 (3.5)[12]	-10.43 (-5.93)[12]
Chlorobenzene-Chlorobenzene	Face-to-Face	3.53	-8.34
	Anti-Face-to-Face	3.40 (3.5)[46]	-10.08 (-1.94)[46]
	T-shape	2.42 (5.0)[46]	-5.39 (-1.80)[46]
	Slipped-Parallel	3.65	-11.14
Benzonitrile-Benzonitrile	Face-to-Face	3.48	-8.15
	Anti-Face-to-Face	3.41 (4.0)[46]	-11.51 (-2.84)[46]
	T-shape	2.45 (5.0)[46]	-4.85 (-1.76)[46]
	Slipped-Parallel	3.81	-10.31

IV. Conclusion

In this study, a computational technique based on (MP2) was used to analyze the π-π interactions in certain benzene derivatives with four fundamental configurations, Such as FF, AFF, SP, and TS. Variations were made to the distance between two molecules of each dimer, but the geometry of each structure remained unchanged. The PES was drawn for each configuration and then fitted to a polynomial equation. The polynomial equation for each configuration was used to determine the minimal distance at which the interaction energy was the lowest. At distances of 3.47 Å, the SP configuration of aniline demonstrated the lowest interaction energies of -8.92 kcal mol^{-1}. The configuration of benzonitrile with the lowest interaction energy of -11.51 kcal mol^{-1} at a distance of 3.41 was determined to be the most stable. With interaction energies of -11.14 kcal mol^{-1} at distances of 3.65 Å, chlorobenzene SP was the most stable compound. Similarly, the SP configuration of toluene was the most stable, with an interaction energy of -10.43 kcal mol^{-1} at a distance of 3.69 Å. These findings have enormous potential in the disciplines of supramolecular chemistry, chemical engineering, protein folding, material sciences, biomedicine, and biotechnology.

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