

MP2 study on the variation of stacking interactions in aniline and some para substituted aniline systems

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ABSTRACT

The use of appropriate level of theories for studying weak van der Waal interactions such as π - π stacking interactions of aromatic molecules has been an important aspect, since the high level methods have limitations for application to large molecules. The differences in the stacking energies of various aromatic molecular structures are found significant. It is also very important for identifying the most favored stacked models of aniline and some of the p-substituted aniline molecules. The effect of basis set in the stacking energies of MP2 calculations is small. The values for HF and MP2 level of theories calculate less electron correlation energy whereas CCSD (T) methods may be used for the calculation of better electron correlation energy. The moderately accurate calculations, MP2 level of theories were found feasible for most of the simple aromatic systems such as benzene, pyridine, aniline etc. In our studies, it has been investigated by using MP2 and DFT methods, to study the π - π stacking interaction energies for the minimized stacked models of aniline and some p-substituted aniline systems.

Keywords: π - π Stacking interactions; Aniline; MP2 methods

INTRODUCTION

Theoretical and quantum mechanical methods encloses a large number of fields in the branch of chemical sciences [1-4]. π - π aromatic stacking interactions are vital in various fields of chemistry and biology [5,6]. Aromatic ring systems are involved in π - π stacking interactions and thus accord to structural stabilization along with molecular recognition. If we observe entropically, stacking interaction is found to be an unfavorable process and results in self-organization of atoms and molecules [15, 16]. They are crucial for the geometry characterization and providing stability to aromatic molecules, in the generation of tertiary structure of proteins and amino

acids, crystal packing of aromatic molecules, regulation of gene expression, intercalation of anticancer drugs into DNA nucleobases, etc. [3-8]. The term π - π stacking interaction implies to the interaction that leads to more or less a parallel arrangement of planar aromatic molecules with an interplanar distance ranging between 3.3–3.8 Å.

Aromatic molecules (benzene, pyridine etc.) show normal ring current through the aromatic ring due to the presence of conjugated π - systems. The aromatic ring current is found maximum at a height of 0.75 Å from the molecular plane. However, the ring current becomes half at

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a height of 1.75\AA from the molecular plane [17]. As a result of which the π - π electron cloud interaction (π - π stacking) is often observed in two parallel placed aromatic molecules, and the π - π electron cloud interaction is much more effective when the interplanar separation ranges from 3.3 - 3.8\AA [18]. Thus these π - π stacking interactions play a crucial role in the field of numerous works of quantum chemistry [3-8]. Benzene and pyridine like aromatic molecules are vastly studied for this kind of stacking interactions [9-13]. Moreover, when substituents are introduced in the aromatic ring systems, the strength of the aromatic system can be attuned [19] π - π stacking interactions play a vital role in the outgrowth of stereoselectivity in many biological and chemical reactions [7-10]. In biological systems, especially in the field of drug discovery, the non-bonded interactions have always been an important strand. These intermolecular non-bonded attractive interactions are responsible for accumulation of macromolecules where the activity and reacting properties of drug molecules depend on its capability of recognition in a particular biological system [20-23]. Aiming at an improved perception of non-covalent interactions (long range) engrossing DNA nucleobases and various aromatic rings, a vast number of theoretical and experimental works have been carried out [29, 30]. Among the different quantum mechanical methods, coupled cluster, CCSD (T) calculations are found to be most accurate in describing stacked complexes.

However, for high level quantum mechanical calculations, MP2 calculations are not acceptable as compared to CCSD calculations for describing interaction energies in macromolecular systems. This is mainly because MP2 calculations overstate the stability of complexes. Thus MP2 calculations are best described for

calculating π - π stacking interactions in small aromatic systems [24]. On the other hand, Density Functional methods are still a vital tool in the field of computational chemistry just because of its reasonable balance of accuracy and low computational cost. But in describing stacking interactions, DFT fails due to involvement of dispersion forces of interactions. However, Truhlar and co-workers have developed a totally new DFT method which has proved to describe π - π stacking interactions [25-28].

In this work, it has been investigated to compare the stacking interaction energies afforded by ab-initio and DFT methods, used to describe the stability and interactions within the stacked models and study the different effect of change in conformations for aniline and some p-substituted aniline systems.

METHODOLOGY

Models for Stacked Structure

The geometries of aniline and para-substituted aniline molecules are completely optimized by using MP2 method with different basis sets. All calculations are carried out using the Gaussian09 program code. These optimized geometries are used for constructing various stacked models of aniline and para-substituted aniline systems using JoinMolecule package of software. Arguslab was also used to visualize and observe the different stacked models. While constructing the models for π - π stacking, all the aromatic ring systems are laterally shifted so that they perfectly fall on top of the other. In these models, all the stacked models of aniline and para substituted aniline systems have been analyzed by horizontally shifting the upper ring and keeping the lower ring at a constant position about the horizontal axis. The lower and upper aniline rings are allowed to stack with a fixed vertical

separation of 3.6 Å to obtain effective π - π stacking interaction.

Stacking interactions for stacked models:

All the constructed geometries of aniline and p-substituted aniline (methyl aniline, chloroaniline and phenylene diamine) were optimized by using MP2 levels of theories with 6-311++G (d, p) basis set (figure 1). Some other basis sets were also used for further calculations and comparison. The optimized models of all the molecules were stacked individually such that the upper ring falls on top of the lower ring. And then lateral horizontal shifting of upper ring was done for both in positive and negative directions, i.e from $-x$ to $+x$ direction. Single-point calculations at MP2 levels were thus carried out for determining the minimized stacked energy using 6-311++G (d,p) as a basis set and to calculate the stacking interaction energies of the stacked models of aniline and p-substituted aniline systems. Other basis sets were also used for stacking energy calculations and to compare among the different stacking energies of stacked models. Other quantum mechanical methods using correlation consistent basis sets like cc-pVDZ and cc-pVTZ for doublet and triplet states respectively, are also carried out for the given aniline systems. But it also gives the same trend as given by MP2 methods with different basis sets (table 1).

The stacking interaction energies (E) are computed from the following equation.

$$E = E_{ST} - 2E_M$$

E_{ST} and E_M are the energies of stacked model and monomer. All the calculations are carried out with Gaussian09 program code [31]

RESULTS AND DISCUSSION

π - π stacking interactions of aniline, 4-methylaniline, 4-chloroaniline and

phenylenediamine systems have been carried out in the present study (figure 1). All the geometries of the molecules have been optimized by MP2 methods. The single point MP2 calculations with 6-311++G (d, p) basis set has been found useful in describing the stability of stacked aniline as well as stacked p-substituted aniline systems. The interaction energies are initially calculated for certain stacked models of aniline and p-substituted aniline systems. The upper rings of the stacked models are laterally shifted with a fixed vertical separation of 3.6 Å to produce various stacked models for each system and the single point calculations are performed for all the stacked models. Figures 2-5 shows the relative changes of the interaction energies of different minimized stacked models of aniline and p-substituted aniline molecules. The calculated stacking interaction energies for minimized models with 6-311++G (d, p) basis set does not show much variation from that of other basis sets (table 1). Among all the stacked models of aniline and p-substituted aniline it has been observed that the stacking interaction energy of stacked aniline model is found to be the most negative (-16.067 kcal/mol) (table 1). On the other hand, for substituted anilines, the stacking interaction energy for phenylenediamine (-10.082 kcal/mol) system has been found to be much more negative than that of Chloroaniline (-8.414 kcal/mol) and Methylaniline (-8.109 kcal/mol). figures 2-5 show the minimized stacked models for all the aniline systems. The more negative stacking interaction energy value represents the calculation of electron-electron correlation and dispersion force. Therefore, we can consider that the stacking interaction for phenylenediamine is more favored than that of chloroaniline and methylaniline. The plots of interaction energies versus stacking positions for lateral shifting of the

aniline systems are shown in figure 6 and certain stable stacked structures are located from the minima in the interaction energy plots i.e. it gives the most favored and stable stacked models (figures 2-5).

The stability of normal stacked aniline molecule is due to its planar and less repulsive structure and it shows effective π - π stacking interaction due to the absence of additional bulky substituents. On the other hand, addition of less bulky substituents such as Cl, CH₃ and NH₂, at para position of the aniline ring results small change in symmetry and electron cloud density (table 2) in the substituents for normal and stacked models, which ultimately leads to the variation in stacking interaction energies. However, ortho and meta substituted aniline systems also shows π - π stacking, but they may not show effective stacking interaction because of the presence of bulky groups adjacent to the -NH₂ group of aniline system, hence it may be considered that para substituted aniline systems give better π - π stacking interactions.

Among all the studied p-substituted aniline systems, it has been observed that minimized stacking interaction energy of phenylenediamine gives more negative value. i.e it gives effective and better π - π stacking interaction than that of other substituted aniline systems. Here the structure of phenyl ring is symmetric and the electron cloud distribution is properly balanced within the aromatic ring due to the presence of same -NH₂ groups at para position (figure 1(d) & table 2).

The standard intermolecular separation between the aniline rings is taken as 3.6 Å. It is also important to locate the most favored π - π stacking distance, so the stacking energies of two stacked aniline molecules at different vertical separations have been calculated and the distance (vertical and lateral) dependent variation of stacking energies are shown in figure 7.

The stacked structures located within certain conformational spaces of two anilines are found favorable as predicted from the results of MP2/6-311++G(d,p) calculations. The maxima and minima in the graphs indicate the two distinguishable regions of total and partial stacking of aromatic rings. The repulsive interaction is found prominent in the total stacking of the aromatic rings, and the maximum points in the graph represent the repulsive and unstable structures. The repulsive interaction is found maximum at 2.8 Å, and it gradually decreases due to the increase of electrostatic interaction energies at longer intermolecular distances.

CONCLUSION

As shown in table 1, the extent of dispersion force calculated in MP2 methods with 6-311++G (d, p) basis set is maximum, which results more negative interaction energy values for different aromatic systems. However, the HF/6-311++G (d, p) method cannot usually estimate more dispersion energies. So the role of dispersion forces demonstrated in these calculations may be useful for studying stacking interactions of aromatic molecules. The high level computational methods with basis sets such as, CCSD(T) and cc-pVQZ may be applied to calculate the effective electron correlation energy and dispersion force to get more accurate calculations, but such high level calculations are quite expensive and time consuming.

In conclusion, the MP2 methods are found more feasible for explaining the π - π type of stacking interaction for all aniline systems. Although effective pi-pi stacking is observed in all aniline and para substituted aniline systems, but in phenylenediamine it is found more favorable and gives minimum stacking interaction energy [figures 5 & 6(d)].

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Table 1. Stacking Interaction energies for minimized stacked models of aniline and p-substituted aniline systems

Basis Sets	Interaction Energies (kcal/mol)			
	Aniline-Aniline	Chloroaniline-Chloroaniline	Methylaniline-Methylaniline	Phenylenediamine-Phenylenediamine
6-311++G (d, p)	-16.0672	-10.3511	-9.6021	-11.7351
6-311++G (2df, 2pd)	-10.2044	-8.4137	-8.1088	-10.0819
cc-pVDZ	-15.1423	-5.1240	-5.9440	-8.6091
cc-pVTZ	-10.3865	-6.9240	-7.3539	-9.6706

Table 2. Mulliken charges for -NH₂ group and substituents (-Cl,-CH₃ and -NH₂) for unstacked and minimized stacked models for different aniline systems

Molecules	Mulliken Charges			
	Groups	Atoms	Unstacked	Stacked
Aniline	NH ₂	N	-0.536	-0.329
		H ₁	0.286	0.238
		H ₂	0.286	0.238
Chloroaniline	NH ₂	N	-0.382	-0.294
		H ₁	0.253	0.236
		H ₂	0.253	0.236
	Cl	Cl	0.211	-0.436
Methylaniline	NH ₂	N	-0.394	-0.363
		H ₁	0.254	0.255
		H ₂	0.254	0.255
	CH ₃	C	-0.692	-0.826
		H ₁	0.134	0.141
		H ₂	0.149	0.164
Phenylenediamine	NH ₂	H ₃	0.133	0.141
		N	-0.397	-0.330
		H ₁	0.244	0.236
	NH ₂	H ₂	0.244	0.236
		N	-0.397	-0.303
		H ₁	0.244	0.248
		H ₂	0.244	0.248

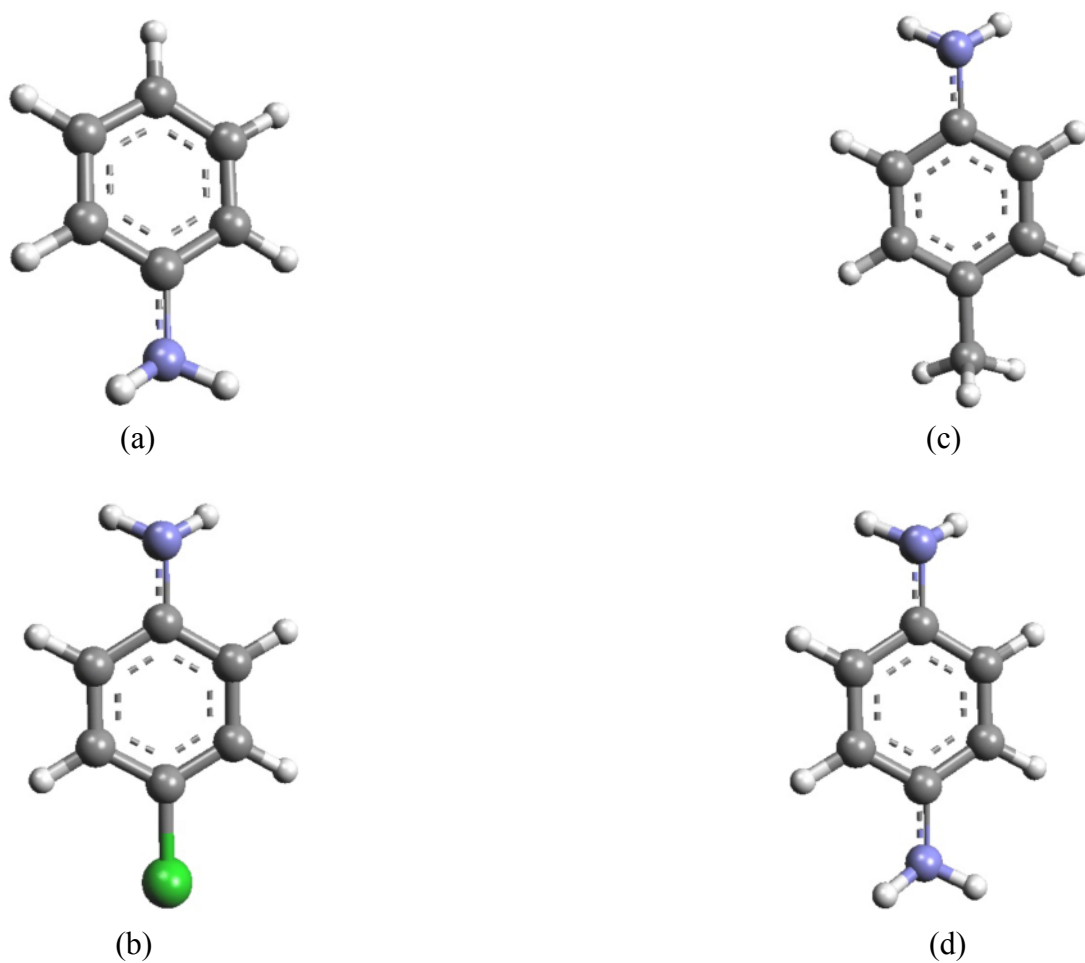


Fig. 1. Optimized models of (a) Aniline (b) 4-methylaniline (c) 4-chloroaniline and (d) Phenylenediamine.

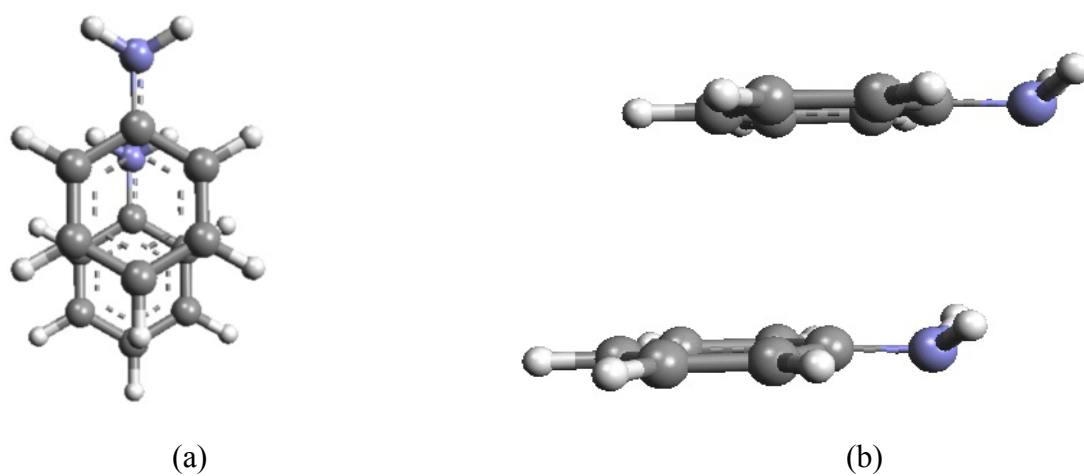


Fig. 2. Minimized stable stacked models of aniline (a) *top view* (b) *side view*.

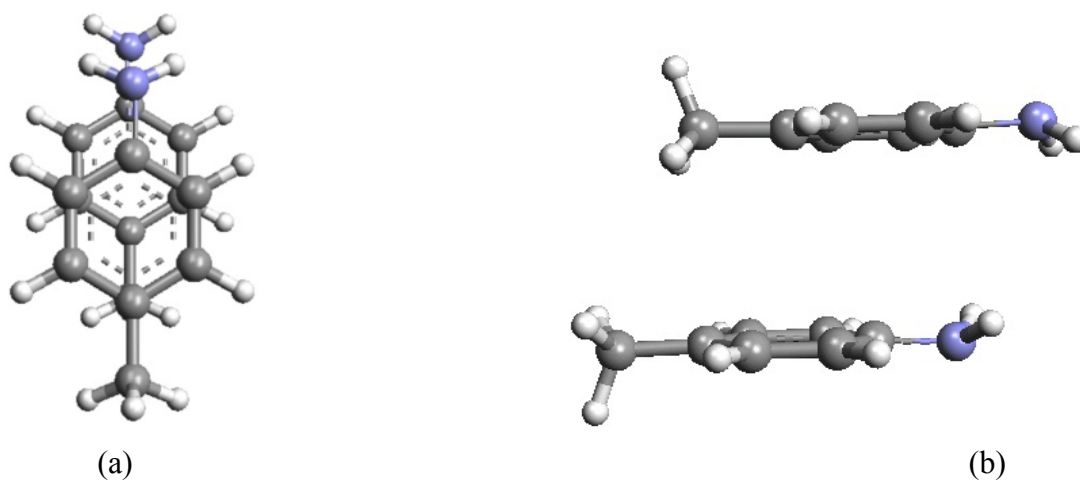


Fig. 3. Minimized stable stacked models of 4-methyl aniline (a) *top view* (b) *side view*.

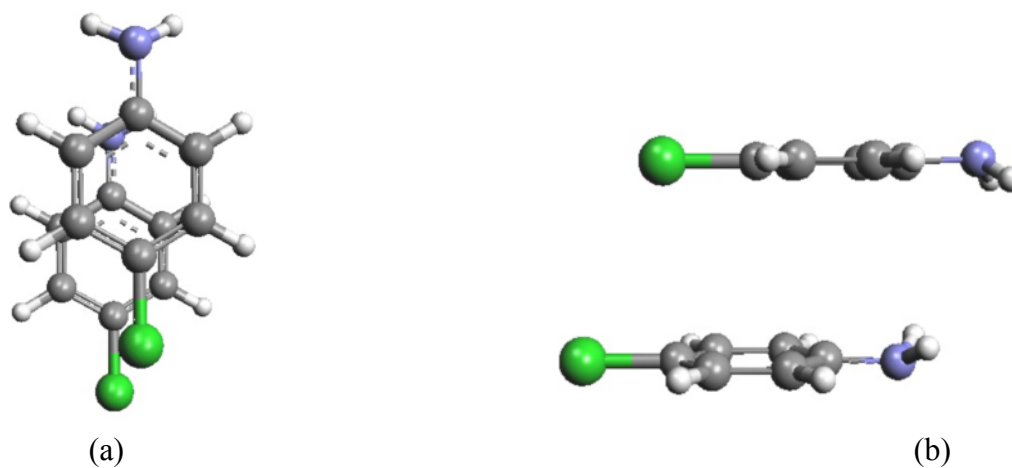
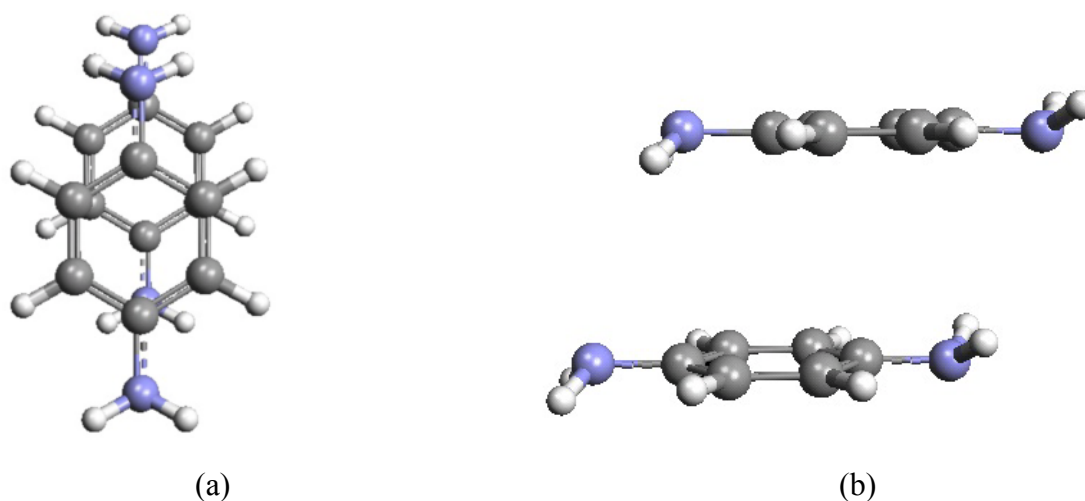


Fig. 4. Minimized stable stacked models of 4-chloro aniline (a) *top view* (b) *side view*.



Fi. 5. Minimized stable stacked models of Phenylenediamine (a) *top view* (b) *side view*.

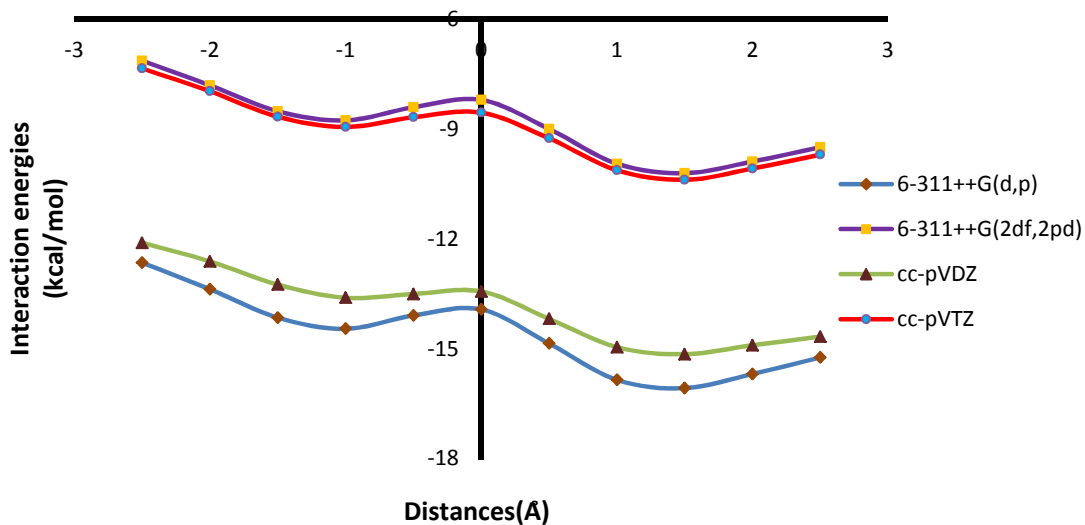


Fig. 6(a). Plot of interaction energies (MP2 single point) versus stacking positions (\AA°) of aniline.

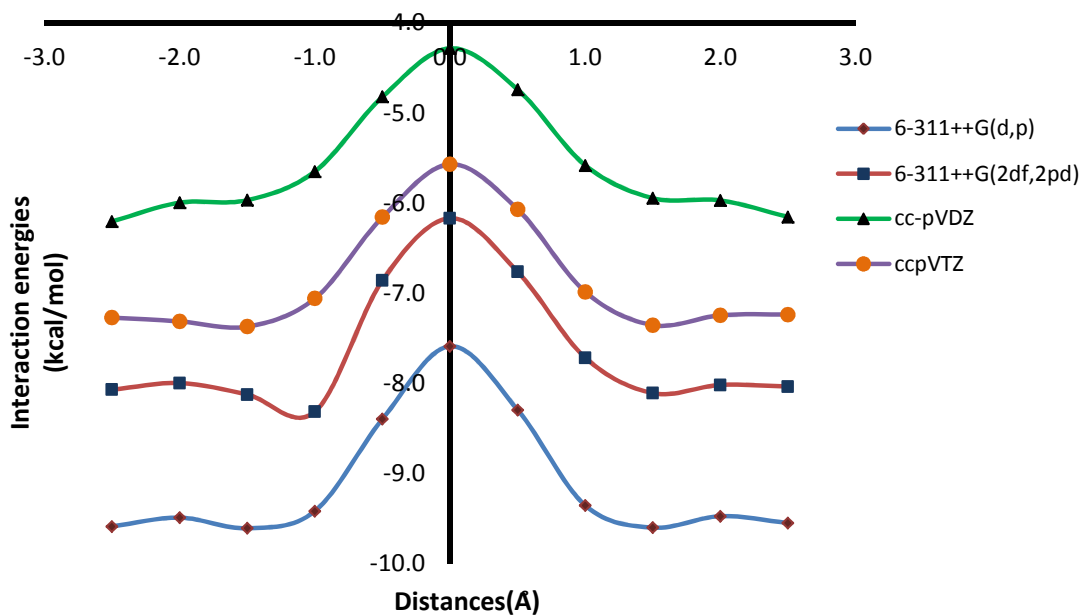


Fig. 6(b). Plot of interaction energies (MP2 single point) versus stacking positions (\AA°) of 4-methylaniline.

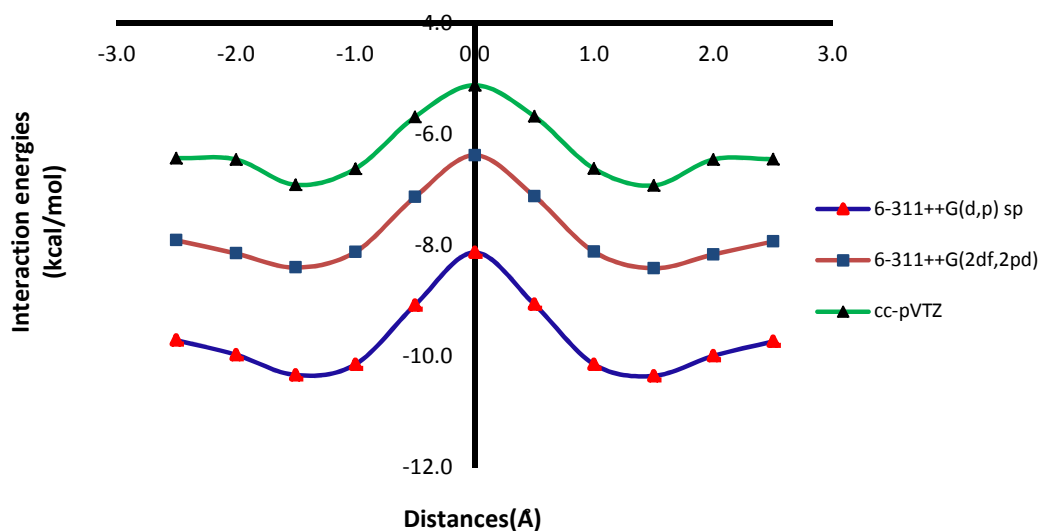


Fig. 6(c). Plot of interaction energies (MP2 single point) versus stacking positions (A°) of 4-chloroaniline.

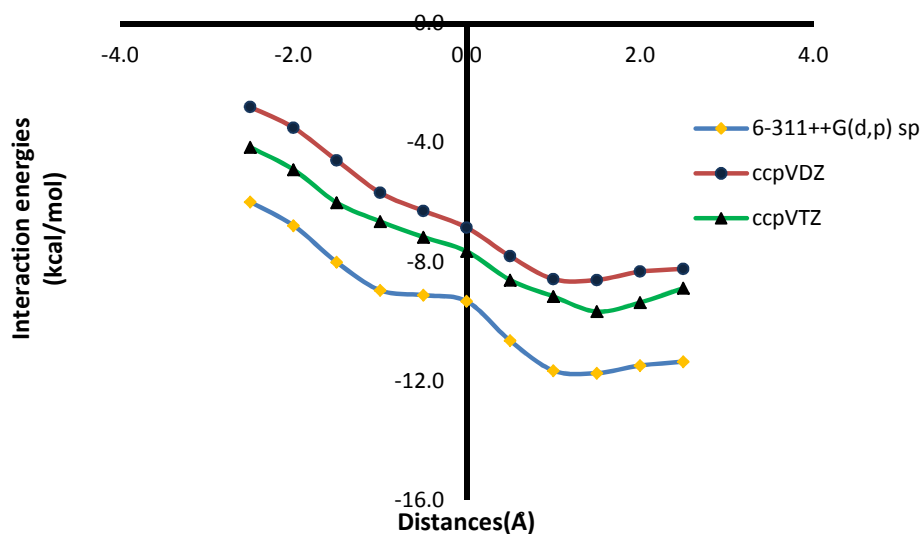


Fig. 6(d). Plot of interaction energies (MP2 single point) versus stacking positions (A°) of phenylenediamine.

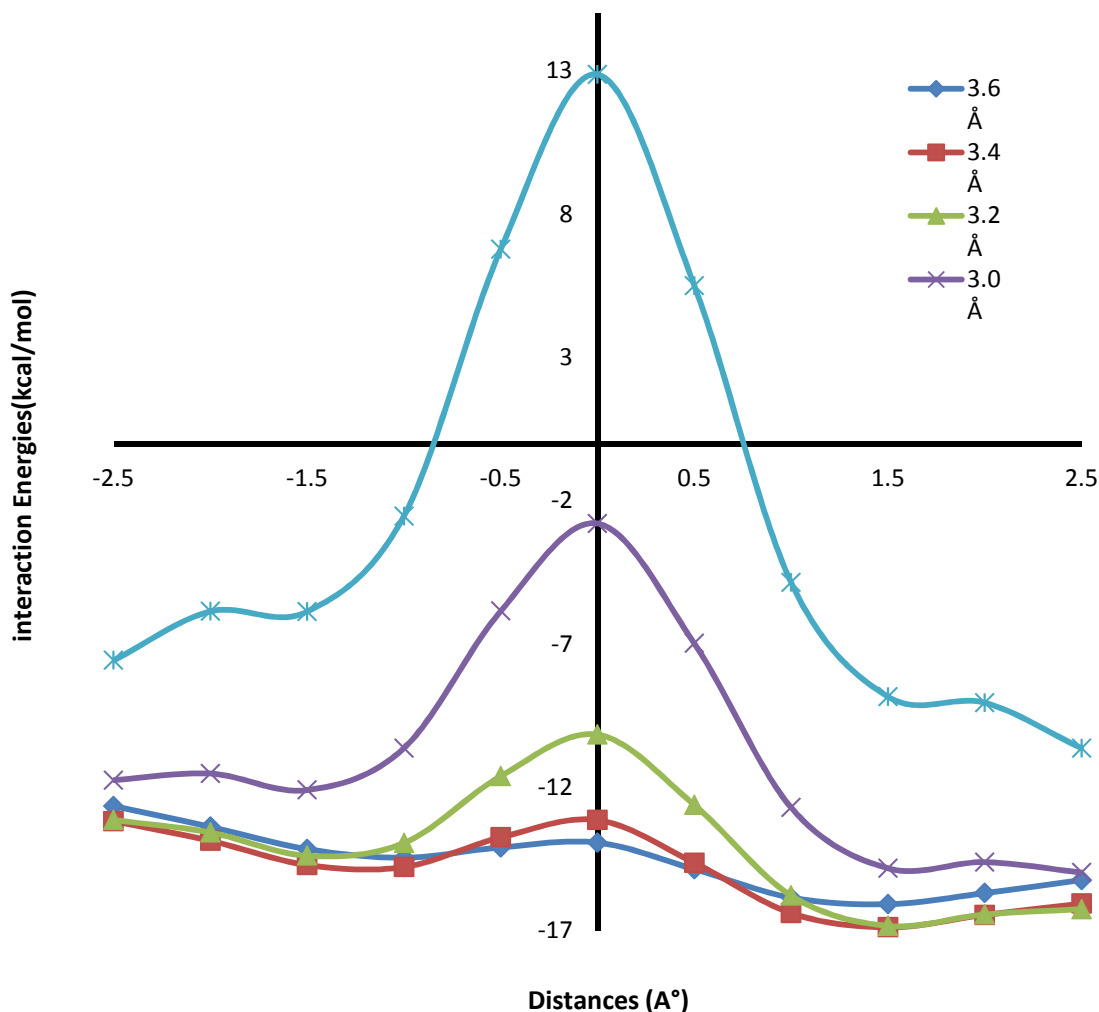


Fig. 7. Plots of interaction energies versus lateral shifting in angstrom (Å) of aniline molecules at different intermolecular distances with MP2/6-311++G(d,p) basis set.

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