QUANTUM MECHANICAL STUDIES ON THE EFFECT OF INTERMOLECULAR ROTATION OF THE STACKING INTERACTION OF DIAZINE ISOMERS

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ABSTRACT

Non-covalent interaction plays an important role in different π -system, aromatic compounds and other biomolecules. The π - π stacking interaction between heteroaromatic systems is an important area of research. Herein, we have taken one simple organic heterocycle such as a diazine molecule and some of its isomers to investigate the π - π stacking interaction. Stacking interactions of heterocycles are highly sensitive towards the position, bond angle and dihedral angle of the heteroatoms and it also results in different interactions for different stacked models. We have chosen the stacked dimers of diazine isomers (1,2-diazine, 1,3-diazine and 1,4-diazine) and quantum mechanical studies have been carried out to compute the π - π stacking interaction using (Møller-Plesset) MPn methods. The diazine isomers show variation in stacking interaction with different intermolecular rotation and we observed a conformational variation in different stacked models of diazine.

Keywords: MPn, Diazine, Dihedral Angle, π - π Stacking etc.

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INTRODUCTION

The non-covalent interactions are important due to their role in the structure and function of supramolecular systems in various areas of chemistry, material science, catalysis, biology, etc. The non-covalent interactions include hydrogen bonding, ion-dipole, dipole-dipole, π - π , van der Waals, metal-ligand interactions.^{1,2} Among the various non-covalent interactions the π - π stacking interaction between heteroaromatic systems has gained the utmost attention in recent years due to its ubiquitous nature in many biological and supramolecular systems. This interaction plays a key role in determining the overall assembly and packing of these systems.^{3,4} The π - π interaction among the aromatic rings plays a crucial role in stabilizing the double-helical structure of DNA and RNA and protein structures.⁵⁻⁷ The π - π interactions are equally important in many material science applications such as in carbon nanotubes, graphene, electronic properties of organic molecules having π -conjugated systems.⁸⁻¹⁰

Heterocyclic molecules are very much important, e.g. naturally occurring indole derivatives have several pharmacological activities.¹¹⁻¹³ Due to the electronegativity difference between the carbon (C) and the heteroatom (X) in the C-X bond of heterocycles, the polarization of the electron cloud takes place and thus these molecules show better stacking interaction compared to non-heterocyclic counterpart. Nitrogen containing heterocycles are the most important one to study for non-covalent interactions, as it shows maximum electron charge density on it. They show better stacking interaction between themselves as the heteroatom plays an important role in the non-covalent interaction. Sponer and Hobza had studied the stacking interaction in dimers of various nitrogen-containing heterocycles using MP2 level of theory.¹⁴ Mignon and co-workers studied the interactions in mixed dimers of pyridine and substituted benzene. Tsuzuki and co-workers studied the interaction of thiophene molecules in several orientations.¹⁵ Sathyamurthy et al. has done a detailed study on the stacking interaction of dimers of pyridine, pyrazine and tetrazine molecule in different orientations.¹⁶⁻¹⁹ The present work is aimed to study the stacking

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interaction in homodimers (12-12, 13-13 and 14-14 diazine) of three isomers of diazine (1,2 diazine, 1,3 diazine and 1,4 diazine) in a different orientation with intermolecular rotation. We also investigated the stacking interactions for the heterodimers (12-13, 13-14 and 12-14 diazine) of diazine isomers. The results would allow us to have a better understanding of the non-covalent interaction of nitrogen containing heterocycles in organic and inorganic systems.

EXPERIMENTAL

Initially, all the diazine and its isomers were constructed and then optimized. Further, these optimized geometries were used for constructing various stacked models of diazine isomers with the help of the *JoinMolecule* package of software. Also, Arguslab was also used to visualize and observe the different stacked models. For studying the long-range non-covalent interaction such as π - π interaction, the quantum mechanical *ab initio* method is the most reliable one. All the stacked models have been computed by using MPn (Møller-Plesset) method with GaussView5.0 and Gaussian09 software packages. MP2/6-311++G(d,p) basis set was used for the optimization of models and the same basis set was used for the calculation of single point energy.

Diazine dimers can be directly stacked like sandwich structure with different dihedral angles (intermolecular rotation), but in our observations, we have taken only 0°, 60°, 120° and 180° dihedral angles, which show preferable stacking interaction among them. Here, 0° dihedral angle can be considered as eclipsed and the rest of them i.e. 60°, 120° and 180° are considered as staggered conformations. The π - π stacking interaction energies for the stacked models of diazine isomers can be calculated by the following equation:

$$\text{Interaction Energy} = E_{\text{stacked}} - 2E_{\text{single}}$$

Where, E_{stacked} = Single point energy of the stacked diazine molecule and E_{single} = Single point energy of the single unstacked diazine molecule. All the calculations were computed by using Gaussian09.²⁰

RESULTS AND DISCUSSION

The current work describes the non-covalent π - π stacking interactions among the diazine isomers both homo and hetero stacked models. Before making the stacked models, the three diazine isomers (1,2-diazine, 1,3-diazine and 1,4-diazine) were optimized by using MP2 level of theories in Gaussian09 software package (Fig.-1).

Fig.-1: Optimized models of Diazine isomers (a) 1,2Diazine, (b) 1,3Diazine and (c) 1,4Diazine

During the construction of stacked models of diazine dimers the intermolecular separation was kept constant at 3.6 Å, which was taken as the standard intermolecular distance for any long-range non-covalent interaction. The stacking interactions of diazine stacked dimers have been studied by horizontal shifting of one ring above others (keeping the second ring at the constant position), both in the positive and negative direction along any axis. Herein, the horizontal shifting for diazine dimers was done along the X-axis from 0 to +3 Å and 0 to -3 Å directions. All the stacked models of diazine stacked dimers were

studied in the gas phase. Moreover, the models for diazine dimers were also constructed by rotating one ring at different rotations keeping the other ring fixed. Here, we calculated the stacking interactions for diazine dimers with different intermolecular rotations (dihedral angle), the preferable intermolecular rotations are viz. 0° , 60° , 120° and 180° (Fig.-2).

Fig.- 2: Pictorial Representation of Intermolecular Rotation for Stacked Diazine Dimmer at 0° , 60° , 120° and 180°

It is well known that more is the negative interaction energy value of the stacked model more is the stability of the stacked model which results in the most stable and favored conformers for any stacked model. The minimum interaction energy can easily be reflected in the interaction of energy plots. Therefore, the minimum points of the interaction energy (kcal/mol) versus horizontal shifting ($\text{\AA}$) plot shows the most negative and most favored structure (Figs.-3 to 6). In our investigations, the most negative value of stacking interaction energy for 1,2-diazine dimer (homo stacked dimer), has been computed as -6.395 kcal/mol, which is for intermolecular rotation of 180° at a horizontal shifting of $+1.0\text{\AA}$ (Table 1). In a 1,2-diazine stacked system, as we increase the intermolecular rotation (dihedral angle) from 0° to 180° for different stacked models, the interaction energy also becomes more negative and it gives the most stable conformation for 180° rotation (Fig.-3 and 7). Thus, for the 1,2-diazine dimer system the stability for stacked models increases in the order $0^\circ < 60^\circ < 120^\circ < 180^\circ$. Similar calculations were also carried out for 1,3- and 1,4-diazine of homo stacked dimer systems. In 1,3- homo stacked dimer system 0° intermolecular rotation is almost equivalent to 180° , therefore we carried out a calculation for the stacking interactions with 0° , 60° and 120° intermolecular rotations.

Fig.-3: Plot of Interaction Energies (kcal/mol) Versus Horizontal Shifting (Å) for 1,2-1,2 Diazine Dimer

Fig.-4: Plot of Interaction Energies (kcal/mol) Versus Horizontal Shifting (Å) for 1,3-1,3 Diazine Dimer

Fig.-5: Plot of Interaction Energies (kcal/mol) Versus Horizontal Shifting (Å) for 1,4-1,4 Diazine Dimer

Fig.-6: Plot of Interaction Energies (kcal/mol) Versus Horizontal Shifting (Å) for Hetero mixed Dimers 1,2-1,3, 1,2-1,4 and 13-14

Fig.-7: Minimized Stacked Models of 1,2 Diazine Stacked Dimers with (a) 0°, (b) 60°, (c) 120° and (d) 180° Intermolecular Rotation

Here, the most stable stacking interaction energy value for the stacked dimer models are computed as -4.379 kcal/mol for the intermolecular molecular rotation of 120°, at +1.0Å horizontal shifting (Fig.-4 and 8). This trend of stability is observed due to the repulsion between the nitrogen atoms of the diazine ring which decreases as we increase the intermolecular rotation of the diazine isomers. But, the repulsion is maximum and gives less negative value in the interaction energy plots when there is no horizontal shifting of the diazine rings and without intermolecular rotation (Figs.- 3 to 6).

On the other hand, since the 1,4-diazine system has purely symmetric stacked conformers, therefore in a 1,4-diazine stacked dimer system, 0° and 60° intermolecular rotations are equivalent to 120° and 180° respectively. Hence, we carried out a calculation for the stacking interactions with only 0° and 60°

intermolecular rotations. In the 1,4-diazine homo dimer system, the most stable interaction was observed at 60° intermolecular rotation with interaction energy value -4.474 kcal/mol at -1.0Å horizontal shifting (Fig.-5 and 9). The overall trend of stability order for all the stacked homo dimer models of diazine isomers is almost the same, i.e. increases the stability with an increase in the intermolecular rotation.

Encouraged by the π - π stacking interaction of homo stacked dimers of different diazine isomers, we further studied the stacking interaction of hetero stacked diazine isomers or mixed diazine isomers. For this we have chosen to study the stacking interaction among 1,2-1,3, 1,3-1,4 and 1,2-1,4 hetero stacked diazine dimer at a normal favored position without any intermolecular rotations and vertical separation was kept constant (3.6Å). Interestingly, all the stacked hetero stacked dimer or mixed stacked systems (1,2-1,3; 1,3-1,4 and 1,2-1,4) are comfortably stacked within them, as we have calculated the interaction energy (Fig.- 6 and 10). The computed stacking interaction energies for 1,2-1,4; 1,3-1,4 and 1,3-1,4-diazine stacked heterodimers were found as -4.212, -4.106 and -4.275 kcal/mol respectively as shown in Table 1. But, the most negative interaction energy value is found for 1,3-1,4 stacked dimeric systems i.e. -4.275 kcal/mol, it happens because of the repulsion between the nitrogen atoms of the two rings is minimum. The actual sequence of stability of the stacking interaction of diazine hetero stacked dimers is found to be; 1,2-1,3 < 1,2-1,4 < 1,3-1,4 diazine dimer.

We also computed the Mulliken charge density of the diazine isomers using MP2/6-311++G(d,p) POP=NPA basis set, for both unstacked diazine molecule as well as stacked diazine molecules for the most stable stacked conformers. The Mulliken charge density shows the change in net charge density at the N atoms of the diazine ring for unstacked as well as stacked diazine molecules, i.e. when the difference in change of charge density at the N atoms are more, the stacked model will be more stable (Table-2 and 3).

Fig.- 8: Minimized Stacked Models of 1,3 Diazine Stacked Dimers with (a) 0° (b) 60° and (c) 120° Intermolecular Rotation

Fig.-9: Minimized Stacked Models of 1,4 Diazine Stacked Dimers with (a) 0° and (b) 60° Intermolecular Rotation

(a) (b) (c)
Fig.-10: Minimized Stacked Models of mixed Diazine Stacked Dimer (a) 1,2-1,3 (b) 1,2-1,4 and (c) 1,3-1,4

Table-1: Stacking Interaction Energies (kcal/mol) for minimized Diazine Dimer stacked Models (MP2/6-311++G(d,p))

Stacked Models	Intermolecular rotation	Horizontal Shifting (Å)	Interaction Energies (kcal/mol)
12-12-Diazine	0°	+2.0	-2.517
	60°	+1.0	-4.330
	120°	+1.0	-6.091
	180°	+1.0	-6.395
13-13-Diazine	0°	-2.0	-3.323
	60°	+1.0	-4.146
	120°	+1.0	-4.379
14-14-Diazine	0°	+1.5	-3.310
	60°	-1.0	-4.474
12-13-Diazine	0°	+1.0	-4.212
12-14-Diazine	0°	-1.5	-4.106
13-14-Diazine	0°	-1.5	-4.275

Table-2: Computed Mulliken Charges for minimized Diazine Dimer Stacked Models (MP2/6-311++G(d,p) POP=NPA)

Models	Intermolecular rotation	Ring (Unstacked)		Ring 1 (stacked)		Ring 2 (stacked)	
		N1	N2	N1	N2	N1	N2
12-12-Diazine	0°	-0.0541	-0.0541	-0.0239	-0.0380	0.0396	-0.0156
	60°	-0.0541	-0.0541	0.0176	-0.0084	-0.0890	0.1457
	120°	-0.0541	-0.0541	-0.0383	0.0257	-0.0952	0.1468
	180°	-0.0541	-0.0541	-0.0293	0.0169	0.0083	-0.0239
13-13-Diazine	0°	-0.2165	-0.2166	-0.0445	-0.0311	-0.1032	-0.1562
	60°	-0.2165	-0.2166	-0.1423	-0.1203	-0.0930	-0.0906
	120°	-0.2165	-0.2166	-0.1327	-0.1394	-0.0604	-0.1381
14-14-Diazine	0°	-0.1148	-0.1148	-0.0193	-0.0447	-0.0170	-0.0409
	60°	-0.1148	-0.1148	-0.0391	-0.0598	-0.0203	-0.0425

Table -3: Computed Mulliken Charges for minimized mixed Diazine Dimer Stacked Models (MP2/6-311++G(d,p) POP=NPA)

Diazine Models	Unstacked Models				Stacked models			
	Ring 1		Ring 2		Ring 1		Ring 2	
	N1	N2	N3	N4	N1	N2	N3	N4
12-13	-0.0541	-0.0541	-0.2165	-0.2166	0.0132	-0.0155	-0.0772	-0.0718
12-14	-0.0541	-0.0541	-0.1148	-0.1148	-0.0508	-0.1852	-0.0107	-0.0367
13-14	-0.2165	-0.2166	-0.1148	-0.1148	-0.0508	-0.1852	-0.0107	-0.0376

CONCLUSION

In this study, we have investigated the quantum mechanical MP2 study on the π - π stacking interaction of nitrogen containing heterocycles, viz. different isomers of diazine molecules. From the above results, we observed that the diazine isomers stacks nicely and shows effective π - π stacking interactions at different intermolecular rotations. The most negative interaction energy is computed for the most stable minimized stacked conformer for each intermolecular rotation. The above results reveal that the diazine stacked dimer shows less negative interaction energy, gives a highly repulsive stacked structure when the intermolecular rotation is 0° . From the interaction energy plots, we have observed that the stability of stacked models of diazine isomers varies with intermolecular rotation, i.e 1,2-diazine stacked dimer highly stabilizes at an intermolecular rotation of 180° and shows the most favoured stacking interactions, while for 1,3- and 1,4-diazine dimer stabilizes at an intermolecular rotation of 120° and 60° , gives the most favoured stacking interaction.

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