

Stacking and Spreading Interaction in N-Heteroaromatic Systems[†]

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$\pi-\pi$ interactions in heteroaromatic systems are ubiquitous in biological systems. In the present study, stabilization energies of stacked and hydrogen-bonded dimers of N-heteroaromatic systems (pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine) have been computed using a benchmark quality coupled cluster through the perturbative triples (CCSD(T)) method at the estimated complete basis set (CBS) limit. In the case of stacking, monomer units are found to be stacked in parallel planes with displaced geometries. The stabilization energies for the most stable stacked geometry of pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine dimers are found to be -3.39 , -4.14 , -4.02 , and -3.90 kcal/mol, respectively at the est. CCSD(T)/CBS level of theory, which is clearly larger than the stabilization energy for the most stable geometry of the benzene dimer. In the case of spreading, hydrogen bonded dimers and trimers are stabilized by weak C–H \cdots N interactions. The stabilization energies for the stacked and the spread out complexes are found to be comparable. The stabilization energy for the trimers is computed using the MP2, MP3, and B3LYP-D methods. The present study is aimed at unraveling the basis of preferred conformations of N-heteroaromatic dimers. These model systems explain partly the stability of double helical DNA and RNA structures that are formed by stacking and hydrogen bonding between nucleic acid bases.

1. Introduction

Noncovalent interactions play an important role in determining the structure and properties of molecular clusters that are important in chemistry, biology, and materials science. Stacking (in vertical plane) through “ $\pi-\pi$ interactions” and spreading (in horizontal plane) through hydrogen bonds are the two types of interactions prevalent in molecular assemblies. These interactions play an important role in the packing of crystals containing aromatic moieties,^{1–4} stabilizing the large three-dimensional helical structures of DNA and RNA,^{5–7} in supramolecular chemistry^{4,8,9} and in molecular recognition processes. It was predicted by Burley and Petsko that nearly 60% of aromatic side chains in proteins participate in $\pi-\pi$ interactions (offset and edge-to-face aromatic pairs).^{10,11} Aromatic–aromatic interactions also influence the structure of host–guest complexes,^{12–16} porphyrin aggregates,¹⁷ and protein folding.¹⁸

The benzene dimer, the simplest prototype model for the $\pi-\pi$ interaction, is perhaps the most-studied system in the last two decades.^{12–35} The combined experimental and theoretical work to date suggests that the two most favorable geometries are the T-shaped (binding energy: 2.46 kcal/mol) and parallel-displaced (binding energy: 2.35 kcal/mol).³⁵ The responsible factor for stabilizing the dimer is found to be primarily a dispersion interaction. Besides this, the role of electrostatic interaction (favorable quadrupole–quadrupole interaction) for the preferred mutual orientation was emphasized by Stone and co-workers.^{36,37} The binding energy for the benzene dimer using multicoefficient

extrapolated density functional methods (namely MCG3-TS, MCG3-MPWB, and MCG3-MPW) was reported by Zhao and Truhlar³⁸ and the computed stabilization energy values were shown to be in excellent agreement with the energy obtained using the CCSD(T) method. The effect of different substituents in aromatic rings on $\pi-\pi$ interactions has been studied in detail by the groups of Kim and Sherrill.^{35,39} The stabilization energy for the dimer is found to be enhanced by substitution.

The $\pi-\pi$ interaction between heteroaromatic moieties has gained a lot of attention in recent years. The stacking interaction in dimers of pyrrole, pyrimidine, triazine, aminotriazine, 4-aminoypyrimidine and 1-aminoypyrimidine was investigated by Šponer and Hobza⁴⁰ at the MP2 theory using 6-31G*(0.25) and aug-cc-pVDZ basis sets. Interactions in mixed dimers of substituted benzene and pyridine were computed by Mignon et al.⁴¹ and the parallel-displaced geometry was found to be the most stable.

The interaction between thiophene molecules in various possible orientations was studied by Tsuzuki et al.,⁴² and the stabilization energies for parallel and perpendicular geometries were computed to be -1.71 and -3.12 kcal/mol. The role of *sym*-triazine units in supramolecular chemistry has been examined recently by Mooibroek and Gamez⁴ using a crystal structure database search. The stacking interaction energies for the toluene dimer in different orientations (parallel, antiparallel, and crossed) were calculated by Tsuzuki et al⁴³ and Rogers et al.⁴⁴ Experimental studies on the *sym*-tetrazine dimer were carried out by Levy and co-workers⁴⁵ and the complexes corresponding to stacked (sandwich) and edge-to-face orientations were observed. The role of the *sym*-tetrazine moiety in crystal structures was reported by Oxtoby et al.⁴⁶ Price and Stone studied the interaction in various heterodimers, including benzene and *sym*-tetrazine,³⁶ and the role of electrostatic interaction was investigated. The interaction in naphthalene dimer was investigated

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theoretically by Tsuzuki et al.⁴⁷ and experimentally by Gilliéron⁴⁸ using resonance enhanced multiphoton ionization coupled with a time-of-flight mass spectrometer. The slipped-parallel geometry with a stabilization energy of -5.73 kcal/mol was found to be more stable than the crossed, T-shaped and sandwiched geometries. An experimental study of the benzene–anthracene heterodimer was carried out by Doxtader et al.⁴⁹ using fluorescence excitation spectra, and an offset-stacked geometry was inferred. The interaction between two azulene rings was reported by Piacenza and Grimme,⁵⁰ and in the most stable geometry ($\Delta E = -9.2$ kcal/mol) two seven-membered rings were found to be stacked and the molecular axes were rotated by $\sim 130^\circ$. The $\pi-\pi$ stacking interaction in cyclophanes and for linear condensed acenes from benzene to tetracene was investigated by Grimme.^{51,52} The $\pi-\pi$ stacking behavior of dimers formed by nitrogen-containing planar polycyclic aromatic hydrocarbons was studied theoretically by Tran et al.,⁵³ and off-centered geometries were predicted to be the most stable ones. The role of nitrogen atoms in aromatic stacking was examined by Itahara et al.⁵⁴ using UV and NMR spectroscopy. Compared to studies on the benzene dimer, there is a scarcity of high quality theoretical studies on heteroaromatic dimers in the literature, in spite of their clear biological importance.

In addition to the hydrogen bonding in adenine–thymine and guanine–cytosine base pairs, stacking interactions between base pairs play a significant role in stabilizing three-dimensional helical structures of DNA. Several reports on spreading and stacking interactions between DNA base pairs have been published by Hobza and co-workers.^{55–60} The role of stacking of substituted-benzene rings in the hydrogen bonding ability of pyrimidine and imidazole bases was studied by Mignon et al.⁶¹ at the MP2 level of theory. The competition between stacked and hydrogen-bonded geometries of pyrimidine dimers was examined by McCarthy and co-workers experimentally as well as theoretically.⁶² Two geometries, one hydrogen-bonded and the other stacked, were proposed and in both the geometries dipole moments were pointed in antiparallel directions.

The importance of stacking interactions in chemistry and biology is reflected in a recently published special issue of PCCP.⁶³ The effect of substituent on the stability of the parallel-displaced geometries in benzene dimer was discussed by Arnstein and Sherrill.⁶⁴ The stacking interaction between polycyclic hydrocarbons (naphthalene, anthracene, and pyrene) has been analyzed by Podeszwa and Szalewicz.⁶⁵ The stacking interaction between nucleic acid bases has been discussed by Šponer et al.⁶⁶ The stacking interaction in solid benzene and graphite by Rubeš and Bludský,⁶⁷ nature and physical origin of C–H $\cdots\pi$ interaction by Tsuzuki and Fujii,⁶⁸ and density functional study of concave–convex $\pi-\pi$ interaction by Zhao and Truhlar⁶⁹ are the other articles of interest in that issue.

The stacking interaction for the pyridine dimer and pyrazine dimer in different orientations has been investigated by us.^{70,71} In the case of the former, an antiparallel-displaced geometry was predicted to be the most stable. It is favored by dipole–dipole interactions. In the case of the pyrazine dimer, T-shaped and cross-displaced geometries were shown to be more stable than sandwich, parallel-displaced, and wedge-shaped geometries. Recently, highly accurate quantum chemical investigation (est. CCSD(T)/CBS limit) for various configurations of benzene–pyridine and pyridine dimers was carried out by Hohenstein and Sherrill.⁷² The parallel-displaced geometry for the benzene–pyridine dimer and the antiparallel displaced geometry for the pyridine dimer were seen to be the most stable.

The aim of the present work is to investigate the influence of the nitrogen heteroatom on the $\pi-\pi$ interaction and also to compare the binding energy between $\pi-\pi$ stacked complexes and their hydrogen bonded complexes. We report the results of an extensive investigation of “stacking interaction” in the vertical plane and “spreading interaction” in the horizontal plane for pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine dimers and trimers. Here, the “spreading interaction” refers to the hydrogen bonding between heteroaromatic molecules lying in a plane. By this study we attempt to provide the basis for insights into experimental observations of N-heteroaromatic systems^{45,54} as well as the role of N-heteroaromatic structures in intermolecular interactions in DNA and RNA.

2. Methodology

The Gaussian 03 suite of programs⁷³ was used for the electronic structure calculations. The core electrons were kept frozen in all the calculations. Stacked dimer and trimer geometries of pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine were optimized using the 6-311++G(d,p) basis set at the MP2 level of theory, and the spread out dimer and trimer geometries were optimized using the 6-311G(d,p) basis set at the same level of theory. The change in the stabilization energy by changing the basis set from 6-311G(d,p) to 6-311++G(d,p) is not significant, as shown in the Supporting Information. It is not feasible to optimize the geometry for such systems with the CCSD(T) method using present computational facilities. Also, it was reported by Sinnokrot et al.,³⁴ (Table 1) that the MP2 and CCSD(T) methods predict slightly different values for the equilibrium separation (R) for the benzene dimer by roughly 0.1–0.2 Å. On careful investigation of potential energy curves produced by the CCSD(T)/ aug-cc-pVDZ* method, it is evident that this small difference in equilibrium separation for the two methods would introduce an error of only ~ 0.10 kcal/mol. Therefore, we inferred that the MP2 method with reasonably higher basis set with diffuse functions adequately describes the geometry for N-heteroaromatic systems. Harmonic vibrational frequency calculations were carried out for all the dimer structures. Using the coordinates from optimized geometry, single-point energy calculations were performed at the MP2 level of theory with Dunning’s augmented correlation-consistent polarized valence basis sets (aug-cc-pVXZ where X = D, T, and Q) and the CCSD(T) method with aug-cc-pVDZ basis set. The BSSE correction was incorporated in each case using the counterpoise correction method developed by Boys and Bernardi.⁷⁴ The stabilization energy for the dimer was obtained using the following equation:

$$\Delta E(AB) = E(AB) - E(A) - E(B) \quad (1)$$

where each computation in eq 1 was performed using the full basis set of the dimer. The stabilization energy at the MP2 method near complete basis set limit (CBS) was obtained using the two-point extrapolation scheme developed by Halkier et al.⁷⁵ For the stacked dimer the aug-cc-pVTZ and aug-cc-pVQZ energy values were used to obtain the MP2/CBS values. For spread out dimers, the MP2/aug-cc-pVQZ energies could not be obtained due to convergence problems. Hence, for these cases the aug-cc-pVDZ and aug-cc-pVTZ points were used in the MP2 extrapolation. The estimated CCSD(T)/CBS energy was then obtained using the following equations:

$$\Delta \text{CCSD(T)} = E_{\text{CCSD(T)}}^{\text{aug-cc-pVDZ}} - E_{\text{MP2}}^{\text{aug-cc-pVDZ}} \quad (2)$$

$$\text{est. } E_{\text{CCSD(T)}}^{\text{CBS}} \approx E_{\text{MP2}}^{\text{CBS}} + \Delta \text{CCSD(T)} \quad (3)$$

It was suggested by Sinnokrot and Sherrill that the change in the $\Delta \text{CCSD(T)}$ is insignificant for basis sets higher than aug-cc-pVDZ, for $\pi-\pi$ stacked systems.³³ We also computed the stabilization energy for the dimers using multicoefficient extrapolated density functional theory (MCG3-TS), a method that has been used previously to predict accurate stabilization energy for the benzene dimer at low computational cost. These calculations were performed using the program MLGAUSS 2.0⁷⁶ in conjunction with Gaussian 03.⁷³

The CCSD(T)/aug-cc-pVDZ calculations for the trimers could not be performed due to the large computational resources requirement. Hence, the stabilization energy for the trimers was computed using MP3, which accounts for first nonadditive dispersion.⁷⁷ The equations used to compute two- and three-body interaction terms between the monomers in trimer are as follows:

$$E(123) = \sum_i E(i) + \sum_{ij} \Delta^2 E(ij) + \Delta^3 E(123) \quad (4)$$

$$\Delta^2 E(ij) = E(ij) - E(i) - E(j) \quad (5)$$

$$\Delta^3 E(123) = E(123) - \sum_i E(i) - \sum_{ij} \Delta^2 E(ij) \quad (6)$$

where $E(123)$ is the total energy of the trimer, $E(i)$ is the energy of monomer “ i ”, $E(ij)$ is the energy of dimer “ ij ”, $\Delta^2 E(ij)$ are two-body (pair) interaction energies, and $\Delta^3 E(123)$ is the three-body nonadditive energy. E_{tot} in Table 3 denotes the sum of two-body and three-body interaction energies. Each computation was performed with the trimer basis set. In addition to this, Grimme’s dispersion-corrected density functional theory (DFT-D) method was employed for both the dimers and trimers; this method has been shown to be reliable and efficient for computing the binding energy of noncovalent complexes including $\pi-\pi$ stacked dimers.^{78–81} The basis sets aug-cc-pVDZ and aug-cc-pVTZ were used for the MP3 and B3LYP-D methods, respectively. The B3LYP-D calculations were performed with Q-Chem 3.2.⁸² The BSSE correction was not applied to the energy obtained using DFT-D method.

3. Results and Discussion

3.1. Stacking Interaction. Pyridine Dimer and Trimer. On full geometry optimization at the MP2 level, two geometries of pyridine dimer “A” and “B” were obtained, with an interplanar separation $R = 3.27 \text{ \AA}$ and $R = 3.25 \text{ \AA}$, respectively, as illustrated in Figure 1 and Table 1. These results validate the earlier results,⁷⁰ with a slight difference in the interplanar separation. Vibrational frequency calculations confirm that both the geometries correspond to minima with no imaginary frequency. In both the geometries the monomer dipole moment vectors point in antiparallel directions and hence contribute to stabilization. Stabilization energies for these two configurations are summarized in Table 1. The BSSE corrected stabilization energies for the dimer “A” and dimer “B” are determined to be -3.39 and -2.64 kcal/mol , respectively, at the est. CCSD(T)/CBS level of theory. Clearly, the most stable pyridine dimer binds stronger than the benzene dimer (-2.74 and -2.78 kcal/mol).³⁰ The stabilization energy values obtained using the MCG3-TS method are (-3.16 for “A” and -2.40 for “B”) in

good agreement with the est. CCSD(T)/CBS energies. The performance of the B3LYP-D method is excellent for the dimer “A”, whereas it produced an error similar to that from the MCG3-TS method for the dimer “B”. Recently, it was shown by Sherrill and co-workers that the B3LYP-D method performs better than the MP2 method for the $\pi-\pi$ stacked benzene dimer and also for the other weakly bound complexes.⁸¹ The MP2 method with Dunning basis sets overestimates the stabilization energy by $\sim 2\text{--}3 \text{ kcal/mol}$, which results in large $\Delta \text{CCSD(T)}$ values. This shows that the coupling of electron pairs and triple substitution are essential for predicting reliable stabilization energy for $\pi-\pi$ interaction. The antiparallel-displaced geometry “A” was found to be the most stable, and this result is in good agreement with the results of crystal structure database search by Janiak.⁸³ The preferred orientation of the monomers in the dimer structure can be explained in terms of favorable electrostatic interaction between the electronegative nitrogen atom and the electropositive hydrogen atom (para to the nitrogen atom) of one pyridine molecule and the hydrogen atom and the nitrogen atom of the other pyridine molecule. Hence, the monomers get locked in this stable dimer configuration. The SAPT analysis for pyridine dimer by Hohenstein and Sherrill⁷² demonstrates that the electrostatic interaction contribution ((Py)₂P2a(−): -3.538 kcal/mol) for antiparallel-displaced configuration is much higher than that of the pyridine dimer in various T-shaped configurations (T1, -1.391 kcal/mol ; T2, -0.392 kcal/mol ; T3, -1.780 kcal/mol ; T4, -0.383 kcal/mol).

In going from the dimer to the trimer, it was found that the minimum energy separation distances between the rings (R_1 and R_2) remain nearly the same (Table 1, Table 3, and Figure 1). The geometries of the dimer served as the initial structure for geometry optimization for the trimer, and two optimized structures “C” and “D” were obtained. In trimer “C”, the top and the bottom rings are perfectly eclipsed to each other and the middle ring is displaced with a uniform interplanar separation. On the other hand, in trimer “D”, the outside rings are tilted toward the middle ring with a tilt angle of $\sim 4^\circ$ for both the rings. The total stabilization energy and many-body interaction terms using the MP2 and B3LYP-D methods are listed in Table 3. Since the trimer configurations are very similar to the respective dimer configurations, intuitively, the stabilization energy of the trimers is expected to be roughly twice the stabilization energy of the corresponding dimers as denoted by ${}^2E_{\text{dimer}}$ in Table 3. The trimer stabilization energy at the MP2 level is found to be 3–4 kcal/mol higher than ${}^2E_{\text{dimer}}$ values. The nearest-neighbor two-body interactions ($\Delta^2 E(12)$ and $\Delta^2 E(23)$) contribute equally in the stabilization energy, and the long-distance two-body interaction $\Delta^2 E(13)$ and three-body interaction terms are negligible except for cyclic configurations. In comparison, the MP3 method, which includes nonadditive dispersion, highly underestimates the stabilization energy. For details the readers can see the Supporting Information. As pointed out elsewhere,⁸⁴ DFT methods perform poorly for nonadditive energies. Alternatively, two-body energy calculations using the CCSD(T) method and three-body energy calculations using the MP3 method would produce accurate energies for the trimers, because the three-body contribution is small. However, the application of CCSD(T)/CBS for all possible dimers in the trimers considered here would impose a prodigious computational requirement. Since B3LYP-D performed well consistently for the dimers (Table 1), we employed B3LYP-D for trimer energies. This is justified by the fact that the MP3 nonadditive energies are negligible for the stacked

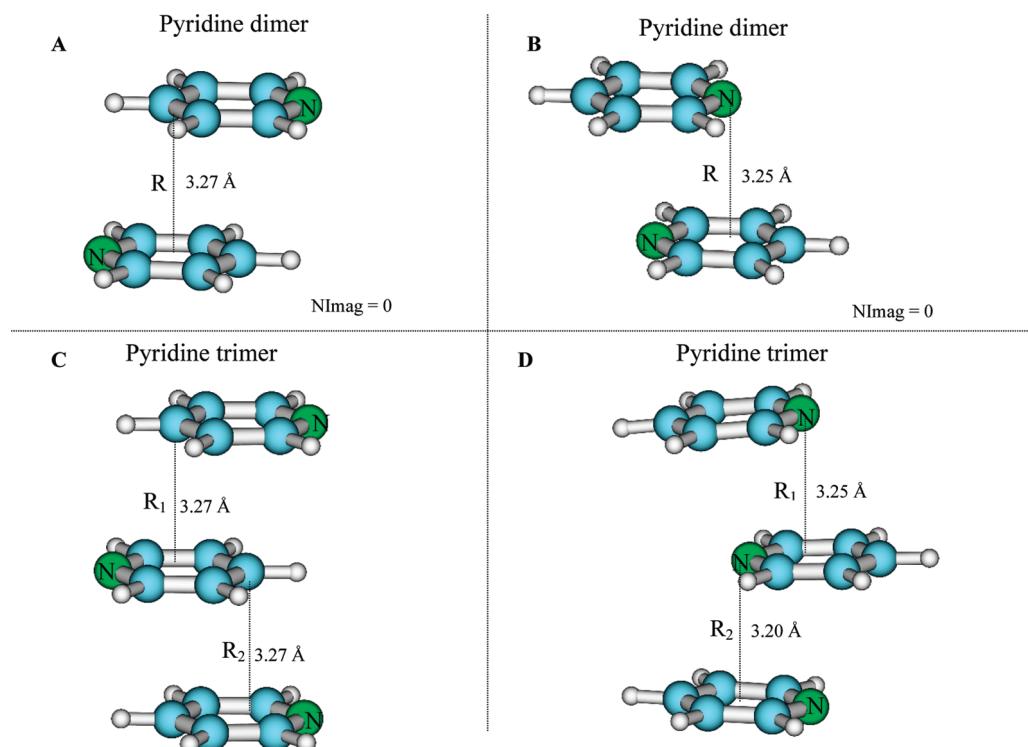


Figure 1. Optimized geometries of pyridine dimer and trimer in a stacked configuration, obtained using the 6-311++G(d,p) basis set at the MP2 level of theory. NImag indicates the number of imaginary frequencies found at the stationary point.

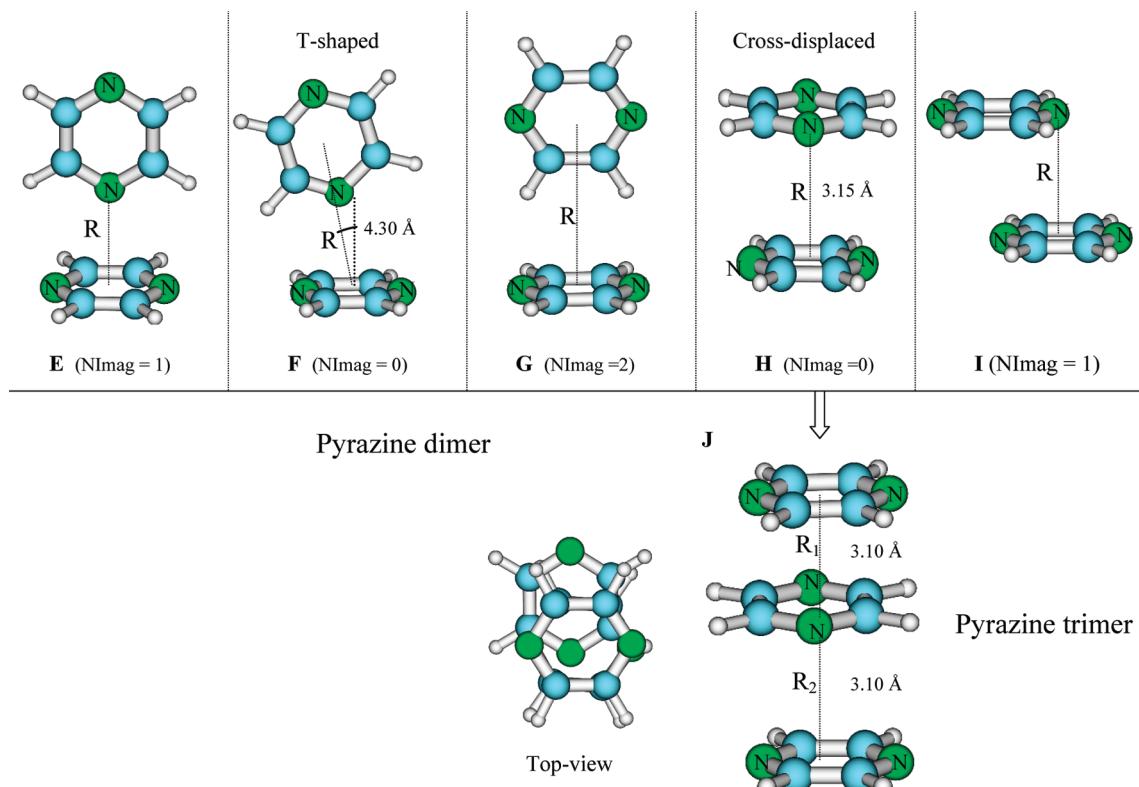


Figure 2. Same as in Figure 1 for the pyrazine dimer and trimer.

trimers and less than ~ 0.25 kcal/mol for the cyclic trimers (Supporting Information). Therefore, the stabilization energy predicted using the B3LYP-D method is expected to fall close to the est. CCSD(T)/CBS energy values. The stabilization energies were computed to be -6.41 and -4.60 kcal/mol for trimers “C” and “D”, respectively, which are in fairly good agreement with ${}^2E_{\text{dimer}}$ values. The study was further extended

to cyclic geometry of pyridine trimer (Figure 5). The optimized trimer geometries at the MP2 level using the 6-311++G** basis set are shown in Figure 5. In contrast to the stacked trimer geometry of benzene, cyclic pyridine trimer “R” is stabilized by three weak hydrogen bonds of C–H \cdots N type with a stabilization energy of -10.11 kcal/mol using the B3LYP-D (Table 3). The cyclic trimer “R” is found to be the most stable

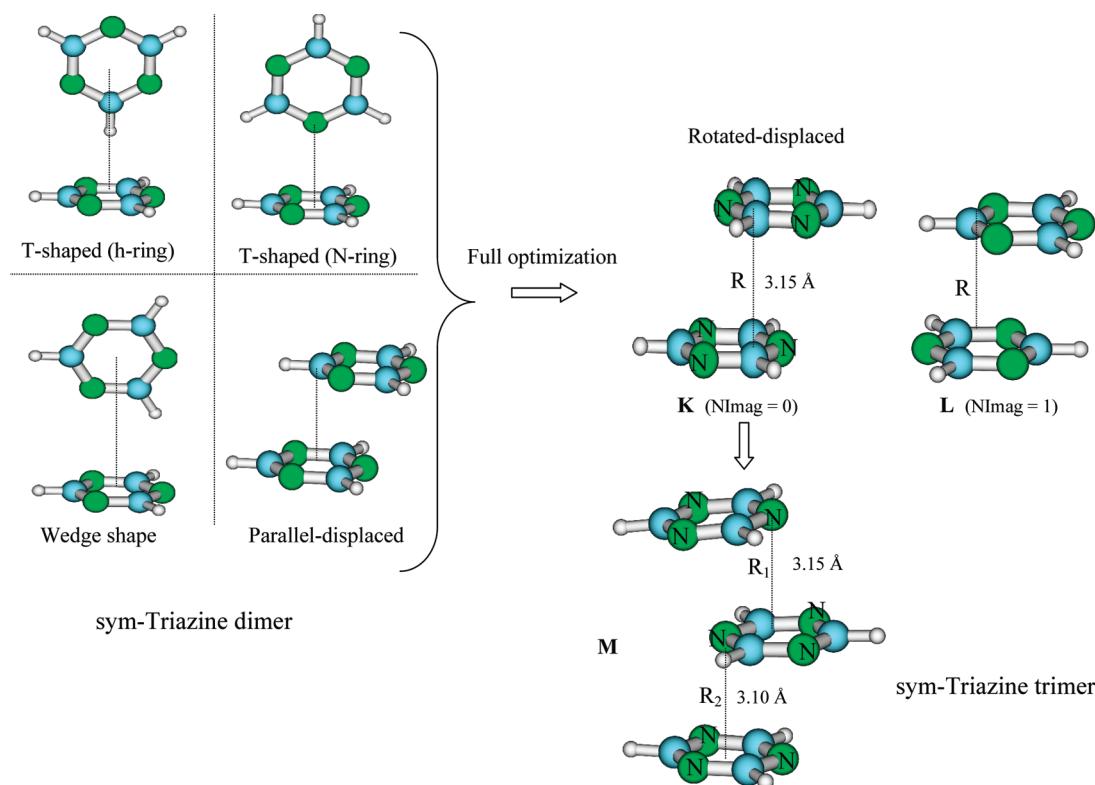


Figure 3. Same as in Figure 1 for the *sym*-triazine dimer and trimer.

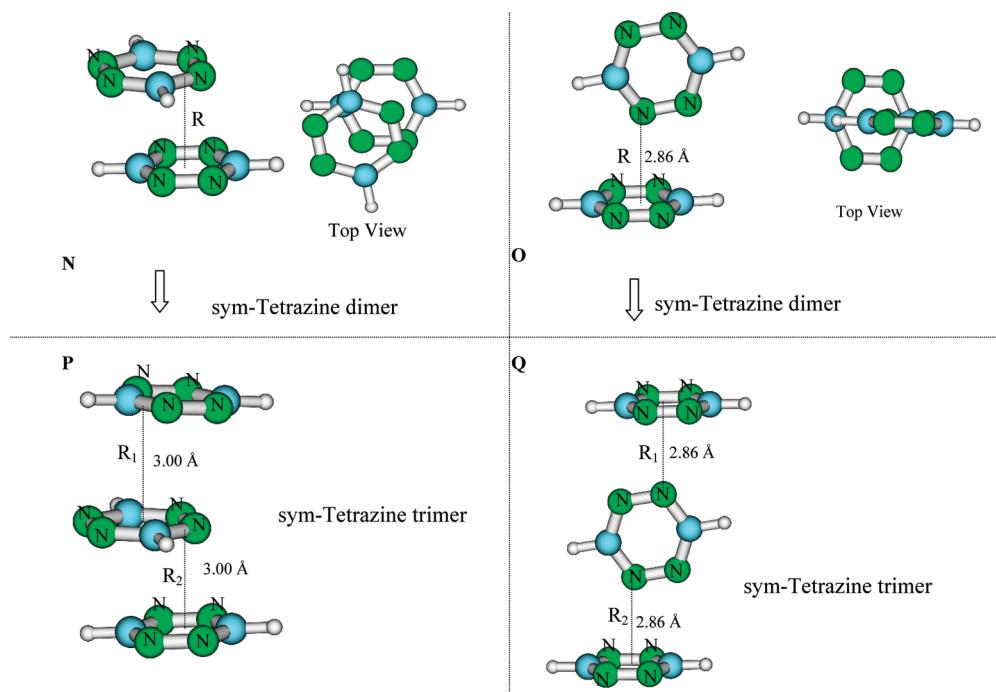


Figure 4. Same as in Figure 1 for the *sym*-tetrazine dimer and trimer.

among the three timers (**C**, **D**, and **R**). The MP3 three-body interaction term is found to be significant for trimer “**R**”.

Pyrazine Dimer and Trimer. The various optimized geometries of pyrazine dimer (T-shaped, wedge-shaped, cross-displaced and N–N-axial-displaced) are illustrated in Figure 2. Vibrational frequency calculations at the MP2 level revealed small imaginary frequencies for some of these geometries (T-shaped, -21 cm^{-1} ; wedge-shaped, -56 and -21 cm^{-1}). The geometry “**F**”, i.e., tilted T-shaped, was found to be a true minimum, with the smallest vibrational frequency $+13\text{ cm}^{-1}$.

In this geometry the N–N axis makes an angle of $\sim 10^\circ$ with the vertical axis, as shown in Figure 2. Pyrazine has a zero dipole moment, but a nonzero quadrupole moment. Therefore, the quadrupole–quadrupole interaction is expected to play an important role in stabilizing the dimer “**F**” similar to the T-shaped benzene dimer. The cross-displaced dimer “**H**” was also found to be a true minimum, with the smallest vibrational frequency $+22\text{ cm}^{-1}$. The N–N-axial-displaced geometry “**T**”, was found to be a saddle point, with one imaginary frequency (-37 cm^{-1}) . The stabilization energies for the dimer “**F**” and

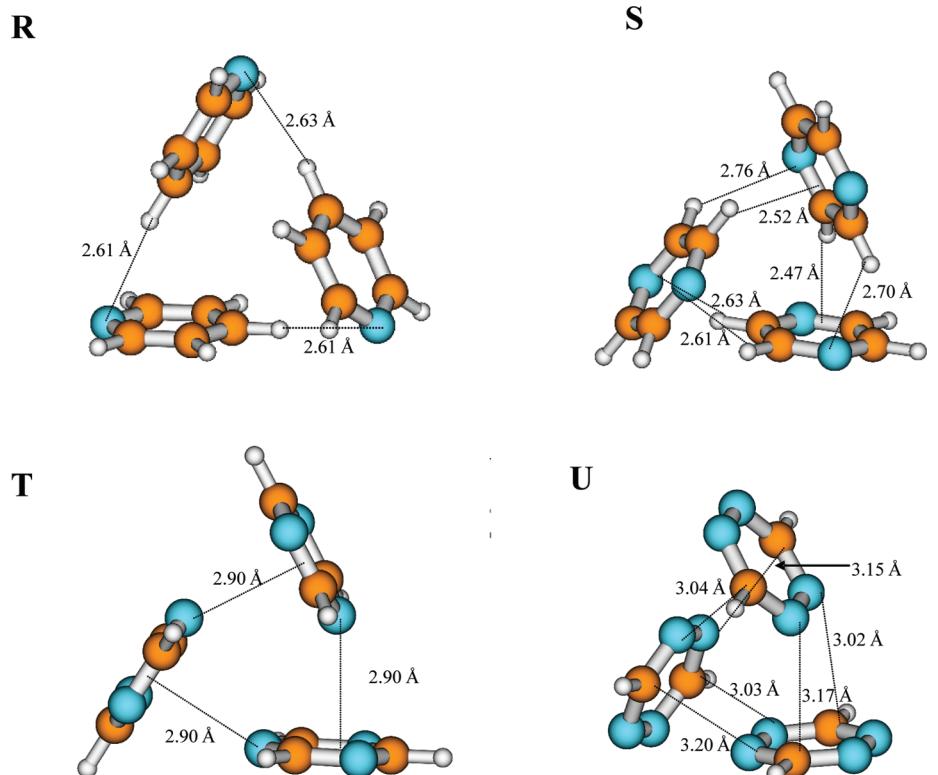


Figure 5. Optimized geometries of pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine trimer in a cyclic configuration, obtained using the 6-311++G(d,p) basis set at the MP2 level of theory.

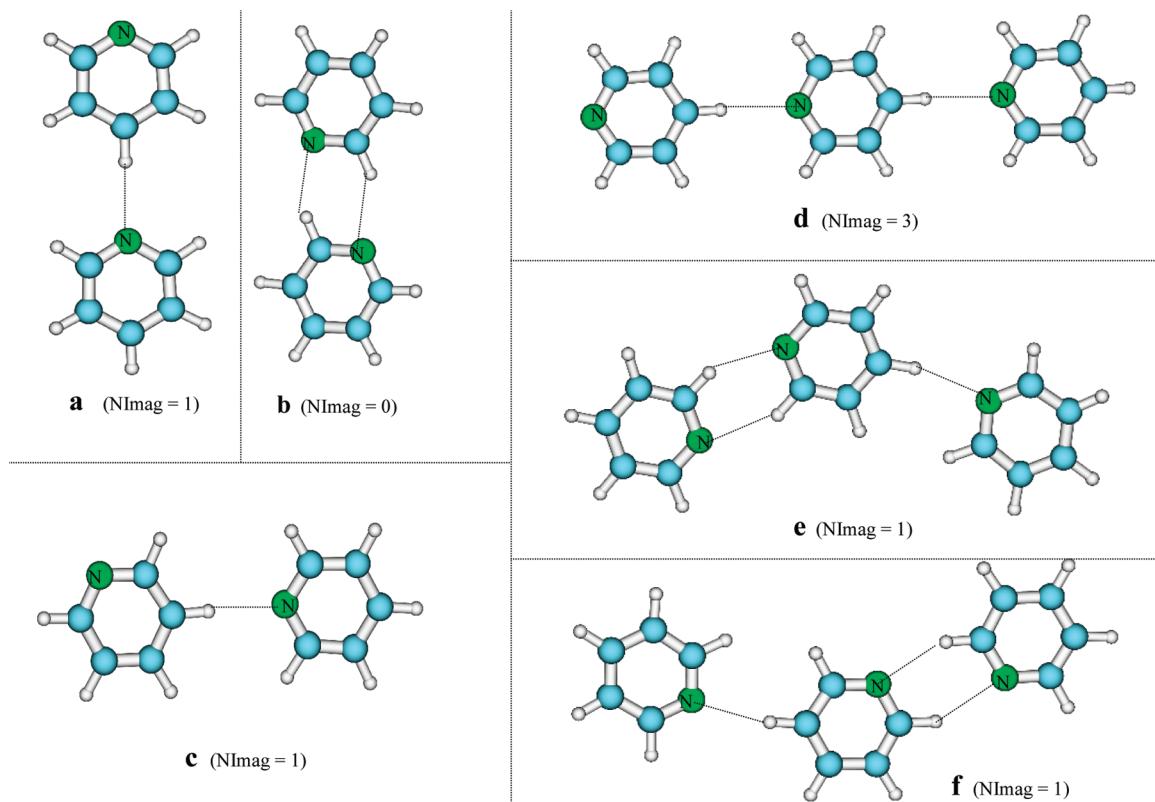


Figure 6. Optimized geometries of the pyridine dimer and trimer in a spread out arrangement obtained using the 6-311G(d,p) basis set at the MP2 level of theory.

the dimer “H”, which represent true minima, were calculated to be -3.47 and -4.14 kcal/mol, respectively, using the est. CCSD(T)/CBS method. The interaction energies -3.44 and -4.11 kcal/mol predicted by the B3LYP-D method are in

excellent agreement with the energies computed at the est. CCSD(T)/CBS level. The MCG3-TS method underestimates the stabilization energy by ~ 0.5 kcal/mol when compared to the est. CCSD(T)/CBS results. In the case of the trimer, only

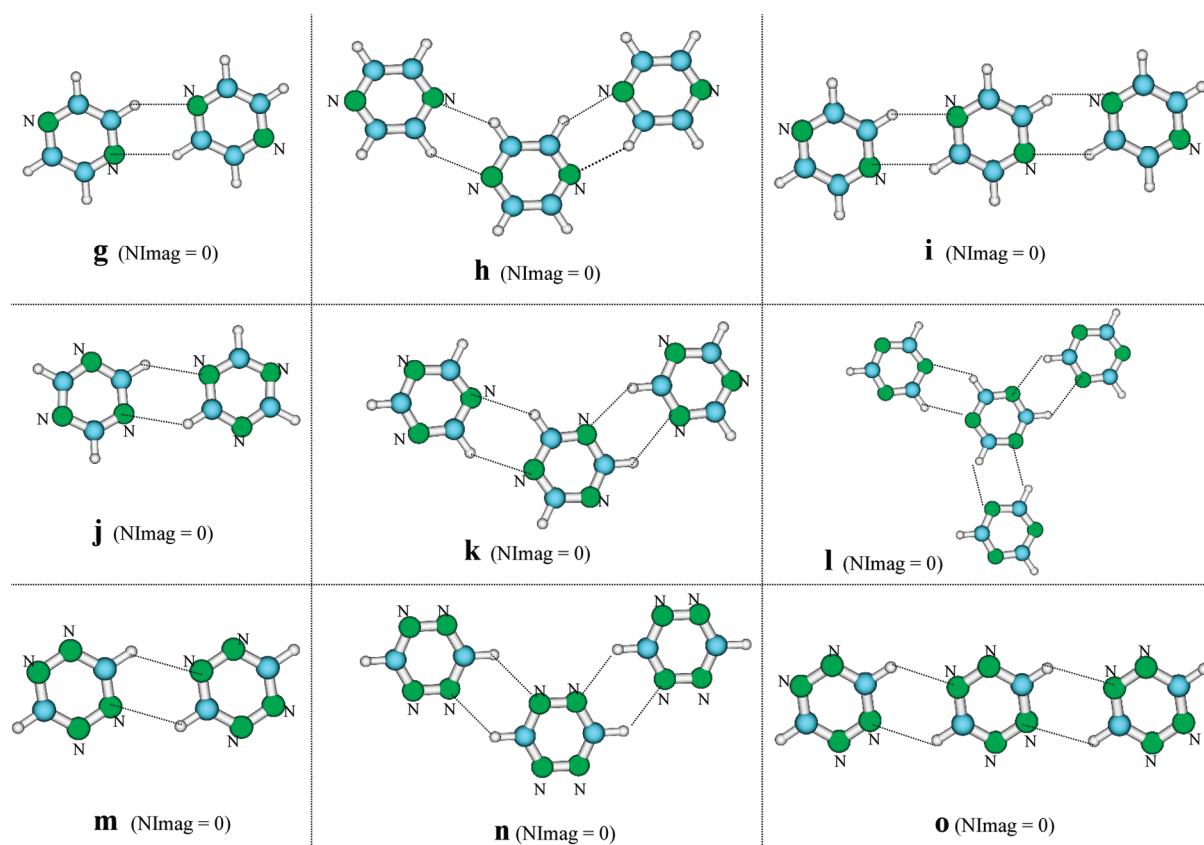


Figure 7. Same as in Figure 5 for the dimer and trimer of pyrazine, *sym*-triazine, and *sym*-tetrazine.

TABLE 1: BSSE Corrected Stabilization Energies (ΔE , kcal/mol) for Various Stacked Dimers

complex	R (Å)	MP2/DZ	MP2/TZ	MP2/QZ	MP2/CBS	$\Delta CCSD(T)$	est. CCSD(T)/CBS	B3LYP-D	MCG3-TS
Pyridine									
A	3.27	-5.25	-5.86	-6.07	-6.22	2.83	-3.39	-3.32	-3.16
B	3.25	-4.08	-4.61	-4.78	-4.90	2.26	-2.64	-2.41	-2.40
Pyrazine									
F	4.30	-3.61	-4.31	-4.69	-4.97	1.50	-3.47	-3.44	-3.04
H	3.15	-6.01	-6.67	-6.90	-7.07	2.93	-4.14	-4.11	-3.72
<i>sym</i> -Triazine									
K	3.15	-4.91	-5.51	-5.71	-5.86	1.84	-4.02	-3.90	-3.41
L	3.25	-4.58	-5.10	-5.29	-5.43	1.59	-3.84	-3.58	-3.28
<i>sym</i> -Tetrazine									
N	3.05	-5.57	-6.27	-6.53	-6.72	2.92	-3.80	-3.56	-3.35
O	4.19	-4.77	-5.23	-5.39	-5.51	1.61	-3.90	-3.55	-3.70

TABLE 2: BSSE Corrected Stabilization Energies (ΔE , kcal/mol) for Various Spread out Dimers

complex	R (Å)	MP2/DZ	MP2/TZ	MP2/QZ	MP2/CBS	$\Delta CCSD(T)$	est. CCSD(T)/CBS	B3LYP-D	MCG3-TS
Pyridine									
(b)	2.43, 2.43	-3.83	-4.22	*	-4.50	0.23	-4.27	-4.55	-3.95
Pyrazine									
(g)	2.43, 2.42	-4.10	-4.49	*	-4.77	0.41	-4.36	-4.70	-4.18
<i>sym</i> -Triazine									
(j)	2.50, 2.50	-3.53	-3.85	-3.97	-4.08	-0.05	-4.13	-4.47	-3.83
<i>sym</i> -Tetrazine									
(m)	2.50, 2.50	-4.62	-4.94	-5.06	-5.17	0.53	-4.64	-4.93	-4.53

the optimized geometry “J” was obtained corresponding to cross-displaced dimers with stabilization energy of -7.97 kcal/mol using the B3LYP-D theoretic method. As in going from the pyrazine dimer (**H**) to the pyrazine trimer (**J**), the change in interplanar separation is negligible; the energy of the trimer is expected to be nearly the $^2E_{\text{dimer}}$ value. The interaction energy

terms at the MP2 and MP3 level show a trend similar to that in the previous case. In the case of cyclic pyrazine trimer “S”, two hydrogen atoms of each pyrazine molecule are seen to be involved in interaction with the other pyrazine molecules in a cyclic manner (one of the hydrogen atoms interacting with the π -cloud of the other pyrazine molecule and the other hydrogen

TABLE 3: Total and Many-Body Stabilization Energies (kcal/mol) for Stacked and Cyclic Trimers Using the MP2/aug-cc-pVDZ, MP3/aug-cc-pVDZ, and B3LYP-D/aug-cc-pVTZ Levels of Theory

MP2	pyridine		pyrazine		triazine		tetrazine		cyclic trimers			
	C	D	J	M	P	Q	R	S	T	U		
$\Delta^2E(12)$	-5.26	-4.04	-5.93	-4.84	-5.60	-4.78	-3.29	-3.18	-3.64	-4.74		
$\Delta^2E(23)$	-5.26	-4.04	-5.90	-4.84	-5.34	-4.78	-3.29	-3.16	-3.64	-4.72		
$\Delta^2E(13)$	-0.01	-0.06	-0.19	-0.22	-0.09	0.03	-3.25	-2.95	-3.64	-4.75		
Δ^2E	-10.53	-8.14	-12.02	-9.90	-11.03	-9.53	-9.83	-9.29	-10.91	-14.21		
Δ^3E	-0.03	0.12	-0.01	0.04	-0.03	0.15	-0.48	-0.31	-0.14	-0.67		
ΔE_{tot}	-10.56	-8.02	-12.03	-9.86	-11.06	-9.38	-10.31	-9.60	-11.05	-14.88		
B3LYP-D	pyridine		pyrazine		triazine		tetrazine		cyclic trimers			
	C	D	J	M	P	Q	R	S	T	U		
	-6.41	-4.60	-7.97	-8.09	-7.06	-7.02	-10.11	-9.82	-9.54	-10.95		
${}^2E_{\text{dimer}}^a$	-6.78	-5.28	-8.28	-8.04	-7.60	-7.80						

^a ${}^2E_{\text{dimer}}$ is the predicted trimer stabilization energy based on sum of purely additive dimer energies obtained at the est. CCSD(T)/CBS level of theory.

TABLE 4: BSSE Corrected Stabilization Energies (ΔE , kcal/mol) for Various Spread out Trimers

complex	$R_{\text{H-bond}} (\text{\AA})$ H \cdots N	bond angle $\angle \text{C}-\text{H}\cdots\text{N}$	MP2/6-311G**	B3LYP-D
(a)	2.44	180.0	-2.25	
(c)	2.42	166.0	-2.30	
(d)	2.42, 2.42	180.0, 180.0	-4.79	
(e)	2.46, 2.41, 2.44	150.6, 152.7, 165.6	-5.38	
(f)	2.46, 2.41, 2.43	149.5, 151.6, 166.3	-5.41	
(h)	2.42, 2.43, 2.43, 2.42	147.0, 46.8, 147.0, 147.1	-7.32	-9.20
(i)	2.42, 2.44, 2.43, 2.42	146.8, 146.1, 147.0, 146.7	-7.19	-9.51
(k)	2.50, 2.50, 2.50, 2.50	139.6, 139.8, 139.1, 139.3	-6.22	-9.12
(l)	2.50, 2.50, 2.50, 2.50	139.7, 139.4, 139.6, 139.4	-9.44	-13.71
(n)	2.49, 2.51, 2.51, 2.49	130.9, 130.4, 130.7, 131.2	-8.39	-9.80
(o)	2.50, 2.50, 2.50, 2.50	130.2, 130.1, 130.7, 130.6	-8.60	-10.09

atom pointing toward the nitrogen atom). The stabilization energy of the cyclic trimer “S” ($\Delta E = -9.82$ kcal/mol) is seen to be considerably larger than the stabilization energy of the cross-displaced trimer “J”.

sym-Triazine Dimer and Trimer. The optimized geometries of the *sym*-triazine dimer and trimer are illustrated in Figure 3. The dipole moment of the *sym*-triazine molecule is zero and the quadrupole moment is very small ($Q_{zz} = 0.47$ debye Å). Therefore, the T-shaped and wedge-shaped structures were given as initial input geometries for optimization and it was found that they converged to two rotated ($\pi/3$)-displaced geometries “K” and “L”. The calculated harmonic vibrational frequencies of “K” were all real, whereas one imaginary frequency was obtained for “L”. Clearly, “K” is the true minimum geometry. The stabilization energy (-4.02 kcal/mol) of dimer “K” is computed to be slightly higher than that of dimer “L” (-3.84 kcal/mol) at the est. CCSD(T)/CBS level of theory. The B3LYP-D energy values are yet again in good agreement with the est. CCSD(T)/CBS energies, producing an error of 0.12 and 0.26 kcal/mol for the dimer “K” and “L”, respectively (Table 1). The stabilization energy computed with the MCG3-TS method shows a trend similar to that in the previous cases. Using the results for the dimer “K”, the initial geometry of the trimer was constructed. On geometry optimization, it was found that the vertical interplanar separation is not uniform, the separation being 3.15 and 3.10 Å between the two rings in succession. As observed for the pyridine trimer, the extreme rings in the *sym*-triazine trimer are seen to be bent toward the middle ring, as illustrated in Figure 3. The stabilization energy for trimer “M” was computed to be -8.09 kcal/mol using the B3LYP-D method. Interestingly, the structure of the cyclic trimer “T” is

found to be similar to the structure of the cyclic benzene trimer with stabilization energy ~1.50 kcal/mol higher than the stacked trimer “M”.

sym-Tetrazine Dimer and Trimer. The optimized geometries of the *sym*-tetrazine dimer and trimer are illustrated in Figure 4. Similar to the earlier cited studies, various dimer geometries were considered as the starting point for optimization and two optimized geometries “N” (parallel-offset) and “O” (wedge-shaped) were obtained. In the dimer geometry “N”, two rings are stacked in a parallel-offset fashion, with the molecular axis rotated by nearly ~97°. On the other hand, in the dimer geometry “O”, the ring planes are oriented in a mutually perpendicular geometry, as shown in the top view in Figure 4. The stabilization energy was computed to be -3.80 and -3.90 kcal/mol for the geometry “N” and “O”, respectively, at the est. CCSD(T)/CBS level of theory. The B3LYP-D and MCG3-TS stabilization energy values are in fairly good agreement with the est. CCSD(T)/CBS energy values. Initial trimer geometries were constructed on the basis of both the dimer geometries, and geometry optimization resulted in two iso-energetic structures “P” and “Q” with the stabilization energy -7.06 and -7.02 kcal/mol, respectively, at the B3LYP-D level of theory. In the case of the cyclic *sym*-tetrazine trimer “U” the stabilization energy (-10.95 kcal/mol) is found to be largest among all the trimers. It is seen that in the case of pyridine, pyrazine, and *sym*-triazine, the relative orientation of the monomers in the cyclic trimer is entirely different from the orientation seen for stacked trimers in Figures 1–3. However, on careful investigation of the cyclic geometry of *sym*-tetrazine, it becomes clear that this geometry retains the dimer orientation similar to that

for the tetrazine dimer “O”. Therefore, the stabilization energy is expected to be larger than in the other cases.

3.2. Spreading Interaction. In addition to the stacking, the dimer and the trimer of pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine could be stabilized by in-plane hydrogen bonding. The dimer and trimer geometries were optimized at the MP2 level of theory using the 6-311G** basis set. The hydrogen bonds in the systems under investigation are of the C–H \cdots N type. The length of the H \cdots N hydrogen bond falls in the range 2.40–2.50 Å and the hydrogen bond angles (\angle C–H \cdots N) vary from 130° to 160°, except when the molecules are arranged in a linear geometry (\angle C–H \cdots N = 180°).

Pyridine Dimer and Trimer. The optimized geometries of the dimer and trimer of pyridine in a spread out arrangement are illustrated in Figure 6. For the pyridine dimer, three optimized geometries “a”, “b”, and “c” were obtained. Among them “a” and “c” have only one hydrogen bond and “b” involves two hydrogen bonds. Unfortunately, the geometries “a” and “c” have one (albeit small) imaginary frequency each (−13.6 and −22.9 cm^{−1}, respectively). The structure “b” has all real frequencies, indicating that it is a true minimum. The stabilization energy for the structure “b” was computed to be −4.27 kcal/mol using the est. CCSD(T)/CBS method, which is nearly 1 kcal/mol higher than the most stable stacked dimer of pyridine. The striking difference between the stabilization energy of stacked and spread out dimer is the Δ CCSD(T) value. For spreading, CCSD(T) correction is much smaller compared to the case of stacked dimers. Therefore, it is deduced that the MP2 method with augmented Dunning’s basis set (aug-cc-pVTZ) predicts reliable stabilization energies for weakly hydrogen bonded complexes. This is consistent with previous assessments.⁸⁵ B3LYP-D overestimates the binding energy by 0.28 kcal/mol whereas the MCG3-TS method underestimates the binding energy by 0.32 kcal/mol, compared to the est. CCSD(T)/CBS results. For pyridine trimer, three optimized geometries, (“d”, “e”, and “f”) were obtained. In the trimer geometry “d”, the three pyridine molecules are connected via a single hydrogen bond between two pyridine molecules. The trimer geometries “e” and “f” involve (2 + 1) hydrogen bonds. The geometries “e” and “f” appear to be identical, but a closer look would reveal the difference in the position of the bonding proton of the pyridine moiety. None of them possesses all real frequencies (“d” has 3 imaginary frequencies, “e” and “f” have 1 imaginary frequency each).

Pyrazine Dimer and Trimer. The optimized geometries of the dimer and trimer of pyrazine, *sym*-triazine and *sym*-tetrazine are illustrated in Figure 7. The presence of an additional nitrogen atom in the pyrazine ring makes it more symmetric than pyridine. As a result, there are fewer possible distinguishable geometries for the dimer and trimer of pyrazine than for pyridine. For the dimer, only one stable geometry (“g”) was obtained, which contains two hydrogen bonds. The stabilization energy for the dimer “g” was computed to be −4.36 kcal/mol using the est. CCSD(T)/CBS method, which is slightly more stable than the stacked dimer of pyrazine. The stabilization energies obtained using the B3LYP-D and MCG3-TS methods show a trend similar to those in the previous cases. For the trimer, two structures, “h” and “i” containing two hydrogen bonds between two pyrazine moieties were obtained. Their stabilization energies were calculated to be −9.20 and −9.51 kcal/mol, respectively, using B3LYP-D, as shown in Table 4. As expected, the trimer energy is seen to be approximately double the dimer energy.

***sym*-Triazine Dimer and Trimer.** In view of the increased symmetry in *sym*-triazine, the number of stable possible dimer and trimer structures becomes fewer. Only one stable dimer configuration, “j”, and one trimer “k”, containing two hydrogen bonds between two adjacent molecules, were obtained. Their stabilization energies were computed to be −4.13 and −9.12 kcal/mol, respectively at the est. CCSD(T)/CBS and B3LYP-D level of theory. These structures also were found to have all real frequencies and hence they represent true minima. The study was extended to a tetramer with a star-like geometry. This structure is significant for molecular self-assembly.⁴ The optimized geometry “l”, belongs to the highly symmetrical D_{3h} point group and is found to have a stabilization energy of −13.71 kcal/mol, which is approximately 3 times the stabilization energy of the dimer (Table 2, −4.47 kcal/mol). The B3LYP-D and MCG3-TS energy values are consistent with the previous cases.

***sym*-Tetrazine Dimer and Trimer.** *sym*-Tetrazine and pyrazine belong to the same point group, D_{2h} . Therefore, the nature of the hydrogen bonded complexes is expected to be similar between these cases. The optimized geometries of the dimer “m” and two trimers “n” and “o” are illustrated in Figure 6. The stabilization energy is determined to be −4.64 kcal/mol at the est. CCSD(T)/CBS level of theory, which is highest among all stacked and spread out dimers. The stabilization energy for the corresponding trimers “n” and “o” are computed to be −9.80 and −10.09 kcal/mol, respectively at the B3LYP-D level of theory. These complexes were identified as true minima by confirming that their vibrational frequencies are all real. The stabilization energy values obtained using the B3LYP-D and MCG3-TS methods show yet again trends similar to those seen in the previous cases (Table 2).

4. Conclusion

Highly accurate quantum chemical calculations were carried out to study “stacking interaction” and “spreading interaction” in several N-heteroaromatic dimers and trimers. Among the stacked structures the antiparallel-displaced geometry for pyridine dimer (ΔE = −3.39 kcal/mol), cross-displaced geometry for pyrazine dimer (ΔE = −4.14 kcal/mol) and rotated-displaced geometry for *sym*-triazine dimer (ΔE = −4.02 kcal/mol) were found to be the most stable at the est. CCSD(T)/CBS level of theory. For the *sym*-tetrazine dimer, two geometries, parallel-offset and wedge-shaped, were the most stable (ΔE = −3.80 and −3.90 kcal/mol, respectively). In the case of spreading, dimer and trimer complexes of pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine are stabilized by weak C–H \cdots N hydrogen bonding. The performance of the B3LYP-D method is excellent for the stacked dimer with an average deviation of 0.17 kcal/mol and fairly well for spread out dimers with an average deviation of 0.31 kcal/mol with respect to the est. CCSD(T)/CBS benchmark. On the other hand, the MCG3-TS method performed better for spread out dimers, exhibiting an average deviation of 0.23 kcal/mol, than for stacked dimers, giving an average deviation of 0.39 kcal/mol. The MCG3-TS error for N-heteroaromatic systems is large compared to the error (0.13 kcal/mol) reported by Zhao and Truhlar for the benzene dimer using this method.³⁸ The binding energies for the stacked and the spread-out dimers lie in the range 3–4.5 kcal/mol, and this is clearly higher than the binding energy for the benzene dimer. The stabilization energy for the cyclic trimers of pyridine, pyrazine, *sym*-triazine, and *sym*-tetrazine trimers were found to lie 2–4 kcal/mol higher than the stabilization energy for the corresponding stacked trimers using B3LYP-D.

It is well-known that the three-dimensional helical structures of DNA and RNA are formed by hydrogen bonding and stacking interaction between nucleic acid bases, which contain nitrogen and oxygen atoms as heteroatoms. In the present work, we show that by introducing heteroatom(s) in the aromatic ring, the stabilization energy of the stacked dimers increases significantly (by ~ 1.5 kcal/mol compared to the stabilization energy of the benzene dimer). Consequently, the presence of the N atom(s) in the aromatic ring partly explains the favorable stacking interaction of DNA and RNA bases. Of course, N-heteroaromatic systems do not completely explain the favorable stacking and spreading interactions of DNA and RNA bases. For example, the oxygen and nitrogen atoms in the bases are positioned in such a way that they form linear hydrogen bonds that are stronger than the type of hydrogen bonds studied here. A more detailed investigation of the stacking and spreading interactions between nucleic acid bases is currently in progress.

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Supporting Information Available: Tables of H bond lengths and interaction energies and total and many-body stabilization energies. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References and Notes

- (1) Claessens, C. G.; Stoddart, J. F. *J. Phys. Org. Chem.* **1997**, *10*, 254.
- (2) Dahl, T. *Acta Chem. Scand.* **1994**, *48*, 95.
- (3) Meyer, E. A.; Castellano, R. K.; Deiderich, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1210.
- (4) Mooibroek, T. J.; Gamez, P. *Inorg. Chim. Acta* **2007**, *360*, 381.
- (5) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984.
- (6) Hunter, C. A.; Singh, J.; Thornton, J. M. *J. Mol. Biol.* **1991**, *218*, 837.
- (7) Jurečka, P.; Hobza, P. *J. Am. Chem. Soc.* **2003**, *125*, 15608.
- (8) Fyfe, M. C. T.; Stoddart, J. F. *Acc. Chem. Res.* **1997**, *30*, 393.
- (9) Brana, M. F.; Cacho, M.; Gradillas, A.; Pascual-Teresa, B.; Ramos, A. *Curr. Pharm. Des.* **2001**, *7*, 1745.
- (10) Burley, S. K.; Petsko, G. A. *Science* **1985**, *229*, 23.
- (11) Burley, S. K.; Petsko, G. A. *Adv. Protein Chem.* **1988**, *39*, 125.
- (12) Askew, B.; Ballester, P.; Buhr, C.; Jeong, K. S.; Jones, S.; Parrish, K.; Williams, K.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 1082.
- (13) Smithrud, D. B.; Diederich, F. *J. Am. Chem. Soc.* **1990**, *112*, 339.
- (14) Hunter, C. A. *Chem. Soc. Rev.* **1994**, *23*, 101.
- (15) Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 3910.
- (16) Sheppard, T. J.; Petti, M. A.; Dougherty, D. A. *J. Am. Chem. Soc.* **1988**, *110*, 1983.
- (17) Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5773.
- (18) Bhattacharya, R.; Samanta, U.; Chakrabarti, P. *Protein Eng.* **2002**, *15*, 91.
- (19) Börnsen, K. O.; Selzle, H. L.; Schlag, E. W. *J. Chem. Phys.* **1986**, *85*, 1726.
- (20) Grover, J. R.; Walters, E. A.; Hui, E. T. *J. Phys. Chem.* **1987**, *91*, 3233.
- (21) Arunan, E.; Gutowsky, H. S. *J. Chem. Phys.* **1993**, *98*, 4294.
- (22) Neusser, H. J.; Krause, H. *Chem. Rev.* **1994**, *94*, 1829.
- (23) Hobza, P.; Selzle, H. L.; Schlag, E. W. *J. Phys. Chem.* **1993**, *97*, 3937.
- (24) Hobza, P.; Selzle, H. L.; Schlag, E. W. *J. Am. Chem. Soc.* **1994**, *116*, 3500.
- (25) Tsuzuki, S.; Uchimaru, T.; Mikami, M.; Tanabe, K. *Chem. Phys. Lett.* **1996**, *252*, 206.
- (26) Hobza, P.; Selzle, H. L.; Schlag, E. W. *J. Phys. Chem.* **1996**, *100*, 18790.
- (27) Jaffe, R. L.; Smith, G. D. *J. Chem. Phys.* **1996**, *105*, 2780.
- (28) Tsuzuki, S.; Uchimaru, T.; Matsumura, K.; Mikami, M.; Tanabe, K. *Chem. Phys. Lett.* **2000**, *319*, 547.
- (29) Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M.; Tanabe, K. *J. Am. Chem. Soc.* **2002**, *124*, 104.
- (30) Sinnokrot, M. O.; Valeev, E. F.; Sherrill, C. D. *J. Am. Chem. Soc.* **2002**, *124*, 10887.
- (31) Sinnokrot, M. O.; Sherrill, C. D. *J. Am. Chem. Soc.* **2004**, *126*, 7690.
- (32) Tauer, T. P.; Sherrill, C. D. *J. Phys. Chem. A* **2005**, *109*, 10475.
- (33) Sinnokrot, M. O.; Sherrill, C. D. *J. Phys. Chem. A* **2006**, *110*, 10656.
- (34) Sinnokrot, M. O.; Sherrill, C. D. *J. Phys. Chem. A* **2004**, *108*, 10200.
- (35) Lee, E. C.; Kim, D.; Jurečka, P.; Tarakeshwar, P.; Hobza, P.; Kim, K. S. *J. Phys. Chem. A* **2007**, *111*, 3446.
- (36) Price, S. L.; Stone, A. J. *J. Chem. Phys.* **1987**, *86*, 2859.
- (37) Stone, A. J. *The Theory of Intermolecular Forces*; Clarendon Press: Oxford, U.K., 1996.
- (38) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 4209.
- (39) Sinnokrot, M. O.; Sherrill, C. D. *J. Phys. Chem. A* **2003**, *107*, 8377.
- (40) Sponer, J.; Hobza, P. *Chem. Phys. Lett.* **1997**, *267*, 263.
- (41) Mignon, P.; Loverix, S.; Proft, F. D.; Geerlings, P. *J. Phys. Chem. A* **2004**, *108*, 6038.
- (42) Tsuzuki, S.; Honda, K.; Azumi, R. *J. Am. Chem. Soc.* **2002**, *124*, 12200.
- (43) Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M. *J. Chem. Phys.* **2005**, *122*, 144323.
- (44) Rogers, D. M.; Hirst, J. D.; Lee, E. P. F.; Wright, T. G. *Chem. Phys. Lett.* **2006**, *427*, 410.
- (45) Young, L.; Haynam, C. A.; Levy, D. H. *J. Chem. Phys.* **1983**, *79*, 1592.
- (46) Oxtoby, N. S.; Blake, A. J.; Champness, N. R.; Wilson, C. *Cryst. Eng. Commun.* **2003**, *5*, 82.
- (47) Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M. *J. Chem. Phys.* **2004**, *120*, 647.
- (48) Gilliéron, C. *Boomerang Trans.* **2006**, *1*, 1.
- (49) Doxater, M. M.; Mangle, E. A.; Bhattacharya, A. K.; Cohen, S. M.; Topp, M. R. *Chem. Phys.* **1986**, *101*, 413.
- (50) Piacenza, M.; Grimme, S. *J. Am. Chem. Soc.* **2005**, *127*, 14841.
- (51) Grimme, S. *Chem. Eur. J.* **2004**, *10*, 3423.
- (52) Grimme, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 3430.
- (53) Tran, F.; Bassam, A.; Jenny, T. A.; Wesolowski, T. A. *J. Phys. Chem. A* **2004**, *108*, 9155.
- (54) Itahara, T.; Imaizumi, K. *J. Phys. Chem. B* **2007**, *111*, 2025.
- (55) Hobza, P.; Sponer, J. *J. Am. Chem. Soc.* **2002**, *124*, 11802.
- (56) Sponer, J.; Jurečka, P.; Hobza, P. *J. Am. Chem. Soc.* **2004**, *126*, 10142.
- (57) Hobza, P.; Sponer, J. *Chem. Rev.* **1999**, *99*, 3247.
- (58) Řehá, D.; Kabelač, M.; Ryáček, F.; Šponer, J.; Šponer, J. E.; Elstner, M.; Suhai, S.; Hobza, P. *J. Am. Chem. Soc.* **2002**, *124*, 3366.
- (59) Jurečka, P.; Hobza, P. *J. Am. Chem. Soc.* **2003**, *125*, 15608.
- (60) Kratochvíl, M.; Šponer, J.; Hobza, P. *J. Am. Chem. Soc.* **2000**, *122*, 3495.
- (61) Mignon, P.; Loverix, S.; Geerlings, P. *Chem. Phys. Lett.* **2005**, *401*, 40.
- (62) McCarthy, W.; Smets, J.; Adamowicz, L.; Plokhotnichenko, C. A. M.; Radchenko, E. D.; Sheina, G. G.; Stepanian, S. G. *Mol. Phys.* **1997**, *91*, 513.
- (63) *Phys. Chem. Chem. Phys.* **2008**, *10*, 2580.
- (64) Arnstein, S. A.; Sherrill, C. D. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2646.
- (65) Podeszwa, R.; Szalewicz, K. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2735.
- (66) Šponer, J.; Riley, K. E.; Hobza, P. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2595.
- (67) Rubeš, M.; Buldský, O. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2611.
- (68) Tsuzuki, T.; Fujii, A. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2584.
- (69) Zhao, Y.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2813.
- (70) Mishra, B. K.; Sathyamurthy, N. *J. Phys. Chem. A* **2005**, *109*, 6.
- (71) Mishra, B. K.; Sathyamurthy, N. *J. Theo. Comput. Chem.* **2006**, *5*, 609.
- (72) Hohenstein, E. G.; Sherrill, C. D. *J. Phys. Chem. A* **2009**, *113*, 878.
- (73) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox,

- D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; and Pople, J. A. *Gaussian 03*, Revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.
- (74) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.
- (75) Halkier, A.; Klopper, W.; Helgaker, T.; Jørgensen, P.; Taylor, P. R. *J. Chem. Phys.* **1999**, *111*, 9157.
- (76) Zhao, Y.; Truhlar, D. G. *MLGAUSS-version 2.0*; University of Minnesota: Minneapolis. 2005.
- (77) Podeszwa, R. *J. Phys. Chem. A* **2008**, *112*, 8884.
- (78) Grimme, S. *J. Comput. Chem.* **2004**, *25*, 1463.
- (79) Grimme, S. *J. Comput. Chem.* **2006**, *27*, 1787.
- (80) Piacenza, M.; Grimme, S. *Chem. Phys. Chem.* **2005**, *6*, 1554.
- (81) Sherrill, C. D.; Takatani, T.; Hohenstein, E. G. *J. Phys. Chem. A* **2009**, *113*, 10146.
- (82) Shao, Y.; Molnar, L. F.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; DiStasio, R. A., Jr.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Voorhis, T. V.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachselt, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B. D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C.-P.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcock, H. L.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer, H. F.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3172–3191.
- (83) Janiak, C. *J. Chem. Soc., Dalton Trans.* **2000**, 3885.
- (84) Tkatchenko, A.; von Lilienfeld, O. A. *Phys. Rev. B* **2008**, *78*, 045116.
- (85) Boese, A. D.; Martin, J. M. L.; Klopper, W. *J. Phys. Chem. A* **2007**, *111*, 11122.

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