QUANTUM CHEMICAL APPROACH ON THE MOLECULAR STRUCTURAL PROPERTIES OF SOME AMINOPYRIDINES

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Abstract

*The quantum chemical calculations by density functional theory method (*DFT*) with 6-311G ++(d, p) basis set were carried out to compute the parameters such as optimized geometry, dipole moment, mullikan atomic charge, HOMO-LUMO energies, natural bond analysis, polarizability, first order hyperpolarizability and hence non-linear optical properties of 2-aminopyridine, 3-aminopyridine,4-aminopyridine and 3,4-diaminopyridine.Total electron density mapped with molecular electrostatic potential surface, contour map with electrostatic potential surface have been constructed by Gaussian 09W package program to predict the reactive sites in the molecules. The study is extended to determine the thermodynamic properties like total energy, zero point vibrational energy, enthalpy, heat capacity and entropy of the chosen aminopyridines. Correlation fitting equations of thermodynamic properties with respect to temperature were also framed for the chosen molecules from 50K to 1000K.*

Keywords: *Aminopyridines, HOMO-LUMO, DFT, NLO, NBO Analysis.*

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1. INTRODUCTION

Aminopyridine has three mono positional isomers named as 2-aminopyridine (2AP), 3-aminopyridine (3AP),4-aminopyridine (4AP). Amino pyridines contribute wide number of applications in the field of pharmacological and agricultural industries. 2-aminopyridine can act as an intermediate for the synthesis of pharmaceutical such as antihistamines, anti-inflammatory and other drugs [1]. 3-amonopyridine also found to be an intermediate for the synthesis of anti-inflammatory drugs like Piroxicam, Tenoxicam, Ampiroxicam and colourants[2]. 4-amonopyridine is an effective medicine in the treatment for multiple sclerosis and the 4AP-therapy shows improvement in sensory, motor and pulmonary function with a decrease in spasticity and pain in the patients who are suffering from spinal-cord injury [3-5]. Di-aminopyridine such as 3, 4-diaminopyridine (34DAP) also discussed in the present study as it plays an effective role in anti-tumour activity, immunosuppressing and symptomatic treatment of multiple sclerosis [6]. The extensive uses of these aminopyridines kindled the interest to study the detailed theoretical investigation of the molecular structural properties. Several authors reported the anharmonic vibrational analysis of certain aminopyridines and their derivatives in the earlier studies[7-12]. Thus the main emphasis of the present study is the analysis of the theoretical study of the physical and chemical properties of the chosen aminopyridines which may provide the knowledge about the significance of the drug materials by applying little modifications in their structure.

2. COMPUTATIONAL DETAILS

Quantum mechanical calculations were carried out for aminopyridines by using the version 8 of Gaussian 09W (revision B.01) program [13].The optimization of the chosen molecules were completed by the DFT calculation of Becke-3-Lee-Yang-Parr hybrid exchange correlation three parameter functional ,B3LYP [14,15] with 6-311G++(d, p)basis set. Self-consistent energy(SCF), dipole moment (μ^0),total polarizability (α^0),first order hyperpolarisibility (β_{tot}), thermodynamic properties, energy distribution in frontier molecular orbitals[16], atomic charges and molecular electrostatic potential surface were estimated at DFT/B3LYP/6-311G++(d, p) framework and it was done on Intel(R)Core(TM) i5-3210M/2.50 GHz processor. Molecular electro static potential surface mapping, contour mapping and HOMO-LUMO orbital energies were analyzed through animation options of Gauss View 5.0.8 visualization program [17].

3. RESULTS AND DISCUSSION

3.1 Analysis of Geometric Parameters

The optimized geometry of the chosen molecules which are energetically most stable and obtained by B3LYP/6-311G++(d, p) level with C_1 point group symmetry of 2AP,3AP,4AP and 34DAP are shown in Fig .1-4 respectively along with the scheme of numbering. The computed bond parameters of the preferred optimized geometry of the chosen molecules at DFT level with 6-311G+ + (d, p) basis set are summarized in the Table-1in addition to the experimental parameters [18] for comparative purpose.

Table 1. Geometrical Parameters of 2AP, 3AP, 4AP & 34DAP calculated at B3LYP/6-311g++(d, p) level

2-Aminopyridine		3-Aminopyridine		4-Aminopyridine		3,4-Diaminopyridine		Experimental [a]
Bond length(Å)		**Bond length(Å)**		**Bond length (Å)**		**Bond length(Å)**		**Bond length(Å)**
N_1-C2	1.338	N_1-C_2	1.330	N_1-C_2	1.338	N_1-C_2	1.320	1.344
N_1-C_6	1.337	N_1-C_6	1.337	N_1-C_6	1.338	N_1-C_6	1.320	1.342
C_2-C_3	1.409	C_2-C_3	1.406	C_2-C_3	1.389	C_2-C_3	1.383	1.385
C_3-H_8	1.084	C_2-H_9	1.089	C_2-H_8	1.087	C_2-H_9	1.076	0.95
C_3-C_4	1.384	C_3-C_4	1.400	C_3-C_4	1.403	C_3-C_4	1.398	1.415
C_2-N_7	1.383	C_3-N_7	1.394	C_4-N_7	1.383	C_3-N_7	1.425	1.405
C_4-C_5	1.398	C_4-C_5	1.389	C_4-C_5	1.403	C_4-C_5	1.393	1.395
C_4-H_9	1.085	C_4-H_8	1.086	C_3-H_9	1.085	-----	-----	-----
C_5-C_6	1.390	C_5-C_6	1.393	C_5-C_6	1.389	C_5-C_6	1.379	1.383
C_5-H_{10}	1.083	C_5-H_{10}	1.084	C_5-H_{10}	1.085	C_5-H_{10}	1.076	0.95
C_6-H_{11}	1.087	C_6-H_{11}	1.085	C_6-H_{11}	1.087	C_6-H_{11}	1.077	0.95
N_7-H_{12}	1.009	N_7-H_{12}	1.009	N_7-H_{12}	1.008	N_7-H_{12}	0.999	0.9
N_7-H_{13}	1.008	N_7-H_{13}	1.009	N_7-H_{13}	1.008	N_7-H_{13}	0.999	0.9
						C_4-N_8	1.381	1.359
						N_8-H_{14}	0.995	0.9
						N_8-H_{15}	0.994	0.9
Bond angle (°)		**Bond angle (°)**		**Bond angle (°)**		**Bond angle (°)**		**Experimental [a]**
C_2-N_1-C_6	118.03	C_2-N_1-C_6	118.23	C_2-N_1-C_6	116.05	C_2-N_1-C_6	116.61	115.69
N_1-C_2-C_3	122.45	N_1-C_2-C_3	124.00	N_1-C_2-C_3	124.49	N_1-C_2-C_3	125.09	125.4
N_1-C_2-N_7	116.27	N_1-C_2-H_9	116.45	N_1-C_2-H_8	116.03	N_1-C_2-H_9	117.02	117.3
C3-C2-N7	121.24	C3-C_2-H_9	119.55	C_3-C_2-H_8	119.48	C_3-C_2-H_9	117.90	117.3
C2-C3-C4	118.41	C2-C3-C4	117.07	C_2-C_3-C_4	119.02	C_2-C_3-C_4	117.69	118.1
C_2-C_3-H_8	120.42	C_2-C_3-N_7	120.95	C_2-C_3-H_9	120.22	C_2-C_3-N_7	118.89	119.63
C_4-C_3-H_8	121.17	C_4-C_3-N_7	121.92	C_4-C_3-H_9	120.77	C_4-C_3-N_7	123.41	122.2
C_3-C_4-C_5	119.53	C_3-C_4-C_5	119.02	C_3-C_4-C_5	116.94	C_3-C_4-C_5	117.54	116.7
C_3-C_4-H_9	119.92	C_3-C_4-H_8	120.25	C_3-C_4-N_7	121.51	C_3-C_4-N_8	121.24	122.3
C_5-C_4-H_9	120.54	C_5-C_4-H_8	120.73	C_5-C_4-N_7	121.51	C_5-C_4-N_8	121.17	121.0
C_4-C_5-C_6	117.55	C_4-C_5-C_6	119.23	C_4-C_5-C_6	119.02	C_4-C_5-C_6	118.94	120.4
C_4-C_5-H_{10}	121.69	C_4-C_5-H_{10}	120.50	C_4-C_5-H_{10}	120.76	C_4-C_5-H_{10}	120.73	119.8
C_6-C_5-H_{10}	120.76	C_6-C_5-H_{10}	120.27	C_6-C_5-H_{10}	120.22	C_6-C_5-H_{10}	120.34	119.8
N_1-C_6-C_5	124.02	N_1-C_6-C_5	122.44	N_1-C_6-C_5	124.49	N_1-C_6-C_5	124.12	123.7
N_1-C_6-H_{11}	115.54	N_1-C_6-H_{11}	116.57	N_1-C_6-H_{11}	116.03	N_1-C_6-H_{11}	116.32	118.1
C_5-C_6-H_{11}	120.44	C_5-C_6-H_{11}	120.99	C_5-C_6-H_{11}	119.48	C_5-C_6-H_{11}	119.55	118.1
C2-N7-H12	114.64	C3-N7-H12	115.88	C_4-N_7-H_{12}	117.40	C_3-N_7-H_{12}	113.43	113.6
C_3-N_7-H_{13}	117.85	C_3-N_7-H_{13}	116.13	C_4-N_7-H_{13}	117.41	C_3-N_7-H_{13}	113.93	115.1
H_{12}-N_7-H_{13}	115.25	H_{12}-N_7-H_{13}	112.45	H_{12}-N_7-H_{13}	114.09	H_{12}-N_7-H_{13}	110.04	113.4
						C_4-N_8-H_{14}	115.86	115.7
						C_4-N_8-H_{15}	116.29	118.3
						H_{14}-N_8-H_{15}	113.03	120.9

[a]Values taken from Ref.[18]

Molecular symmetry is a fundamental concept as it is a tool to predict the properties such as dipole moment, planar structure of aromatic ring and electronic transitions in the molecules. It is observed that the mean C-C bond distance estimated in between the carbon atoms of the pyridine ring are found to be 1.395Å, 1.397 Å, 1.396 Å and 1.388 Å for 2AP, 3AP, 4AP and 34DAP respectively and these values are not significantly deviated from one another although they contain –NH_2 group at different positions. The mean C-N bond length in the aromatic ring also calculated as 1.337 Å, 1.334 Å, 1.338 Å and 1.320 Å in 2AP, 3AP, 4AP and 34DAP respectively which are found to be slightly lesser than the experimental (1.343 Å) value.

The exo-bond C-N_7 distance are computed as 1.383 Å, 1.394 Å and 1.383 Å for 2AP, 3AP and 4AP respectively and it is observed that the bond length in 2AP and 4AP are found to be equal and relatively low when compared with 3AP.This can be explained with the fact that the 2AP & 4AP exhibit imine-enamine tautomerism [19] and hence the aromatic ring π-electrons get delocalized with C-N_7 bond consequently the single bond resonates as C=N_7 so that the bond length of C-N_7 in 2AP and 4AP are lowered to certain extent.

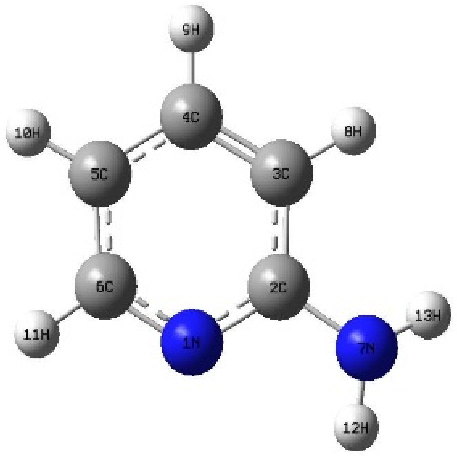


Fig-1: Optimized structure of 2-Aminopyridine

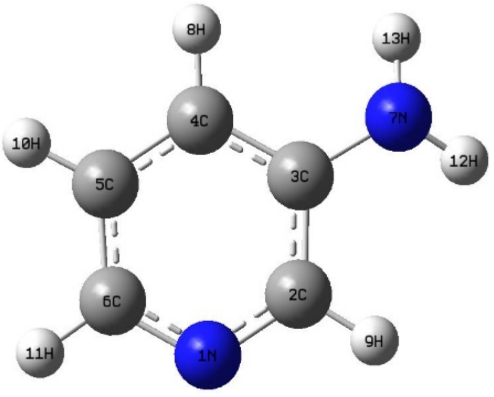


Fig-2: Optimized structure of 3-Aminopyridine

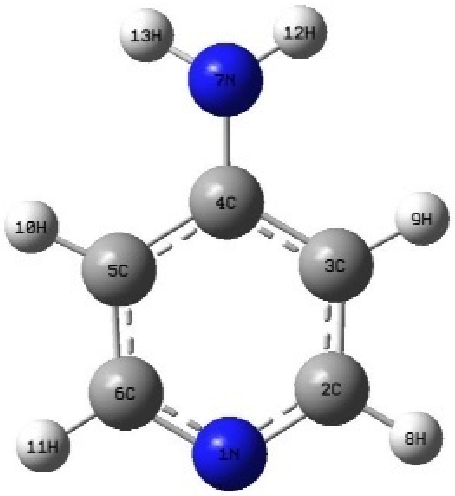


Fig-3: Optimized structure of 4-Aminopyridine

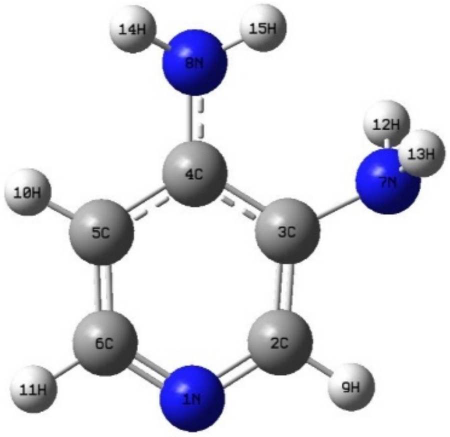
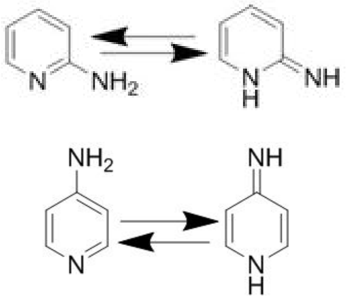


Fig-4: Optimized structure of 3, 4-Diaminopyridine



Imine-Enamine Tautomerism in 2AP and 4AP

Whereas in di-substituted aminopyridine, 34DAP, the C_3-N_7 and C_4-N_8 bond lengths are measured as 1.425 Å and 1.381 Å respectively and even in this case also the C_4-N_8 bond length found to be at lower end due to imine-enamine tautomerism while the C_3-N_7 bond length just exists as such without any resonance like 3AP.

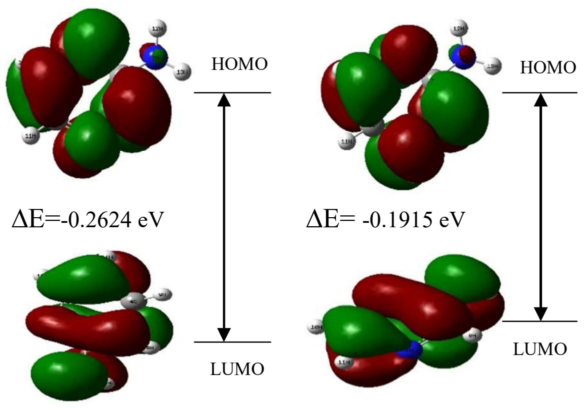
All possible N-H bond length in the chosen aminopyridines are found to be within the range of 0.999 Å – 1.009 Å and no marked positional effect is observed with respect to amino group.

The calculated bond angles in all the amino pyridines are observed to be slightly towards lower end than the experimental values. The exo bond angles N1-C2-N7 and C3-C2-N7 in 2AP are found to be 116.27° and 121.24 ° respectively and in the case of 3AP, the exo angles such as C2-C3-N7 and C4-C3-N7 are obtained as 120.95 ° and 121.92 ° respectively .In the same way ,in 4AP, the exo angles, C3-C4-N7 and C5-C4-N7 show same value 121.51 ° whereas C2-C3-N7/C4-C3-N7 and C3-C4-N8/C5-C4-N8 in 34DP are calculated as 118.89 ° /123.41 ° and 121.24 ° /121.17 ° respectively. The exo bond angles in these cases are found to be almost equal to 120 ° /121 °, hence the presence of $–NH_2$ substituent in different positions of the pyridine ring leads not a significant distortion in the exo bond angles except in few cases such as N1-C2-N7 in 2 AP and C2-C3-N7 in 34DAP which are observed to be lesser than ideal value 120Å and measured as 116.27 ° and 118.89 ° respectively but these computed values satisfactorily accede with the experimental value. The deviation in the bond angle N1-C2-N7 (116.27 °) occur because of the involvement of different hybridizations in the atoms N_1, C2 and N7 (N1-sp^2, C2-sp^2 and N7-sp^3) [20] in addition to the presence of unshared electron pairs on both the nitrogen and thereby bond angle is reduced by 3.73° than the expected angle (120°).Similarly, the distortion in the bond angle C2-C3-N7 (118.89 °) in 34DAP can be explained with the steric repulsion between the $–NH_2$ groups present in the adjacent carbon atoms (C3 & C4) in 34DAP.

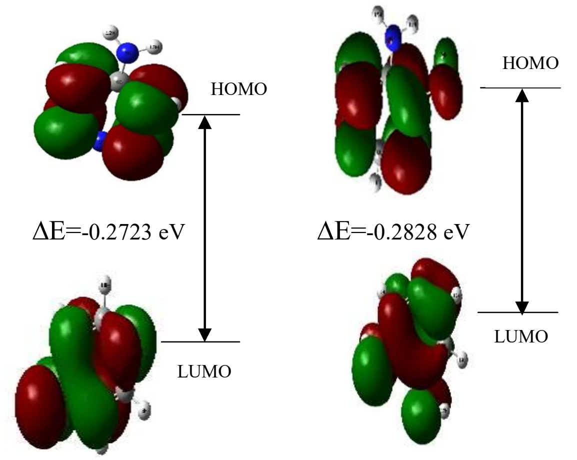
The C-C-C and C-N-C bond angles in the pyridine ring are found to be in the range of 116.05 ° to 119.53 ° which indicates that the presence of –NH2 group as substituents in the different positions do not influence the bond angles of the aromatic ring of aminopyridines whereas the C5-C6-N1 and N1-C2-C3 bond angles are obtained in the range of 122.00° to 125.09° which are observed to be more than the other C-C-C bond angles inside the ring because of the lone pair –bond pair repulsion that give a significant deviation in all the aminopyridine. In general, the bond angle parameters of the pyridine ring and amino group have good agreement with the reported experimental values.

3.2 Frontier Molecular Orbital Analysis

The chemical reactivity and also the stability the molecules have been associated with energy between highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) [21]. HOMO is the orbital which represents the ability to donate an electron and LUMO is the orbital that represents the capacity to accept an electron. The HOMO energy is directly related to the ionization potential ($I = - E_{HOMO}$) whereas the LUMO energy is correlated to electron affinity ($A = - E_{LUMO}$). In addition, with the aid of HOMO- LUMO energy gap, the global hardness of the molecule, $\eta=1/2(E_{LUMO} - E_{HOMO})$,electronic potential $\mu=1/2(E_{HOMO} + E_{LUMO})$ and global electrophilicity index $\omega= \mu^2 /2\eta$ are also calculated for the chosen molecules at B3LYP level with 6-311G++(d, p) basis set and summarized in Table-2 along with the energies of HOMO, LUMO, HOMO-1 and LUMO+1.



2-Aminopyridine **3-Aminopyridine**



4-Aminopyridine **3,4-Diaminopyridine**

Fig-5: Frontier molecular orbitals (Homo and Lumo) of Aminopyridines at DFT level

The HOMO-LUMO energy gap of 2AP, 3AP, 4AP and 34DAP are computed as -0.2624 eV,-0.1915 eV, -0.2723 eV and -0.2828 eV at DFT method. It is observed that except 3AP, all the other three values of energy gap of aminopyridines are invariable. The low values of energy gap reveal that all the selected molecules are more polarizable with high chemical reactivity and possess low kinetic stability as well as soft molecules. The negative and positive phases of the homo and lumo are appeared as green and red in colour respectively as depicted in the Fig-5.A significant degree of an intra molecular charge transfer is expected from HOMO → LUMO energy level as the estimated orbital energy gap is low at DFT level. It is visible from Fig-5 that the HOMO is located over the pyridine ring of all the aminopyridines and the LUMO resides on the amino groups of the molecules hence the intramolecular charge transfer takes place from pyridine ring to amino group.

3.3 Analysis of Mullikan Charge

The atomic population and charge distribution in the selected molecules at DFT/6-311G++ (d, p) level have been reported in the Table-3. The computation of effective atomic charges plays an important role in the application of quantum mechanical calculation of molecular system [22]. The atomic charges of nitrogen atoms are found to be negative because of the presence of unshared pair of electrons and electronegativity nature of nitrogen whereas all the hydrogen atoms, C3 and C5 of aminopyridines in the present study have positive charges except 3AP. The C2 and C6 carbon atoms in the chosen amino pyridines experience negative charge as the lone pair of electrons oriented on the nitrogen atom of the pyridine ring which is flanked between these two carbon atoms. The variation in the charge distribution and magnitude of the atomic charges within the molecules are also attributed with the delocalization of pi-electrons in the aromatic ring of the molecules.

3.4 Analysis of Molecular Electrostatic Potential

The molecular electrostatic potential surface (MEPS) is a method of mapping of electrostatic potential with electron density which displays the charge distributions of the molecules in a three dimensional way, molecular shape, size and dipole moment of the molecule. Knowledge of the charge distributions provide information to decide reactive sites and hence to predict the nucleophilic and electrophilic behaviour of the molecules [23-25].

The total electron density mapped with electrostatic potential surface and the contour map of electrostatic potential surface of negative and positive potential of the chosen aminopyridines are constructed at B3LYP/6-311G++ (d, p) level and shown in Fig-6.The negative electrostatic potential in MEPS are shown as red in colour and the positive electrostatic potentials are as blue in colour while the areas with green colour are the surface where the potential energy is almost zero. In the present molecules, the red shade region is located over the nitrogen atoms which are the negative electrostatic potential whereas the blue region is located over the hydrogen atoms which are considered as the positive electrostatic potential. The green area is placed over the C-C and C-H bonds where the electrostatic potential closes to zero. In the present study, it is revealed that the aminopyridines may undergo nucleophilic attack at the site of nitrogen atoms in the molecules.

Table-2: Comparison of HOMO-LUMO Energy gaps and related molecular properties at DFT/6-311G++(d, p) level

Molecular properties	2-amino pyridine	3-amino pyridine	4-amino pyridine	3,4-diamino pyridine
E_{LUMO+1}	0.0237	0.0189	0.0163	0.0235
E_{LUMO}	0.0061	-0.0344	0.0119	0.0215
E_{HOMO}	-0.2563	-0.2259	-0.2604	-0.2613
E_{HOMO-1}	-0.2628	-0.2590	-0.2606	-0.2630
Homo- lumo energy gap	-0.2624	-0.1915	-0.2723	-0.2828
Global hardness(η)	0.1412	0.1458	0.1362	0.1414
Electronic chemical potential(μ)	-0.1250	-0.1301	-0.1243	-0.1199
Global electrophilicity (ω)	0.0553	0.0581	0.0567	0.0508

Table-3: Mullikan charge distribution of Aminopyridines

Atom with Numbering	2-amino pyridine	3-amino pyridine	4-amino pyridine	Atom with Numbering	3,4-diamino pyridine
N1	-0.1386	-0.0741	-0.0932	N1	-0.0929
C2	-0.5475	-0.2899	-0.5057	C2	-0.3473
C3	0.5643	-0.1330	0.4333	C3	0.0448
C4	-0.5335	0.1468	-0.5805	C4	-0.2975
C5	0.0792	-0.0482	0.4332	C5	0.3870
C6	-0.3133	-0.3975	-0.5057	C6	-0.4821
N7	-0.2699	-0.3141	-0.2937	N7	-0.4467
H8	0.1614	0.1603	0.1620	N8	-0.2776
H9	0.1624	0.1546	0.1546	H9	0.2016
H10	0.1568	0.1640	0.1546	H10	0.1542
H11	0.1811	0.1590	0.1620	H11	0.1585
H12	0.2631	0.2378	0.2396	H12	0.2503
H13	0.2345	0.2343	0.2396	H13	0.2655
				H14	0.2397
				H15	0.2423

3.5 Thermodynamic Properties

The values of some thermodynamic parameters such as thermal energy, heat capacity, rotational constant, dipole moment, enthalpy, entropy and zero point vibrational energy of all the chosen molecules are computed at ground state at DFT/B3LYP/6-311G++(d, p) level at 298.15 K and summarized in the Table-4. The self-consistent field (SCF) energy obtained for the optimized geometry at DFT framework also computed as -303.73907410 a.u.,-303.838278 a.u., -303.73316560 a.u., -356.10778763 a. u., for 2AP,3AP,4AP and 34DAP respectively. As the SCF energy is found to be relatively more in the case of 34DAP, the later may show high stability factor than other aminopyridines. The thermodynamic functions especially heat capacity (Cp), entropy (S) and enthalpy(H) changes of the chosen molecules under investigation are estimated for a wide range of temperature from 50K to 1000K and tabulated in Table-5 at DFT level. A linear increase of entropy(S_m), heat capacity($C_{p,m}$) and enthalpy(H_m) change as a function of temperature is observed and depicted as correlation graphic in Fig.7-9 [26]. The correlation equations of $C_{p,m}$, S_m and H_m as a function of temperature were fitted by quadratic formulas and the corresponding fitting factors (R^2) of these thermodynamic properties for the compounds under study are determined at DFT/6-311G++(d, p) framework and their fitting equations are given as:

For 2-aminopyridine,
$C_{p,m}^{o} = -0.7245 + 0.08975\,T - 5 \times 10^{-4}\,T^{2}$ ($R^2 = 0.9972$)
$H_{m}^{o} = 65.385 + 0.0008\,T - 5 \times 10^{-3}\,T^{2}$ ($R^2 = 0.9993$)
$S_{m}^{o} = 48.402 + 0.0954\,T - 5 \times 10^{-2}\,T^{2}$ ($R^2 = 0.9998$)

Table-4: Thermochemical properties of aminopyridines at B3LYP/6-311G++(d, p) level

Theoretically computed Dipole moment (Debye), Energy (au), Zero point vibrational energy(kcal mol^{-1}), Entropy (Cal $mol^{-1}K^{-1}$), Rotational temperature (Kelvin), Rotational constant (GHZ), Thermal energy (kcal mol^{-1}) and Molar capacity at constant volume (Cal $mol^{-1}Kelvin^{-1}$)

Parameters	**2-amino pyridine**	**3-amino pyridine**	**4-amino pyridine**	**3,4-diamino pyridine**
Dipole moment (Debye)	2.1198	3.3934	4.1154	3.6542
Total energy (a.u)	-303.73907410	-303.72838278	-303.73316560	-359.10778763
Zero point energy (kcal mol^{-1})	65.92772	65.74192	65.88713	76.74756
Entropy (Cal $mol^{-1}K^{-1}$)				
Total	74.991	75.414	75.217	80.780
Translational	39.535	39.535	39.535	39.977
Rotational	26.794	26.835	26.833	27.832
Vibrational	8.662	9.044	8.849	12.971
Rotational temperature(Kelvin)	0.27826	0.27853	0.28622	0.16280
	0.13100	0.12775	0.12524	0.10786
	0.08917	0.06423	0.08721	0.06515
Rotational constants (GHZ)	5.79800	5.80358	5.96386	3.39212
	2.72968	2.66178	2.60962	2.24738
	1.85796	1.82734	1.81708	1.35760
Thermal Energy (Kcal/mol)				
Total	69.471	69.345	69.466	80.441
Translational	0.889	0.889	0.889	0.889
Rotational	0.889	0.889	0.889	0.889
Vibrational	67.693	67.567	67.688	78.663
Molar capacity at constant volume(Cal/mol-Kelvin)				
Total	22.190	22.363	22.326	25.711
Translational	2.981	2.981	2.981	2.981
Rotational	2.981	2.981	2.981	2.981
Vibrational	16.228	16.401	16.365	19.749

For 3-aminopyridine,
$C_{p,m}^{o} = -0.4506 + 0.0892\,T - 5 \times 10^{-4}\,T^{2}$ ($R^2 = 0.9977$)
$H_{m}^{o} = 65.07 + 0.0074T - 5 \times 10^{-3}\,T^{2}$ ($R^2 = 0.9993$)
$S_{m}^{o} = 48.441 + 0.0968\,T - 5 \times 10^{-2}\,T^{2}$ ($R^2 = 0.9998$)

For 4-aminopyridine,
$C_{p,m}^{o} = -0.5561 + 0.0894\,T - 5 \times 10^{-4}\,T^{2}$ ($R^2 = 0.9977$)
$H_{m}^{o} = 65.315 + 0.007\,T - 5 \times 10^{-3}\,T^{2}$ ($R^2 = 0.9993$)
$S_{m}^{o} = 48.507 + 0.0962\,T - 5 \times 10^{-3}\,T^{2}$ ($R^2 = 0.9994$)

For 3, 4-diaminopyridine,
$C_{p,m}^{o} = 0.6274 + 0.0973\,T - 5 \times 10^{-4}\,T^{2}$ ($R^2 = 0.9971$)
$H_{m}^{o} = 75.474 + 0.0094\,T - 5 \times 10^{-3}\,T^{2}$ ($R^2 = 0.9993$)
$S_{m}^{o} = 49.624 + 0.1122\,T - 5 \times 10^{-3}\,T^{2}$ ($R^2 = 0.9998$)

These thermodynamic data contribute helpful information for the further application of the compounds and can also be used to calculate the other thermodynamic energies which aid the directions of chemical reactions as per the second law of thermodynamics in thermochemical field.

3.6 Non-Linear Optical Properties

Dipole moment, polarizability and hyper polarizability of the organic molecules are the properties which are used for an intense investigation of the non-linear optical materials. The dipole moment computed at DFT/6-311G++(d, p) level are 2.1198D, 3.3934D, 4.1154D and 3.6542D for 2AP,3AP,4AP and 34DAP respectively which is a measure to analyse the inter molecular attraction of the molecules.In the present study, the output of Gaussian 09W provides the polarizability tensors, α_{xx}, α_{xy}, α_{yy}, α_{xz},α_{yz},α_{zz} and the first order hyper polarizability tensors which can be described by 3x3x3 matrix and reduced to ten components as β_{xxx}, β_{xxy}, β_{xyy}, β_{yyy}, β_{xxz}, β_{xyz}, β_{yyz}, β_{xzz}, β_{yzz}, β_{zzz} due to Kleimman symmetry[27]. The mean polarizability and the average value of the first order hyper polarizability values are calculated by using the following equations,

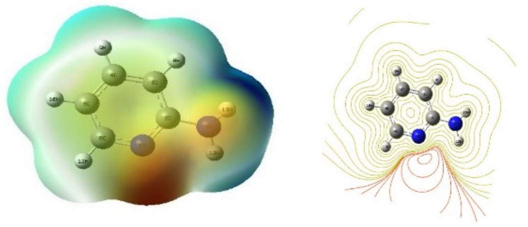
$$\alpha_{total} = 1/3(\alpha_{xx} + \alpha_{yy} + \alpha_{zz})$$

$$\beta_{total} = (\beta_x^2 + \beta_y^2 + \beta_z^2)^{1/2} = [(\beta_{xxx} + \beta_{xyy} + \beta_{xzz})^2 + (\beta_{yyy} + \beta_{yzz} + \beta_{yxx})^2 + (\beta_{zzz} + \beta_{zxx} + \beta_{zyy})^2]^{1/2}$$

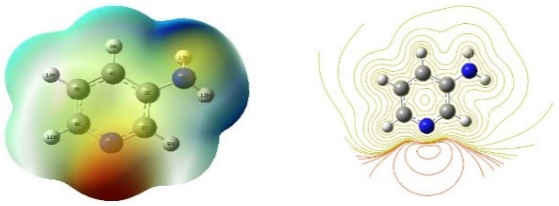
The first hyper polarizability values are found to be 2.5687×10^{-30}, 2.6802×10^{-30}, 1.4935×10^{-30} and 2.6015×10^{-30} cm^{-5} $esu^{-1}$for the molecules 2AP,3AP, 4AP and 34DAP respectively and are presented in the Table-6 .Urea is a prototypical molecule used in the study of NLO properties of the molecular system and therefore applied frequently as a threshold value for the comparative study. The molecules under investigation, aminopyridines at DFT level have the calculated β values greater than the β values of urea (0.2991×10^{-30} cm^{-5} esu^{-1}) and hence all the aminopyridines under study are expected to be good NLO materials. The value of the β components calculated theoretically clearly indicate the direction of charge delocalization and the intramolecular charge transfer process.

Table-5: Temperature dependence of thermodynamic parameters of aminopyridine at DFT/6-311G++(d, p) level

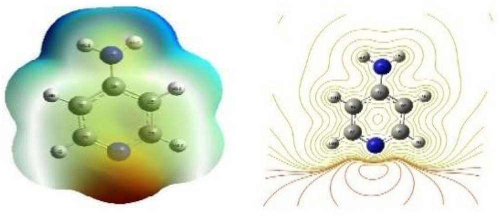
Temperature	Enthalpy(Hm)(k cal mol-1)				Heat capacity(Cp,m)(cal mol-1 k-1)				Entropy(Sm)(cal mol-1 k-1)			
(K)	2AP	3AP	4AP	34DAP	2AP	3AP	4AP	34DAP	2AP	3AP	4AP	34DAP
50	66.24	66.04	66.19	76.53	6.18	6.16	6.13	6.89	52.18	52.21	52.21	53.88
100	66.59	66.39	66.53	76.94	7.87	8.13	7.94	9.86	58.27	58.37	58.28	60.87
150	67.05	66.48	67.00	77.53	10.86	11.22	11.10	13.65	62.80	63.03	62.87	66.37
200	67.68	67.52	67.65	78.31	14.49	14.80	14.75	17.70	66.98	67.31	67.13	71.42
250	68.51	68.36	68.48	79.30	18.39	18.63	18.59	21.80	71.08	71.46	72.28	76.26
298.15	69.48	69.35	69.47	80.44	22.19	22.36	22.33	25.71	74.99	75.41	75.22	80.78
300	69.52	69.39	69.51	80.49	22.34	22.51	22.47	25.85	75.14	75.57	75.37	80.95
350	70.74	70.61	70.73	81.88	26.15	26.27	26.23	29.75	79.18	79.63	79.43	85.54
400	72.13	72.01	72.13	83.46	29.72	29.79	29.75	33.40	83.17	83.63	83.43	90.02
450	73.70	73.58	73.70	85.22	32.97	33.02	32.97	36.76	87.10	87.56	87.35	94.38
500	75.43	75.31	75.42	87.13	35.90	35.93	35.89	39.81	90.94	91.41	91.19	98.63
550	77.29	77.17	77.28	89.19	38.53	38.55	38.50	42.55	94.67	95.14	94.93	102.74
600	79.27	79.16	79.26	91.38	40.88	40.89	40.85	45.02	98.30	98.77	98.55	106.72
650	81.37	81.26	81.36	93.69	42.99	43.00	42.95	47.24	101.82	102.29	102.06	110.58
700	83.57	83.45	83.56	96.10	44.89	44.90	44.85	49.25	105.22	105.70	105.47	114.30
750	85.86	85.74	85.84	98.61	46.61	46.62	46.58	51.08	108.52	108.99	108.76	117.90
800	88.23	88.11	88.21	101.21	48.17	48.18	48.14	52.74	111.70	112.18	111.94	121.38
850	90.67	90.56	90.65	103.89	49.60	49.62	49.57	54.27	114.79	115.26	115.02	124.74
900	93.19	93.07	93.17	106.63	50.91	50.93	50.89	55.68	117.77	118.25	118.01	128.00
950	95.76	95.65	95.74	109.45	52.12	52.14	52.10	56.98	120.67	121.14	120.90	131.15
1000	98.40	98.28	98.37	112.33	53.23	53.25	53.21	58.19	123.47	123.95	123.70	134.21



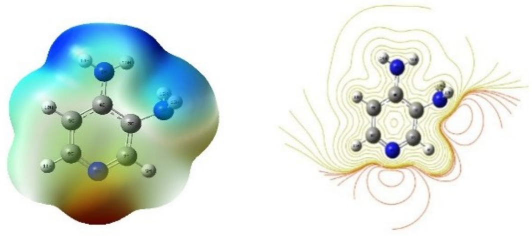
(a) 2-Aminopyridine **(b)**



(a) 3-Aminopyridine **(b)**



(a) 4-Aminopyridine **(b)**



(a) 3, 4--Diaminopyridine **(b)**

Fig-6: (a) The total electron density surface mapped with electrostatic potential (b) contour mapping of aminopyridine

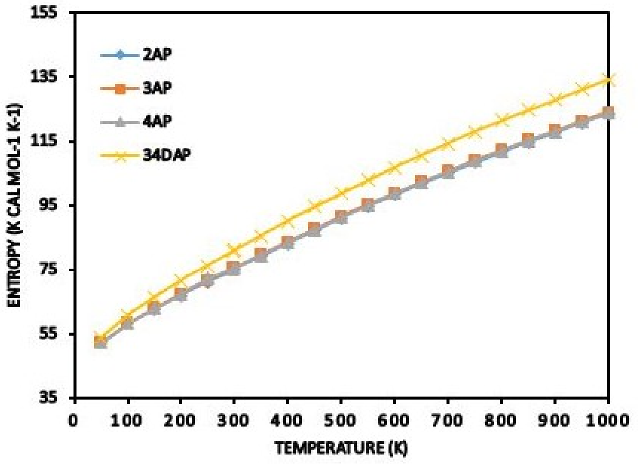


Fig-7: Correlation graphic of entropy vs temperature of Aminopyridines

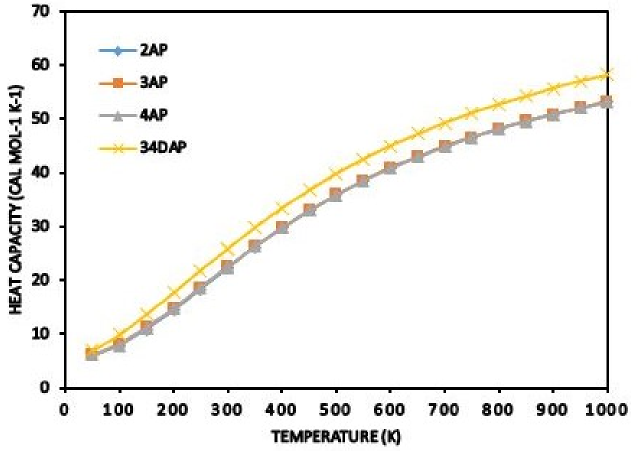


Fig-8: Correlation graphic of heat capacity vs temperature of Aminopyridines

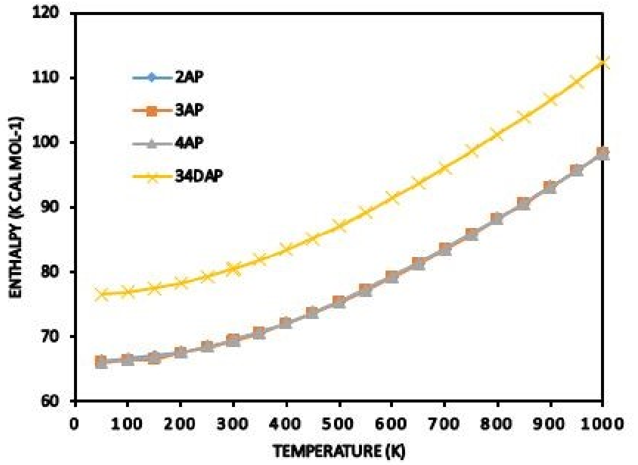


Fig-9: Correlation graphic of enthalpy vs temperature of Aminopyridines

Table-6: Comparison of Polarizability and Hyper Polarizability values of Aminopyridines at DFT/6-311G++(d, p) level

Polarizability	2-amino pyridine	3-amino pyridine	4-amino pyridine	3,4-diamino pyridine
α_{XX}	98.3237	97.3819	94.6586	99.6622
α_{XY}	-1.3030	-2.0389	-0.0105	4.5058
α_{YY}	78.5360	78.5653	80.6387	81.3362
α_{XZ}	0.3821	-0.3864	-0.3310	0.0027
α_{YZ}	0.0615	0.0580	-0.0027	-0.0010
α_{ZZ}	44.4051	43.8899	43.9424	46.7709
α_{Total} (a.u)	73.7549	73.2790	73.0799	75.9231
Hyperpolarisibility				
β_{XXX}	321.6275	-294.8016	-263.5833	-241.9757
β_{XXY}	-27.4388	23.0892	0.0030	-27.9420
β_{XYY}	-49.3038	2.0041	71.5116	-87.9337
β_{YYY}	0.5241	12.4900	-0.0057	62.8138
β_{XXZ}	11.7685	12.1450	9.6463	1.2501
β_{XYZ}	2.0375	-0.5149	0.0043	-17.1939
β_{YYZ}	3.2267	6.5467	5.7375	0.7854
β_{XZZ}	23.5165	-9.5923	21.4054	34.9235
β_{YZZ}	11.0881	26.0639	0.0009	25.5907
β_{ZZZ}	10.2739	13.0935	12.2048	1.0548
β_{TOTAL} ($cm^{-5}\ esu^{-1}$)	2.5687×10^{-30}	2.6802×10^{-30}	1.4935×10^{-30}	2.6015×10^{-30}

3.7 Donor-Acceptor Interaction

Natural Bonding Orbital (NBO) analysis is an efficient basis to study donor-acceptor interaction, bond order, type of hybridization, resonance effect within the molecule and emphasis the charge transfer within the molecular system [28].A bonding or lone pair orbital acts as a donor and a filled or empty anti-bonding orbital can act as an acceptor. The computation of stabilization energy (E^2) of all possible interactions between filled donors Lewis-type NBO's and empty (acceptors) non-Lewis can be done by second order perturbation theory. The stabilization of orbitals interaction is proportional to the energy difference between the interacting orbitals. Hence the strongest interaction takes place when the stabilization energy (E^2) is more between the efficient donor and efficient acceptor and it is also associated with i (donor) → j (acceptor) delocalization. [29].The stabilization energy (E^2) is estimated from the second order perturbation approach as

$$E^2 = q_i \frac{F^2(i,j)}{\sum_i - \sum_j}$$

where q_i is the donor orbital occupancy, $\sum_i$and $\sum_j$ are diagonal elements (orbital energies) and $F_{(i,\ j)}$is the off-diagonal Fock matrix element. The second order perturbation analysis of Fockmatrix of 2AP,3AP,4AP and 34DAP are tabulated in the Table-7 for different types of donor-acceptor interactions with their stabilization energy of not less than 4.0 Kcal mol^{-1}. The bond pair-bond pair interaction and lone pair - lone pair interactions with their high stabilization energies for all amino pyridines are analyzed in the present study. The interactions between nitrogen lone pair (non-bonding) and pyridine ring C-C anti bonding orbital $n_N \rightarrow \sigma^*_{C-C}$ in the aminopyridines are found to have strong stabilization energy (E^2) > 8 Kcal/mole. The interaction between nitrogen lone pair (non-bonding) to aromatic ring C-C antibonding π orbital $n_N \rightarrow \pi^*_{C-C}$ also obtained with very strong stabilization energies (E^2) 35.27, 26.75, 32.09 and 29.50 Kcal $mole^{-1}$ for2AP, 3AP, 4AP and 34DAP respectively.

The stabilization energy between $\sigma_{C-C} \rightarrow \sigma^*_{C-C}$ orbital are estimated and found to be less than 5 Kcal/mole .The interaction/transition between π_{C-C} → π^{*}_{C-C} orbital are determined as 14.23/25.24, 20.95/20.18, 13.86/24.8, and 14.50/24.67 Kcal mole^{-1}for 2AP, 3AP, 4AP and 34DAP respectively and these E^2 are more than the stabilization energy calculated for n → σ^* orbital interaction. Similarly, π_{N-C} → π^{*}_{C-C} orbital interaction are also accompanied with very strong stabilization energies (E^2) range from 10.31 to 30.27 Kcal mole^{-1}.

Table-7: Second order perturbation theory analysis of Fock-Matrix of aminopyridines by NBO method

2-AMINOPYRIDINE

	Donor (i) →Acceptor(j)				E(2)Kcal mol-1	Ej-Ei (a.u)	F(i, j) a.u
π	N1-C2	→	π*	C3-C4	10.31	0.32	0.052
π	N1-C2	→	π*	C5-C6	29.41	0.33	0.088
π	C3-C4	→	π*	N1-C2	27.43	0.27	0.08
π	C3-C4	→	π*	C5-C6	14.23	0.29	0.058
σ	C3-C8	→	σ*	N1-C2	4.84	1.06	0.064
π	C5-C6	→	π*	C3-C4	25.24	0.28	0.75
π	C5-C6	→	π*	N1-C2	13.40	0.026	0.055
σ	C5-H10	→	σ*	N1-C6	4.42	1.07	0.061
σ	C6-H11	→	σ*	N1-C2	4.55	1.05	0.062
σ	N7-H12	→	σ*	C2-C3	4.15	1.19	0.063
n	N1(LP)	→	σ*	C2-C3	10.06	0.88	0.085
n	N1(LP)	→	σ*	C5-C6	8.54	0.91	0.08
n	N7(LP)	→	π*	N1-C2	35.27	0.3	0.098

3-AMINOPYRIDINE

	Donor (i) →Acceptor(j)				E(2)Kcal mol-1	Ej-Ei (a.u)	F(i,j) a.u
π	N1-C2	→	π*	C3-C4	14.69	0.32	0.063
π	N1-C2	→	π*	C5-C6	21.72	0.32	0.076
σ	C2-H9	→	σ*	N1-C6	4.77	1.07	0.064
σ	C2-H9	→	σ*	C3-C4	4.01	1.08	0.059
π	C3-C4	→	π*	N1-C2	23.1	0.27	0.071
π	C3-C4	→	π*	C5-C6	20.95	0.29	0.07
σ	C4-C5	→	σ*	C3-N7	4.4	1.14	0.063
π	C5-C6	→	π*	N1-C2	20.18	0.26	0.066
π	C5-C6	→	π*	C3-C4	20.18	0.27	0.067
σ	C5-H10	→	σ*	N1-C6	4.21	1.07	0.06
σ	C6-H11	→	σ*	N1-C2	4.71	1.07	0.063
σ	N7-H12	→	σ*	C3-C4	4.12	1.21	0.063
n	N1(LP)	→	σ*	C2-C3	9.42	0.88	0.082
n	N1(LP)	→	σ*	C5-C6	8.87	0.9	0.081
n	N7(LP)	→	π*	C3-C4	26.75	0.32	0.088

3,4-DIAMINOPYRIDINE

	Donor (i) →Acceptor(j)				E(2)Kcal mol-1	Ej-Ei (a.u)	F(i, j) a.u
π	N1-C2	→	π*	C3-C4	11.71	0.32	0.56
π	N1-C2	→	π*	C5-C6	30.27	0.32	0.089
σ	C2-C3	→	σ*	C4-N8	4.44	1.15	0.064
σ	C2-H9	→	σ*	N1-C6	4.8	1.09	0.065
σ	C2-H9	→	σ*	C3-C4	4.22	1.08	0.061
σ	C3-C4	→	σ*	C4-C5	4.16	1.28	0.065
π	C3-C4	→	π*	N1-C2	31.51	0.28	0.85
π	C3-C4	→	π*	C5-C6	14.5	0.29	0.059
σ	C4-C5	→	σ*	C3-C4	4.16	1.28	0.065
σ	C4-C5	→	σ*	C3-N7	4.4	1.11	0.063
σ	C5-C6	→	σ*	C4-N8	4.65	1.15	0.037
π	C5-C6	→	π*	N1-C2	13.66	0.28	0.057
π	C5-C6	→	π*	C3-C4	24.67	0.28	0.077
σ	C5-H10	→	σ*	N1-C6	4.28	1.11	0.062
σ	C6-H11	→	σ*	N1-C2	4.71	1.1	0.064
n	N1(LP)	→	σ*	C2-C3	9.08	0.91	0.082
n	N1(LP)	→	σ*	C5-C6	9.46	0.92	0.084
n	N7(LP)	→	σ*	C3-C4	9.55	0.87	0.082
n	N8(LP)	→	π*	C3-C4	29.5	0.33	0.095

4-AMINOPYRIDINE

	Donor (i) →Acceptor(j)				E(2)Kcal mol-1	Ej-Ei (a.u)	F(i,j) a.u
π	N1-C2		π*	C3-C4	11.24	0.31	0.054
π	N1-C2	→	π*	C5-C6	29.45	0.31	0.087
σ	C2-C3	→	σ*	C4-N7	4.49	1.15	0.064
σ	C2-H8	→	σ*	N1-C6	4.63	1.06	0.063
π	C3-C4	→	π*	N1-C2	32.52	0.27	0.085
π	C3-C4	→	π*	C5-C6	13.86	0.28	0.057
σ	C3-H9	→	σ*	N1-C2	4.37	1.07	0.061
σ	C5-C6	→	σ*	C4-N7	4.49	1.15	0.064
π	C5-C6	→	π*	N1-C2	13.06	0.27	0.055
π	C5-C6	→	π*	C3-C4	24.8	0.27	0.076
σ	C5-H10	→	σ*	N1-C6	4.37	1.07	0.061
σ	C6-H11	→	σ*	N1-C2	4.63	1.06	0.063
σ	N7-H12	→	σ*	C4-C5	4.12	1.22	0.063
σ	N7-H13	→	σ*	C3-C4	4.11	1.22	0.063
n	N1(LP)	→	σ*	C2-C3	9.18	0.91	0.083
n	N1(LP)	→	σ*	C5-C6	9.18	0.91	0.083
n	N7(LP)	→	π*	C3-C4	32.09	0.32	0.096

4. CONCLUSION

Based on the quantum mechanical approach, a complete molecular structural analysis of 2AP, 3AP, 4AP and 34DAP have been performed by DFT with 6-311G++ (d, p) basis set. The presence of amino group in 2 and 4 positions of the pyridine ring exhibits imine-enamine tautomerism which is proved by the geometric parameters measured at DFT level. The $\pi_{N-C} \longrightarrow \pi^*_{C-C}$ orbital interaction is computed with very strong stabilization energies (E^2) in Kcal/mole than in $\pi_{C-C} \rightarrow \pi^*_{C-C}$ transition in the chosen aminopyridines. The correlation equation of entropy, heat capacity and enthalpy change with respect to temperature were fitted by quadratic formula with the corresponding fitting factors (R^2). It has been noticed that the thermodynamic properties such as entropy, heat capacity and enthalpy increase with wide range of temperature from 50K to 1000K.The reported geometric parameters, molecular electro static potential surface mapping and contour mapping by DFT/B3LYP/6-311G++ (d, p) calculation stand as the evidences for the reactive sites in the chosen molecules for nucleophilic and electrophilic attack. NLO behavior of the chosen aminopyridines also identified from the computed values of polarizability and hyper polarizability by B3LYP method.

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