Research Article

# Am1 and Mass Spectrometry Study of the Fragmentation of 4-aminoantipyrine Schiff Base Ligand

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**ABSTRACT**
The mass spectrum of 4-aminoantipyrine ligand has been studied in the context of correlating fragmentation pathways with electronic charges of atoms. The atomic charges were found to be good prediction for the fragmentation pathways. In this connection, considering an isolated molecular fragment in the gas phase, which was surrounded by vacuum using semi-empirical molecular orbital AM1 method, the heats of formation ($\Delta H_f^o$), dipole moment (μ), ionization potential (IP), full atomic charges and energies of frontier molecular orbitals ($E_{HOMO}$ and $E_{LUMO}$) have been performed and discussed to evaluate stable fragments.

**Keywords:** AM1, mass spectrometry, fragments, 4-amino-antipyrine, ligand.

## INTRODUCTION

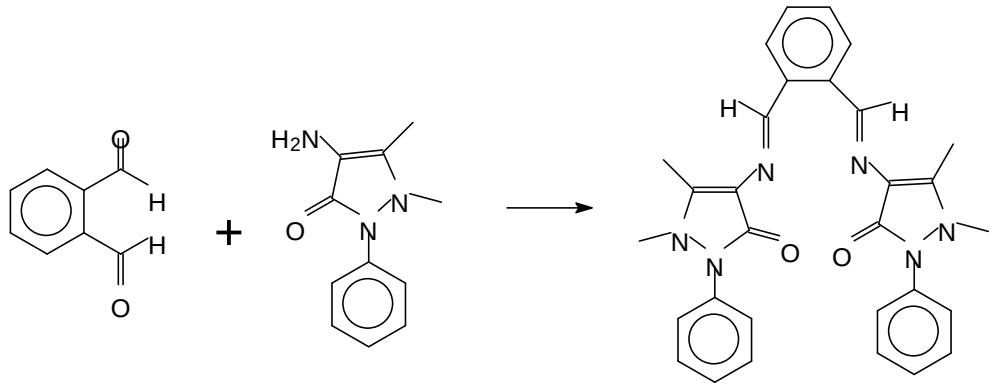
The transition metal complexes of 4-aminoantipyrine derivatives have been extensively examined in various fields like biological, analytical and therapeutics[1-3]. The emergence of new diseases, such as human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS) and the re-emergences of tuberculosis (TB) have led to increase in the incidence of fungal infections[4]. The antimicrobial activity of antipyrine Schiff bases and their complexes have been discussed[5-9]. Recently a new approach of analysis of fragmentation processes of organic compounds in electron impact mass spectrometry has been described to give a good correlation with the electronic charges of each atom[10]. The fragmentation process has been taken place mainly at the level of atoms bearing high negative or positive charges[11, 12]. It has been found that the AM1 method presents a good reliability[13, 14]. This is prompted us to investigate the electronic charges of atoms became a valuable instrument for understanding the fragmentation processes of 4-aminoantipyrine Schiffs base ligand in mass spectrometry. Austin Model-1 (AM1) is one of the semi-empirical quantum calculation methods, which is based on the neglect of differential diatomic overlap integral approximation, it includes experimental parameters and extensive simplification of the Schrodinger's equation (HΨ=EΨ) to optimize molecules for calculation of various properties and solve chemical problems[15]. In this way quantum chemistry simulates chemical structure and allows studying chemical phenomena by running calculations on computer rather than by examining reactions experimentally. In this connection, theoretical investigation was considered worthwhile to study the fragmentation process of 4-aminoantipyrine Schiff base ligand with a view to calculate their heats of formation ($\Delta H_f^o$), dipole moment (μ), ionization potential (IP), full atomic charges and energies of frontier molecular orbitals ($E_{HOMO}$ and $E_{LUMO}$), which are an advantage for investigating the stability of fragments during the electron impact mass spectrum.

Electronic properties of 4-amino-antipyrine Schiff base ligand (**1**) in gas phase usually considering isolated molecules which was surrounded by vacuum and it has been evaluated by AM1 method. From the obtained optimized electronic structure of 4-amino-antipyrine ligand (**1**) and its fragments (**2 - 6**) which are observed from mass spectrum (Figure-2). The mechanism of fragmentation processes (Scheme-2 to -6) have been studied by comparison of the relative values of net charges at different atoms of the molecule and also observed the predominated fragment using semi-empirical molecular orbital AM1 method.

**Experimental**

**Synthesis of the Schiff base of 4-aminoantipyrine**[16]

A solution of 4-aminoantipyrine (16.24 g 0.04mmol) in methanol (25 ml) was added to a solution of orthophthalaldehyde (2.68 g , 0.02mmol) in methanol (25 ml). The mixture obtained was refluxed for an hour, then stirred for 3 hrs at room temperature and left at the same temperature for a day. The resulting a deep orange coloured solid was separated on evaporation of solvent and dried. Elemental analysis: Calc. C% , 71.43; N%, 16.67; Found. C%, 72.13; N%, 16.06.

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**Scheme - 1: Formation of Schiff base 4-aminoantipyrine ligand**

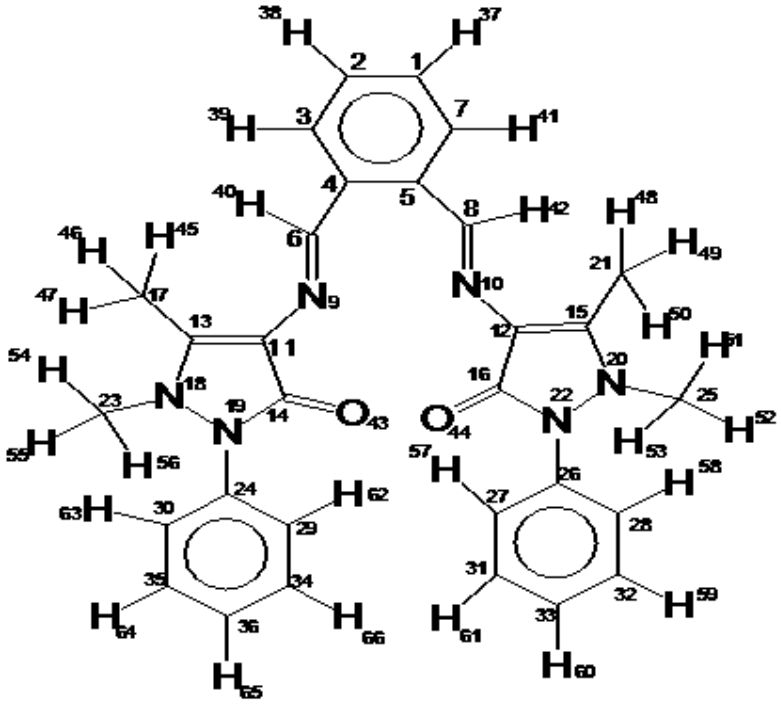


**Fig. 1:**

**Mass spectrum**

The mass spectrum was obtained by electron impact mass spectrometry (EIMS) on a CPG-JSM AX505 apparatus at 70 eV as shown in Figure- 2 and the data is presented in Table-I.

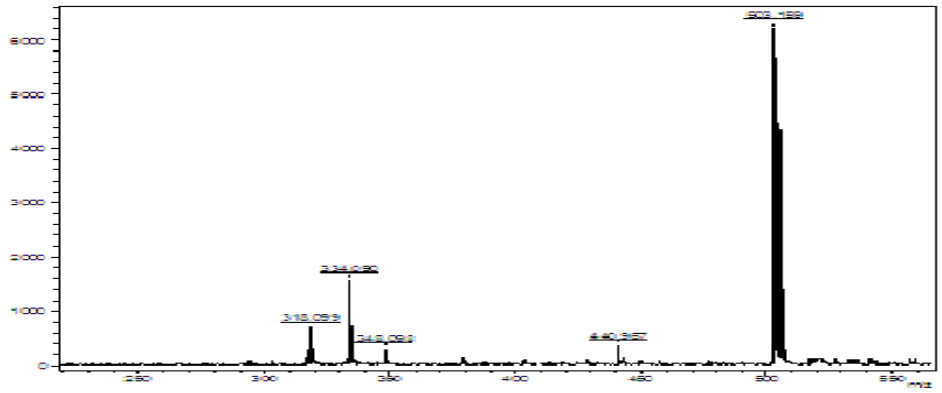


Figure 2: - Mass spectrum of 4-Aminoantipyrine Schiff base Ligand

**Computational methods**[15]

Austin Model 1 (AM1) Semi-empirical molecular orbital calculations were performed on the fragments as shown in Scheme-2, 3, 4, 5 & 6 using the MOPAC93 in WinMOPAC ver 5.13 program by means of Intel Dualcore D102GGC2 DDR2 1GB SDRAM PC. The AM1 semi-empirical method is a modification of MNDO, offering more accurate parameterizations for polar systems and transition states. Geometry calculations in the ground state (keywords: PRECISE, equivalent to GNORM=5.0, CHARGE, GEO-OK, and MMOK to correct the increase in the barrier to rotation of the amide linkage) were completely optimized until the lowest energy was found. The position of the atom in the molecule is mentioned as subscript as shown in Figure- 1.

**RESULTS AND DISCUSSION**

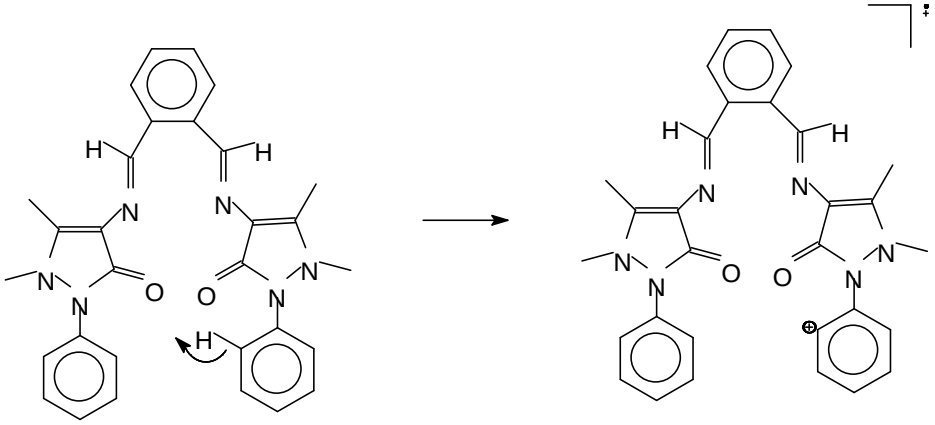
**Electronic structure of 4-aminoantipyrine ligand (1) and its fragments (2 to 6)**

The optimized electronic structure of 4-aminoantipyrine ligand (**1**) and its fragments (**2** to **6**) are shown in Scheme-1 to -6. The calculated heats of formation ($\Delta H_f^o$), ionization potential (IP), dipole moment (μ), the energies of frontier molecular orbitals ($E_{HOMO}$ and $E_{LUMO}$) are presented in Table-I. Net charges on carbon, nitrogen and oxygen- atoms of the fragments (**1** to **6**) are presented in Table-II.

The calculated values of frontier orbital energies ($E_{HOMO}$ and $E_{LUMO}$) reveal that molecules **1** to **6** have more electron-donor character. The results so obtained reveal that the electronic properties and reactivity of molecule depend on its conformational structure. The promotion of an electron from HOMO to LUMO, in a photochemical reaction, the supra-facial path way is allowed in the case of molecules **1** to **6,** due to the presence of same sign[17]. The dipole moment of molecules depends on the nature of the atoms and bonds comprising the molecules and on their arrangement. The dipole moment is increasing in the order of molecules **5** < **1** < **6** < **3** < **4** < **2.** Fragment (**4**) shows higher dipole moment. The electronegative hetero-atoms cause displacement of electrons that induces an additional dipole moment in the molecule. According to the heat of formation ($\Delta H_f^o$) data, the stability of compounds have increased in the order of **3 < 2 < 1 < 4< 5 < 6**. But geometry calculations in the ground state were completely optimized until the lowest energy conformation was found in the individual fragment.

**Formation of base peak from molecular ion (M-H) m/z 503**

The m/z ratio of molecular ion of the 4-aminoantipyrine ligand is in good agreement with the expected molecular weight is an indication of the stability of the ion. According to the charges of different atoms, the most probable point of impact of the electron beam is the oxygen of the carbonyl-group ($O_{43}$, $O_{44}$). The significant fragmentation processes have been investigated, and observed the most important fragments take place on most negative charge carbon atoms or are induced by hetero-atoms (oxygen or nitrogen). The most negative charge atoms are the most electron donating nature. It is observed that the molecular ions of the compound and the base peak is found through the process (Scheme-2) with relative abundance of 100% and is very stable.

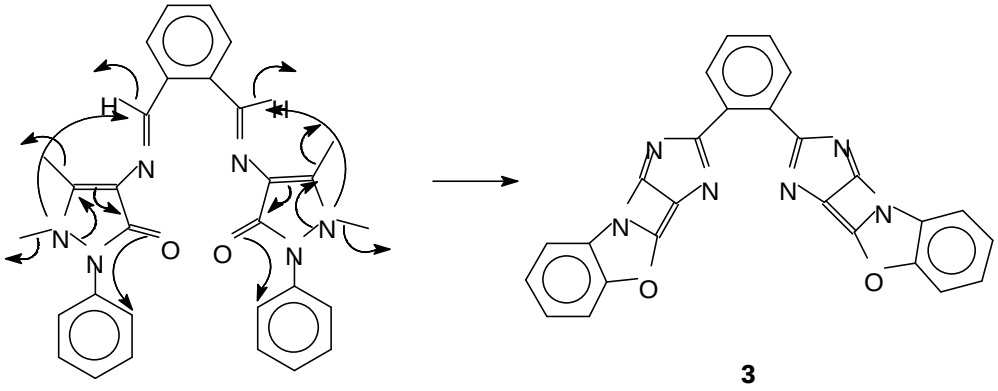


1 2

**Scheme-2**

**Formation of the fragment m/z 440**

This fragment had been observed with the taking away of four methyl groups bearing $C_{13}$, $C_{15}$, $N_{18}$ and $N_{20}$ atoms. The fragmentation process has been shown with rearrangement as shown in Scheme-3. It is found with less relative abundance of 4.79%.



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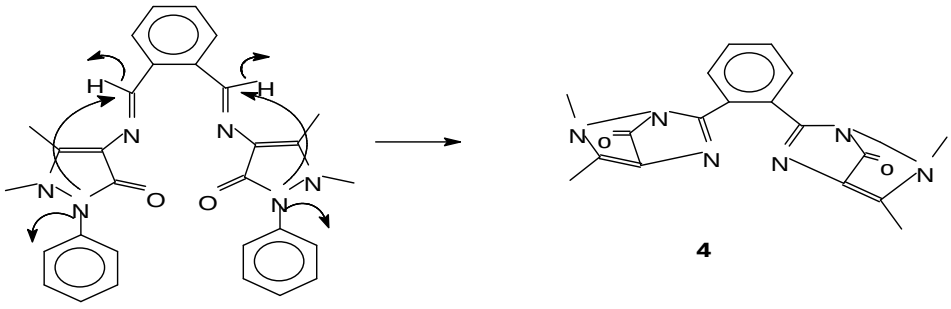
**Scheme- 3**

**Formation of the fragment m/z 348**

This fragment is formed by direct elimination of two phenyl groups from $N_{19}$ and $N_{22}$-atoms due to high negative charge. The fragmentation process has been given as per Scheme-4 with simultaneous rearrangement. It is also observed that fragment is more stable than molecular ion as per $\Delta H_f$ values. But it is formed with 3.59% relative abundance.



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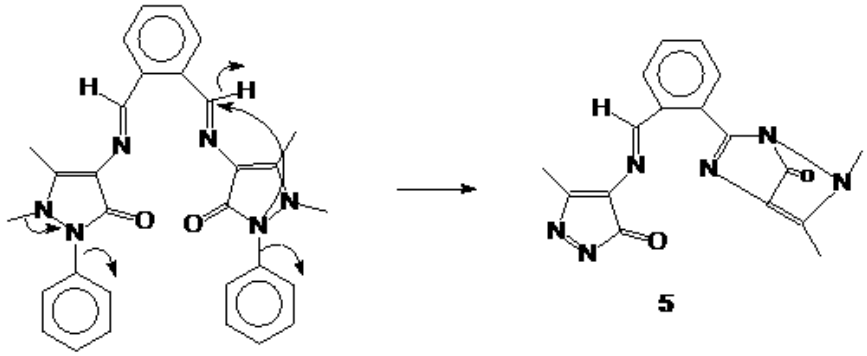
**Scheme - 4**

**Formation of the fragment m/z 334**

This fragment is formed by simultaneous removal of two phenyl groups from $N_{19}$ and $N_{22}$-atoms due to high negative charge and expulsion of one methyl group from $N_{18}$- atom. The fragmentation process has been agreed as per Scheme-5 with simultaneous rearrangement. It is also observed that fragment is more stable base peak ion as per $\Delta H_f$ values. But it is formed with 3.59% relative abundance.

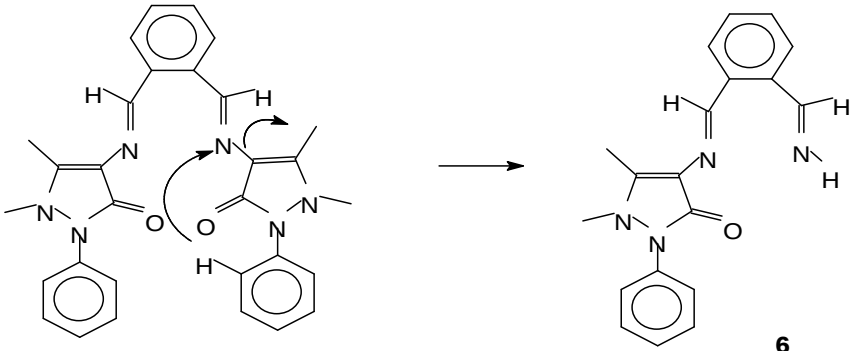



5

**Scheme - 5**

**Formation of the fragment m/z 318**

It is investigated with direct taking away of pyrazolone group from $N_{10}$- atom, due to high negative charge. The fragmentation process has been given as per Scheme-6 with expulsion of pyrazolone group parent molecule. It is also observed that fragment is more stable fragment as per $\Delta H_f$ values. But it is formed with 23.95% relative abundance.




6

**Scheme - 6**

**CONCLUSION**

Mass spectrometry is useful tool in the prediction of the ease of fragmentation process for 4-aminoantipyrin Schiff base ligand that has been considered in this investigation but also provides the experimental spectrometric strategy by the theoretical methodology employed. AM1 semi-empirical method appeared as a useful for understanding and explaining the process of the fragmentation. In this study, it has been formed logic and good explanations of all fragments obtained formation of base peak ion of the target compound and most of their fragments bearing high positive or negative charge. So, loss of proton (M-H) and rearrangement of molecule with removal of phenyl or methyl groups from hetero-atoms and formation of fragments m/z 503, 440, 348, 334 and 318 can be justified by exploiting electronic charges of atoms. The correlation between charges of atoms and fragmentation process of the molecule had been found to be very appropriate. The utility of theoretical predictions is important for evaluating the fragmentation mechanism and stability of fragments.

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**Table I: Heat of formation ($\Delta H_f^o$ in kcal/mol), dipole moment (μ in Debye), energies of frontier molecular orbitals (in eV) and of pyrazalone ligand (1) and its fragments (2 to 6) from AM1 calculation along with observed molecular weight (m/z) and relative abundance (%) from mass spectrum**

| Parameters | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| $\Delta H_f^o$ (kcal/mol) | 203.48 | 393.59 | 478.17 | 193.58 | 171.92 | 134.38 |
| μ (Debye) | 4.65 | 13.11 | 5.29 | 7.96 | 3.19 | 4.75 |
| $E_{HOMO}$ (eV) | -8.496 | -10.367 | -8.929 | -7.740 | -9.542 | -8.705 |
| $E_{LUMO}$ (eV) | -0.760 | -4.798 | -1.747 | -1.140 | -2.000 | -0.831 |
| Ionization potential (eV) | 8.49 | 10.36 | 8.93 | 7.74 | 9.54 | 8.70 |
| Molecular weight | 504.590 | 503.582 | 440.420 | 348.363 | 334.337 | 318.377 |
| *m/z values | - - | 503 | 440 | 348 | 334 | 318 |
| *Relative abundance (%) | - - | 100 | 4.79 | 3.59 | 8.98 | 23.95 |
| *Measured from mass spectrometry | | | | | | |

**Table II: Atomic charges on Carbon, Nitrogen and Oxygen atoms of 4-amino-2,3-dimethyl-1- phenyl-5- pyrazalone ligand (1) and its fragments (2 to 6) from AM1 calculations**

| Charges | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| $C_1$ | -0.1332 | -0.1290 | -0.1194 | -0.1259 | -0.1213 | -0.1287 |
| $C_2$ | -0.1219 | -0.0964 | -0.1198 | -0.1191 | -0.1127 | -0.1263 |
| $C_3$ | -0.1071 | -0.1022 | -0.0974 | -0.1048 | -0.0944 | -0.0964 |
| $C_4$ | -0.0334 | -0.0055 | +0.0090 | -0.0006 | -0.0131 | -0.0458 |
| $C_5$ | -0.0428 | -0.0896 | +0.0101 | +0.0148 | -0.0358 | -0.0436 |
| $C_6$ | -0.0255 | -0.0696 | +0.0460 | +0.1104 | +0.0759 | -0.0296 |
| $C_7$ | -0.0951 | -0.0816 | -0.0978 | -0.0945 | -0.0877 | -0.0988 |
| $C_8$ | -0.0181 | +0.0606 | +0.0436 | +0.0767 | +0.0107 | -0.0254 |
| $C_{11}$ | -0.1632 | -0.2133 | -0.1519 | -0.0580 | -0.0427 | -0.1644 |
| $C_{12}$ | -0.1581 | -0.0233 | -0.1527 | -0.1987 | -0.1326 | - - |
| $C_{13}$ | +0.0478 | +0.0965 | -0.0031 | -0.0726 | +0.0252 | +0.0501 |
| $C_{14}$ | +0.3025 | +0.3097 | +0.1607 | +0.2444 | +0.2298 | +0.3044 |
| $C_{15}$ | +0.0466 | +0.0956 | -0.0044 | +0.0328 | -0.0604 | - - |
| $C_{16}$ | +0.2999 | +0.1154 | +0.1596 | +0.2495 | +0.1941 | - - |
| $C_{17}$ | -0.1799 | -0.1898 | - - | -0.1800 | -0.2245 | -0.1799 |
| $C_{21}$ | -0.1790 | -0.2011 | - - | -0.2224 | -0.1621 | - - |
| $C_{23}$ | -0.1197 | -0.1108 | - - | -0.1043 | - - | -0.1192 |
| $C_{24}$ | +0.0427 | +0.0166 | -0.0664 | - - | - - | +0.0450 |
| $C_{25}$ | -0.1185 | -0.1120 | - - | -0.1562 | -0.1578 | - - |
| $C_{26}$ | +0.0418 | -0.0458 | -0.0694 | - - | - - | - - |
| $C_{27}$ | -0.1225 | +0.0176 | -0.0782 | - - | - - | - - |
| $C_{28}$ | -0.1495 | -0.0700 | -0.0766 | - - | - - | - - |
| $C_{29}$ | -0.1219 | -0.1056 | +0.0136 | - - | - - | -0.1506 |
| $C_{30}$ | -0.1496 | -0.1182 | -0.0782 | - - | - - | -0.1245 |
| $C_{31}$ | -0.1176 | -0.0719 | -0.1064 | - - | - - | - - |
| $C_{32}$ | -0.1216 | -0.1089 | -0.1314 | - - | - - | - - |
| $C_{33}$ | -0.1408 | -0.0855 | -0.1154 | - - | - - | - - |
| $C_{34}$ | 0.1181 | -0.1284 | -0.1059 | - - | - - | -0.1201 |
| $C_{35}$ | -0.1220 | -0.1265 | -0.1311 | - - | - - | -0.1167 |
| $C_{36}$ | -0.1412 | -0.1156 | -0.1159 | - - | - - | -0.1406 |
| $N_9$ | -0.1189 | -0.0860 | -0.0603 | -0.0851 | -0.0893 | -0.2245 |
| $N_{10}$ | -0.1303 | -0.1560 | -0.0792 | -0.1794 | -0.1213 | -0.1244 |
| $N_{18}$ | -0.1136 | -0.1247 | -0.0582 | +0.1027 | -0.1436 | -0.1125 |
| $N_{19}$ | -0.1886 | -0.1736 | -0.0794 | -0.2798 | -0.1753 | -0.1902 |
| $N_{20}$ | -0.1152 | -0.0629 | -0.0446 | -0.1523 | +0.0259 | - - |
| $N_{22}$ | -0.1877 | -0.0579 | -0.0400 | -0.1648 | -0.0525 | - - |
| $O_{43}$ | -0.3105 | -0.3461 | -0.0818 | -0.2067 | -0.1871 | -0.3230 |
| $O_{44}$ | -0.3121 | -0.0279 | -0.0815 | -0.1331 | -0.1978 | - - |
| *subscript numbers of atom are given as per Figure-1 | | | | | | |

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