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**Original Article**

# AM1 study on the conformations of keto-enol tautomerism in methicillin

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**Abstract**

The geometry, conformation and electronic structure of keto-enol tautomerism in methicillin have been optimized and calculated in the gas phase usually considering an isolated molecule surrounded by vacuum using semi-empirical molecular orbital AM1 method. The mechanism of protonation in enol tautomer of methicillin has been studied by comparison of the different positions of net charges at nitrogen atoms in the molecule. Further, 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. The conformational analyses of mono- and di-protonated enol tautomers have also been performed for their stable conformations.

**Key words:** AM1, keto-enol tautomerism, methicillin, induction effect, frontier molecular orbital.

## INTRODUCTION

Methicillin was used to treat infections caused by certain gram-positive bacteria and also against gram-negative cocci [1]. Methicillin inhibits the growth of both penicillin susceptible and penicillinase-producing staphylococci [2]. Methicillin is insensitive to β-lactamase enzymes and the presence of the ortho-dimethoxyphenyl group increases the β-lactamase resistance [3]. The importance of tautomeric equilibria has recognised for the study of the processes of both organic chemistry and biochemistry [4]. The tautomerism of organic compounds was reported extensively theoretical and statistical-physical approaches [5]. Theoretical models of the salvation energies of tautomers [6] were reported. The stability of tautomers [7] and equilibrium constants in electrostatic reaction field for heterocyclic compounds in aqueous solution [8] was studied. It is assumed that dipolar character of the drug could improve oral absorption [9].

Austin Model-1 (AM1) is one of the semi-empirical quantum calculation methods based on the neglect of differential diatomic overlap integral approximation, which includes experimental parameters and extensive simplification of the Schrodinger's equation (HΨ=EΨ) to optimize molecules for calculation of various properties [10]. It is important to know the conformational changes in the molecule for the prediction of its reactivity and pharmacological action to simulating chemical structure and reactions numerically studying chemical phenomena through the calculations on computer instead of examining reactions experimentally. These observations together with earlier work on methicillin conformational analyses and electronic structure [11] prompted us to incorporate the study of keto-enol tautomerism in methicillin. It has attracted much to carry out optimization of protonated forms with a view to evaluate the polarity.

The present study reveals on molecular conformation and electronic properties of methicillin (**1**) and its tautomerism in gas phase usually considering an isolated molecule surrounded by vacuum has been evaluated by AM1 method. Keto-enol tautomerism of methicillin involves the shifting of hydrogen atom from α-carbon atom of keto (-HC-C=O) group to the oxygen atom in the same molecule to form enol (-C=C-O-H) group as shown in Figure-2. It is also observed that the keto-form predominates in the methicillin. From the obtained optimized electronic structure of keto-enol tautomerism of methicillin, the mechanism of protonation has been studied by

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comparison of the relative values of net charges at nitrogen atoms in different positions of the molecule. Taking enol form of methicillin as a neutral molecule (**2)**, the molecular geometry and conformations of mono-protonated (**3** & **4**), di-protonated (**5**) and anion (**6**) systems have been determined by full optimization calculations using semi-empirical molecular orbital AM1 method.

**Computational methods [10]:** Semi-empirical molecular orbital calculations (Austin Model-1, (AM1)) were performed on the molecules shown in Scheme-1 using the MOPAC93 in WinMOPAC ver 5.13 program by means of Intel Dualcore D102GGC2 DDR2 1GB SDRAM PC. 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 conformation was found. The position of the atom in the molecule is mentioned as subscript (as shown in Figure-1). The initial molecular geometry was adopted as Pople's standard data [12], and subsequently fully optimized using an energy gradient method. The conformations were designated by Klyne-Prelog terms [13] using *s* = syn, *a* = anti, *p* = peri-planar ($0\pm30^0$ & $180\pm30^0$) and all other angles *c* = clinal.

## RESULTS AND DISCUSSION

**Electronic structure of methicillin (1) and its enol tautomer (2) mono-protonated (3 & 4), di-protonated (5) and anion (6):** The optimized electronic structure of methicillin (**1**) and its enol tautomer (**2**) mono-protonated (**3** & **4**), di-protonated (**5**) and anion (**6**) are shown in Scheme-1. In this context, the numbering of enol form of methicillin (**2)** is shown in Figure -1. The calculated heats of formation ($\Delta H_f^o$), ionization potential (IP), dipole moment (μ), the energies of frontier molecular orbitals ($E_{HOMO}$ and $E_{LUMO}$) and net charges on hetero atoms of the molecules (**1** to **6**) are presented in Table-I. It is observed that the net charges on $N_7$- and $N_{13}$- atoms are -0.1523 and -0.2763 respectively in the case of methicillin enol-form (**2**). It is also investigated that the sequence of protonation for nitrogen atoms of methicillin enol-form (**2**) is increasing in the order of $N_7 < N_{13}$. Thus, $N_{13}$- atom is predicted to be main protonation site of methicillin enol-form (**2**), according to the negative charge distribution on nitrogen atoms.

The calculated values of frontier orbital energies ($E_{HOMO}$ and $E_{LUMO}$) reveal that molecules **1** and **5** have more electron-donor character whereas other molecules have electron-acceptor property. 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 5**, due to the presence of same sign and anion (**6**) is allowed antara-facial path way due to the opposite sign [14].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 **2** < **4** < **5** < **3** < **1** < **6**. Anion (**6**) shows higher dipole moment. The electronegative hetero-atoms cause displacement of electrons that induces an additional dipole moment in the molecule. The magnitude of the induction effect [15] ($\mu_{ind}$) of molecules can be estimated with respect to methicillin enol form (**2**). It is found that the induction effect is increasing in the order of $\Delta\mu_{ind}$ (**4**) 1.104 D < $\Delta\mu_{ind}$ (**5**) 1.212 D < $\Delta\mu_{ind}$ (**3**) 1.873 D < $\Delta\mu_{ind}$ (**1**) 2.016 D < $\Delta\mu_{ind}$ (**6**) 15.656 D. According to the heat of formation ($\Delta H_f^o$) data, the stability of compounds have increased in the order of **5** < **3** < **4** < **2** < **1** < **6**. But geometry calculations in the ground state were completely optimized until the lowest energy conformation was found in the individual ions or molecules. It can be assumed that the electronic properties and reactivity of the molecule depend on its conformational structure. It is predicted that the protonation would take place preferably at $N_{13}$-atom than $N_7$-atom in the case of methicillin enol-form (**2**). It is confirmed that the stability of mono-protonated enol form of methicillin **4** ($\Delta H_f^o$, +13.2664 kcal/mol) is more stable than **3** ($\Delta H_f^o$, +15.9283 kcal/mol). The enol form of di-protonated methicillin **(5)** is possible (with the heat of formation ($\Delta H_f^o$) of +251.9399 kcal/mol**)** from mono-protonated enol form of methicillins (**3** & **4**). The protonation at $N_{13}$- atom in the case of enol form of methicillin (**2**) to mono-protonated form (**3**) is considered by decreasing net atomic charges at $N_{13}$-, $O_{10}$-, $O_{12}$-, and $O_{36}$- atoms and increased at $O_{19}$-, $O_{21}$-, and $O_{33}$- atoms. The protonation site of enol form of methicillin (**2**) at $N_7$- atom to mono-protonated form (**4**) is considered by decreasing net atomic charges at $N_7$-, $N_{13}$-, $O_{10}$-, $O_{12}$-, $O_{33}$- and $O_{36}$-atoms and increased at $O_{19}$- and $O_{21}$- atoms. In the case of di-protonated form (**5**), the negative atomic charges are decreased at all hetero atoms except at $O_{19}$-atom and $O_{21}$-atoms. Anion of enol form of methicillin (**6**) is formed by the removal of a proton on $O_{10}$-atom with increasing net charges at $N_7$-, $O_{10}$-, $O_{12}$-, $O_{19}$-, $O_{21}$-, $O_{33}$-, and $O_{36}$-, and decreasing at $N_{13}$- atom.

**The acid – base equilibrium of methicillin enol form and its protonated forms:** Equilibrium is normally established in polar solvents, in order to investigate the basicity and it is found out the

protonation sites of enol form of methicillin (**2**) as per Scheme-1. $N_{13}$-atom is main basic centre in accordance with the negative charge distribution on nitrogen atoms (Table-1). Ionization potential (IP) is increasing in the order of **6 < 2 < 1 < 4 < 3 < 5**. To determine the exact protonation centres of enol form of methicillin (**2**), the proton affinities (PA) for the different nitrogen atoms of the molecule have been calculated through AM1 method. The electron excitation energies are increasing in the order of **5 < 6 < 4 < 2 < 3 < 1**. It indicates that di-protonated enol form of methicillin (**5**) and anion (**6**) are more reactive. The stable conformation of the cations formed by the protonation of each nitrogen atom of the molecule is determined; the heats of formation are calculated with full geometry optimization. The cations formed by the protonation at $N_7$- or $N_{13}$- atoms of enol form of methicillin (**2**) can exist in *anti*- or *syn*-conformations, according to the position of nitrogen atoms as shown in Scheme-1. Its conformation can be assigned by comparison of its geometry and electronic structure. The proton affinity (PA) [16] values for the different nitrogen atoms of enol form of methicillin RH (**2**) were calculated by using the equation (1) and found to be 215.1736 kcal/mol and 217.8355 kcal/mol respectively in the case of mono-protonated methicillins ( **3** and **4**). Di-protonated form (**5**) was formed from either of mono-protonated methicillins (**3** and **4**) respectively with PA 131.1884 kcal/mol and 128.5265 kcal/mol.

$$PA=\Delta H_f^o(H^+) + \Delta H_f^o(B) - \Delta H_f^o(BH^+) \ldots (1).$$

Where PA is the proton affinity, $\Delta H_f^o(B)$ is the heat of formation for enol form of methicillin (**2**), $\Delta H_f^o(BH^+)$ is the heat of formation for the cation, and $\Delta H_f^o(H^+)$ is heat of formation for the proton (367.2kcal/mol). The proton affinity is in the order of $N_{13}$ (215.1736 kcal/mol) < $N_7$ (217.8355 kcal/mol) and mono-protonated methicillin (**4**) appears to be more stable. All cations are solvated to form hydrogen bonds with the polar solvents which would affect the position of the equilibrium. As per electron excitation energies (ΔE) (in eV), it is observed the reactivity is decreased in the order of **5** > **6** > **4** > **2** > **3** > **1**. It is confirmed that methicillin (**1**) is more stable than its enol-form (**2**).

**The conformations of keto-enol tautomerism in methicillin:** Figure - 2 illustrates the formation of two tautomeric forms of methicillin (**1**), which may possible at chemical equilibrium under ordinary conditions. Instances are known when tautomeric forms are stable under ordinary conditions, which are capable of inter-conversion at higher temperatures, frequently in the presence of catalyst. Fully optimized AM1 calculations scrutinize only the main data of bond lengths (Table-II) and dihedral angles (Table-III) of molecules (**1** to **6**) for the sake of simplicity.

The tautomeric equilibrium constants $\log K_T$ was calculated [17] from the heat of formation, according to the equation (2):

$$\log K_T = \frac{\Delta GT}{2.303\ R\ T} \approx \frac{\delta\Delta H_f^o}{2.303\ R\ T} \quad \text{- - (2)}$$

Where ΔGT is the free energy of the tautomeric equilibrium, $\delta\Delta H_f^o$ is the difference in the calculated heats of formation of the tautomeric species participating in this equilibrium. R is the gas constant and T is the absolute temperature. From this equation (2), $\log K_T$ value was calculated as 15.7256.

From the Table-II, Table-III, Figure-2 and Scheme-1, it is observed that methicillin (**1**) would undergo keto-enol tautomerism and form enol of methicillin (**2**) with increasing bond length of $O_{12}$-$C_9$ (1.3502 Å) and decreasing bond length of $C_{11}$-$C_9$ (1.3779 Å). The change of conformation from *–ap* of $C_{10}C_8C_4C_3$, *-ac* of $C_{14}N_{13}C_{11}C_9$ and ***+ap*** of $C_{15}C_{14}N_{13}C_{11}$ are changed respectively to *+sc*, *+ac* and *+ap* conformations. Dihedral angle of $O_{33}C_8C_4C_3$ and $H_{35}N_{13}C_{11}C_9$ are changed respectively *+sp* to *–ac* and *+sc* to *–sc* conformation. After keto-enol rearrangement, the enol form of methicillin (**2**) is formed with the *-sp* conformation in the case of dihedral angle of $H_{46}O_{12}C_9N_7$.

**The conformations of methicillin enol form (2) and its mono-protonated (3 & 4), di-protonated (5) and anion (6):** The spatial arrangement of atoms in a molecule was considered to study the conformations of methicillin (**1**), and its enol form of methicillin (**2**), mono-protonated forms (**3 & 4**), di-protonated form (**5**) and anion (**6**) with a view to investigate molecular deformations. These can exist in *anti*- or *syn*- conformation, according to the position of atoms. In this context, the change in energy content of the protonation may depend on the changes in the parameters of dihedral angles. Fully optimized AM1 calculations scrutinize only the main data of bond lengths (Table-II) and dihedral angles (Table-III) of molecules (**1** to **6**) for the sake of simplicity.

From the Table-II, and Table-III, it is observed that as per Scheme-1, mono-protonated enol form of methicillin (**3**) is formed by the addition of proton at $N_{13}$-atom of enol tautomer of methicillin (**2**), with increasing bond lengths at $C_{14}$-$N_{13}$, $H_{46}$-$O_{12}$ and $C_{11}$-$C_9$ and decreasing bond lengths at $C_9$-$N_7$, $O_{12}$-$C_9$, $O_{36}$-$C_{14}$ and $C_{15}$-$C_{14}$. The conformations of

$H_{35}N_{13}C_{11}C_9$, and $O_{36}C_{14}N_{13}C_{11}$ are changed respectively from -*sc* to -*sp* and –*sp* to +*sp* conformations and all other conformations are moderately changed. It is observed that the protonation at $N_{13}$-atom in the case of $HN_{13}C_{11}C_9$ is shown -*ac* conformation. If the mono-protonated enol form of methicillin (**4**) is formed by the addition of proton at $N_7$- atom of methicillin enol tautomer (**2**), with increasing bond lengths at $C_{14}$-$N_{13}$, $H_{46}$-$O_{12}$ and $C_9$-$N_7$ and decreasing bond lengths at $C_{15}$-$C_{14}$, $O_{36}$-$C_{14}$ and $O_{12}$-$C_9$. The change of dihedral angle of $C_{14}N_{13}C_{11}C_9$, $H_{35}N_{13}C_{11}C_9$ and $H_{46}O_{12}C_9N_7$ are converted from +*ac* to +*ap*, -*sc* to -*sp* and -*sp* to +*sc* conformations respectively and all other conformations are unaltered. It is observed that the protonation at $N_7$-atom is shown -*ap* conformation. In the case of formation of di-protonated methicillin enol (**5**), it is found that the dihedral angle of $H_{35}N_{13}C_{11}C_9$, $O_{36}C_{14}N_{13}C_{11}$ and $H_{46}O_{12}C_9N_7$ are changed conformation, -*sc* to -*sp*, -*sp* to +*sp* and -*sp* to -s*c* conformations respectively. It is also investigated that the protonation at $N_7$-atom and $N_{13}$-atom are shown -*ac* conformations to form stable di-protonated methicillin enol (**5**).

It can be concluded that the anion (**6**) is formed with the removal of a proton on $O_{10}$- atom of methicillin enol tautomer (**2**), and the change of conformation from ***+sc*** of $O_{10}C_8C_4C_3$, and ***–sc*** of $C_{16}C_{15}C_{14}N_{13}$ are changed to ***-ac*** conformation, ***-ac*** of $O_{33}C_8C_4C_3$, ***-sp*** of $O_{36}C_{14}N_{13}C_{11}$ and ***–sp*** of $H_{46}O_{12}C_9N_7$ are changed to ***+sc, +sp*** and ***+sc*** conformations respectively to form stable anion (**6**) and rest of positions have moderate changes.

## CONCLUSION

AM1 calculations show that keto-enol tautomerism of methicillin and its protonated forms are nearly non-planar skeleton geometry, and the sequence of proton transfer at nitrogen atom is $N_{13}$> $N_7$. In order to gain insight into the structure of methicillin, it is desirable to perform rigorous theoretical analysis on the different geometries of methicillin and its protonated forms. The utility of theoretical predictions is important for evaluating the biochemical mechanism to prevent cell wall synthesis and binding to plasma protein. This study reveals about the stability of keto-enol tautomerism, conformations and molecular deformations.

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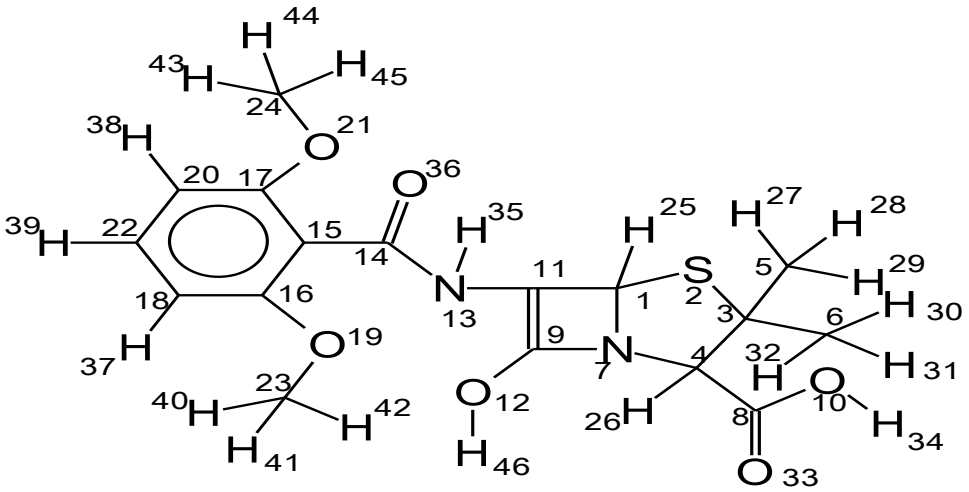



**Figure - 1**

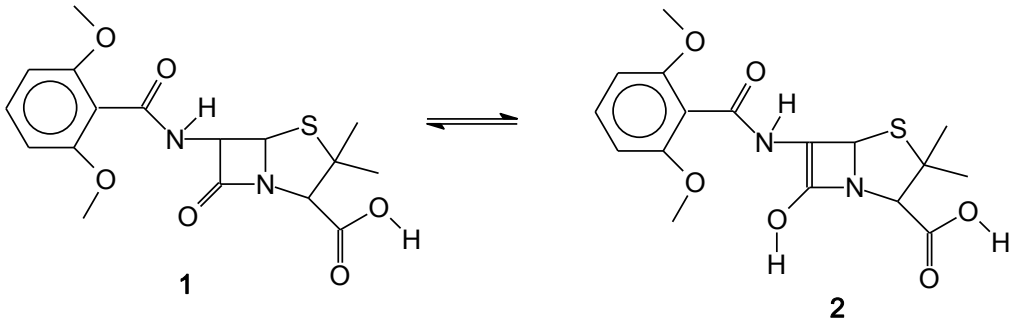
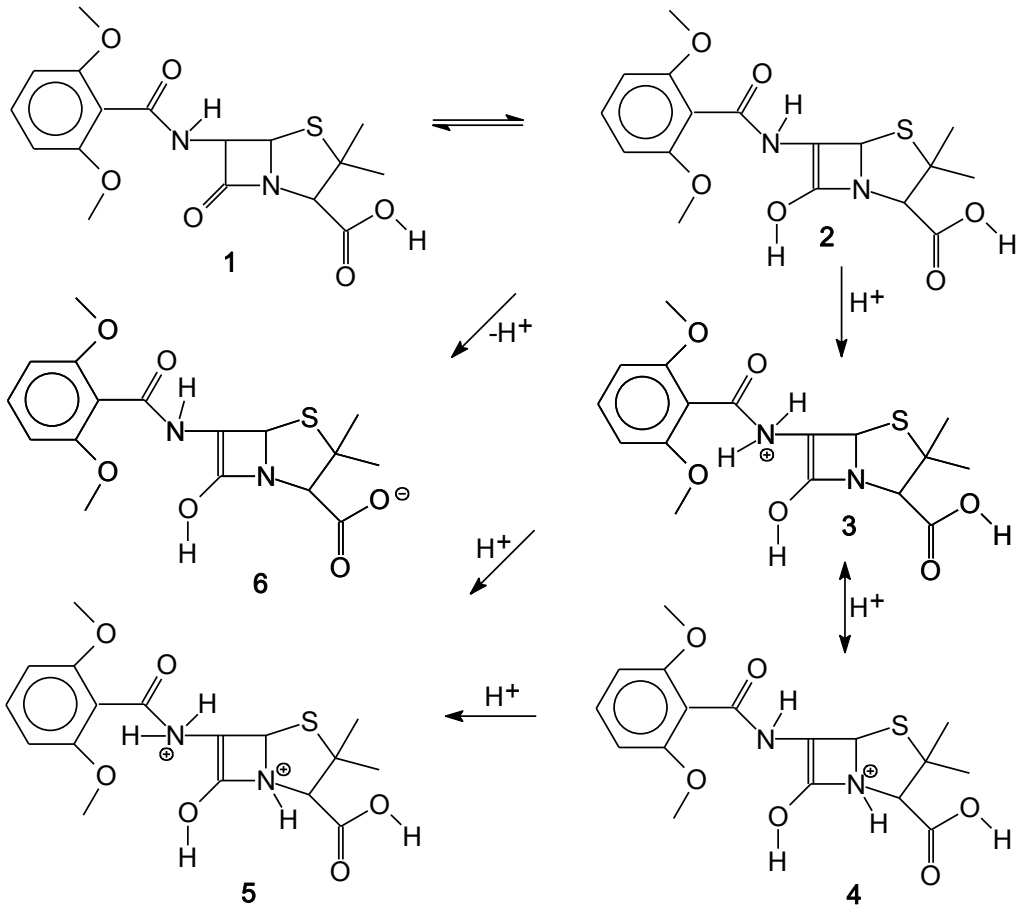


Figure - 2: Methicillin keto- enol rearrangement



Scheme - 1

Table –I : Heat of formation ($\Delta H_f^o$ in kcal/mol), ionization potential (eV), dipole moment (μ in Debye), energies of frontier molecular orbitals (in eV), electron excitation energies (ΔE) (in eV) and the atomic charges on hetero-atoms of methicillin(**1**) and its enol form(**2**), mono-protonated forms (**3** & **4**), di-protonated form (**5**), and anion (**6**) from AM1 calculations.

| Parameters | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|
| $\Delta H_f^o$ (kcal/mol) | -157.5533 | -136.098 | +15.9283 | +13.2664 | +251.9399 | -170.5982 |
| Ionization potential(eV) | 8.910 | 8.002 | 11.860 | 11.642 | 14.628 | 5.108 |
| μ (Debye) | 5.428 | 3.412 | 5.285 | 4.516 | 4.624 | 19.068 |
| $E_{HOMO}$ (eV) | -8.910 | -8.002 | -11.860 | -11.642 | -14.628 | -5.108 |
| $E_{LUMO}$ (eV) | -0.204 | -0.051 | -3.807 | -4.073 | -8.054 | +1.785 |
| Electron excitation energies ($\Delta E= E_{LUMO} - E_{HOMO}$) (eV) | 8.706 | 7.951 | 8.053 | 7.569 | 6.574 | 6.893 |
| $S_2$ (atomic charge) | +0.0544 | +0.0949 | +0.1228 | +0.2465 | +0.2993 | -0.0412 |
| $N_7$ (atomic charge) | -0.2440 | -0.1523 | -0.1569 | -0.0274 | -0.0532 | -0.1555 |
| $N_{13}$ (atomic charge) | -0.3571 | -0.2763 | +0.0172 | -0.2716 | -0.0507 | -0.2360 |
| $O_{10}$ (atomic charge) | -0.2851 | -0.3072 | -0.2798 | -0.5790 | -0.2491 | -0.5850 |
| $O_{12}$ (atomic charge) | -0.2410 | -0.2192 | -0.1951 | -0.1642 | -0.1623 | -0.2534 |
| $O_{19}$ (atomic charge) | -0.2126 | -0.2103 | -0.2662 | -0.2409 | -0.2892 | -0.2290 |
| $O_{21}$ (atomic charge) | -0.1920 | -0.1890 | -0.2101 | -0.2031 | -0.2204 | -0.1900 |
| $O_{33}$ (atomic charge) | -0.3570 | -0.3745 | -0.3871 | -0.3347 | -0.3719 | -0.5355 |
| $O_{36}$ (atomic charge) | -0.3335 | -0.3407 | -0.1563 | -0.3025 | -0.1762 | -0.3779 |

Table –II : Bond lengths of methicillin(**1**) and its enol form (**2**), mono-protonated forms (**3** & **4**), di-protonated form (**5**), and anion (**6**) from AM1 calculations.

| Bond lengths (Å) | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|
| $C_9$-$N_7$ | 1.4480 | 1.4624 | 1.4503 | 1.5195 | 1.5154 | 1.4558 |
| $N_{13}$-$C_{11}$ | 1.4102 | 1.3701 | 1.4109 | 1.3444 | 1.4159 | 1.3764 |
| $C_{14}$-$N_{13}$ | 1.3987 | 1.3912 | 1.5328 | 1.4270 | 1.5751 | 1.3754 |
| $C_{11}$-$C_9$ | 1.5685 | 1.3779 | 1.3857 | 1.3836 | 1.3703 | 1.3847 |
| $O_{10}$-$C_8$ | 1.3585 | 1.3623 | 1.3522 | 1.3515 | 1.3427 | 1.2642 |
| $O_{33}$-$C_8$ | 1.2343 | 1.2347 | 1.2366 | 1.2325 | 1.2344 | 1.2579 |
| $O_{12}$-$C_9$ | 1.2184 | 1.3502 | 1.3300 | 1.3380 | 1.3212 | 1.3380 |
| $O_{36}$-$C_{14}$ | 1.2421 | 1.2431 | 1.2177 | 1.2369 | 1.2147 | 1.2485 |
| $C_{15}$-$C_{14}$ | 1.4881 | 1.4911 | 1.4625 | 1.4739 | 1.4452 | 1.5004 |
| $H_{46}$-$O_{12}$ | - - | 0.9736 | 0.9834 | 0.9793 | 0.9896 | 0.9867 |
| $H_{34}$-$O_{10}$ | 0.9729 | 0.9727 | 0.9761 | 0.9773 | 0.9823 | - - |
| $H_{35}$-$N_{13}$ | 0.9932 | 0.9955 | 1.0282 | 1.0023 | 1.0300 | 0.9945 |
| H-$N_7$ | - - | - - | - - | 1.0181 | 1.0243 | - - |

Table – III Dihedral angle (°) of methicillin (**1**) and its enol form (**2**), mono-protonated forms (**3** & **4**), di-protonated form (**5**), and anion (**6**) from AM1 calculations.

| Dihedral angle (°) | **1** | | **2** | | **3** | | **4** | | **5** | | **6** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Angle | (*) | Angle | (*) | Angle | (*) | Angle | (*) | Angle | (*) | Angle | (*) |
| $C_4C_3S_2C_1$ | -19.69 | *-sp* | -18.08 | *-sp* | -17.73 | *-sp* | -27.62 | *-sp* | -25.06 | *-sp* | -18.71 | *-sp* |
| $C_8C_4C_3S_2$ | +162.71 | *+ap* | +157.71 | *+ap* | +154.76 | *+ap* | +159.74 | *+ap* | +154.59 | *+ap* | +159.91 | *+ap* |
| $O_{10}C_8C_4C_3$ | -167.36 | *-ap* | +68.46 | *+sc* | +68.73 | *+sc* | +48.89 | *+sc* | +69.69 | *+sc* | -102.24 | *-ac* |
| $C_{14}N_{13}C_{11}C_9$ | -124.04 | *-ac* | +144.67 | *+ac* | +106.43 | *+ac* | +159.23 | *+ap* | +110.79 | *+ac* | +121.19 | *+ac* |
| $C_{15}C_{14}N_{13}C_{11}$ | +178.79 | *+ap* | -179.92 | *-ap* | -171.19 | *-ap* | -179.21 | *-ap* | -170.61 | *-ap* | -176.89 | *-ap* |
| $C_{16}C_{15}C_{14}N_{13}$ | -59.83 | *-sc* | -61.95 | *-sc* | -56.77 | *-sc* | -51.19 | *-sc* | -53.32 | *-sc* | -99.64 | *-ac* |
| $O_{33}C_8C_4C_3$ | +18.48 | *-sp* | -113.51 | *-ac* | -112.60 | *-ac* | -135.26 | *-ac* | -111.57 | *-ac* | +76.86 | *+sc* |
| $O_{12}C_9N_7C_4$ | +58.22 | *+sc* | +65.88 | *+sc* | +70.02 | *+sc* | +43.50 | *+sc* | +81.89 | *+sc* | +67.73 | *+sc* |
| $H_{34}O_{10}C_8C_4$ | +179.77 | *+ap* | +179.16 | *+ap* | +178.60 | *+ap* | +177.55 | *+ap* | +178.97 | *+ap* | - - | - - |
| $H_{35}N_{13}C_{11}C_9$ | +45.99 | *+sc* | -39.89 | *-sc* | -16.32 | *-sp* | -24.29 | *-sp* | -11.31 | *-sp* | -15.84 | *-sp* |
| $O_{36}C_{14}N_{13}C_{11}$ | -2.71 | *-sp* | -0.84 | *-sp* | +8.09 | *+sp* | -1.19 | *-sp* | +7.93 | *+sp* | +4.87 | *+sp* |
| $H_{46}O_{12}C_9N_7$ | - - | - - | -2.35 | *-sp* | -12.60 | *-sp* | +76.54 | *+sc* | -43.35 | *-sc* | -25.33 | *-sc* |
| $HN_7C_4C_3$ | - - | - - | - - | - - | - - | - - | -153.35 | *-ap* | -143.79 | *-ac* | - - | - - |
| $HN_{13}C_{11}C_9$ | - - | - - | - - | - - | -133.23 | *-ac* | - - | - - | -128.90 | *-ac* | - - | - - |

* Conformational analyses using prefixes *a* = anti, *s* = syn, *p* = peri-planar, *c* = clinal, and + & - signs [13].

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