Natural Bonding Orbital and Frontier Molecular Orbital study of 2-Aminoethanethiol

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Abstract :   2-Aminoethanethiol is a drug used to treat cystinosis. In the current investigation, the molecular structure of the molecule was modeled using ab initio HF (Hartree-Fock) and DFT (Densiy functional theory) calculations at 6-311+G(d, p) levels. The theoretical vibrational frequencies and parameters like bond lengths and bond angles are calculated and compared with the experimental values. HOMMO-LUMO energies calculated. Stability of the molecule arising from hyperconjugative interactions, charge delocalization have been analyzed using natural bond orbital analysis (NBO). Natural bond orbital (NBO) analysis calculated with DFT/B3LYP/6-311+G(d,p) level shows that charge transfer takes place among the molecule. Besides, molecular electrostatic potential (MESP), HOMO and LUMO analysis, and several other thermodynamic properties were performed at both methods.

Keywords:2-Aminoethanethiol**,**HF; DFT; NBO;

1. Introduction

2-Aminoethanethiol, a stable organic compound containing both an amine and a thiol functional groups is white and water soluble solid. It is commonly used as salts of ammonium derivatives[$HSCH_2CH_2NH_3$] including hydrochloride, phosphocysteamine andbitartrate[1-2].It is used in the treatment of cystinosis [3], a lysosomal storage disease which is characterized by abnormal accumulation of the amino acid cystine. It is a disorder resulting in intracellular crystal formation throughout the body. This drug is usually prescribed to decrease intralysosomalcystine accumulation. [3-4].This drug is a mercaptoethylamine compound and is readily transported into Lysosomes where it reacts with Cystine to form cysteine-cysteamine disulfide and Cysteine has led to its use in cystine depleting agents for the treatment of Cystinosis [5].

2. Experimental: Structure and Spectra

The sample was obtained from M/s. Sigma Aldrich Co., with a stated purity of 99% and was used as such without further purification. The Fourier transform infrared spectra are recorded using Perkin Elmer spectrometer in KBr dispersion in the range of 4000 to 400 cm^{-1}. The FT-Raman spectrum was recorded using the 1054 line of a Nd:YAG laser as excitation wavelength in the region 4000-100 cm^{-1} on a Bruker model IFS 66 V spectrophotometer equipped with an FRA 106 FT-Raman module accessory.

3. Computational Details

In the present work, the density functional theory (DFT/B3LYP) at the 6-311 +G(d,p) higher basis set level was adopted to calculate the properties of the title molecule [6].All the calculations was performed by employing Becke's three parameter hybrid exchange functional with the Lee-Yang –Parr correlation functional [7] to optimize the structure of the molecule and also to calculate the electronic structure of the title molecule. The entire calculations were performed on a Pentium V/ 1.6 GHz personal computer using Gaussian 09W program package [8-9] and applying geometry optimization Initial geometry generated was minimized at the HartreeFock level using 6-311+G (d,p) basis set. The natural bonding orbitals (NBO) calculations were performed using NBO 3.1 program as implemented in the Gaussian 09W package at DFT/B3LYP/6-311 +G(d,p) level[10-12].

4.   Results and Discussion

2-Aminoethanethiol has 11 atoms with 27 degrees of freedom corresponding to the Cartesian coordinates of each atom in the molecule. In a nonlinear rmolecule, 3 of these degrees belong to the rotational, 3 of these degrees belong to translational motions and remaining (3N-6) corresponds to its vibrational motions. Therefore the net number of   modes of vibrations is 27. The molecular structure of the molecule is shown in Fig.1
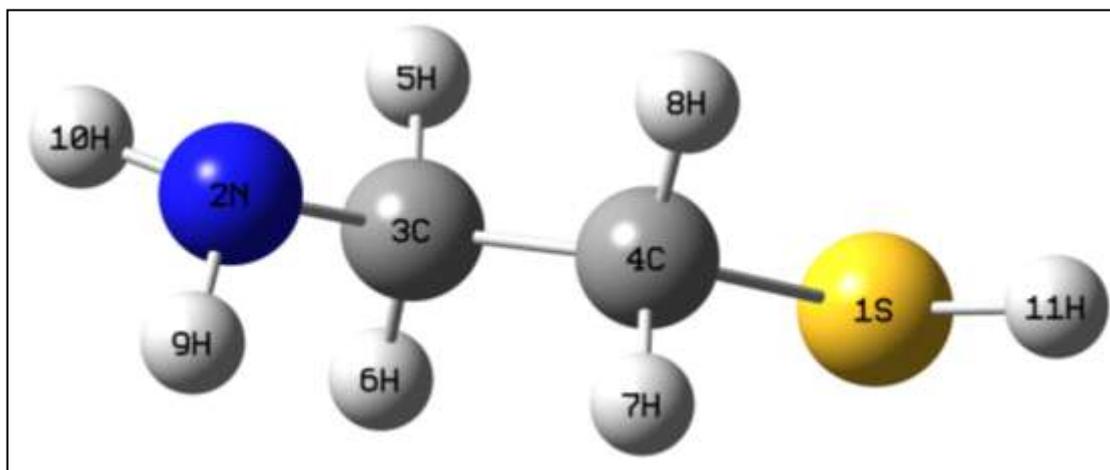
Fig.1 Molecular Structure and atom numbering adopted in the Study

4.1 NBO analysis

The natural bond orbital (NBO) calculation was performed using NBO3.1program implemented in the Gaussian 09 package [12] at the DFT/B3LYP level in order to understand various second-order interactions between the filled or bital of one subsystem and vacant orbital of another subsystem, which is a measure of the delocalization or hyper conjugation. The hyperconjugative interaction energy was deduced from the second-order perturbation approach [13-14.]. Delocalization of electrondensity between occupied Lewis- type(bondor lone pair) NBO orbitals and formally unoccupied (antibondor Rydberg)non-Lewis NBO orbitals corresponds to a stabilizing donor–acceptor interaction. The corresponding results of possible intensive interactions have been tabulated in Table 1. In NBO analysis, the larger $E^{(2)}$ value shows the intensive interaction between electron-donor and electron-acceptors and greater the extent of conjugation of the whole system. The second order perturbation theory analysis of Fock matrix in NBO analysis shows strong intramolecular hyperconjugative interactions of electrons.

NBO analysis provides the most accurate possible 'natural Lewis structure 'picture of ø, because all orbital details are mathematically chosen to include the highest possible percentage of the electron density. A useful aspect of NBO method is that it gives information about interactions in both filled and virtual or bital spaces that could enhance the analysis of intra-

and intermolecular interactions.

The second order Fock matrix was carried out to evaluate the donor–accept or interactions in the NBO analysis[14]. The interactions result is a loss of occupancy from the localized NBO of the idealized Lewis structure into an emptyn on-Lewis orbital. Foreach donor(i) and acceptor(j), the stabilization energy $E^{(2)}$ associated with the delocalization ij is estimated

$$E^{(2)} \longrightarrow = \Delta E_y = q_i \frac{F^2_{(ij)}}{\varepsilon_j - \varepsilon_i}$$

whereq$_i$ is the donororbitaloccupancy,are e$_i$ and e$_j$ diagonal elementsand F(i,j) is the off diagonal NBO Fockmatrix element.

Table 1. NBO results showing the formation of Lewis and non-Lewis orbitals for 2-Aminoethanethiol

Bond (A-B)	Type	ED/energy(a.u.)	ED$_A$ (%)	ED$_B$ (%)	NBO	S (%)	p (%)
S1-C4	σ	1.98633 0.58499	48.33	51.67	0.6952(sp$^{5.32}$)S+ 0.7188(sp$^{3.79}$)C	15.73 20.86	83.76 78.98
S 1 - H 11	σ	1.99023 0.54340	56.23	43.77	0.7499(sp$^{6.30}$)S+ 0.6616(sp$^{0.00}$)H	13.62 99.68	85.85 0.32
N 2 - C 3	σ	1.99085 0.72761	59.10	40.90	0.7687(sp$^{2.08}$)N 0.6395(sp$^{2.98}$)C	32.40 25.09	67.54 25.09
N 2 - H 9	σ	1.99076 0.62328	67.69	32.31	0.8227(sp$^{3.14}$)N 0.5685(sp$^{0.00}$)H	24.12 99.94	75.80 0.06
C 3 - C 4	σ	1.98874 0.63247	49.29	50.71	0.7020 (sp$^{2.48}$)C 0.7121 (sp$^{2.34}$)C	28.70 29.96	71.25 70.00
C3 – H5	σ	1.98033 0.50491	59.82	40.18	0.7735 (sp$^{3.38}$)C 0.6338 (sp$^{0.00}$)C	22.83 99.96	77.10 0.04
C3 – C4	σ *	0.01778 0.37115	50.71	49.29	0.7121 (sp$^{2.48}$)C -0.7020(sp$^{2.34}$)C	28.70 29.96	71.25 70.00
C4 – H8	σ *	0.02084 0.39428	38.93	61.07	0.6239 (sp$^{3.02}$)C -0.7815(sp$^{0.00}$)H	24.89 99.96	75.05 0.04
S1 – H11	σ *	0.00489 0.17825	43.77	56.23	0.6616 (sp$^{6.30}$)S -0.7499(sp$^{0.00}$)H	13.32 99.68	85.85 0.32
N2 – C3	σ *	0.01001 0.34395	4.090	59.10	0.6395 (sp$^{2.08}$)N -0.7687(sp$^{2.98}$)C	32.40 25.09	67.54 74.79
S1	LP	1.99301 0.63501	-	-	Sp$^{0.41}$	70.87	29.12
N2	LP	1.95737 0.31793	-	-	Sp$^{4.18}$	19.29	80.66

Table 2.Second order perturbation theory of Fock matrix in NBO basis for 2-Aminoethanethiol

Donor	Type	ED/e	Acceptor	Type	ED/e	E(2) kcal/mol	E(j)-E(i) a.u.	F(i,j) a.u.
S1 - C 4	σ	1.98633	N2 - C 3	σ*	0.01001	3.05	0.93	0.048
S1–H 11	σ	1.99023	C 3 - C 4	σ*	0.01778	1.36	0.91	0.031
N2- C 3	σ	1.99085	S 1- C4	σ*	0.01322	2.41	0.87	0.041
N2 - H 9	σ	1.99076	C3 - H5	σ*	0.01716	1.99	1.01	0.040
N2-H 10	σ	1.98902	C3 - C4	σ*	0.01778	2.21	0.99	0.042
C3-C4	σ	1.98874	N2-H10	σ*	0.00540	1.79	1.06	0.039
C3-H5	σ	1.98033	N2-H9	σ*	0.00808	3.08	0.93	0.048
C3-H5	σ	1.98033	C4-H7	σ*	0.02299	2.72	0.89	0.044

C3-H6	σ	1.98758	C4-H8	σ*	0.02084	2.49	0.90	0.042
S 1	LP (1)	1.99301	C4 - H 8	σ*	0.02084	0.50	1.03	0.020
S 1	LP (2)	1.97238	C4 - H 7	π*	0.02299	4.12	0.63	0.046
S 1	LP (2)	1.97238	C 4-H8	π*	0.02084	3.39	0.64	0.042
N 2	LP (1)	1.95737	S 1 – C4	σ*	0.01322	0.85	0.46	0.018
N 2	LP (1)	1.95737	C3-C4	σ*	0.01778	1.73	0.69	0.031
N 2	LP (1)	1.95737	C3-H5	σ*	0.01716	0.63	0.70	0.019
N 2	LP (1)	1.95737	C3-H6	σ*	0.03243	7.20	0.69	0.063

[a] E(2) means energy of hyperconjugative interaction (stabilization energy).
[b] Energy difference between donor and acceptor i and j NBO orbitals
[c] F(i, k) is the Fock matrix element between i and j NBO orbitals.

A strong interaction exists from lone pair interaction and also between bonding and anti-bonding (σ→ σ*) electron with greater energy contributions. The intramolecular interaction are formed by the orbital overlap between σ(C-H)σ(S-H)σ(N-H)σ(N-C)σ*(C-H)σ*(S-H)σ*(N-H)σ*(C-C)σ*(N-C) bond orbital that results in intramolecular charge transfer (ICT) causing stabilization of the system. These interactions are observed as increase in electron density (ED) in C-H anti-bonding orbital that weakens the respective bonds.The electron density of C-H (≈ 1.97 e) clearly shows strong delocalization.

The strong intramolecular hyper conjugation of σ electrons of C-H,S-H,N-C,N-H to the anti-bonding C-H,N-H,S-H,C-C bond lead to stabilization of the compound and it is shown in Table 2. The intramolecular hyperconjugative interaction of S1 and C4 is σ (S1-C4) with anti-bonding orbital of σ*(N2 - C 3)   leads to strong delocalization of 3.05 kcal/mol   .

There occurs a strong intramolecular hyperconjugative interaction from LP N1 σ* (C3-H6) andLP S1 σ* (C4-H8) which increases ED from 1.957 to 1.993 that weakens the respective bonds leading to stabilization of 7.20 and 0.50 kcal/mol respectively. [15-16].

4.2 Molecule Electrostatic Potential

The molecule electrostatic potential (MEP) at a given point p(x,y,z) acting on the molecule is the force acting on a proton located at p through electric charge cloud generated through the molecules electrons and nuclei. The electrostatic potential of a molecule helps to assess the molecules reactivity towards positively or negatively charged reactants. In order to calculate the MEP of thismolecule, the optimized geometry at DFT/B3LYP/6-311 +G(d,p) level is mapped with electron density and MEP on the molecular surface using a color coding scheme. Visualization of the MEP represented by different colors, gives details on attractive potential which appears in red and regions of negative potential that appears in blue. The maximum negative region represents the site for electrophilic attackindicated by red colors while the maximum positive region represents nucleophilic attack. [16]. The MEP of the compound at B3LYP/6-311+G(d,p) basis set is shown in Fig 2.
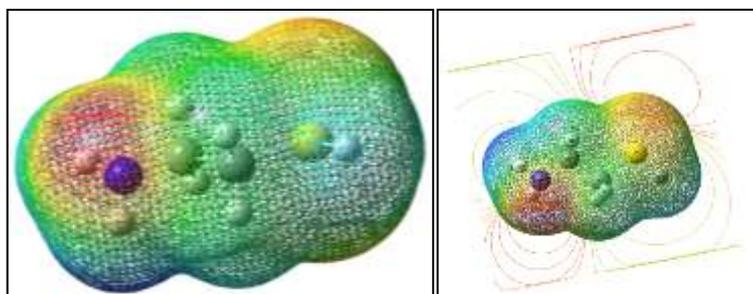
Fig.2: MEP of 2-Aminoethanethiol

Molecular Transport Properties

The most important orbitals in the molecule are frontier orbitals. HOMO and LUMO are types of molecular orbitalswhere HOMO stands for highest occupied molecular orbital and LUMO stands for lowest unoccupied molecular orbital.The energy difference between the HOMO and LUMO is termed the HOMO–LUMOgap. The difference in energy between these two frontier orbitals can be used to predict the strength and stability of the molecule. The electrons from HOMO are donated and are available for bonding. They are characteristic for nucleophilic component while LUMO is the lowest energy orbital that receives electrons. They are characteristic for electrophilic component.The contour map of electrostatic potential of the molecule has been constructed by the DFT method and is shown in Fig.2 also confirms the different negative and positive potential sides of the molecule in accordance with the total electron density surface [17].

The quantum bonding features of the molecule depicted by a plot of HOMO-LUMO gives information on other parameters like Chemical Hardness (η), Softness (S), Chemical Potential (μ), Electronegativity (χ) and Electrophilicity (ω) and they are defined as follows:

Chemical softness $S = 1/2\eta$
Chemical Hardness$\eta = I-A/2$
Chemical Potential$\mu = -(I+A)/2$,
Electronegativity$\chi = (I+A)/2$,
Electrophilicity$\omega = \mu^2/2\eta$.Where I and A are ionization potential and electron affinity;
$I = -E_{HOMO}$ and $A = -E_{LUMO}$
Using the above equations, the parameters are calculated and tabulated in Table.3.

Table.3   Molecular properties of 2-Aminoethanethiol

Molecular properties	DFT/B3LYP/6-311 +G(d,p)	Molecular properties	B3LYP/6-311 +G(d,p)
E_{HOMO} (eV)	-6.5519	Chemical Hardness (η)	3.1385
E_{LUMO} (eV)	-0.2819	Softness (S)	0.3186
$E_{HOMO\ -LUMO}$(eV)	6.27	Chemical Potential (μ)	-3.4169
IonisationPotential (I)	6.5519	Electronegativity (χ)	3.4169
Electron affinity (A)	0.2819	Electrophilicity (ω)	5.8376

LUMO PLOT
First Excited state

$E_{LUMO} = 0.2819$ eV

$\Delta E = 6.27$ eV

$E_{HOMO} = 6.5519$ eV

HOMO PLOT
Ground state
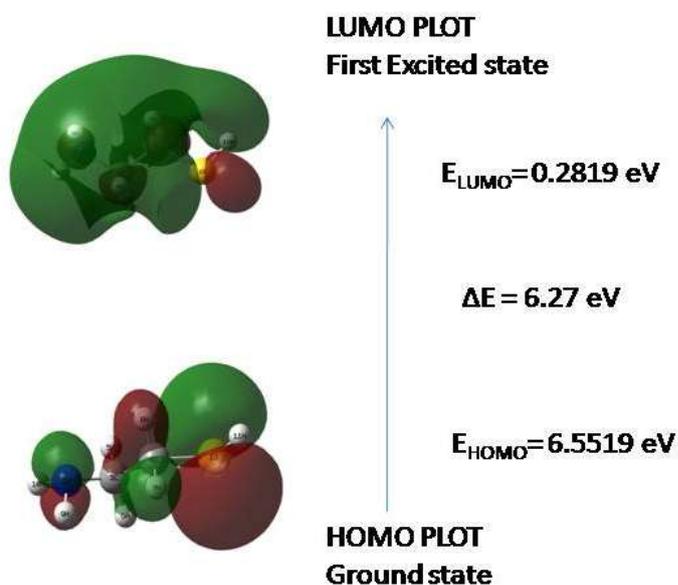
Fig.2. HOMO-LUMO composition of frontier molecular orbital of2-Aminoethanethiol

5. Conclusions

The optimized molecular structure, thermodynamic and electronic properties calculated by DFT method using B3LYP/6-311 +G(d,p)basis set. The optimized geometric parameters (bond lengths and bond angles) of **2-Aminoethanethiol** are theoretically determined by DFT theory and compared with experimental data. The NBO analysis indicates the intermolecular charge transfer between the bonding and antibonding orbital of σ(C-H)σ(S-H)σ(N-H)σ(N-C)σ*(C-H)σ*(S-H)σ*(N-H)σ*(C-C)σ*(N-C) bond orbital that results in intramolecular charge transfer (ICT) causing stabilization of the system.The lowering of the HOMO-LUMO energy gap value has substantial influence on the intermolecular charge transfer and bioactivity of the molecule. The MEP map shows the negative potential sites are on Nitrogen and Sulphur atoms as well as the positive potential sites around the hydrogen atoms.

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