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Density Functional Theory Studies On Molecular Structure And Electronic Properties Of sulfanilamide, Sulfathiazole, E7070 And Furosemide Molecules

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Abstract: *The complete computational study of the Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4** was performed by DFT method with the B3LYP functional and 6-31G (d,p) basis set using Gaussian 09 program. The optimized molecular structure and their parameters such as bond lengths, bond angles and dihedral angles are computed by DFT method. The molecular electrostatic potential mapped onto total density surface has been interpreted.The frontier molecular orbitals analysis shows that the lower energy gap of the molecule, gives the charge transfer process in the molecular system. The global reactivity descriptors that could help to understand the chemical reactivity of the compounds are also predicted. The computation of the Mulliken atomic charges allows schematizing a Mulliken's plot and interpreted it.The change in electron density (ED) in the σ *and π* anti-bonding orbital's and stabilization energies E(2) have been calculated by Natural Bond Orbital (NBO) analysis to give clear evidence of stabilization originating in the hyperconjugation of hydrogen-bonded interaction. First hyperpolarizability value has been calculated to describe the nonlinear optical (NLO) property of the compounds **1-4** and results,show thatare might be not used as non-linear optical (NLO) material.*

Keywords: *sulfamide; density functional theory; computational chemistry; quantum chemical calculations.*

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I. Introduction

Sulfonamides represent classes of synthetic antibiotic drugs that are widely used in human and veterinary medicine [1,2]. Furthermore the Sulfonamide compounds were discovered in 1935 [3], and nowadays are extensively used for the treatment of infections in human [4], aquaculture, livestock production [5], catalysis [6], and organic syntheses [7].

Density Functional Theory (DFT) provides a considerable theoretical framework for deriving quantum chemistry properties [8,9]. Within DFT, the electron density contains information about the molecular properties and takes a fundamental role in calculating chemical reactivity properties. B3LYP is one of the most commonly used exchange-correlation energy functional, in which Becke three parameter hybrid functional combined [10] with the Lee-Yang-Parr correlation functional [11].

The present paper gives a complete description of the molecular geometry, MEP, electronic transitions, global reactivity descriptors, Mulliken atomic charges, intramolecular interactions, and NLO features of the Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4** illustrated in literature[12] using DFT/B3LYP method with 6-31G (d,p) basis set.

II. Materials And Methods

All the quantum chemical calculations of the studied compounds were performed by applying DFT method with the B3LYP functional and 6-31G (d,p) basis set using Gaussian 09 software [13].

III. Results And Discussion

3.1. Molecular Geometry:

The molecular structures of the compounds **1-4** with atom numbering scheme adopted in the computations by DFT/B3LYP method with 6-31G (d,p) basis set is shown in Figure 1. The optimized structural parameters such as bond lengths, bond angles and dihedral angles of Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4** are listed in Tables 1-4.

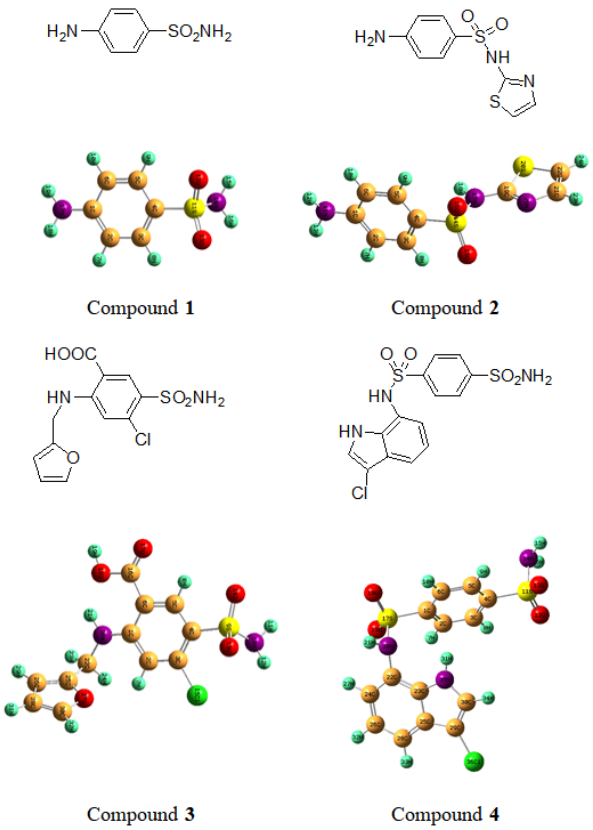

Figure 1. Optimized molecular structure of Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4**

Table 1. Optimized geometric parameters of compound **1**

Bond Length(Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.409	A(2,1,17)	120.612	D(2,3,4,11)	179.896
R(1,17)	1.385	A(1,2,3)	120.636	D(4,5,6,10)	179.783
R(2,7)	1.087	A(2,3,4)	119.800	D(6,1,2,7)	179.363
R(3,4)	1.397	A(2,3,8)	120.460	D(1,2,3,8)	178.637
R(4,5)	1.397	A(3,4,11)	119.807	D(3,4,5,9)	178.216
R(4,11)	1.779	A(4,11,12)	107.833	D(17,1,2,3)	177.633
R(5,6)	1.388	A(4,11,14)	104.471	D(2,1,17,19)	160.071
R(6,10)	1.087	A(12,11,13)	122.246	D(5,4,11,13)	156.570
R(11,12)	1.468	A(12,11,14)	106.564	D(12,11,14,16)	126.238
R(11,13)	1.468	A(13,11,14)	106.555	D(4,11,14,15)	119.683
R(11,14)	1.703	A(11,14,15)	108.543	D(3,4,11,14)	90.279
R(14,15)	1.017	A(15,14,16)	110.846	D(5,4,11,12)	22.757
R(14,16)	1.017	A(1,17,18)	116.588	D(2,1,17,18)	22.002
R(17,18)	1.010	A(1,17,19)	116.588	D(12,11,14,15)	5.683
R(17,19)	1.010	A(18,17,19)	113.241	D(17,1,6,10)	2.672

Table 2. Optimized geometric parameters of compound **2**

Bond Length(Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.411	A(3,4,5)	120.614	D(19,20,22,24)	180.000
R(1,11)	1.380	A(3,4,14)	119.682	D(17,19,20,22)	179.994
R(4,14)	1.780	A(1,11,12)	117.218	D(14,17,19,20)	179.960
R(5,9)	1.085	A(12,11,13)	113.844	D(4,5,6,10)	179.907
R(11,12)	1.009	A(4,14,16)	109.222	D(6,1,2,7)	179.322
R(14,15)	1.461	A(4,14,17)	97.546	D(2,3,4,14)	179.218
R(14,16)	1.461	A(15,14,16)	121.049	D(1,2,3,8)	178.586
R(14,17)	1.731	A(16,14,17)	108.618	D(3,4,5,9)	177.999
R(17,18)	1.010	A(14,17,19)	123.998	D(11,1,2,3)	177.777
R(17,19)	1.380	A(18,17,19)	120.340	D(2,1,11,12)	161.450
R(19,20)	1.775	A(17,19,20)	120.056	D(5,4,14,15)	156.356
R(19,25)	1.296	A(17,19,25)	124.713	D(15,14,17,18)	113.172
R(20,22)	1.750	A(20,19,25)	115.232	D(3,4,14,17)	90.872
R(21,22)	1.359	A(22,21,23)	124.492	D(16,14,17,19)	66.735
R(21,23)	1.084	A(22,21,25)	116.870	D(5,4,14,16)	21.929

Table 3. Optimized geometric parameters of compound **3**

Bond Length(Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.418	A(4,3,15)	121.630	D(26,28,30,32)	179.998
R(1,20)	1.363	A(4,9,10)	103.460	D(29,26,28,30)	179.936
R(3,15)	1.751	A(4,9,13)	108.821	D(31,28,30,27)	179.778
R(4,9)	1.792	A(4,9,14)	106.693	D(6,16,18,19)	179.617
R(6,16)	1.480	A(10,9,13)	108.455	D(3,4,5,8)	179.598
R(9,10)	1.693	A(13,9,14)	121.495	D(8,5,6,1)	179.549
R(9,13)	1.464	A(11,10,12)	111.922	D(22,25,27,30)	179.110
R(9,14)	1.466	A(6,16,17)	125.233	D(20,1,2,3)	177.852
R(10,11)	1.017	A(6,16,18)	114.776	D(6,1,20,22)	177.586
R(16,17)	1.214	A(17,16,18)	119.991	D(2,3,4,9)	177.355
R(16,18)	1.372	A(16,18,19)	105.359	D(6,1,2,7)	176.414
R(18,19)	0.972	A(1,20,21)	116.178	D(3,4,9,14)	174.422
R(20,21)	1.009	A(1,20,22)	126.482	D(2,1,20,21)	173.799
R(20,22)	1.460	A(20,22,25)	115.608	D(23,22,25,27)	163.662
R(25,27)	1.370	A(25,27,30)	107.203	D(21,20,22,24)	145.887

Table 4. Optimized geometric parameters of compound **4**

Bond Length(Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.394	A(2,1,6)	121.900	D(29,30,35,31)	179.912
R(11,12)	1.465	A(3,4,5)	121.835	D(22,24,26,32)	179.895
R(11,13)	1.465	A(3,4,11)	119.163	D(32,26,28,25)	179.867
R(11,14)	1.690	A(4,11,14)	103.275	D(34,30,35,23)	179.680
R(14,15)	1.017	A(12,11,13)	122.656	D(22,23,35,30)	179.620
R(17,18)	1.466	A(13,11,14)	106.855	D(2,3,4,11)	179.537
R(17,19)	1.464	A(11,14,16)	110.042	D(29,25,28,26)	179.471
R(17,20)	1.713	A(15,14,16)	111.816	D(35,23,25,28)	179.399
R(20,21)	1.019	A(18,17,19)	121.715	D(7,2,3,4)	179.370
R(20,22)	1.438	A(17,20,21)	105.931	D(17,1,6,5)	179.120
R(23,35)	1.374	A(17,20,22)	119.574	D(27,24,26,28)	178.787
R(25,29)	1.434	A(22,23,25)	121.729	D(20,22,23,25)	178.773
R(29,30)	1.370	A(23,35,30)	109.381	D(5,4,11,12)	160.841
R(29,36)	1.737	A(23,35,31)	124.524	D(1,17,20,21)	142.588
R(31,35)	1.007	A(30,35,31)	126.094	D(17,20,22,23)	107.817

3.2. Molecular Electrostatic Potential (MEP):

Molecular electrostatic potential (MEP) is related to the electronic density and is a very useful descriptor in understanding sites for electrophilic attack and nucleophilic reactions as well as hydrogen bonding interactions [14-16]. To predict reactive sites for electrophilic attack for the title compounds, MEP was calculated at the B3LYP/6-31G (d,p) optimized geometries. The negative (red) regions of MEP were related to electrophilic reactivity and the positive (blue) ones to nucleophilic reactivity shown in Figure 2.

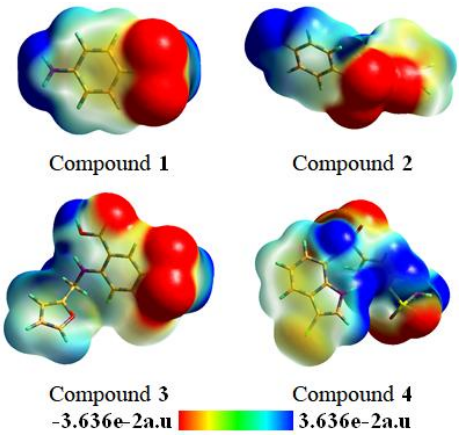

Figure 2. Molecular electrostatic potential surface of Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4**

In all molecules, the regions exhibiting the negative electrostatic potential are localized on sulfamide function, also on thiazole for compound **2** and on carbonyl of acid function for compound **3**; while the regions presenting the positive potential are localized vicinity of the hydrogen atoms.

3.3. Basin Analysis:

The concept of basin was first introduced by Bader in his atom in molecular (AIM) theory, after that, this concept was transplant to the analysis of ELF by Savin and Silvi. In fact, basin can be defined for any real

space function, such as molecular orbital, electron density difference, electrostatic potential and even Fukui function.

A real space function in general has one or more maxima, which are referred to as attractors or (3,-3) critical points. Each basin is a subspace of the whole space, and uniquely contains an attractor. The basins are separated with each other by interbasin surfaces (IBS), which are essentially the zero-flux surface of the real space functions; mathematically, such surfaces consist of all of the points **r** satisfying $\nabla f(\mathrm{r}).\mathrm{n}(\mathrm{r}) = 0$, where n(r) stands for the unit normal vector of the surface at position r.

Interbasin surfaces (IBS) dissect the whole molecular space into individual basins, each IBS actually is a bunch of gradient paths derived from a (3,-1) critical points (CP). The interbasin surfaces of compounds **1-4** generated by (3,-1) critical points are illustrated below.

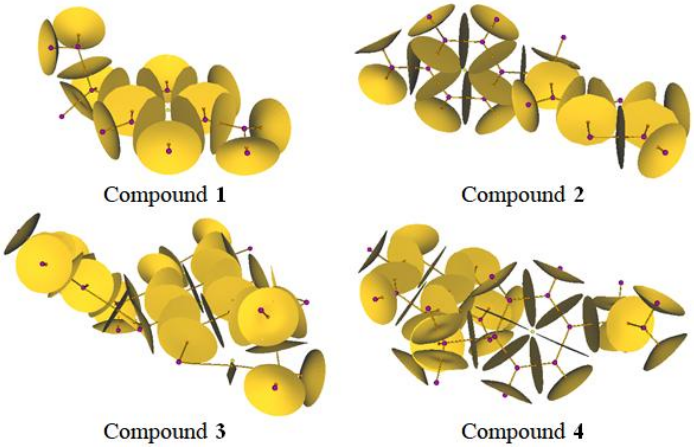

Figure 3. Plots of the interbasin surfaces of compounds **1-4**

The number of interbasin surfaces is 19, 26, 38 and 38 for compounds **1-4** respectively.

3.4. Frontier Molecular Orbitals (FMOs):

Molecular orbital and their properties such as energy are very useful for physicists and chemists. This is also used by the frontier electron density for predicting the most reactive position in π-electron systems and also explains several types of reactions in conjugated system [17]. The eigen values of LUMO and HOMO and their energy gap reflect the chemical activity of the molecule [18]. Recently the energy gap between highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) has been used to prove the bio activity from intramolecular charge transfer (ICT) [19,20]. Figure 4illustrate the distributions and energy levels of the HOMO-1, HOMO, LUMO and LUMO+1orbitals computed at the B3LYP/6-31G (d,p)level for the compound **4** which is the most reactive.

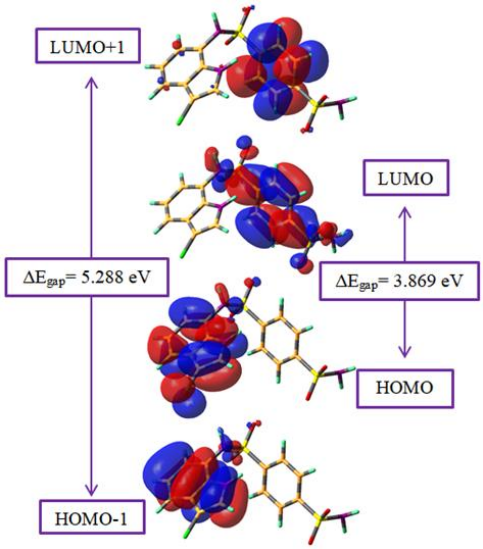

Figure 4.HOMO-LUMO Structure with the energy level diagram of compound **4**

HOMO-1 and HOMO are confined over the indole ring, while LUMO and LUMO+1 are on benzene ring for compound **4** which gives charge transfer process in the molecular system.

3.5. Global Reactivity Descriptors:

Energies of HOMO and LUMO are popular quantum mechanical descriptors. It has been shown [21] that these orbital's play a major role in governing many chemical reactions, and are also responsible for charge transfer complexes [22]. The energy of the HOMO is directly related to the ionization potential and characterizes the susceptibility of the molecule towards attack of electrophiles.The concept of hard and soft nucleophiles and electrophiles has been also directly related to the relative energies of the HOMO and LUMO orbital's. Hard nucleophiles have alow energy HOMO, soft nucleophiles have a high energy HOMO, hard electrophiles have a high energy LUMO and soft electrophileshave a low energy LUMO [23]. The energy of LUMO is directly related to the electron affinity and characterizes the susceptibility of the molecule towards attack of nucleophiles.Frontier orbital densities can strictly be used to describe the reactivity of different atoms in the same molecule [22,24]. The electronegativity and hardness are of course used extensively to make predictions about chemical behavior. The quantum chemical descriptors such as; E_{HOMO}, E_{LUMO}, ΔE_{gap}, the ionization potential (I), the electron affinity (A), the absolute electronegativity (χ), the absolute hardness (η) and softness (S) for the Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4**have been calculated at B3LYP/6-31G (d,p) basis set and the result are given in Table 5.

Table 5. Quantum chemical descriptors of Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4**

Parameters	Compound 1	Compound 2	Compound 3	Compound 4
E_{HOMO}(eV)	-5.983	-5.795	-6.071	-5.864
E_{LUMO}(eV)	-0.471	-0.888	-1.610	-1.995
ΔE_{gap} (eV)	5.512	4.907	4.461	3.869
I (eV)	5.983	5.795	6.071	5.864
A (eV)	0.471	0.888	1.610	1.995
μ (eV)	-3.227	-3.342	-3.840	-3.930
χ (eV)	3.227	3.342	3.840	3.930
η (eV)	2.756	2.453	2.231	1.934
S (eV)	0.181	0.204	0.224	0.258
ω (eV)	1.889	2.276	3.306	3.992

The compound which has the lowest energy gap is the compound **4** (ΔE_{gap} = 3.869 eV). This lower gap allows it to be the softest molecule. The compound that has the highest energy gap is the compound **1** (ΔE_{gap} = 5.512 eV). The compound that has the highest HOMO energy is the compound **2** (E_{HOMO} = -5.795 eV). This higher energy allows it to be the best electron donor. The compound that has the lowest LUMO energy is the compound **4** (E_{LUMO} = -1.995 eV) which signifies that it can be the best electron acceptor. The two properties like *I* (potential ionization) and *A* (affinity) are so important, the determination of these two properties allows us to calculate the absolute electronegativity (χ) and the absolute hardness (η). These two parameters are related to the one-electron orbital energies of the HOMO and LUMO respectively. Compound **2** has the lowest value of the potential ionization (*I* = 5.795 eV), so that will be the better electron donor. Compound **4** has the largest value of the affinity (*A* = 1.995 eV), so it is the better electron acceptor. The chemical reactivity varies with the structure of molecules. Chemical hardness (softness) value of compound **4** (η = 1.934 eV, **S** = 0.258 eV) is lesser (greater) among all the molecules. Thus, compound **4** is found to be more reactive than all the compounds. Compound **4** possesses higher electronegativity value (χ = 3.930 eV) than all compounds so; it is the best electron acceptor. The value of ω for compound **4** (ω = 3.992 eV) indicates that it is the stronger electrophiles than all compounds. Compound **4** has the smaller frontier orbital gap so, it is more polarizable and is associated with a high chemical reactivity, low kinetic stability and is also termed as soft molecule.

3.6. Mulliken analysis:

Mulliken charge is directly associated with the vibrational properties of the molecule, and quantifies how the electronic structure changes under atomic displacement; it is, therefore, connected on to the chemical bonds present in the molecule. Mulliken atomic charge calculation plays an important role in the application of quantum chemical calculation to molecular systems [25]. The parameters like dipole moment, polarizability, reactivity depend on the atomic charges of the molecular systems. The Mulliken atomic charges of compound **4** which is the most reactive are calculated by DFT/B3LYP method and 6-31G (d,p) basis set and detailed in a Mulliken's plot as visualized in Figure 5.

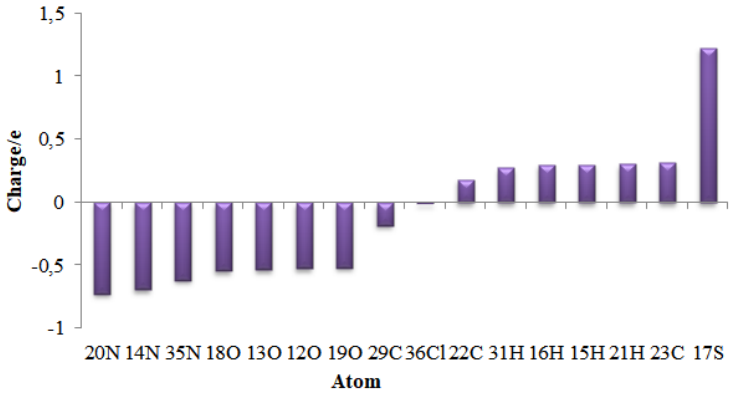

Figure 5. Mulliken's plot of compound **4**

The atom 20N shows more negative (-0.727235e) charge and 17S more positive (1.228342e) charge, which suggests extensive charge delocalization in the entire molecule. The charge noticed on the 14N and 35N is smaller and equal to -0.693207e and -0.619502e respectively. This can be explained by the high degree of conjugation, with a strong push-pull effect on the whole molecule. Negatively chargedoxygen (18O, 13O, 12O and 19O) atoms shows that charge is transferred from sulfur to oxygen. Carbon atom 29C is more negatively charged which is due to thedirect attachment ofthe chlorine atom.The negativecharge of 36Cl is equal to -0.001257e, which explain that, is due to the electronegativity and attractive force of halogen atom and the strong conjugation throughout the molecule.The maximum atomic charge of carbons is obtained for 22C and 23C. This is due to the attachment of negatively charged atoms (20N and 35N) respectively.The positive charges are localized on the hydrogen atoms.Very similar values of positive charges are observed for the hydrogen atoms (31H, 16H, 15H and 21H (0.273878, 0.299221, 0.300352 and 0.305337e) respectively) bonded to the negative atoms (35N, 14N, 14N and 20N) respectively.

3.7. Natural Bond Orbital Analysis (NBO):

Natural bond orbital (NBO) analysis provides an efficientmethod for studying intra and intermolecular bonding and interaction among bonds and also provides a convenient basis for investigating charge transfer or conjugative interaction in molecularsystems [26]. It is also provides orbital picture that is as closeand possible to classical Lewis structure for a molecule. NBO theoryalso allows the assignment of the hybridization of atomic lonepairs and of the atoms involved in bond orbitals. Some electrondonor orbital, acceptor orbital and the interacting stabilizationenergy resulted from the second-order micro-disturbance theoryare reported [27,28]. The second-order Fock matrix is carried outto evaluate the donor-acceptor interactions in NBO analysis [29]. The stabilization energy E (2) values of the Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4** were calculated on the basis of second-order Fock matrix perturbation theory using DFT/B3LYP method with 6-31G (d,p) basis set. The larger E (2) values were listed in Tables 6-9.

Table 6. Second order perturbation theory analysis of Fock matrix on NBO of compound **1**

Donor(i)	ED/e	Acceptor(j)	ED/e	E(2) Kcal/mol	E(j)-E(i) a.u	F(i.j) a.u
LP (1) N17	1.82141	π*(C1-C6)	0.40571	31.14	0.32	0.094
π (C1-C6)	1.60864	π*(C4-C5)	0.41739	28.79	0.27	0.080
π (C4-C5)	1.69083	π*(C2-C3)	0.31173	24.01	0.29	0.075
π (C2-C3)	1.70721	π*(C1-C6)	0.40571	22.91	0.28	0.073
LP (3) O12	1.78132	σ*(S11-O13)	0.15690	21.45	0.57	0.100
LP (3) O13	1.78133	σ*(S11-O12)	0.15692	21.45	0.57	0.100
LP (2) O12	1.82251	σ*(C4-S11)	0.19272	15.50	0.46	0.076
LP (2) O13	1.82251	σ*(C4-S11)	0.19272	15.50	0.46	0.076
π (C1-C6	1.60864	π*(C2-C3)	0.31173	14.95	0.28	0.059
π (C2-C3)	1.70721	π*(C4-C5)	0.41739	14.83	0.27	0.059
π (C4-C5)	1.69083	π*(C1-C6)	0.40571	14.23	0.28	0.058
LP (2) O12	1.82251	σ*(S11-N14)	0.24694	13.75	0.41	0.068
LP (2) O13	1.82251	σ*(S11-N14)	0.24694	13.75	0.41	0.068
LP (3) O12	1.78132	σ*(S11-N14)	0.24694	11.50	0.40	0.061
LP (3) O13	1.78133	σ*(S11-N14)	0.24694	11.49	0.40	0.061
π (C4-C5)	1.69083	σ*(S11-N14)	0.24694	5.47	0.39	0.042
σ (C3-C4)	1.97658	σ*(C4-C5)	0.02398	4.39	1.27	0.067
σ (C4-C5)	1.97658	σ*(C3-C4)	0.02398	4.39	1.27	0.067
σ (N17-H18)	1.98872	σ*(C1-C6)	0.02278	4.10	1.20	0.063
σ (N17-H19)	1.98872	σ*(C1-C2)	0.02278	4.10	1.20	0.063

Table 7. Second order perturbation theory analysis of Fock matrix on NBO of compound **2**

Donor(i)	ED/e	Acceptor(j)	ED/e	E(2) Kcal/mol	E(j)-E(i) a.u	F(i.j) a.u
LP (1) N17	1.78606	π*(C19-N25)	0.38696	42.46	0.29	0.103
LP (1) N11	1.80977	π*(C1-C2)	0.40578	33.25	0.31	0.096
LP (3) O15	1.77964	σ*(S14-N17)	0.31454	31.30	0.37	0.099
LP (3) O16	1.77964	σ*(S14-N17)	0.31454	31.29	0.37	0.099
π (C1-C2)	1.59963	π*(C3-C4)	0.42818	30.20	0.27	0.081
LP (2) S20	1.69384	π*(C19-N25)	0.38696	25.95	0.26	0.074
π (C3-C4)	1.69941	π*(C5-C6)	0.30467	23.98	0.29	0.075
π (C5-C6)	1.70797	π*(C1-C2)	0.40578	22.95	0.28	0.073
π (C19-N25)	1.88092	π*(C21-C22)	0.25417	19.86	0.34	0.076
LP (1) N25	1.87248	σ*(C19-S20)	0.09087	18.22	0.52	0.087
LP (2) S20	1.69384	π*(C21-C22)	0.25417	17.43	0.28	0.063
LP (2) O15	1.79657	σ*(C4-S14)	0.19653	16.72	0.45	0.078
LP (2) O16	1.79656	σ*(C4-S14)	0.19653	16.71	0.45	0.078
LP (2) O16	1.79656	σ*(S14-O15)	0.15353	16.30	0.57	0.087
LP (2) O15	1.79657	σ*(S14-O16)	0.15348	16.28	0.57	0.087
π (C1-C2)	1.59963	π*(C5-C6)	0.30467	14.55	0.28	0.059
π (C5-C6)	1.70797	π*(C3-C4)	0.42818	14.50	0.27	0.058
π (C3-C4)	1.69941	π*(C1-C2)	0.40578	13.39	0.29	0.057
π (C21-C22)	1.92646	π*(C19-N25)	0.38696	9.25	0.28	0.049
σ (C21-N25)	1.97632	σ*(N17-C19)	0.04012	7.56	1.20	0.085

Table 8. Second order perturbation theory analysis of Fock matrix on NBO of compound **3**

Donor(i)	ED/e	Acceptor(j)	ED/e	E(2) Kcal/mol	E(j)-E(i) a.u	F(i.j) a.u
LP (1) C6	1.14687	π*(C4-C5)	0.34731	85.50	0.14	0.115
LP (1) C6	1.14687	π*(C16-O17)	0.27084	75.68	0.13	0.105
LP (2) O18	1.84382	π*(C16-O17)	0.27084	40.55	0.35	0.110
LP (2) O17	1.83509	σ*(C16-O18)	0.10685	35.32	0.58	0.130
LP (2) O27	1.70215	π*(C25-C26)	0.27870	28.21	0.36	0.091
LP (2) O27	1.70215	π*(C28-C30)	0.25552	26.97	0.36	0.089
π (C4-C5)	1.71049	π*(C2-C3)	0.34898	24.26	0.28	0.074
LP (3) O13	1.77472	σ*(S9-O14)	0.15215	21.37	0.56	0.100
LP (3) O14	1.79045	σ*(S9-O13)	0.16276	21.30	0.57	0.100
LP (2) O17	1.83509	σ*(C6-C16)	0.06503	18.72	0.69	0.104
LP (2) O13	1.80914	σ*(C4-S9)	0.20944	17.44	0.44	0.079
LP (2) O14	1.81276	σ*(C4-S9)	0.20944	16.89	0.44	0.078
π (C25-C26)	1.86118	π*(C28-C30)	0.25552	15.28	0.30	0.062
π (C28-C30)	1.87700	π*(C25-C26)	0.27870	14.80	0.31	0.062
LP (3) Cl15	1.91622	π*(C2-C3)	0.34898	13.91	0.33	0.065
LP (2) O13	1.80914	σ*(S9-N10)	0.24176	13.52	0.41	0.067
LP (2) O14	1.81276	σ*(S9-N10)	0.24176	13.48	0.41	0.068
LP (3) O13	1.77472	σ*(S9-N10)	0.24176	12.69	0.41	0.064
π (C2-C3)	1.74025	π*(C4-C5)	0.34731	11.95	0.30	0.055
LP (3) O14	1.79045	σ*(S9-N10)	0.24176	11.41	0.41	0.062

Table 9. Second order perturbation theory analysis of Fock matrix on NBO of compound **4**

Donor(i)	ED/e	Acceptor(j)	ED/e	E(2) Kcal/mol	E(j)-E(i) a.u	F(i.j) a.u
LP (1) N35	1.62393	π*(C29-C30)	0.33945	39.19	0.28	0.094
LP (1) N35	1.62393	π*(C23-C25)	0.49744	37.92	0.29	0.097
LP (3) O18	1.79357	σ*(S17-O19)	0.16347	21.94	0.57	0.101
LP (3) O13	1.78081	σ*(S11-O12)	0.15775	21.60	0.57	0.100
LP (3) O12	1.77766	σ*(S11-O13)	0.15518	21.34	0.57	0.100
π (C26-C28)	1.71376	π*(C22-C24)	0.36518	21.15	0.28	0.069
LP (3) O19	1.76925	σ*(S17-N20)	0.27755	20.53	0.40	0.081
π (C5-C6)	1.64124	π*(C3-C4)	0.35385	20.14	0.27	0.067
π (C5-C6)	1.64124	π*(C1-C2)	0.35584	20.08	0.27	0.066
π (C3-C4)	1.67089	π*(C1-C2)	0.35584	19.76	0.28	0.067
π (C23-C25)	1.58436	π*(C29-C30)	0.33945	19.58	0.26	0.065
π (C1-C2)	1.67224	π*(C5-C6)	0.28378	19.53	0.29	0.068
π (C3-C4)	1.67089	π*(C5-C6)	0.28378	19.51	0.29	0.068
π (C23-C25)	1.58436	π*(C26-C28)	0.29879	19.49	0.28	0.069
π (C22-C24)	1.73064	π*(C23-C25)	0.49744	19.43	0.29	0.071
π (C1-C2)	1.67224	π*(C3-C4)	0.35385	19.40	0.28	0.067
LP (2) O19	1.80594	σ*(C1-S17)	0.20864	19.07	0.44	0.082
π (C23-C25)	1.58436	π*(C22-C24)	0.36518	18.92	0.27	0.065
LP (3) O19	1.76925	σ*(S17-O18)	0.14483	17.59	0.56	0.091
π (C26-C28)	1.71376	π*(C23-C25)	0.49744	17.11	0.27	0.064

The intra molecular interaction for the title compounds is formed by the orbital overlap between: π (C1-C6) and π*(C4-C5) for compound **1**, π (C1-C2) and π*(C3-C4) for compound **2**, π (C4-C5) and π*(C2-C3) for compound **3** andπ (C26-C28) and π*(C22-C24) for compound **4** respectively, which result into intermolecular charge transfer (ICT) causing stabilization of the system. The intra molecular hyper conjugative interactions π (C1-C6) to π*(C4-C5) for compound **1**, π (C1-C2) to π*(C3-C4) for compound **2**, π (C4-C5) to π*(C2-C3) for compound **3** and π (C26-C28) to π*(C22-C24) for compound **4** lead to highest stabilization of 28.79, 30.20, 24.26 and 21.15 kJ mol^{-1} respectively. In case of LP (1) N17 orbital to the π*(C1-C6) for compound **1**, LP (1) N17 orbital to π*(C19-N25) for compound **2**, LP (1) C6 orbital to π*(C4-C5) for compound **3**, LP (1) N35 orbital to π*(C29-C30) for compound **4** respectively, show the stabilization energy of 31.14, 42.46, 85.50 and 39.19 kJ mol^{-1} respectively.

3.8. Nonlinear Optical Properties (NLO):

Molecules with non-linear optical responses are of great importance as they find application in optical modulation, optical switching, optical logic, and optical memory for areas such as telecommunication, signal processing and optical interconnections [30,31]. Molecules with delocalized electronic system have been found to possess non-linear optical properties.Theoretically calculated values of first order hyperpolarizability, dipole moments, total polarizability and anisotropy of thepolarizability of Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4** are calculated at the DFT method with B3LYP/6-31G (d,p) basis set andcollectedin Table 10.

Table 10. Nonlinear optical properties of Sulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4**

Parameters	Compound 1	Compound 2	Compound 3	Compound 4
β_{xxx}	56.0974	-134.6517	-23.2779	187.3034
β_{yyy}	-0.0103	-1.7458	18.0280	41.6256
β_{zzz}	-1.8721	-0.0101	2.3069	-3.4986
β_{xyy}	16.2770	7.9931	-45.2505	-18.5876
β_{xxy}	-0.0190	-35.8278	-23.9913	-56.9187
β_{xxz}	13.2977	-0.0221	-53.3657	60.3275
β_{xzz}	-17.8681	-37.4639	-15.6210	17.2956
β_{yzz}	0.0146	-6.7062	1.2121	0.6225
β_{yyz}	6.8208	0.0105	-4.8823	-16.7968
β_{xyz}	0.0024	0.0132	25.3875	1.2205
β(esu)x10^{-33}	60.2012	169.9909	101.1588	190.8351
μ_x	4.4263	-5.8473	-6.3051	2.2741
μ_y	-0.0006	-5.1836	0.0283	-0.7005
μ_z	1.9230	-0.0002	-3.4781	-0.9979
μ(D)	4.8259	7.8141	7.2008	2.5803
α_{xx}	-53.6646	-62.2548	-117.0817	-134.1256
α_{yy}	-67.0538	-115.4308	-128.3872	-185.4369
α_{zz}	-74.4408	-104.5742	-134.1110	-152.0637
α_{xy}	0.0039	0.0502	-13.6433	-0.2911
α_{xz}	-14.4145	0.0014	-13.7813	5.2439
α_{yz}	0.0016	-0.0078	-1.7501	4.3085
α(esu)x10^{-24}	30.9205	48.6647	36.9143	46.6116
$\Delta\alpha$(esu)x10^{-24}	4.5824	7.2121	5.4707	6.9078

Since the values of the polarizabilities (Δα) and the hyperpolarizabilities (β) of the GAUSSIAN 09 output are obtained in atomic units (a.u.), the calculated values have been converted into electrostatic units (e.s.u.) (for α; 1 a.u = 0.1482 x 10^{-24} e.s.u., for β; 1 a.u = 8.6393 x 10^{-33} e.s.u.). The calculated values of dipole moment (μ) for the title compounds were found to be 4.8259, 7.8141, 7.2008 and 2.5803D respectively, which are approximately four, seven and two times respectively than to the value for urea (μ = 1.3732 D). Urea is one of the prototypical molecules used in the study of the NLO properties of molecular systems. Therefore, it has been used frequently as a threshold value for comparative purposes. The calculated values of polarizability are 30.9205 x 10^{-24}, 48.6647 x 10^{-24}, 36.9143 x 10^{-24} and 46.6116 x 10^{-24} esu respectively; the values of anisotropy of the polarizability are 4.5824, 7.2121, 5.4707 and 6.9078 esu, respectively. The magnitude of the molecular hyperpolarizability (β) is one of the important key factors in a NLO system. The DFT/6-31G (d,p) calculated first hyperpolarizability value (β) of Sulfanilamide, Sulfathiazole, E7070 and Furosemide molecules are equal to 60.2012 x 10^{-33}, 169.9909 x 10^{-33}, 101.1588 x 10^{-33} and 190.8351 x 10^{-33} esu. The first hyperpolarizability of title molecules is approximately 0.17, 0.49, 0.29 and 0.55 times than those of urea (β of urea is 343.272 x10^{-33} esu obtained by B3LYP/6-311G (d,p) method). The above results show that all studied compounds **1-4**might have not the NLO applications.

IV. Conclusion

TheSulfanilamide, Sulfathiazole, E7070 and Furosemide **1-4** were theoretically studied usingdensity functional theory employing Becke's three parameter hybrid exchange functional with Lee-Yang-Parr (B3LYP)

co-relational functional involving 6-31G (d,p) basis set.The structures of the studied molecules were analyzed in parameters like bond lengths, bond angles and dihedral angles through DFT method.As can be seen from the molecular electrostatic potential map of the title molecules, negative region is mainly localized over the sulfamide function in all molecules, also on thiazole for compound **2** and on carbonyl of acid function for compound **3**and the maximum positive region is localized on the hydrogen atoms. FMO analysis identifies the presence of delocalized electron density within the molecule.Insight into the global reactivity properties has been obtained by analysis of frontier molecular orbitals, from results we obtained lower energy gap for compound **4**which shows that is the most reactive.Moreover, the Mulliken analysis was predicted and interpreted in detail. The NBO analysis discloses the fact that the π-π^* interactions are responsible for the stabilization of the molecules. The values of dipole moment (μ), polarizability (α) and hyper polarizability (β) of the molecule were calculated and results give information that compounds **1-4**might have not the NLO applications.

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