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THEORETICAL STUDY OF THE STRUCTURE AND REACTIVITY DESCRIPTORS OF SULFAMIDES DERIVATIVES (SULFACETAMIDE, SULFAGUANIDINE, SULFAMETHOXAZOLE AND SULFATHIAZOLE)

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ABSTRACT

In this report a complete theoretical calculations of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 were performed by using Density Functional Theory (DFT) method with 6-31G (d,p) basis set. The molecular geometries and their parameters such as bond lengths, bond angles and dihedral angles of title compounds 1-4 are determined. Also, the MEP map contour shows that the negative potential sites are generally on sulfamide function as well as the positive potential sites are around the hydrogen atoms. The HOMO and LUMO analysis is used to determine the charge transfer within the molecule. In addition, the molecular properties such as ionization potential, electronegativity, chemical potential, electrophilicity have been deduced from HOMO-LUMO analysis and the results show that the compound 3 is the more reactive. The distribution of Mulliken charges of present molecules were calculated and were interrelated with the architecture of the molecular bonds. Stability of the molecules arising from hyperconjugative interactions and charge delocalization were analyzed using natural bond orbital (NBO) analysis. The results show that electron density (ED) in the σ^* and π^* anti-bonding orbitals and second order delocalization energies (E2) confirm the occurrence of intramolecular charge transfer (ICT) within the molecules. The dipole moment (μ) and polarizability (α), anisotropy polarizability ($\Delta\alpha$) and hyperpolarizability (β) of the molecules 1-4 have been reported and

the results show that (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) compounds are not an attractive object for future studies of nonlinear optical properties.

KEYWORDS: Sulfamide; density functional theory; computational chemistry; quantum chemical calculations.

INTRODUCTION

Sulfonamides have been used as one of the successful antibacterial agents applicable to animal and human. Moreover, they are used in agriculture field as well as insecticides and herbicides. Indeed, sulfanilamide as lead compound, the period from 1935 to the present day many thousands of molecules containing the sulfanilamide structure have been developed since its discovery, yielding improved formulations with greater effectiveness and less toxicity because they are less toxic as compared to other drugs and are scalable.[1-3]

In recent years, density functional theory has been exploited to understand many intricate features in chemistry and biology.[4-7] In particular, the conceptual DFT studies have gained a lot of interest in different areas of research.[7-10] Conceptual DFT has been proven to describe the reactivity between reaction partners. Several different reactivity descriptors such as electronegativity, chemical potential, global hardness, global softness, local hardness, local softness and Fukui functions are used to determine the nature of reactive sites and their consequences in both chemistry and biology.[8-10]

The aim of the present work is to determine the optimized molecular geometries, the reactive sites in molecules, electrons transition state, chemical reactivity, Mulliken atomic charge, the second-order perturbation and first hypepolarizability (β) of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 reported in literature[11] at DFT/B3LYP method and 6-31G (d,p) basis set.

1. MATERIALS AND METHODS

The quantum chemical calculation of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 have been performed using the DFT method and B3LYP level with 6-31G (d,p) basis set with the Gaussian 09 program.[12]

2. RESULTS AND DISCUSSION

2.1. Molecular Geometry

Molecular geometry plays a major role in determining the structure-activity relationship. The optimized structures of the (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 with numbering scheme for the atoms are shown in Figure 1. The optimized structural parameters of compounds 1-4 calculated by B3LYP method with 6-31G (d,p) basis set are listed in Tables 1-4.

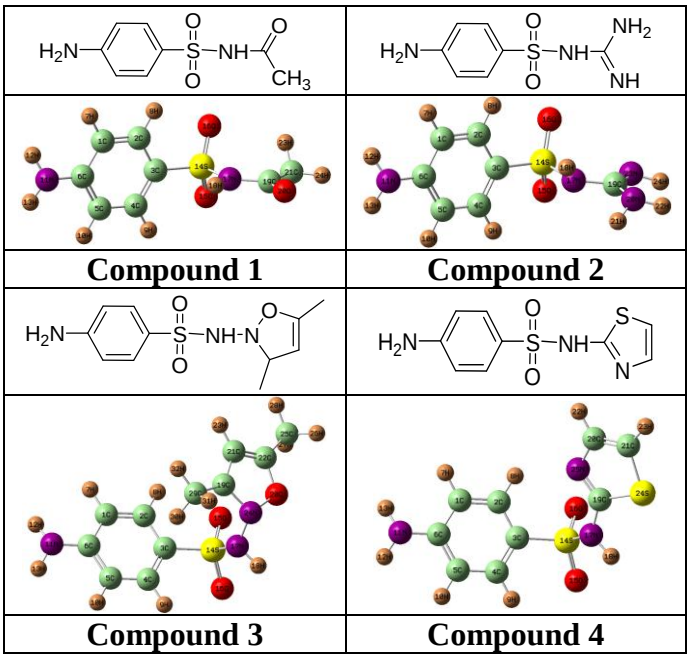

Figure 1: Optimized molecular structure of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4.

Table 1: Optimized geometric parameters of compound 1.

Bond Length (Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.386	A(2,1,6)	120.621	D(6,1,2,8)	178.777
R(1,6)	1.411	A(2,1,7)	119.852	D(2,1,6,11)	177.695
R(1,7)	1.086	A(2,3,4)	120.687	D(7,1,6,5)	179.312
R(3,14)	1.774	A(2,3,14)	119.650	D(1,2,3,14)	179.575
R(6,11)	1.378	A(1,6,11)	120.557	D(2,3,4,9)	178.154
R(11,12)	1.009	A(6,11,12)	117.609	D(2,3,14,17)	90.648
R(14,15)	1.466	A(3,14,15)	109.615	D(4,3,14,16)	156.054
R(14,16)	1.466	A(3,14,16)	109.614	D(3,4,5,10)	179.928
R(14,17)	1.721	A(3,14,17)	99.615	D(1,6,11,13)	162.331
R(17,18)	1.014	A(16,14,17)	108.146	D(3,14,17,19)	179.994
R(17,19)	1.401	A(14,17,18)	116.310	D(15,14,17,19)	65.551
R(19,20)	1.217	A(18,17,19)	115.380	D(16,14,17,18)	114.410
R(19,21)	1.510	A(17,19,20)	118.750	D(14,17,19,20)	179.984
R(21,23)	1.094	A(17,19,21)	116.637	D(17,19,21,23)	59.263

R(21,24)	1.089	A(19,21,23)	110.389	D(20,19,21,22)	120.742

Table 2: Optimized geometric parameters of compound 2.

Bond Length (Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.389	A(2,1,6)	120.582	D(6,1,2,8)	178.651
R(1,6)	1.409	A(3,4,9)	119.708	D(2,1,6,11)	177.643
R(1,7)	1.087	A(1,6,11)	120.658	D(7,1,6,5)	179.383
R(3,14)	1.785	A(6,11,12)	116.659	D(1,2,3,14)	178.839
R(6,11)	1.384	A(12,11,13)	113.289	D(2,3,4,9)	178.231
R(11,12)	1.010	A(3,14,16)	107.554	D(2,3,14,17)	102.696
R(14,15)	1.460	A(15,14,17)	107.016	D(4,3,14,16)	165.867
R(14,17)	1.731	A(14,17,18)	110.463	D(3,4,5,10)	179.941
R(17,18)	1.017	A(14,17,19)	120.687	D(1,6,11,13)	160.096
R(17,19)	1.417	A(18,17,19)	113.179	D(3,14,17,19)	176.825
R(19,20)	1.400	A(17,19,20)	109.624	D(15,14,17,19)	63.983
R(19,23)	1.272	A(17,19,23)	121.260	D(16,14,17,18)	64.174
R(20,21)	1.013	A(20,19,23)	129.085	D(14,17,19,20)	179.500
R(20,22)	1.012	A(19,20,21)	114.469	D(18,17,19,20)	45.368
R(23,24)	1.020	A(19,23,24)	111.387	D(17,19,20,22)	172.453

Table 3: Optimized geometric parameters of compound 3.

Bond Length (Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,2)	1.388	A(2,1,6)	120.653	D(6,1,2,8)	179.573
R(3,14)	1.780	A(2,1,7)	119.851	D(2,1,6,11)	177.590
R(6,11)	1.384	A(4,3,14)	119.724	D(7,1,6,5)	179.704
R(11,12)	1.009	A(1,6,11)	120.620	D(1,2,3,14)	179.060
R(14,15)	1.466	A(5,6,11)	120.549	D(2,3,4,9)	178.598
R(14,16)	1.470	A(6,11,13)	116.765	D(4,3,14,15)	166.011
R(14,17)	1.780	A(3,14,16)	108.841	D(3,4,5,10)	179.889
R(17,18)	1.020	A(3,14,17)	103.897	D(1,6,11,13)	160.576
R(17,24)	1.377	A(15,14,17)	111.729	D(3,14,17,18)	136.118
R(19,24)	1.432	A(14,17,24)	123.061	D(16,14,17,24)	151.834
R(19,29)	1.489	A(21,19,24)	108.058	D(29,19,21,22)	171.719
R(20,24)	1.479	A(20,22,25)	115.782	D(24,19,29,32)	177.215
R(21,22)	1.377	A(17,24,19)	117.359	D(22,20,24,17)	131.663
R(25,26)	1.097	A(17,24,20)	111.914	D(19,21,22,25)	176.430
R(29,30)	1.096	A(19,29,30)	112.338	D(23,21,22,20)	178.216

Table 4: Optimized geometric parameters of compound 4.

Bond Length (Å)		Bond Angles (°)		Dihedral Angles (°)	
R(1,6)	1.410	A(2,1,7)	119.735	D(7,1,2,3)	179.773
R(1,7)	1.087	A(1,6,11)	120.552	D(2,1,6,11)	177.814
R(3,14)	1.772	A(6,11,12)	116.976	D(1,2,3,14)	178.518
R(6,11)	1.382	A(12,11,13)	113.636	D(8,2,3,4)	179.390
R(11,12)	1.009	A(3,14,15)	109.041	D(2,3,4,9)	178.828
R(14,15)	1.466	A(3,14,17)	104.750	D(2,3,14,17)	87.313
R(14,17)	1.734	A(15,14,17)	101.141	D(4,3,14,16)	148.642

R(17,18)	1.014	A(14,17,19)	123.524	D(3,4,5,10)	179.727
R(17,19)	1.385	A(17,19,24)	120.433	D(1,6,11,12)	160.987
R(19,24)	1.771	A(17,19,25)	124.555	D(3,14,17,18)	130.215
R(19,25)	1.299	A(24,19,25)	114.997	D(15,14,17,19)	162.271
R(20,21)	1.360	A(21,20,22)	124.474	D(18,17,19,25)	176.801
R(20,25)	1.379	A(20,21,23)	129.250	D(17,19,25,20)	178.622
R(21,23)	1.080	A(23,21,24)	121.062	D(22,20,25,19)	179.918
R(21,24)	1.746	A(19,25,20)	110.474	D(23,21,24,19)	178.637

2.2. Molecular Electrostatic Potential (MEP)

MEP plays a vital role in order to analyze the physical-chemical properties in chemical structures.[13-15] Also, MEP is an invaluable tool in predicting and analyzing the molecular interactions such as drug-receptor and enzyme-substrate interactions. MEP map is very useful for the qualitative interpretation of the electrophilic and nucleophilic reactions for the study of biological recognition process and hydrogen bonding interactions.[16] Electrostatic potential is enhanced in the order of red < orange < yellow < green < blue.[17] To predict reactive sites for electrophilic and nucleophilic attack for the investigated molecules, the MEP at the B3LYP/6-31G (d,p) optimized geometries were calculated and presented in Figure 2.

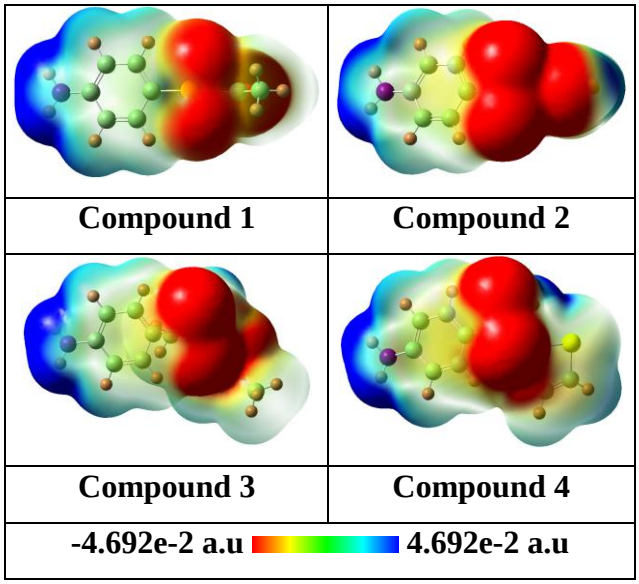

Figure 2: Molecular electrostatic potential surface of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4.

In all molecules, the regions exhibiting the negative electrostatic potential are localized on sulfamide function and on carbonyl of ketone function for compound 1, Amidine group for compound 2 and on methoxazole group for compound 3; while the regions presenting the positive potential are localized vicinity of the hydrogen atoms.

2.3. 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.

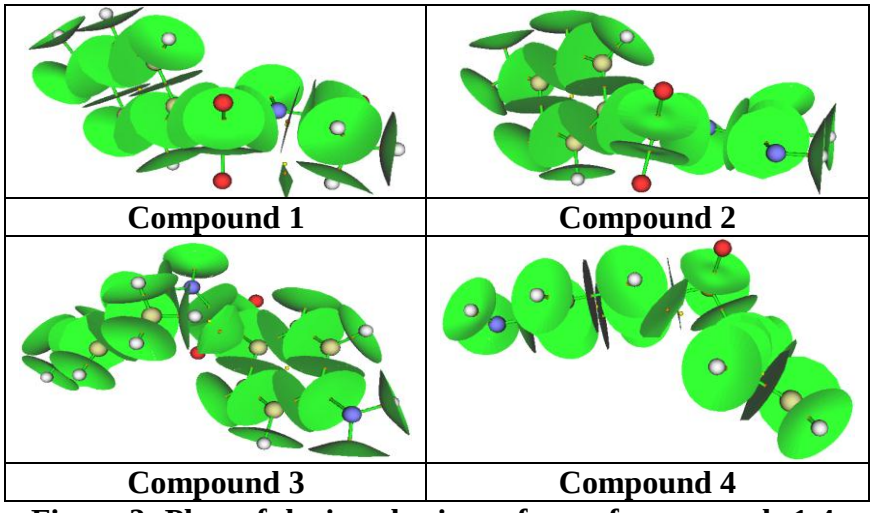

Figure 3: Plots of the interbasin surfaces of compounds 1-4.

The number of interbasin surfaces is 26, 24, 35 and 27 for compounds **1-4** respectively.

2.4. Frontier Molecular Orbitals (FMOs)

The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are very important parameters for quantum chemistry. HOMO which can be thought as the outer orbital containing electrons tends to give these electrons as an electron donor and on the other hand, LUMO can accept electrons and the LUMO energy is directly

related to electron affinity.[18] HOMO and HOMO-1 and second highest and lowest unoccupied molecular orbitals LUMO and LUMO+1and their transition state were shown for the most reactive compound (compound **3**) in Figure 4.

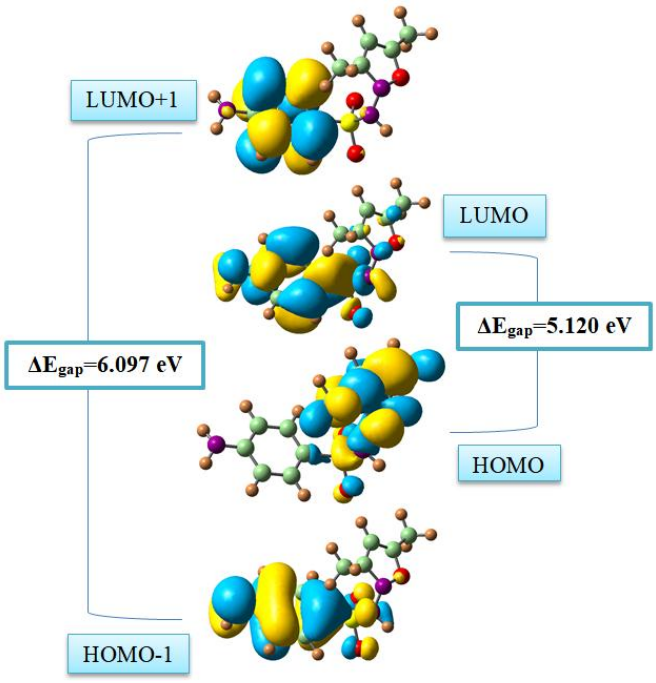

Figure 4: HOMO-LUMO Structure with the energy level diagram of compound 3.

HOMO-1, LUMO and LUMO+1 are confined over the phenylamine group, while HOMO is on methoxazole group and sulfamide function for compound **3** which gives charge transfer process in the molecular system.

2.5. Global Reactivity Descriptors

The understanding of chemical reactivity and site selectivity of the molecular systems has been effectively handled by the conceptual density functional theory (DFT).[19] Chemical potential, global hardness, global softness, electronegativity and electrophilicity are global reactivity descriptors, highly successful in predicting global chemical reactivity trends. The global parameters ionization potential (*I*), electron affinity (*A*), electrophilicity (ω), electronegativity (χ), hardness (η) and softness (*S*) of the molecules **1-4** are determined using B3LYP/6-31G (d,p) basis set and displayed in Table 5.

Table 5: Quantum chemical descriptors of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4.

Parameters	Compound 1	Compound 2	Compound 3	Compound 4
E_{HOMO} (eV)	-6.414	-6.109	-6.103	-5.932
E_{LUMO} (eV)	-0.979	-0.579	-0.983	-0.644
ΔE_{gap} (eV)	5.435	5.530	5.120	5.288
I (eV)	6.414	6.109	6.103	5.932
A (eV)	0.979	0.579	0.983	0.644
μ (eV)	-3.697	-3.344	-3.543	-3.288
χ (eV)	3.697	3.344	3.543	3.288
η (eV)	2.718	2.765	2.560	2.644
S (eV)	0.184	0.181	0.195	0.189
ω (eV)	2.515	2.022	2.452	2.045

The compound which has the lowest energy gap is the compound 3 (ΔE_{gap} = 5.120 eV). This lower gap allows it to be the softest molecule. The compound that has the highest energy gap is the compound 2 (ΔE_{gap} = 5.530 eV). The compound that has the highest HOMO energy is the compound 4 (E_{HOMO} = -5.932 eV). This higher energy allows it to be the best electron donor. The compound that has the lowest LUMO energy is the compound 3 (E_{LUMO} = -0.983 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 4 has the lowest value of the potential ionization (*I* = 5.932 eV), so that will be the better electron donor. Compound 3 has the largest value of the affinity (*A* = 0.983 eV), so it is the better electron acceptor. The chemical reactivity varies with the structure of molecules. Chemical hardness (softness) value of compound 3 (η = 2.560 eV, S = 0.195 eV) is lesser (greater) among all the molecules. Thus, compound 3 is found to be more reactive than all the compounds. Compound 1 possesses higher electronegativity value (χ = 3.697 eV) than all compounds so; it is the best electron acceptor. The value of ω for compound 1 (ω = 2.515 eV) indicates that it is the stronger electrophiles than all compounds. Compound 3 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.

2.6. Mulliken analysis

Mulliken atomic charge calculation plays an important role in the application of quantum chemical calculation to molecular systems.[20] The parameters like dipole moment, polarizability and reactivity depend on the atomic charges of the molecular systems. Mulliken

atomic charges calculated at the DFT/B3LYP levels with 6-31G (d,p) basis set of compound 3 which is the most reactive and are detailed in a Mulliken's plot as visualized in Figure 5.

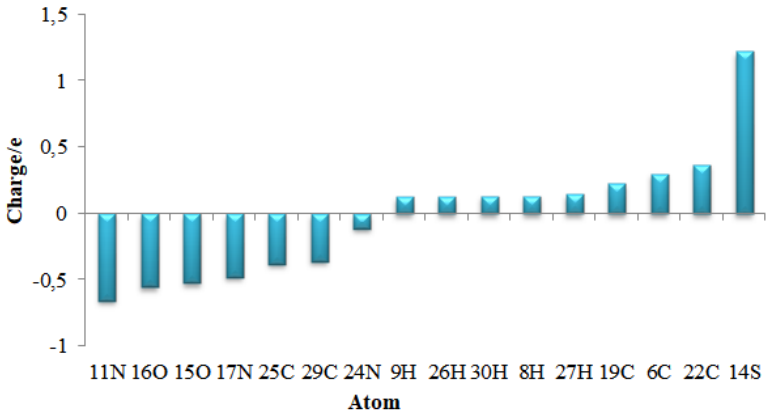

Figure 4: Mulliken's plot of compound 5.

The atom 11N shows more negative (-0.65558e) charge and 14S more positive (1.223347e) charge, which suggests extensive charge delocalization in the entire molecule. The charge noticed on the 17N and 24N is smaller and equal to -0.481419e and -0.112042e respectively. This can be explained by the high degree of conjugation, with a strong push-pull effect between the sulfamide group and methoxazole group. Negatively charged oxygen (15O,16O) atoms shows that charge is transferred from sulfur to oxygen. Carbon atoms 25C and 29C are more negatively charged which indicate that the charge transfer from sulfamide group to methoxazole group. The maximum atomic charge of carbons is obtained for 19C, 6C and 22C. This is due to the attachment of negatively charged atoms (24N, 11N and 20O) respectively. The positive charges are localized on the hydrogen atoms. Very similar values of positive charges are observed for the hydrogen atoms (9H, 26H, 30H, 8H and 27H (0.12~0.14e)) bonded to the negative carbon atoms (4C, 25C, 29C, 2C and 25C) respectively.

2.7. Natural Bond Orbital Analysis (NBO)

The NBO analysis provides an efficient method for studying intra- and intermolecular bonding and provides a convenient basis for investigating charge transfer or conjugative interaction in molecular systems.[21] Hyperconjugation may be given as a stabilizing effect that arises from an overlap between an occupied orbital with another neighboring electron deficient orbital when these orbitals are properly oriented. The hyperconjugative interaction energy was deduced from the second-order perturbation approach of Fock matrix in NBO basis between donor-acceptor orbitals.[22] The stabilization energy E (2) values of the (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 were calculated on

the basis of second-order Fock matrix perturbation theory using B3LYP/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	1.76644	π*(C19-O20)	0.21934	48.74	0.30	0.108
LP (1) N11	1.80457	π*(C5-C6)	0.40660	34.34	0.31	0.097
π (C5-C6)	1.59588	π*(C3-C4)	0.43343	30.66	0.27	0.081
LP (2) O20	1.85429	σ*(N17-C19)	0.08914	29.21	0.65	0.125
LP (3) O15	1.79217	σ*(S14-N17)	0.29882	27.02	0.39	0.093
LP (3) O16	1.79215	σ*(S14-N17)	0.29882	27.00	0.39	0.093
π (C3-C4)	1.70001	π*(C1-C2)	0.30181	23.99	0.30	0.075
π (C1-C2)	1.70949	π*(C5-C6)	0.40660	22.88	0.28	0.073
LP (2) O20	1.85429	σ*(C19-C21)	0.05264	18.57	0.64	0.099
LP (2) O15	1.79897	σ*(C3-S14)	0.19172	18.28	0.46	0.082
LP (2) O16	1.79897	σ*(C3-S14)	0.19172	18.28	0.46	0.082
π (C5-C6)	1.59588	π*(C1-C2)	0.30181	14.44	0.28	0.059
π (C1-C2)	1.70949	π*(C3-C4)	0.43343	14.35	0.27	0.058
π (C3-C4)	1.70001	π*(C5-C6)	0.40660	13.23	0.29	0.057
LP (2) O15	1.79897	σ*(S14-O16)	0.15532	12.17	0.57	0.075
LP (2) O16	1.79897	σ*(S14-O15)	0.15531	12.14	0.57	0.075
LP (3) O16	1.79215	σ*(S14-O15)	0.15531	10.20	0.56	0.069
LP (3) O15	1.79217	σ*(S14-O16)	0.15532	10.18	0.56	0.068
LP (1) N17	1.76644	σ*(S14-O16)	0.15532	7.44	0.55	0.058
LP (1) N17	1.76644	σ*(S14-O15)	0.15531	7.43	0.55	0.058

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) N20	1.85150	π*(C19-N23)	0.24737	31.71	0.34	0.096
LP (1) N11	1.81923	π*(C1-C6)	0.40190	31.57	0.32	0.094
π (C1-C6)	1.61198	π*(C2-C3)	0.41454	28.89	0.27	0.080
LP (3) O15	1.78595	σ*(S14-N17)	0.29459	28.30	0.37	0.094
LP (3) O16	1.77827	σ*(S14-N17)	0.29459	26.99	0.38	0.092
LP (1) N17	1.84837	π*(C19-N23)	0.24737	24.55	0.36	0.086
π (C2-C3)	1.70052	π*(C4-C5)	0.30252	23.56	0.29	0.074
π (C4-C5)	1.70995	π*(C1-C6)	0.40190	22.87	0.28	0.073
LP (2) O16	1.80345	σ*(C3-S14)	0.19773	18.99	0.45	0.083
LP (2) O15	1.79685	σ*(C3-S14)	0.19773	18.35	0.45	0.081
LP (1) N23	1.91272	σ*(C19-N20)	0.05944	18.31	0.77	0.107
π (C1-C6)	1.61198	π*(C4-C5)	0.30252	14.63	0.28	0.059
π (C4-C5)	1.70995	π*(C2-C3)	0.41454	14.61	0.27	0.058

π (C2-C3)	1.70052	π*(C1-C6)	0.40190	13.76	0.29	0.057
LP (2) O15	1.79685	σ*(S14-O16)	0.16139	13.75	0.56	0.079
LP (3) O16	1.77827	σ*(S14-O15)	0.14611	12.83	0.57	0.078
σ (N23-H24)	1.96509	σ*(N17-C19)	0.06147	12.00	0.97	0.097
LP (2) O16	1.80345	σ*(S14-O15)	0.14611	9.21	0.57	0.066
LP (3) O15	1.78595	σ*(S14-O16)	0.16139	9.11	0.56	0.065
LP (1) N17	1.84837	σ*(S14-O16)	0.16139	8.84	0.62	0.066

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) N17	1.78285	π*(C19-N20)	0.42678	37.92	0.29	0.099
π (C22-C24)	1.62573	π*(N21-C23)	0.36812	36.34	0.26	0.087
π (N21-C23)	1.74233	π*(C19-N20)	0.42678	35.13	0.30	0.096
π (C19- N20)	1.69881	π*(C22-C24)	0.31817	31.73	0.33	0.092
LP (1) N11	1.81954	π*(C1-C6)	0.40718	31.42	0.32	0.094
π (C1-C6)	1.60916	π*(C2-C3)	0.41755	29.55	0.27	0.081
π (C2-C3)	1.68657	π*(C4-C5)	0.30947	24.68	0.29	0.076
π (C4-C5)	1.70905	π*(C1-C6)	0.40718	23.13	0.28	0.074
LP (3) O16	1.76294	σ*(S14-N17)	0.28387	21.43	0.39	0.083
LP (3) O15	1.79308	σ*(S14-O16)	0.15868	20.09	0.57	0.097
LP (2) O16	1.81104	σ*(C3-S14)	0.19046	17.97	0.46	0.081
LP (3) O16	1.76294	σ*(S14-O15)	0.14583	16.98	0.56	0.089
LP (2) O15	1.81593	σ*(C3-S14)	0.19046	16.27	0.46	0.078
π (C1-C6)	1.60916	π*(C4-C5)	0.30947	14.64	0.28	0.059
π (C4-C5)	1.70905	π*(C2-C3)	0.41755	14.21	0.28	0.058
π (C2-C3)	1.68657	π*(C1-C6)	0.40718	13.86	0.28	0.057
LP (1) N20	1.90969	σ*(C19-N21)	0.04000	13.68	0.85	0.098
LP (1) N21	1.91425	σ*(C19-N20)	0.03791	13.47	0.88	0.098
LP (3) O15	1.79308	σ*(S14-N17)	0.28387	12.72	0.40	0.065
LP (1) N17	1.78285	π*(C19-N20)	0.42678	37.92	0.29	0.099

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) N11	1.81504	π*(C5-C6)	0.40722	32.31	0.31	0.095
LP (1) N17	1.80466	π*(C19-N25)	0.39078	31.40	0.31	0.092
π (C5-C6)	1.60590	π*(C3-C4)	0.42765	29.84	0.27	0.081
LP (2) S24	1.67670	π*(C19-N25)	0.39078	27.08	0.25	0.075
LP (3) O16	1.75663	σ*(S14-N17)	0.30655	23.84	0.37	0.085
π (C3-C4)	1.69842	π*(C1-C2)	0.29635	23.83	0.30	0.075
π (C1-C2)	1.70303	π*(C5-C6)	0.40722	23.68	0.28	0.074
π (C19-N25)	1.88020	π*(C20-C21)	0.25641	19.60	0.34	0.076
LP (2) S24	1.67670	π*(C20-C21)	0.25641	17.98	0.28	0.064

LP (2) O16	1.80895	σ*(C3-S14)	0.18649	17.86	0.47	0.082
LP (3) O15	1.79104	σ*(S14-O16)	0.15809	17.60	0.58	0.091
LP (1) N25	1.87835	σ*(C19-S24)	0.08947	17.38	0.53	0.086
LP (2) O15	1.81440	σ*(C3-S14)	0.18649	17.10	0.47	0.080
LP (3) O15	1.79104	σ*(S14-N17)	0.30655	16.81	0.38	0.073
LP (3) O16	1.75663	σ*(S14-O15)	0.14637	15.99	0.56	0.087
π (C1-C2)	1.70303	π*(C3-C4)	0.42765	14.45	0.27	0.058
π (C5-C6)	1.60590	π*(C1-C2)	0.29635	14.11	0.29	0.058
π (C3-C4)	1.69842	π*(C5-C6)	0.40722	13.48	0.28	0.057
LP (2) O15	1.81440	σ*(S14-N17)	0.30655	8.92	0.38	0.054
LP (2) O16	1.80895	σ*(S14-N17)	0.30655	8.46	0.38	0.052

The intra molecular interaction for the title compounds is formed by the orbital overlap between: π (C5-C6) and π*(C3-C4) for compound 1, π (C1-C6) and π*(C2-C3) for compound 2, π (C22-C24) and π*(N21-C23) for compound 3 and π (C5-C6) and π*(C3-C4) for compound 4 respectively, which result into intermolecular charge transfer (ICT) causing stabilization of the system. The intra molecular hyper conjugative interactions of π (C5-C6) to π*(C3-C4) for compound 1, π (C1-C6) to π*(C2-C3) for compound 2, π (C22-C24) to π*(N21-C23) for compound 3 and π (C5-C6) to π*(C3-C4) for compound 4 lead to highest stabilization of 30.66, 28.89, 36.34 and 29.84 kJ mol^{-1} respectively. In case of LP (1) N17 orbital to the π*(C19-O20) for compound 1, LP (1) N20 orbital to π*(C19-N23) for compound 2, LP (1) N17 orbital to π*(C19-N20) for compound 3, LP (1) N11 orbital to π*(C5-C6) for compound 4 respectively, show the stabilization energy of 48.74, 31.71, 37.92 and 32.31 kJ mol^{-1} respectively.

2.8. Nonlinear Optical Properties (NLO)

Non-Linear Optical (NLO) effect is the forefront of current research because of its importance in providing the key functions of frequency shifting, optical modulation, optical switching, optical logic and optic memory for the emerging technologies in areas such as telecommunications, signal processing and optical inter-connections.[23-25] It is known that the significance of the polarizability and the first hyperpolarizability of molecular systems are dependent on the efficiency of electronic communication between acceptor and the donor groups as that will be the key to intramolecular charge transfer.[26] The dipole moment (μ), polarizability (α), anisotropy of polarizability (Δα) and first hypepolarizability (β_0) of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 were calculated using B3LYP/6-31G (d,p) basis set and illustrated in Table 10.

Table 10: Nonlinear optical properties of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4.

Parameters	Compound 1	Compound 2	Compound 3	Compound 4
β_{xxx}	-139.1782	-52.6621	133.9865	-116.5116
β_{yyy}	-12.8907	25.7198	-24.4687	-33.3365
β_{zzz}	0.0009	-3.8064	0.0702	-4.3405
β_{xyy}	-17.2148	22.9729	-6.7514	3.7006
β_{xxy}	-27.9413	56.3871	-23.9375	-55.5952
β_{xxz}	0.0157	2.0720	-31.1506	-16.1674
β_{xzz}	-20.9671	-19.3548	3.4825	-8.4201
β_{yzz}	8.2129	3.4189	1.1896	3.0251
β_{yyz}	0.0030	5.7439	-1.9348	9.0560
β_{xyz}	0.0008	-12.3322	8.9371	6.0752
β_0 (esu)x10^{-33}	187.8184	98.6714	142.1099	149.0237
μ_x	-7.4926	-4.7092	4.6116	-2.9315
μ_y	0.6594	5.9982	-4.3671	-3.8766
μ_z	0.0005	-1.2111	-0.0146	-1.9698
μ(D)	7.5216	7.7215	6.3512	5.2443
α_{xx}	-63.6572	-55.4208	-82.1033	-70.0047
α_{yy}	-102.5066	-88.8911	-115.1321	-106.3120
α_{zz}	-84.4302	-88.8863	-109.5377	-108.7017
α_{xy}	-6.1282	16.3626	-1.3451	3.8585
α_{xz}	0.0022	-2.5719	-0.5813	-1.8074
α_{yz}	0.0017	4.4683	9.5536	-10.0428
α(esu)x10^{-24}	35.3049	44.7554	34.8952	42.0444
$\Delta\alpha$(esu)x10^{-24}	5.2322	6.6327	5.1715	6.2310

Since the values of the polarizabilities (Δα) and the hyperpolarizabilities (β_0) 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 7.5216, 7.7215, 6.3512 and 5.2443 D respectively, which are approximately between five and seven times 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 35.3049 x 10^{-24}, 44.7554 x 10^{-24}, 34.8952 x 10^{-24} and 42.0444 x 10^{-24} esu respectively; the values of anisotropy of the polarizability are 5.2322, 6.6327, 5.1715 and 6.2310 esu, respectively. The magnitude of the molecular hyperpolarizability (β_0) is one of the important key factors in a NLO system. The DFT/6-31G (d,p) calculated first hyperpolarizability value (β_0) of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) molecules are equal to 187.8184 x 10^{-33}, 98.6714 x 10^{-33},

142.1099 x 10^{-33} and 149.0237 x 10^{-33} esu. The first hyperpolarizability of title molecules is approximately 0.55, 0.29, 0.41 and 0.43 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.

3. CONCLUSION

This paper describes the various theoretical calculations of (sulfacetamide, sulfaguanidine, sulfamethoxazole and sulfathiazole) 1-4 have been performed using DFT/B3LYP method and 6-31G (d,p) basis set. The study of the molecular geometry reveals that there is no appreciable change in the bond lengths, bond angles and dihedral angles of the molecules by the change of the substitution groups. Information about the size, shape, charge density distribution and site of chemical reactivity of the molecules has been obtained by mapping electron density with molecular electrostatic potential (MEP) using the same level of basis set. The lowering of energy separation between the HOMO and LUMO on compound 3 clearly explicates the charge transfer interactions taking place within the molecule. According to the calculated Mulliken atomic charges, the 14S atom has a largest positive atomic charge and 11N atom has a largest negative atomic charge. The NBO analysis shows strong intermolecular hyperconjugative interactions of π-electrons, the strong delocalization of π-electrons in the molecules leading to stabilization of the molecules. On the basis of first hyperpolarizability of compounds 1-4, we conclude that title compounds cannot be used as an attractive material for non-linear optical (NLO) applications.

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