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Theoretical analysis and molecular orbital studies of a series of 1,4,3,5-oxathiadiazepane-4,4-dioxides derived of sarcosine

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ABSTRACT

The optimized molecular structure of a series of 1,4,3,5-oxathiadiazepane 4,4-dioxides derived of sarcosine have been investigated theoretically using Gaussian09 software package. The HOMO and LUMO analysis were used to determine the charge transfer within the molecule and some molecular properties such as ionization potential, electron affinity, electronegativity, chemical potential, hardness, softness and electrophilicity. The linear polarizability (α) and the first hyperpolarizability (β_{tot}) values of the investigated molecule have been computed using B3LYP with 6-31G (d,p) basis set. Stability of the molecules arising from hyper conjugative interaction and charge transfer delocalization has been analyzed using natural bond orbital (NBO) analysis. Finally, Fukui function analyses on atomic charges, electrophilic and nucleophilic descriptors of the title molecules have been calculated.

Keywords: Oxathiadiazepane; Density functional theory; Computational chemistry; Quantum chemical calculations

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INTRODUCTION

The biological activity of compounds is mainly dependent on their molecular structures [1].Heterocyclic compounds are acquiring more importance in recent years as these can be found in a large number of compounds which display biological activities [2]. Heterocyclic compounds particularly five, six and seven member heterocyclic have attracted the attention of pharmaceutical community over the years due to their therapeutic values [3,4]. Polyfunctionalized heterocyclic compounds containing nitrogen, sulphur, oxygen as heteroatom play important roles in the drug discovery process [5]. Analysis of drugs in late development stages or in the market shows that 68% of them are heterocycles. Heterocyclic containing sulfonamide moieties have occupied an important place in drug discovery, they have received considerable attention because of their wide pharmaceutical and non-pharmaceutical uses such as antimicrobial, antiviral, anti-inflammatory agents, HIV protease [6,7], agonists of the 5-HTID receptor [8,9], carbonic anhydrase inhibitors [10,11], antitumor[12], glycogen phosphorylase inhibitory [13], cholestrolacyl transferase inhibitory [14], pesticidal, dyes and lubricants[15].

Previously, we have synthesized and characterized a new class of heterocyclic compounds: 1,4,3,5-oxathiadiazepane 4,4-dioxides [16] and in the aim to study their properties and to predict their applications, the present study gives a complete description of the molecular geometry and chemical reactivity as HOMO-LUMO energy gap, natural bond orbital (NBO) analysis, chemical hardness, chemical potential and delocalization activity of the electron clouds in the optimized molecular structure.

All these investigations have been done on the basis of the optimized geometry by using the density functional theory method (DFT/B3LYP) with 6-31G (d,p) basis sets. Theoretical studies on bioactive compounds are of interest in order to gain a deeper insight on their action and thus helping in the design of new compounds with therapeutic effects. The knowledge of physico-chemical properties and sites of reaction of investigated compound will provide a deeper insight of its probable action. Particularly, molecular electrostatic potential (MESP) 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.

MATERIALS AND METHODS

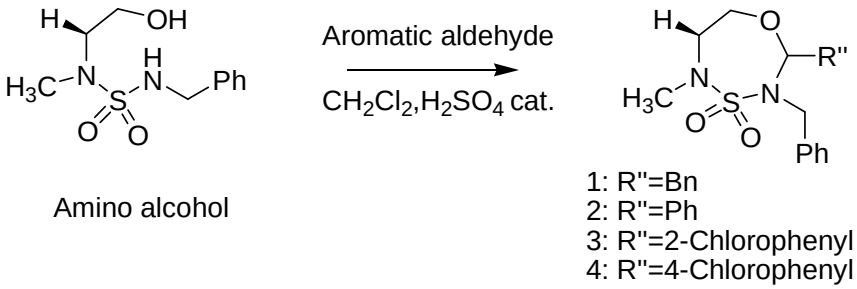
All computational calculations have been performed on personal computer using the Gaussian 09W program packages developed by Frisch and coworkers. The Becke's three parameter hybrid functional using the LYP correlation functional (B3LYP), one of the most robust functional of the hybrid family, was herein used for all the calculations, with 6.31G(d,p) basis set. Gaussian output files were visualized by means of GAUSSIAN VIEW 05 software.

RESULTS AND DISCUSSION

3.1. Chemistry:

In a previous work [16], we have described the synthesis of a new class of 1,4,3,5-oxathiadiazepane 4,4-dioxides derived of sarcosine **1-4** indicated in Scheme 1. The synthesis of these compounds was carried out using a cycolodehydration reaction of substituted amino alcohol and various aromatic aldehydes by treatment with sulfuric acid (cat.) in dichloromethane at ambient temperature, these new heterocycles were obtained in 50%, 50%, 43% and 41% yields, respectively.

Scheme 1.Syntheticroute for the preparation of1,4,3,5-oxathiadiazepane 4,4-dioxides1-4



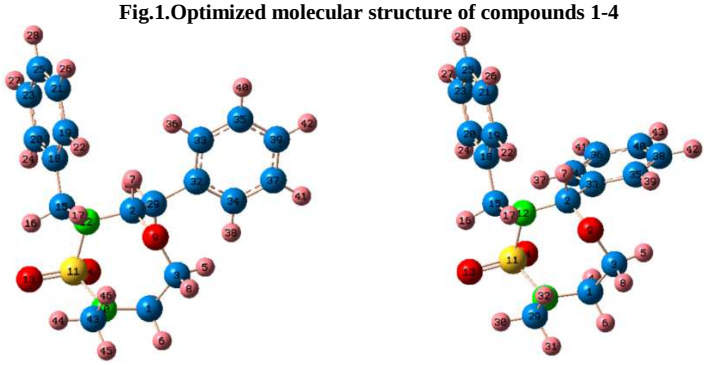
Amino alcohol

1: R''=Bn
2: R''=Ph
3: R''=2-Chlorophenyl
4: R''=4-Chlorophenyl

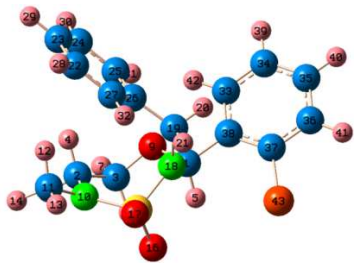
3.2. Molecular Geometry:

The optimized parameters (bond lengths, bond angles and dihedral angles) of 1,4,3,5-oxathiadiazepane 4,4-dioxides derived of sarcosine**1-4** have been obtained using the B3LYP/6-31G(d,p) method. No solvent corrections were made with these calculations. The computations were converged upon a true energy minimum, which were supported by the absence of imaginary frequencies. The chemical structure of the title molecules are shown in scheme 1 and thefinal optimized molecular structures of compounds in accordance with the atom numbering scheme were shown in Fig. 1. Some selected geometrical parameters calculated are listed in Tables**1-4**.

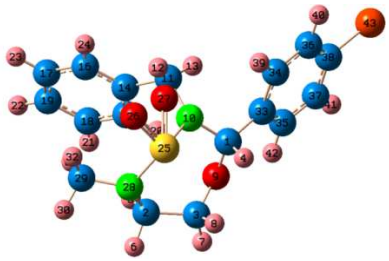
Fig.1.Optimized molecular structure of compounds 1-4



Compound 1 **Compound 2**



Compound3



Compound4

Table 1:Optimized geometric parameters of compound 1

Bond length(Å)		Bond Angles (°)		Dihedral Angles (°)	
$N_{10}S_{11}$	1.691	$S_{11}N_{10}C_1$	114.993	$N_{12}C_2O_9C_3$	94.214
C_1N_{10}	1.464	$N_{10}S_{11}N_{12}$	109.370	$H_{30}C_{29}C_2N_{12}$	44.577
$S_{11}O_{13}$	1.460	$N_{10}S_{11}O_{13}$	106.826	$N_{12}S_{11}N_{10}C_{43}$	72.889
$S_{11}N_{12}$	1.706	$N_{10}S_{11}O_{14}$	105.600	$C_{43}N_{10}C_1H_6$	59.399
C_2N_{12}	1.479	$O_{13}S_{11}O_{14}$	121.774	$C_1N_{10}C_{43}H_{46}$	62.092
C_2O_9	1.426	$S_{11}N_{12}C_2$	117.224	$O_{13}S_{11}N_{12}C_{15}$	25.490
$N_{10}C_{43}$	1.465	$C_2O_9C_3$	121.772	$N_{12}C_2C_{29}C_{32}$	165.065
$N_{12}C_{15}$	1.485	$O_9C_2N_{12}$	111.795	$O_{14}S_{11}N_{12}C_{15}$	156.769
C_2C_{29}	1.539	$N_{12}C_{15}C_{18}$	111.259	$H_{44}C_{43}N_{10}S_{11}$	41.853
C_1H_4	1.090	$C_1N_{10}C_{43}$	116.873	$H_{17}C_{15}N_{12}S_{11}$	92.360

Table 2:Optimized geometric parameters of compound 2

Bond length(Å)		Bond Angles (°)		Dihedral Angles (°)	
$N_{10}S_{11}$	1.685	$S_{11}N_{10}C_1$	114.387	$N_{12}C_2O_9C_3$	92.081
C_1N_{10}	1.465	$N_{10}S_{11}N_{12}$	109.358	$H_7C_2C_{33}C_{35}$	71.133
$S_{11}O_{13}$	1.460	$N_{10}S_{11}O_{13}$	106.936	$N_{12}S_{11}N_{10}C_{29}$	76.036
$S_{11}N_{12}$	1.721	$N_{10}S_{11}O_{14}$	105.667	$H_6C_1N_{10}C_{29}$	65.051
C_2N_{12}	1.478	$O_{13}S_{11}O_{14}$	121.269	$N_{10}C_1C_3H_8$	80.902
C_2O_9	1.434	$S_{11}N_{12}C_2$	119.242	$O_{13}S_{11}N_{12}C_{15}$	19.422
$N_{10}C_{29}$	1.466	$C_3O_9C_2$	121.827	$N_{12}C_2C_{33}C_{34}$	12.112
$N_{12}C_{15}$	1.488	$O_9C_2N_{12}$	112.610	$O_{14}S_{11}N_{12}C_{15}$	150.320
C_2C_{33}	1.524	$N_{12}C_{15}C_{18}$	111.503	$H_{30}C_{29}N_{10}S_{11}$	44.041
C_1H4	1.090	$C_1N_{10}C_{29}$	117.000	$C_2N_{12}S_{11}N_{10}$	43.610

Table 3:Optimized geometric parameters of compound 3

Bond length(Å)		Bond Angles (°)		Dihedral Angles (°)	
$N_{10}S_{15}$	1.679	$S_{15}N_{10}C_2$	120.876	$H_5C_1N_{18}C_{19}$	154.723
C_2N_{10}	1.471	$N_{10}S_{15}N_{18}$	107.954	$C_{38}C_1N_{18}C_{19}$	36.313
$S_{15}O_{16}$	1.462	$N_{10}S_{15}O_{16}$	107.016	$N_{18}S_{15}N_{10}C_2$	43.828
$S_{15}N_{18}$	1.689	$N_{10}S_{15}O_{17}$	106.938	$C_{11}C_2N_{10}C_{11}$	171.473
C_1N_{18}	1.465	$O_{16}S_{15}O_{17}$	121.584	$H_4C_2C_3O_9$	48.020
C_1O_9	1.424	$C_1N_{18}S_{15}$	115.554	$O_{16}S_{15}N_{10}C_{11}$	137.242
$N_{10}C_{11}$	1.463	$C_1O_9C_3$	114.876	$N_{18}C_1C_{38}C_{37}$	71.430
$N_{18}C_{19}$	1.477	$O_9C_1C_{18}$	112.956	$O_{17}S_{15}N_{18}C_1$	166.370
C_2H_4	1.099	$N_{18}C_{19}C_{26}$	118.479	$H_6C_2N_{10}S_{15}$	137.058
$C_{37}Cl_{43}$	1.758	$Cl_{43}C_{37}C_{38}$	120.837	$N_{10}S_{15}N_{18}C_{19}$	84.805

Table 4:Optimized geometric parameters of compound 4

Bond length(Å)		Bond Angles (°)		Dihedral Angles (°)	
$S_{25}N_{28}$	1.728	$S_{25}N_{28}C_2$	118.315	$C_1O_9C_3C2$	85.704
C_2N_{28}	1.470	$N_{10}S_{25}N_{28}$	108.176	$S_{25}N_{28}C_2H_6$	139.917
$S_{25}O_{26}$	1.503	$N_{28}S_{25}O_{26}$	104.588	$N_{28}S_{25}N_{10}C_{11}$	85.732
$N_{10}S_{25}$	1.724	$N_{28}S_{25}O_{27}$	106.593	$H_{30}C_{29}N_{28}C_2$	66.655
C_1N_{10}	1.453	$O_{26}S_{25}O_{27}$	121.590	$N_{28}C_2C_3H_7$	165.005
C_1O_9	1.428	$C_1N_{10}S_{25}$	111.153	$O_{26}S_{25}N_{28}C_2$	156.728
$N_{28}C_{29}$	1.463	$C_3O_9C_1$	114.674	$N_{10}C_1C_{33}C_{34}$	46.118
$N_{10}C_{11}$	1.485	$O_9C_1N_{10}$	113.267	$O_{27}S_{25}N_{28}C_2$	92.392
C_2H_5	1.099	$N_{10}C_{11}C_{14}$	115.183	$H_{31}C_{29}N_{28}S_{25}$	93.048
$C_{38}Cl_{43}$	1.758	$C_{36}C_{38}C_{143}$	119.445	$C_1N_{10}S_{25}O_{26}$	166.102

3.3. Molecular Electrostatic Potential:

The molecular electrostatic potential, V(r), at a given point r (x, y, z) in the vicinity of a molecule, is defined in terms of the interaction energy between the electrical charge generated from the molecule electrons and nuclei and a positive test charge (a proton) located at r. The molecular electrostatic potential (MEP) is related to the electronic

density and is a very useful descriptor for determining sites for electrophilic attack and nucleophilic reactions as well as hydrogen-bonding interactions [17,18]. To predict reactive sites for electrophilic and nucleophilic attack for the title molecule, MEP was calculated at the B3LYP/6-31G (d,p) basis set optimized geometry.

The negative (red) regions of MEP were related to electrophilic reactivity and the positive (bleu) regions to nucleophilic reactivity shown in Fig.2, the negative regions are mainly localized on the sulfoxide group (SO_2). A maximum positive region is localized on the hydrogen atoms indicating a possible site for nucleophilic attack. The MEP map shows that the negative potential sites are on electronegative atoms as well as the positive potential sites are around the hydrogen atoms. These sites give information about the region from where the compound can have noncovalent interactions.

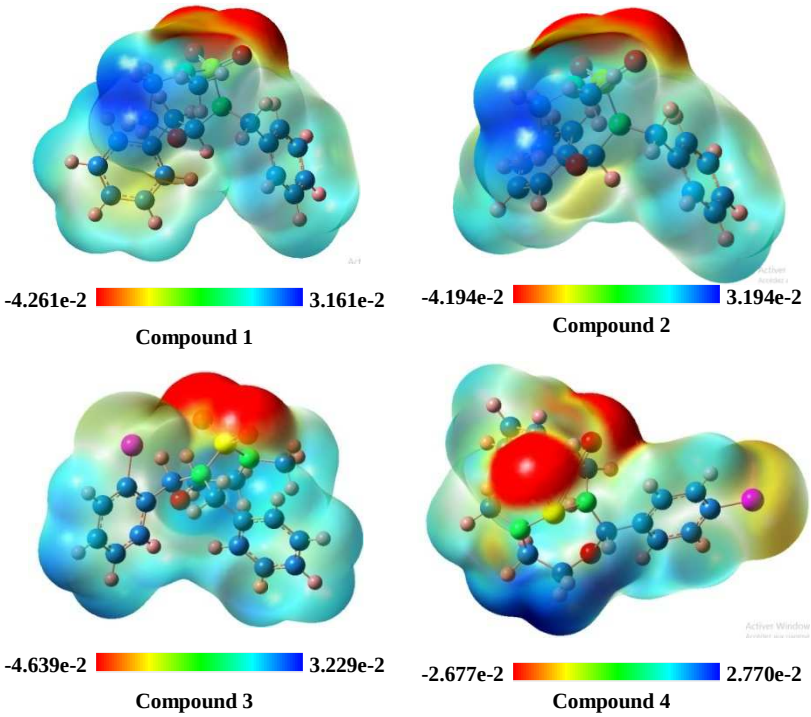


Fig.2.Molecular electrostatic potential surface of compounds 1-4

3.4. Frontier Molecular Orbitals (FMOs):

The frontier molecular orbital determine the way in which the molecule interacts with other species. HOMO (highest occupied molecular orbital), which can be thought the outermost orbital containing electrons, tends to give these electrons such as an electron donor. On the other hand, LUMO (lowest unoccupied molecular orbital) can be thought the innermost orbital containing free places to accept electrons [19]. Therefore, while the energy of the HOMO is directly related to the ionization potential, LUMO energy is directly related to the electron affinity. Energy difference between HOMO and LUMO orbital is called as energy gap that is an important stability for structures [20], in this case, the order of stability of the title compounds is **1**, **2**, **4** and **3**. HOMO-LUMO helps to characterize the chemical reactivity and kinetic stability of the molecule [21]. A molecule with a small gap is more polarized and is known as soft molecule. Recently, the energy gap between HOMO and LUMO has been used to prove the bioactivity from intramolecular charge transfer (ICT) [22,23] because it is a measure of electron conductivity. The frontier orbital (HOMO, LUMO) of the starting product (amino alcohol) and the final product (compound **3)**, with B3LYP/6-31G(d,p) method is plotted in Fig. 3. The HOMO and LUMO energy gap of 1,4,3,5-oxathiadiazepane 4,4-dioxides**1**-**4** calculated by B3LYP/6-31G(d,p) method are given in Table 5.

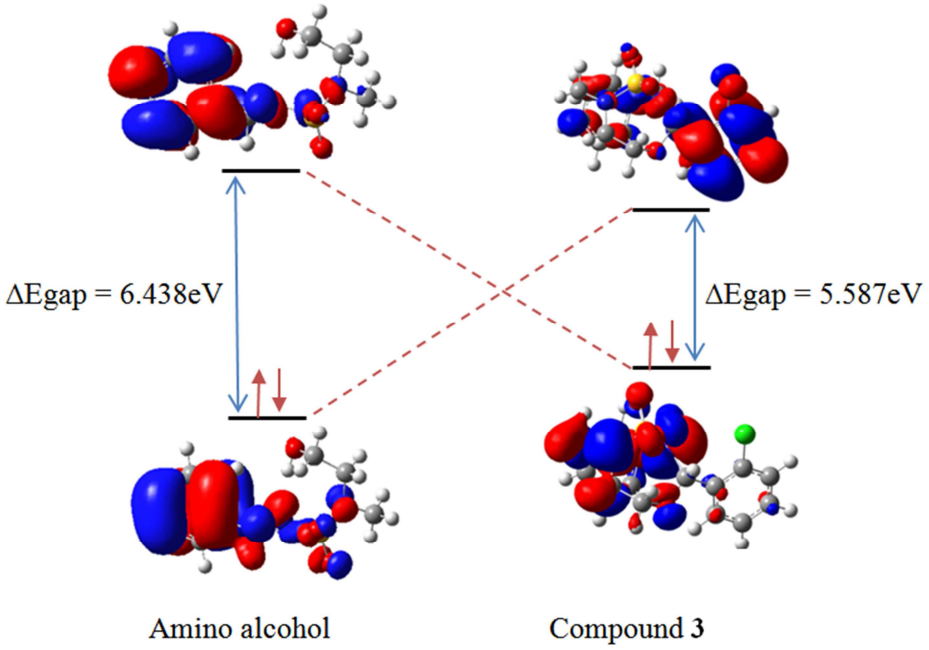


Fig. 3.Highest occupied molecular orbitals and lowest unoccupied molecular orbitals of amino alcohol and compound 3

3.5. Global Reactivity Descriptors:

The global reactivity indices such as chemical hardness, chemical potential and electrophilicity are used for rationalizing, interpreting and predicting diverse aspects of chemical bonding and reaction mechanism whereas the local quantities such as Fukui functions, local softness and local philicity indices are employed to probe site selectivity of different molecules. The calculated values of the global reactivity descriptors for the title molecule are collected in Table 5.

The ionization potential (I) and electron affinity (A) are defined as the difference in ground state energies between the cationic and the neutral system and between the neutral and the anionic system i.e.

$$I = E(N-1) - E(N) \text{ and } A = E(N) - E(N+1)$$

According to Koopman's theorem, the energies of the HOMO and the LUMO orbitals of the molecule are related to the ionization potential (I) and the electron affinity (A), respectively, by the following equations

$$I = -E_{HOMO} \text{ and } A = -E_{LUMO}$$

Chemical potential (μ) can be defined as the first order partial derivative of total energy (E) with respect to the number of electrons (N) at constant external potential V(r).

$$\mu = [\partial E/\partial N]_v$$

The most important application of the chemical potential μ is that it enables us to predict whether a change in substance happens voluntarily or not. Chemical hardness demonstrates the resistance to alteration in electron distribution under small perturbation, usually developed during the event of chemical reaction and is well correlated with the stability and reactivity of the chemical system. The global hardness is given as the second derivative of the energy E, with respect to the number of electrons, N, at constant external potential V(r).

$$\eta = 1/2[\partial\mu/\partial N]_v = 1/2[\partial^2 E/\partial N^2]_v$$

According to Koopmans' theorem, μ and η can be represented in terms of HOMO and LUMO, as follows:

$$\eta = (-E_{HOMO} + E_{LUMO})/2 \text{ and } \mu = (E_{HOMO} + E_{LUMO})/2$$

If a molecule has large HOMO-LUMO gap, it is a hard molecule or small HOMO-LUMO gap it is a soft molecule. One can also relate the stability of molecule to hardness. A small gap increases quantum mixing and therefore enhances chemical reactivity. The inverse of the hardness is expressed as the global softness.

$$S = 1/\eta$$

The global electrophilicity index (ω) categorizes, within a unique absolute scale, the propensity of electron acceptors to acquire additional electronic charge from the environment. The local extension of this index provides useful information about the active sites of electrophiles, thereby allowing the characterization of the intramolecular selectivity in these systems. For electrophilicity, Parr proposed ω index which is directly related to the energy difference for the change in electronic charge in the system containing the charge transfer.

$$\omega = \mu^2/2\eta$$

A good electrophile is, in this sense, characterized by a high value of μ and a low value of η.

Table 5: Energetic parameters of compounds1-4

Compounds	Compound 1	Compound 2	Compound 3	Compound 4
E_{HOMO} (eV)	-6.306	-6.321	-6.290	-6.373
E_{LUMO} (eV)	-0.299	-0.418	-0.703	-0.686
ΔE_{gap}(eV)	6.007	5.903	5.587	5.687
I (eV)	6.306	6.321	6.290	6.373
A (eV)	0.299	0.418	0.703	0.686
μ(eV)	-3.302	-3.369	-3.496	-3.529
x(eV)	3.302	3.369	3.496	3.529
η(eV)	3.003	2.951	2.793	2.843
S(eV)	0.166	0.169	0.179	0.176
ω(eV)	1.815	1.923	2.187	2.190

As shown in table 5, the compound which have the lowest energetic gap is the compound **3** (ΔEgap = 5.587eV). This lower gap allows it to be the softest molecule. The compound that have the highest energy gap is the compound **1** (ΔEgap = 6.007eV).The compound that has the highest HOMO energy is the compound **3** (E_{HOMO} = -6.290eV). 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} = -0.703eV) 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 allow us to calculate the absolute electronegativity (χ) and the absolute hardness (). These two parameters are related to the one-electron orbital energies of the HOMO and LUMO respectively. Compound **3** has lowest value of the potential ionization (I = 6.290eV), so that will be the better electron donor. Compound **3** also has the largest value of the affinity (A = 0.703eV), so it is the better electron acceptor. The chemical reactivity varies with the structural of molecules. Chemical hardness (softness) value of compound **3** (η = 2.793eV) is lesser (greater) among all the molecules. Thus, compound **3** is found to be more reactive than all the compounds. Compound **4** possesses higher electronegativity value (= 3.529eV) than all compounds so; it is the best electron acceptor. The value of ω for compound **4** (ω = 2.190eV) 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.

3.6. Local Reactivity Descriptors:

Parr and Yang [24] have demonstrated that most of the frontier-electron density theory of chemical reactivity can be rationalized from the DFT. Parr and Yang defined a Fukui function (f_k) to describe electrophilic attack (f_k^-), nucleophilic attack (f_k^+) and neutral (radical) attack (f_k^0). Yang and Mortier proposed a finite difference approach to calculate Fukui function indices [25]. In a finite difference approximation, the condensed Fukui function values are given by Yang et al. as

$$\text{For nucleophilic attack } f_k^+ = [q_k(N+1) - q_k(N)]$$

$$\text{For electrophilic attack } f_k^- = [q_k(N) - q_k(N-1)]$$

$$\text{For radical attack } f_k^0 = [q_k(N+1) - q_k(N-1)]/2$$

where q_k is the gross charge of the kth atom in the neutral (N), anionic (N+1) and cationic (N−1) molecule, respectively, all with the ground state geometry of the N electron molecule. Gross charges may be determined by

Mulliken, Hirshfeld and Natural charge analysis. In a molecular system, the atomic site, which possesses the highest condensed Fukui function, favors the higher reactivity.

Table 6:Order of the reactive sites on compounds1 and 2

	Compound 1					Compound 2			
Atom	C_{18}	C_{20}	C_{32}	C_{34}	Atom	N_{10}	N_{12}	O_{14}	O_9
f^+	0.059	0.026	0.018	-0.001	f^+	0	-0.006	-0.007	-0.008
Atom	C_{32}	C_{33}	C_{18}	C_{34}	Atom	C_{34}	C_{33}	C_{35}	C_2
f^-	0.006	-0.002	-0.013	-0.015	f^-	0.013	0.01	-0.015	-0.017
Atom	C_{18}	C_{32}	C_{33}	C_{20}	Atom	C_{33}	C_{34}	N_{10}	C_2
f^0	0.023	0.012	-0.005	-0.005	f^0	-0.002	-0.011	-0.016	-0.022

Table 7:Order of the reactive sites on compounds 3 and 4

	Compound 3					Compound 4			
Atom	C_{38}	O_9	N_{10}	C_{27}	Atom	N_{10}	C_{33}	C_{15}	C_{35}
f^+	0.089	0.047	0.047	0.028	f^+	0.231	0.115	0.027	0.005
Atom	C_{26}	C_{38}	C_{37}	C_{25}	Atom	C_{11}	O_{27}	S_{25}	C_{34}
f^-	0.02	0.015	0.005	-0.012	f^-	0.203	0.172	0.036	0.017
Atom	C_{38}	O_9	N_{10}	C_{26}	Atom	C_{33}	C_{15}	C_{35}	C_{38}
f^0	0.052	0.006	0.003	-0.002	f^0	0.045	0.009	0.003	-0.001

In this study, gross charges were calculated by using Mulliken charge analysis in order to calculate the condensed Fukui functions. The condensed Fukui functions for the compounds are given in Table 6 and 7. These tables show that the most reactive site of compounds**1**, **2**, **3** and **4**are the C18, N10, C38 and N10respectively,for the nucleophilic attack and C32, C34, C26 and C11respectively, for electrophilic attack and C18, C33, C38 and C33 respectively, for radical attack

3.7. Natural Bond Orbital Analysis (NBO):

NBO analysis has been performed on the title molecules at B3LYP/6-31G (d,p) level of theory. Natural bond or bital (NBO) analysis is a useful tool for understanding delocalization of electron density from occupied Lewis-type(donor)NBO to properly unoccupied non-Lewis type(acceptor) NBOs within the molecule. The stabilization of orbital interaction is proportional to the difference energy between the interacting orbitals. Therefore, the interaction having strongest stabilization takes place between effective donors and effective acceptors. The interaction between bonding and anti-bonding molecular orbitals can be quantitatively described in terms of NBO approach that is expressed by means of second-order perturbation interaction energy E(2). This energy represents the estimate of the off-diagonal NBO Fock matrix element. The stabilization energy E(2) associated with *i* (donor) → *j* (acceptor) delocalization is estimated from the second-order perturbation approach as given below [26]:

$$E(2) = \Delta E_{ij} = q_i \frac{F^2(i,j)}{E_j - E_i}$$

where q_i is the donor orbital occupancy, E_i and E_j are diagonal elements (orbital energies) and F(i,j) is the off-diagonal Fock matrix element.

In NBO analysis large E(2) value shows the intensive interaction between electron-donors and electron- acceptors, and greater the extent of conjugation of the whole system, the possibleintensiveinteractionaregiveninTables8-11.

The intra molecular interaction for the title compounds is formed by the orbital overlap between: π(C18-C19) and π*(C20-C23) for compound **1**, π(C18-C19) and π*(C20-C23) for compound **2**, π(C26-C27) and π*(C22-C23) for compound **3** and π(C37-C38), π*(C33-C35) and π*(C34-C36) for compound **4** respectively, which result into intermolecular charge transfer (ICT) causing stabilization of the system. The intra molecular hyper conjugative interactions of π(C18-C19) to π*(C20-C23) for compound **1**, π(C18-C19) to π*(C20-C23) for compound **2**, π(C26-C27) to π*(C22-C23) for compound **3** and π (C37-C38) to π*(C33-C35) and π*(C34-C36) for compound **4** lead to highest stabilization of 19.20, 19.18, 20.36, 19.01 and 19.00 kJ mol^{-1} respectively. In case of LP(2) O13 and LP(3) O13 orbitals to the σ*(S11-N12) andσ* (S11-O14) for compound **1**,LP(2) O13 and LP(3) O13 orbitals to σ*(S11-N12) and σ*(S11-O14) for compound **2**,LP(2) O16 and LP(3) O16 orbitals to σ*(N10-S15) and σ*(S15-O17) for compound **3** and LP(3) O26 orbitals to σ*(N10-S25) for compound **4** respectively, show the stabilization energy of (18.64, 21.24) , (20.63, 20.81), (19.15, 21.22) and 17.06 kJ mol^{-1} respectively.

Table 8: 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
σ (N_{10}-S_{11})	1.96577	σ*(S_{11}-N_{12})	0.28039	2.63	0.89	0.046
		σ*(S_{11}-O_{13})	0.14336	3.13	1.05	0.052
		σ*(S_{11}-O_{14})	0.14783	3.60	1.05	0.056
σ (N_{10}-C_{43})	1.98798	σ*(S_{11}-O_{14})	0.14783	1.08	1.03	0.031
σ (S_{11}-N_{12})	1.96452	σ* (N_{10}-S_{11})	0.27060	2.79	0.88	0.047
		σ*(S_{11}-O_{13})	0.14336	3.42	1.03	0.055
		σ*(S_{11}-O_{14})	0.14783	3.54	1.04	0.056
		σ*(C_{15}-C_{18})	0.02822	1.28	1.16	0.034
σ (N_{12}-C_{15})	1.98039	σ*(C_2-C_{29})	0.03593	1.77	1.08	0.039
		σ*(C_{18}-C_{19})	0.02168	1.15	1.31	0.035
π (C_{18}-C_{19})	1.66833	σ* (N_{12}-C_{15})	0.02922	3.74	0.56	0.044
		π *(C_{20}-C_{23})	0.31047	19.20	0.29	0.066
LP(1) N_{10}	1.85840	σ*(C_1-C_3)	0.04452	8.64	0.64	0.068
		σ*(S_{11}-N_{12})	0.28039	11.94	0.42	0.066
		σ*(S_{11}-O_{13})	0.14336	1.64	0.58	0.028
LP(1) O_{13}	1.97924	σ*(S_{11}-O_{14})	0.14783	2.06	1.07	0.043
LP(2) O_{13}	1.80423	σ*(S_{11}-N_{12})	0.28039	18.64	0.42	0.080
		σ* (N_{10}-S_{11})	0.27060	15.95	0.42	0.075
LP(3) O_{13}	1.79142	σ* (N_{10}-S_{11})	0.27060	8.19	0.42	0.053
		σ*(S_{11}-O_{14})	0.14783	21.24	0.58	0.100

Table 9: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
σ (C_1-N_{10})	1.98518	σ*(S_{11}-O_{13})	0.14347	1.27	1.03	0.033
σ (C_2-O_9)	1.99028	σ*(C_{33}-C_{34})	0.02264	1.16	1.41	0.036
σ (N_{10}-S_{11})	1.96552	σ*(C_1-H_6)	0.01797	1.36	1.20	0.036
		σ*(S_{11}-N_{12})	0.29080	2.61	0.88	0.046
		σ*(S_{11}-O_{13})	0.14347	3.06	1.05	0.052
		σ*(S_{11}-O_{14})	0.14805	3.54	1.05	0.056
σ (N_{10}-C_{29})	1.98810	σ*(S_{11}-O_{14})	0.14805	1.09	1.03	0.031
σ (S_{11}-N_{12})	1.96353	σ* (N_{10}-S_{11})	0.26494	2.91	0.88	0.048
		σ*(S_{11}-O_{13})	0.14347	3.54	1.03	0.055
		σ*(S_{11}-O_{14})	0.14805	3.72	1.03	0.057
σ (N_{12}-C_{15})	1.98049	σ*(C_2-C_{33})	0.04213	1.90	1.12	0.041
π (C_{18}-C_{19})	1.66900	σ* (N_{12}-C_{15})	0.02895	3.93	0.55	0.045
		π *(C_{20}-C_{23})	0.30951	19.18	0.29	0.067
LP(1) N_{10}	1.85718	σ*(C_1-C_3)	0.04065	7.97	0.66	0.066
		σ*(S_{11}-N_{12})	0.29080	12.36	0.41	0.066
LP(1) O_{13}	1.97889	σ*(S_{11}-O_{14})	0.14805	1.98	1.07	0.042
LP(2) O_{13}	1.80089	σ*(S_{11}-N_{12})	0.29080	20.63	0.40	0.083
		σ* (N_{10}-S_{11})	0.26494	14.11	0.43	0.071
LP(3) O_{13}	1.79563	σ* (N_{10}-S_{11})	0.26494	9.89	0.43	0.059
		σ*(S_{11}-O_{14})	0.14805	20.81	0.58	0.099

Table 10:Secondorder perturbation theoryanalysis 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
σ (C_2-C_3)	1.98886	σ*(N_{10}-C_{11})	0.01354	2.03	0.97	0.040
σ (N_{10}-S_{15})	1.97064	σ*(S_{15}-O_{16})	0.15855	3.46	1.07	0.056
		σ*(S_{15}-O_{17})	0.14462	3.27	1.07	0.054
σ (N_{10}-C_{11})	1.98696	σ*(C_2-C_3)	0.02752	2.08	1.10	0.043
σ (S_{15}-N_{18})	1.96653	σ* (N_{10}-S_{15})	0.26816	2.45	0.92	0.045
		σ*(S_{15}-O_{16})	0.15855	3.70	1.06	0.058
π (C_{26}-C_{27})	1.65702	σ* (N_{18}-C_{19})	0.03543	4.94	0.57	0.052
		π *(C_{22}-C_{23})	0.32753	20.36	0.28	0.068
LP(1) N_{10}	1.84920	σ*(C_2-H_4)	0.02508	5.35	0.71	0.057
		σ*(S_{15}-N_{18})	0.27210	9.37	0.42	0.057
		σ*(S_{15}-O_{16})	0.15855	7.18	0.57	0.057
		σ*(S_{15}-O_{16})	0.15855	2.09	0.56	0.031
LP(1) O_{16}	1.97834	σ*(S_{15}-O_{17})	0.14462	2.07	1.07	0.043
LP(2) O_{16}	1.81941	σ*(S_{15}-N_{18})	0.27210	13.98	0.42	0.070
		σ* (N_{10}-S_{15})	0.26816	19.15	0.43	0.083
LP(3) O_{16}	1.77324	σ* (N_{10}-S_{15})	0.26816	4.49	0.43	0.040
		σ*(S_{15}-O_{17})	0.14462	21.22	0.57	0.100
LP(1) Cl_{43}	1.99322	σ*(C_{37}-C_{38})	0.03377	1.36	1.46	0.040
LP(2) Cl_{43}	1.96862	σ*(C_{37}-C_{38})	0.03377	4.41	0.86	0.055
LP(3) Cl_{43}	1.92525	σ*(C_{36}-C_{37})	0.02459	12.24	0.33	0.061

Table 11:Secondorder perturbation theoryanalysis 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
σ (C_2-C_3)	1.98943	σ*(N_{28}-C_{29})	0.01735	1.94	0.98	0.039
σ (C_1-O_9)	1.98909	σ*(C_{33}-C_{34})	0.02123	1.77	1.39	0.044
σ (N_{10}-S_{25})	1.97461	σ*(C_1-C_{33})	0.03769	2.64	1.10	0.048
		σ*(S_{25}-N_{28})	0.20902	1.45	0.82	0.032
		σ*(S_{25}-O_{26})	0.03255	1.60	0.95	0.035
σ (S_{25}-N_{28})	1.97527	σ*(S_{25}-O_{26})	0.03255	1.80	0.95	0.037
σ (N_{28}-C_{29})	1.99009	σ*(C_2-C_3)	0.02861	2.18	1.09	0.044
π (C_{37}-C_{38})	1.68011	π*(C_{33}-C_{35})	0.34946	19.01	0.30	0.068
		π *(C_{34}-C_{36})	0.31073	19.00	0.30	0.067
LP(1) N_{28}	1.84996	σ*(C_{29}-H_{31})	0.02082	6.53	0.74	0.064
		σ*(N_{10}-S_{25})	0.21299	11.47	0.40	0.061
LP(1) O_{26}	1.98324	σ* (H_{12}-O_{27})	0.02987	3.60	1.26	0.060
LP(2) O_{26}	1.85450	σ*(S_{25}-N_{28})	0.20902	10.99	0.41	0.061
		σ* (N_{10}-S_{25})	0.21299	9.26	0.40	0.055
LP(3) O_{26}	1.80251	σ* (S_{25}-N_{28})	0.20902	13.70	0.41	0.067
		σ*(N_{10}-S_{25})	0.21299	17.06	0.40	0.074
LP(1) Cl_{43}	1.99341	σ*(C_{36}-C_{38})	0.02680	1.25	1.47	0.038
LP(2) Cl_{43}	1.97325	σ*(C_{36}-C_{38})	0.02680	3.86	0.87	0.052
		σ*(C_{37}-C_{38})	0.02675	3.83	0.88	0.052
LP(3) Cl_{43}	1.93064	σ*(C_{37}-C_{38})	0.02675	12.15	0.33	0.061

3.8. Nonlinear Optical Properties (NLO):

Density functional theory has been used as an effective method to investigate the organic NLO materials. Recent research works have illustrated that the organic non-linear optical materials are having high optical non-linearity than inorganic materials [27]. Recently Lornoxicam has identified as new organic material for NLO applications [28]. The first order hyperpolarizability (β total) of the title compound Lornoxicam along with related properties (μ, (α) and Δα) are calculated by using the DFT-B3LYP method with 6-31G (d,p) basis set. Based on the finite-field approach, the energy of a system is a function of the electric field. First order hyperpolarizability is a third rank tensor that can be described by a 3 x 3 x 3 array. The 27 components of the 3D matrix can be reduced to 10 components due to the Kleinman symmetry [29]. It can be given in the lower tetrahedral format. The components of β total are defined as the coefficients in the Taylor series expansion of the energy in the external electric field. When the external electric field is weak and homogeneous, this expansion becomes:

$$E = E^0 - \mu_\alpha F_\alpha - 1/2\alpha_{\alpha\beta} F_\alpha F_\alpha - 1/6\beta_{\alpha\beta\gamma} F_\beta F_\beta F_\gamma + \ldots$$

where E^0 is the energy of unperturbed molecule, Fα the field at the origin, μ_α, $\alpha_{\alpha\beta}$, and $\beta_{\alpha\beta\gamma}$ are the components of dipole moment, polarizability and the first order hyperpolarizabilities, respectively.

The total static dipole moment (μ), the mean dipole polarizability (α), the anisotropy of the polarizability (Δα) and the total first order hyperpolarizability β total , using x, y, z components they are defined as:

$$\mu_{tot} = \left[\mu_x^2 + \mu_y^2 + \mu_z^2\right]^{1/2}$$

$$\alpha = \left(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}\right)/3$$

$$\Delta\alpha = 2^{-1/2}\left[\left(\alpha_{xx} - \alpha_{yy}\right)^2 + \left(\alpha_{yy} - \alpha_{zz}\right)^2 + \left(\alpha_{zz} - \alpha_{xx}\right)^2 + 6\alpha_{xz}^2 + 6\alpha_{xy}^2 + 6\alpha_{yz}^2\right]^{1/2}$$

$$\beta_{tot} = \left(\beta_x^2 + \beta_y^2 + \beta_z^2\right)^{1/2}$$

$$\beta_x = \beta_{xxx} + \beta_{xyz} + \beta_{xzz}$$

$$\beta_y = \beta_{yyy} + \beta_{xxy} + \beta_{yzz}$$

$$\beta_z = \beta_{zzz} + \beta_{xxz} + \beta_{yyz}$$

In the present work, the calculated dipole moment, polarizability and first order hyperpolarizability values are obtained from B3LYP/6-31G(d,p) method and listed in Table 12. It is well known that the higher values of dipole moment, molecular polarizability, and hyperpolarizability are important for more active NLO properties. The polarizabilities and hyperpolarizability are reported in atomic units (a.u), the calculated values have been converted into electrostatic units (esu) (for α; 1 a.u = 0.1482 x10^{-24} esu, for β; 1 a.u = 8.6393 x10^{-33} esu). The calculated values

of dipole moment (μ) for the title compounds were found to be 4.4664, 4.1735, 5.5508 and 4.4799D respectively, which are approximately 3 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 -21.4164 x 10^{-24}, -20.2045 x 10^{-24},-21.9732x 10^{-24} and -22.7084x 10^{-24} esu respectively, the values of anisotropy of the polarizability are 4.2943, 3.7741, 3.7365and 2.5866esu, respectively. The magnitude of the molecular hyperpolarizability β, is one of important key factors in a NLO system. The DFT/6-31G (d,p) calculated first hyperpolarizability value (β) of oxathiadiazepane 4,4-dioxides are equal to 712.1012x 10^{-33}, 534.0003x 10^{-33}, 407.3274x 10^{33} and 1087.7630 x 10^{-33} esu. The first hyperpolarizability of title molecules is approximately 2.07, 1.58, 1.18 and 3.17 times than those of urea (β of urea is 343.272 x10^{-33} esu obtained by HF/6-311G(d,p) method).

Table 12: The dipole moments μ (D) polarizability*α*, the average polarizability α_0(esu), the anisotropy of the polarizability Δα(esu), and the first hyperpolarizabilityβ (esu)of oxathiadiazepane 4,4-dioxides 1-4 calculated by B3LYP/6-31 G(d,p) method

Parameters	Compound 1	Compound 2	Compound 3	Compound 4
β_{xxx}	63.1631	9.8972	4.5507	-106.7930
B_{xxy}	-2.8331	-2.0393	30.9821	10.3068
B_{xyy}	11.5566	34.6647	-8.0345	-23.6398
β_{yyy}	-6.9110	5.6437	14.5585	-29.1412
B_{zxx}	13.8951	28.9496	-12.1792	-12.7039
B_{xyz}	24.1704	-3.1684	-8.0778	-11.4669
B_{zyy}	38.8241	16.1145	25.1092	-9.9716
B_{xzz}	-21.9757	-8.9893	14.0839	12.7681
B_{yzz}	0.7662	11.7632	-9.1092	-3.8787
β_{zzz}	9.9824	3.0917	15.0584	-15.9515
B_{tot}(esu) x10^{-33}	712.1012	534.0003	407.3274	1087.7630
μ_x	2.4769	0.2076	0.9327	-2.0862
μ_y	1.0674	1.2020	4.7184	-1.8386
μ_z	3.5602	3.9913	2.7709	-3.5124
μ_{tot}(D)	4.4664	4.1735	5.5508	4.4799
α_{xx}	-147.5728	-129.4828	-136.0673	-157.9528
α_{yy}	-135.6668	-137.1845	-160.9386	-150.9550
α_{zz}	-150.2919	-142.3311	-147.7973	-150.7774
α_{xy}	-9.2207	-1.5001	-4.4177	-5.2799
α_{xz}	-5.1576	8.6180	4.2866	6.9153
α_{yz}	-10.3803	-9.8917	-4.3807	3.0170
α_0(esu) x10^{-24}	-21.4164	-20.2045	-21.9732	-22.7084
Δα(esu) x10^{-24}	4.2943	3.7741	3.7365	2.5866

CONCLUSION

In this present investigation molecular structure, HOMO, LUMO, and polarizability analysis of a serie of 1,4,3,5-oxathiadiazepane 4,4-dioxides derived of sarcosine have been studied using DFT (B3LYP/6-31G (d,p)) calculation. The MEP analysis presents a visual representation of chemically active sites and comparative reactivity of atoms. The global reactivity descriptors reveal differences between the investigated compounds with respect to their chemical stability. The calculated fukui functions show the reactivity order for electrophilic attack and predict that the preferred sites for nucleophilic attack. NLO behavior of the title molecule has been investigated by dipole moment, polarizability and first hyperpolarizability. The calculated first hyper polarizability of the title compound are 0.712 x 10^{-30} esu, 0.534 x 10^{-30} esu, 0.407 x 10^{-30} esu, 1.087 x 10^{-30} esu, respectively implies that the title molecule may be useful as a nonlinear optical material. The lowest singlet excited state of the molecule is mainly derived from the HOMO→LUMO (π → π*) electron transition, NBO analysis reveals that the some important intramolecular charge transfer can induce large nonlinearity to the title molecule and the intramolecular conjugative interaction around the sulfonamide group can induce the large bioactivity in the compound. We conclude that the title compound and its derivatives are an attractive object for future studies of nonlinear optical properties.

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