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Theoretical studies on S–N interactions in sulfonamides

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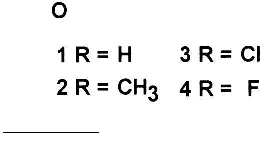
Abstract—Theoretical studies using ab initio molecular orbital and density functional methods have been carried out on sulfonamide $HS(O)_2NH_2$ to understand the S–N interactions present in the sulfonamide. Complete optimisation at HF/6-31+G*, MP2/6-31+G* and B3LYP/6-31+G* levels have shown that the NH_2 and SO_2 units are in an eclipsed arrangement. The effect of substituent on the S–N interactions has been analysed by studying, $CH_3S(O)_2NH_2$, $ClS(O)_2NH_2$ and $FS(O)_2NH_2$. Natural bond orbital analysis has been carried out to understand various interactions present in these systems. The S–N rotational barrier obtained using G2MP2 method is 6.74 kcal/mol which has been found to be more due to the repulsive interactions than the anomeric interactions. © 2002 Published by Elsevier Science Ltd.

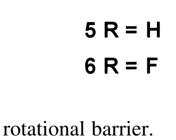
1. Introduction

The sulfonamide moiety, O_2SNR is found in several classes of biologically active compounds including antibacterials, sweeteners and herbicides etc.[1] More than 30 drugs containing this moiety are in clinical use.[2] Chiral sulfonamides[3] serve admirably as ligands for a number of different metals in the catalytic enantioselective synthesis of organic molecules. Sulfonamide S–N bonds are also formed while protecting the nitrogen center in amines, amides etc. with the tosyl group.[4] However, the removal of the tosyl group by breaking the S–N bond requires drastic conditions, which affect the rest of the molecule.[4,5]

Several studies are being carried out to efficiently break the S–N bonds;[6] increasing the acid lability of tosyl group by introducing suitable substituent in the benzene ring has led to limited success.[4] Nyasse et al.[5] have reported the use of the 2-naphthalenesulfonyl unit as a tosyl substitute for easy dissociation of the sulfonyl moiety. Microwave irradiation is being used as an effective means to break the S–N bond.[7] Understanding the basic interactions present in sulfonamides is important for efficient modification of these interactions and to design an effective protecting/leaving group. In this paper, we explore the strength of S–N interactions in sulfonamides (**1**–**4**) using ab initio MO and NBO methods and compare with S–N interactions in sulfenamides (**5**,**6**).



1 R = H **3** R = Cl
2 R = CH_3 **4** R = F



5 R = H
6 R = F

The S–N bond length in sulfonamides (~1.66 Å) is much shorter than the S–N single bond distance ~1.75 Å.[8] This is in spite of the fact that sulfonamides do not participate in N-lone pair delocalisation as in carboxamides.[9] Several theoretical studies have been performed on sulfonamide, albeit using simple theoretical methods but none of them pay attention to S–N interactions. Extensive studies using molecular mechanics and QSAR methods on sulfonamides have been reported[10] mainly to study the properties as ligands in biological host guest interactions. Topiol et al.[11] have performed semiempirical studies and ab initio calculations using a minimal basis set to obtain the conformational aspects. Mo et al.[12] have reported that the d-orbitals on sulfur are not important in describing the S–N bond, but important in describing the S–O bond from their study on sulfamide using HF/6-31+G* level. Bindal and coworkers[13] have studied the torsional potential of *N*-methylmethanesulfonamide along the S–N bond using the HF/6-31+G* level of theory for the development of force field torsional parameters. Houk and co-workers[14] have compared the conformations and electrostatic potentials of *N*-methylmethanesulfonamide with the tetrahedral intermediate for base catalysed amide hydrolysis using the HF/6-31+G* level. It had been shown that the eclipsed arrangement of the NR_2 and SO_2 is more preferred than a staggered arrangement in sulfonamide, however the origin of this preference has not been explored. The theoretical methods employed in the earlier studies include only SCF method with simple basis sets. Because of the presence of several lone pairs of electrons in sulfonamides, inclusion of electron correlation and diffuse functions in the conformational analysis is essential. The electrostatic interactions, electron delocalisation and substituent effects on the conformational aspects of these molecules have not been explored. In this paper we

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Keywords: S–N interactions; sulfonamides; rotational barrier.

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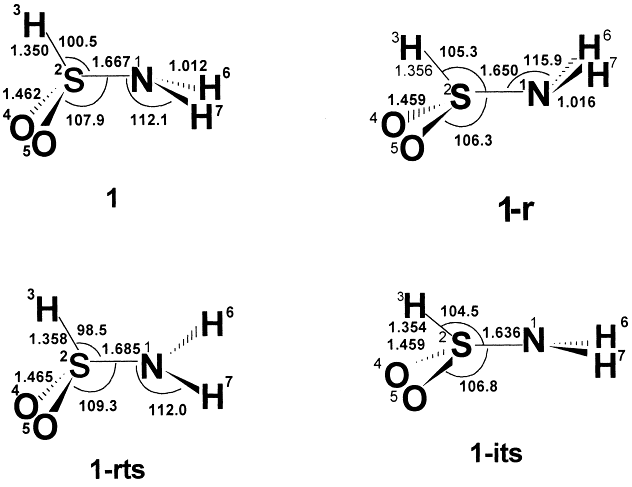

Figure 1. The structure and the geometrical parameters of **1**, **1-r**, **1-rts** and **1-its** and MP2/6-31+G* level.

Table 2. Atomic charges (NPA) of **1**, **1-r**, **1-rts**, **1-its** obtained at MP2/6-31+G* level, MP2 densities

Atom	1	1-r	1-rts	1-its
N1	−1.175	−1.152	−1.174	−1.203
S2	2.171	2.162	2.121	2.129
H3	0.029	0.010	0.023	0.035
O4	−0.953	−0.928	−0.931	−0.934
O5	−0.953	−0.953	−0.931	−0.934
H6	0.440	0.426	0.443	0.454
H6	0.440	0.435	0.443	0.454

report S–N rotational barriers and N-inversion barriers in sulfonamide **1** and analyse the anomeric interactions present to understand the S–N interactions, using high accuracy G2MP2 method. Substituent effects on the electron delocalisation have been explored using MP2/6-31+G* level and NBO analysis on CH_3, Cl, F substituted sulfonamides (**2**–**4**). This is in continuation of our work in S–N interactions in sulfinimines,[15a,b] sulfenamides,[15c] sulfilimines[15d] etc.

2. Results and discussion

On the potential energy surface of sulfonamide, $HS(O)_2NH_2$, two minima **1** and **1-r**, one rotational transition state, **1-rts** and one inversion transition state, **1-its** could be located (Fig. 1). The structural data corresponding to these structures obtained at HF/6-31+G*, MP2/6-31+G*, B3LYP/6-31+G* levels are given in Table 1. Both ground state structures **1** and **1-r** are found to have C_s symmetry, the basic difference between the two structures arising from the arrangement of $-NH_2$ group *syn* (**1**) or anti (**1-r**) with respect to the SO_2 group. The topomerisation between the two structures **1** and **1-r** is probable either through rotation around S–N or through inversion at nitrogen.

The S–N bond length in **1** is 1.636 Å at HF/6-31+G* level. After including electron correlation at MP2 and B3LYP levels the bond length elongates to 1.667 and 1.682 Å, respectively. The MP2 estimate matches well with the average (~1.66 Å) distance reported using X-ray crystal data.[8] The longer bond length at the B3LYP level is due to the overestimation of electron–electron repulsions, such overestimation by DFT methods has been reported earlier.[15,27] The S–N bond distance in **1** (1.667 Å) is shorter than the S–N single bond distance of 1.733 Å calculated for **5** but longer than the S=N double bond distance (1.596 Å) in HN=S both obtained at MP2/6-31+G* level, a similar trend is observed at HF and B3LYP levels also. This reduction in the S–N distance may be attributed to: (a) partial double bond character due to $n_N \rightarrow \sigma_{S-H}^*$ anomeric π interactions as in sulfenamides, (b) partial double bond character due to sulfur d-orbital participation, (c) electrostatic interaction between S and N, (d) a combination of these factors. The S–N bond order in **1** calculated using AIM method is 0.741, which is much smaller than the S–N bond order in **5** (1.170). Wiberg bond index in **1** (0.856) is also much smaller than that in **5** (0.971). The smaller S–N bond order and Wiberg bond order in **1** indicate that the S–N anomeric π character is very weak in **1**. The arrangement of atoms around N(1) shows pyramidal character[28] with the sum of angles around N(1) being 336.7°. The strong pyramidalisation at nitrogen also indicates a weak anomeric S–N interaction.

Table 1. Important geometrical parameters of $HS(O)_2NH_2$ and their rotational and inversion transition states obtained at HF/6-31+G*, MP2/6-31+G* and B3LYP/6-31+G* levels. Distances in Å and angles in degrees

Parameters	HF/6-31+G*				MP2/6-31+G*				B3LYP/6-31+G*			
	1	1-rts	1-r	1-its	1	1-rts	1-r	1-its	1	1-rts	1-r	1-its
N1–S2	1.636	1.652	1.620	1.612	1.667	1.685	1.650	1.636	1.682	1.701	1.663	1.647
S2–H3	1.322	1.328	1.327	1.326	1.350	1.358	1.356	1.354	1.358	1.367	1.365	1.362
S2–O4	1.425	1.421	1.423	1.424	1.462	1.465	1.459	1.459	1.462	1.465	1.458	1.460
S2–O5	1.425	1.428	1.423	1.424	1.462	1.457	1.459	1.459	1.462	1.457	1.458	1.460
N1–H6	1.001	1.002	0.996	0.997	1.019	1.021	1.016	1.013	1.018	1.020	1.015	1.012
N1–H7	1.001	1.003	0.998	0.997	1.019	1.021	1.016	1.013	1.018	1.020	1.015	1.012
N1–S2–H3	101.3	99.0	104.9	104.5	100.5	98.5	105.3	104.5	100.0	98.4	105.0	104.2
N1–S2–O4	108.3	110.1	107.1	107.3	107.9	108.8	106.3	106.8	108.3	109.1	106.6	107.0
N1–S2–O5	108.3	108.9	107.1	107.3	107.9	109.3	106.3	106.8	108.3	109.4	106.6	107.0
H6–N1–S2	113.1	113.4	117.1	119.4	112.1	109.7	115.9	119.7	111.6	109.3	115.6	119.7
H7–N1–S2	113.1	111.0	117.1	119.4	112.1	112.0	115.9	119.7	111.6	111.5	115.6	119.7
N1–S2–H3–O4	112.5	112.6	112.9	−113.3	111.8	113.4	112.6	−112.7	111.8	113.5	112.7	112.3
N1–S2–H3–O5	−112.5	246.4	−112.9	113.3	−111.8	248.0	−112.6	112.7	−111.8	248.0	−112.7	−112.3
H6–N1–S2–H3	114.6	11.6	73.3	84.1	116.2	225.8	70.3	85.5	116.8	226.5	69.6	86.5
H7–N1–S2–H3	−114.6	137.0	−73.3	−84.1	−116.2	348.2	−70.3	−85.5	−116.8	348.2	−69.6	−86.5

Table 3. Occupancy of important molecular orbitals of **1** obtained from NBO analysis

Orbital	Occupancy	Orbital	Occupancy
n_N	1.952	σ_{S-N}^*	0.136
$n_{O(1)}$	1.987	σ_{S-H}^*	0.163
$n_{O(2)}$	1.864	σ_{S-O}^*	0.111
$n_{O(3)}$	1.833		

Atomic charges obtained by using the NPA method are given in Table 2. The data indicates that the nitrogen atom possesses 1.175 units of negative charge and sulfur possesses 2.171 units of positive charge in **1**. The charge distribution is indicative of the role of strong electrostatic interactions between S and N. Schleyer and co-workers[30] argued that generalized anomeric (negative hyperconjugative) interactions lead to bond polarisation and bond shortening, accordingly the S–N bond polarisation in **1** might be due to anomeric interactions. Natural bond orbital (NBO) analysis has been carried out on **1** to understand the bonding characteristics (Table 3). The electron density on the lone pair of nitrogen $\rho(n_N)$ in **1** is 1.952, 0.048 less than is expected (2.0). NBO data shows three lone pairs each on the two oxygen atoms due to the strong ionic character of the $S^+–O^-$ bond. The electron density on the three lone pairs of O4 in **1** is 1.987, 1.864 and 1.833. This indicates that the delocalization of the oxygen lone pair is stronger than that of nitrogen in **1**. The electron density from these lone pairs on oxygen and nitrogen is distributed to the σ^* orbitals of S–H, S–N, S–O4, S–O5 bonds, as indicated by the electron density 0.136, 0.163, 0.111 and 0.111 in these orbitals, respectively. This indicates that the delocalization of lone pair electron density is in all directions in sulfonamides (which may be termed as three dimensional delocalization). Such an observation was made in CF_4 type compounds also.[28] Table 4 lists the data from the second order energy analysis, where it is clearly shown that the energies for the $n_N \rightarrow \sigma_{S-H}^*$ (5.86 kcal/mol) and $n_N \rightarrow \sigma_{S-O}^*$ (3.23 kcal/mol) interactions are weaker than the $n_O \rightarrow \sigma_{S-H}^*$ (22.01 kcal/mol), $n_O \rightarrow \sigma_{S-O}^*$ (30.04 kcal/mol) and $n_O \rightarrow \sigma_{S-N}^*$ (16.48 kcal/mol) interactions. In **1** the anomeric π_{S-N} strength gained through the $n_N \rightarrow \sigma_{S-H}^*$ (or σ_{S-O}^*) gets nullified due to the $n_O \rightarrow \sigma_{S-N}^*$ interactions. The second order energy associated with $n_N \rightarrow \sigma_{S-H}^*$ in **5** is 4.6 kcal/mol, smaller than that in **1** (5.86 kcal/mol). This indicates the $n_N \rightarrow \sigma_{S-H}^*$ anomeric interaction in **1** is stronger, but this does not increase the S–N bond order because of the $n_O \rightarrow \sigma_{S-N}^*$ interactions. The kind of three dimensional negative hyperconjugation present in **1** seems to provide additional strength to S–N and S–O bonds. As a consequence of this extra strength, the S–N bond cleavage becomes difficult in sulfonamides. Any reduction in this strength would facilitate the easy removal of the protecting tosyl group, say for example using neighbouring group assistance.[6i]

Table 4. The second order energy analysis $E^{(2)}$, energy differences (ΔE) and Fock matrix elements (F) between interacting orbitals associated with various anomeric interactions in sulfonamide **1**

Structure		$E^{(2)}$ (kcal/mol)	E_j-E_j (a.u.)	F_{ij} (a.u.)
1	$n_N \rightarrow \sigma_{S-H}^*$	5.86	0.89	0.07
	$n_N \rightarrow \sigma_{S-O}^*$	3.23	1.07	0.05
	$n_O \rightarrow \sigma_{S-N}^*$	16.48	0.82	0.11
	$n_O \rightarrow \sigma_{S-H}^*$	22.01	0.82	0.12
	$n_O \rightarrow \sigma_{S-O}^*$	30.04	0.99	0.16
1-r	$n_N \rightarrow \sigma_{S-H}^*$	10.78	0.85	0.09
	$n_N \rightarrow \sigma_{S-O}^*$	2.73	1.05	0.05
	$n_O \rightarrow \sigma_{S-N}^*$	24.61	0.80	0.13
	$n_O \rightarrow \sigma_{S-H}^*$	22.61	1.00	0.14
	$n_O \rightarrow \sigma_{S-O}^*$	27.79	0.79	0.13
1-rts	$n_N \rightarrow \sigma_{S-H}^*$	0.71	0.88	0.02
	$n_N \rightarrow \sigma_{S-O}^*$	5.83	1.07	0.07
	$n_N \rightarrow \sigma_{S-O}^*$	7.77	1.08	0.08
	$n_O \rightarrow \sigma_{S-N}^*$	14.62	0.81	0.10
	$n_O \rightarrow \sigma_{S-H}^*$	23.25	1.00	0.12
	$n_O \rightarrow \sigma_{S-O}^*$	29.38	0.99	0.16
1-its	$n_N \rightarrow \sigma_{S-H}^*$	11.66	0.82	0.09
	$n_N \rightarrow \sigma_{S-O}^*$	3.60	1.01	0.05
	$n_O \rightarrow \sigma_{S-N}^*$	14.59	0.85	0.10
	$n_O \rightarrow \sigma_{S-H}^*$	22.65	0.82	0.12
	$n_O \rightarrow \sigma_{S-O}^*$	29.34	0.99	0.16

The S–N bond length in **1-r** is 1.650 Å (Table 1) at MP2/6-31+G* level which is smaller as compared to that in conformation **1** by 0.017 Å. The decrease in S–N bond distance is accompanied by an increase in S–H bond distance (0.005 Å), and an increase in the N1–S2–H3 angle (3.6°), decrease in N pyramidalisation (sum of angles around nitrogen 339.7°) increase in $n_N \rightarrow \sigma_{S-H}^*$ interaction energy (Table 4) suggesting an increase in the negative hyperconjugation.[20] The absolute energies and the ZPE values of **1** and its related structures are given in Table 5, the relative energy values are reported in Table 6. The conformation **1-r** is 1.59 kcal/mol higher in energy compared to **1** at HF/6-31+G* level. The ΔE between **1** and **1-r** decreases with the increase in the complexity of the quantum mechanical level, at the G2MP2 level it is 0.66 kcal/mol. Conformer **1** has an eclipsed arrangement and **1-r** has a staggered arrangement, hence **1-r** is expected to have lower energy. The lower energy for **1-r** is also expected because of the stronger $n_N \rightarrow \sigma_{S-H}^*$ hyperconjugation in **1-r** compared to that in **1**. But the energy of conformer **1** is lowest at all the levels. This indicates that the repulsions between the lone pairs of electrons on N and O are very strong in **1-r** (stronger than the destabilization in **1** due to eclipsing and the extra stabilization due to the stronger anomeric effect in **1-r**) and make it relatively unstable.

The inversion transition structure **1-its** has S–N bond distance of 1.636 Å (decreases by 0.031 Å relative to **1**) at MP2/6-31+G* level. The S2–H3 bond distance increases by 0.004 Å and the bond angle N1–S2–H3 increases by 4.0° (Table 1) and the $E^{(2)}$ for the $n_N \rightarrow \sigma_{S-H}^*$ delocalisation increases by 6.80 kcal/mol relative to **1**. All these factors indicate stronger negative hyperconjugation in **1-its** compared to that in **1**. This is also reflected by low inversion barriers. The N-inversion barrier in **1** is 1.20 kcal/mol at MP2/6-31+G* and 0.64 kcal/mol at G2MP2 level (Table 6). The N-inversion barrier in **5** at G2MP2 level is 1.79 kcal/mol. The smaller inversion barrier in **1** relative to **5** indicates stronger donation of the nitrogen lone pair in **1**, which is also supported by the second order energy analysis.

In the rotational transition state **1-rts**, the lone pair of nitrogen is in plane with one of the S–O bonds. The $n_N \rightarrow \sigma_{S-O}^*$ interaction is stronger than the $n_N \rightarrow \sigma_{S-H}^*$

Table 5. Absolute energies (in a.u.) and zero point vibrational energies (ZPE) (in kcal/mol) of $HS(O)_2NH_2$ in its **1**, **1-r**, **1-rts** and **1-its** conformation at various levels

Method	**1**	**1-rts**	**1-r**	**1-its**
HF/6-31+G*	−603.335589	−603.322639	−603.332606	−603.332569
HF/6-31+G*	−603.344493	−603.331359	−603.342087	−603.341957
MP2/6-31+G*	−604.019915	−604.007189	−604.017407	−604.017011
B3LYP/6-31+G*	−605.121764	−605.110576	−605.119516	−605.119007
B3PW91/6-31+G*	−604.995928	−604.984568	−604.993876	−604.993432
G2MP2	−604.442791	−604.432045	−604.441738	−604.441759
ZPE	29.23	28.88	29.06	28.61

Table 6. Relative energies (ΔE) and S–N rotational barrier (in kcal/mol) and N-inversion barriers of sulfonamide at various theoretical levels. ZPE corrected values are given in parentheses

Method	**1→1-r** ΔE	**1→1-rts** rotational barrier	**1→1-its** inversion barrier
HF/6-31+G*	1.87 (1.59)	8.13 (7.64)	1.90 (1.25)
HF/6-31+G*	1.51 (1.34)	8.24 (7.71)	1.59 (0.97)
MP2/6-31+G*	1.57 (1.40)	7.98 (7.63)	1.82 (1.20)
B3LYP/6-31+G*	1.41 (1.24)	7.02 (6.67)	1.73 (1.11)
B3PW91/6-31+G*	1.29 (1.12)	7.13 (6.78)	1.57 (0.95)
G2MP2	– (0.66)	– (6.74)	– (0.64)

interaction (Table 4) and hence stronger anomeric stabilization is expected in **1-rts** compared to **1** and **1-r**. For example, the S–N distance in **1** increases only by 0.016 Å during rotation, whereas the S–N distance increases by 0.042 Å in **5** during rotation. However, in **1-rts** the repulsions between lone pairs on nitrogen and oxygen are stronger, which destabilizes the structure. These two opposing factors influence the S–N rotational path. The S–N rotation barrier in **1** at HF/6-31+G* (+ZPE) level is 7.64 kcal/mol. With the inclusion of electron correlation using MP2/6-31+G* level, the barrier is calculated to be 7.63 kcal/mol. After including the diffused functions, the barrier increased by ~0.07 kcal/mol. Inclusion of electron correlation using density functional B3PW91 and B3LYP methods reduces the barrier significantly to 6.78 and 6.67 kcal/mol, respectively. At the G2MP2 level the S–N rotational barrier in **1** is 6.74 kcal/mol. The higher rotational barrier in **1** can be attributed to the lone pair–lone pair repulsions in **1-rts**. The negative hyperconjugative ($n_N \rightarrow \sigma_{S-H}{}^*$) interaction is not responsible to the high rotational barrier in sulfonamides because both **1** and **1-rts** have anomeric interactions. This is in contrast with the observations made on **5** where the equally high rotational barriers (6.57 kcal/mol at G2MP2) have been found to be due to anomeric interactions.[29b]

3. Substituent effects

Electronegative substituents like –F and –Cl reduce the energy of the σ^* orbitals and increase the strength of the negative hyperconjugative interaction. To understand the influence of methyl, chlorine and fluorine substitution on the S–N interactions in substituted sulfonamides, HF/6-31+G* and MP2/6-31+G* calculations on $CH_3S(O)_2NH_2$ (**2**), $ClS(O)_2NH_2$ (**3**) and $FS(O)_2NH_2$ (**4**) have been performed. Important geometrical parameters, rotational barriers, charges and orbital occupation of some molecular orbitals corresponding to **1**–**4** are listed in Table 7. The S–N and S–O bond lengths decrease with an increase in the electron withdrawing nature of X in $XS(O)_2NH_2$ in the order $CH_3>H>Cl>F$. The N-inversion barriers in **3**,**4** are much less than that in **1** and the inversion barrier in **2** is larger than that in **1**. Table 8 shows the details of second order interactions in **2**–**4**. The $n_N \rightarrow \sigma_{S-X}{}^*$ and $n_O \rightarrow \sigma_{S-X}{}^*$ delocalisations are much stronger in **3** and **4** supporting the increased anomeric interactions. The stabilization due to CH_3, Cl and F substitution in **1** is 13.55, 16.2 and 32.6 kcal/mol, respectively, calculated using isodesmic equation (Eq. (1)) (Table 9). The variation in the bond lengths, angles, inversion barriers, stabilization energies, atomic charges and second order interactions indicate stronger anomeric interactions in **4** compared to **1**.

Table 7. Important geometrical parameters, rotational barriers, inversion barriers, NPA charges and orbital occupancies of sulfonamide $XS(O)_2NH_2$ at MP2/6-31+G* level

Parameters	H (**1**)	CH_3 (**2**)	Cl (**3**)	F (**4**)
S–N[a]	1.667	1.685	1.650	1.645
S–O[a]	1.462	1.468	1.454	1.448
N–S–O[b]	107.9	107.5	108.3	109.7
N–S–X[b]	100.5	102.1	101.7	99.1
Sum of angles around nitrogen	336.7	335.2	345.0	320.4
ΔE[c]	1.57	2.55	−1.00	−1.64
S–N rotational barrier[d]	7.98	7.57	4.79	4.13
N-Inversion barrier[d]	1.82	3.63	0.18	0.45
Atomic charges				
S	2.171	2.335	2.261	2.592
N	−1.174	−1.166	−1.154	−1.157
O	−0.953	−0.962	−0.906	−0.195
X	0.029	−0.119	−0.195	−0.506
Electron density				
$\rho(n_N)$	1.952	1.956	1.934	1.931
$\rho(\sigma_{S-X}{}^*)$	0.136	0.124	0.277	0.307
$\rho(\sigma_{S-O}{}^*)$	0.111	0.112	0.124	0.107

[a] Bond length in Å.
[b] Angles in degrees.
[c] In kcal/mol.
[d] In kcal/mol.

Table 8. The second order energy analysis $E^{(2)}$, energy differences (ΔE) and Fock matrix elements (F) between interacting orbitals associated with various anomeric interactions in substituted sulfonamide **1**

Structure		$E^{(2)}$ (kcal/mol)	E_j-E_i (a.u.)	F_{ij} (a.u.)
2	$n_N \rightarrow \sigma_{S-C}^*$	10.25	0.86	0.09
	$n_N \rightarrow \sigma_{S-O}^*$	2.32	1.05	0.04
	$n_O \rightarrow \sigma_{S-N}^*$	20.56	0.81	1.11
	$n_O \rightarrow \sigma_{S-C}^*$	22.60	0.81	0.12
	$n_O \rightarrow \sigma_{S-O}^*$	27.56	0.99	0.15
3-r	$n_N \rightarrow \sigma_{S-Cl}^*$	19.04	0.62	0.10
	$n_N \rightarrow \sigma_{S-O}^*$	1.67	1.06	0.04
	$n_O \rightarrow \sigma_{S-N}^*$	29.33	0.83	0.14
	$n_O \rightarrow \sigma_{S-Cl}^*$	46.79	0.54	0.15
	$n_O \rightarrow \sigma_{S-O}^*$	18.14	1.00	0.12
4-r	$n_N \rightarrow \sigma_{S-F}^*$	20.48	0.73	0.11
	$n_N \rightarrow \sigma_{S-O}^*$	1.25	1.09	0.03
	$n_O \rightarrow \sigma_{S-O}^*$	26.05	0.85	0.13
	$n_O \rightarrow \sigma_{S-F}^*$	54.51	0.65	0.17
	$n_O \rightarrow \sigma_{S-O}^*$	10.64	1.48	0.14

Table 9. Stabilization energies of the ground state, rotational transition state and inversion transition state of substituted sulfonamide $XS(O)_2NH_2$ at MP2/6-31+G* level

X	-r	-rts	-its
2	12.5	17.0	11.6
3	18.8	22.6	17.9
4	35.8	40.0	38.3

$$XS(O)_2NH_2 + SH_2 \rightarrow HS(O)_2NH_2 + XSH \quad (1)$$

$$XS(O)_2NH_2(RTS) + SH_2 \rightarrow HS(O)_2NH_2(RTS) + XSH \quad (2)$$

The increased anomeric interactions upon substitution by electronegative elements should increase the S–N rotation barriers if anomeric π interactions are important. This has been observed in the case of **5**, the rotational barrier of which increases from 8.04 to 20.20 kcal/mol at MP2/6-31+G* level upon fluorine substitution. However, the S–N rotational barriers in sulfonamides **3** and **4** (4.79 and 4.13 kcal/mol, respectively) are less than the rotational barrier in **1** (7.98 kcal/mol, all values at MP2/6-31+G* level). This might be due to two reasons: (1) the anomeric interactions in sulfonamides do not induce additional π character between S and N. This might be originating from the fact that the $n_N \rightarrow \sigma_{S-R}^*$ as well as $n_O \rightarrow \sigma_{S-N}^*$ interactions are strongly operative in sulfonamides; (2) the rotational transition states **3-rts** and **4-rts** possess stronger anomeric interactions in comparison to ground state structures **3** and **4**, respectively. This is evident from the greater stabilization energies (isodesmic Eq. (2)) of **4-rts** (40.0 kcal/mol) compared to **4** (3.58 kcal/mol).

The above observations indicate that the anomeric interactions in sulfonamides do not lead to any additional π character. Hence, the smaller bond lengths in sulfonamides are not due to anomeric interactions but due to electrostatic interactions between positively charged sulfur and negatively charged nitrogen. The importance of electrostatic interactions in sulfonamides is furthur evidenced by the fact that for $FS(O)_2NH_2$, a staggered arrangement (**4-r**) is more stable than an eclipsed arrangement (**4**) by 1.64 kcal/mol in an apparent reversal of stability order found in **1** and **1-r**.

4. Computational methods

Ab initio molecular orbital (MO)[16] and density functional calculations (DFT)[17] have been carried out using the GAUSSIAN94W[18] package, windows version of GAUSSIAN94 suite of programs. Complete optimizations have been performed on sulfonamide, **1** its rotational, N-inversion conformers and corresponding transition states using the HF/6-31+G*[19] basis set. Since the molecule possesses several lone pairs of electrons, inclusion of diffuse functions in the basis set is important[16] and hence all the structures have been completely optimised at HF/6-31+G* level also. To study the effect of electron correlation on the geometries and energies, complete optimisations have been performed using MP2/6-31+G*,[20] B3LYP/6-31+G*[21] and B3PW91/6-31+G*[22] levels. Final energies have been calculated using the high accuracy G2MP2[23] method. Frequencies were computed analytically for all optimised species at HF/6-31+G* level in order to characterize each stationary point as a minimum or a transition state and to determine the zero point vibrational energies (ZPE). The ZPE values obtained at HF/6-31+G* level have been scaled by a factor of 0.9153.[24] Atomic charges in all the structures were obtained using the natural population analysis (NPA) method within the NBO approach[25] with the MP2 densities using MP2/6-31+G* geometries to understand the electron distribution in these molecules. Second order energy analysis has been carried out using the NBO method to understand the delocalizations present in sulfonamides at Mp2/6-31+G* level. Wiberg bond indices have been obtained using the NBO method and bond orders have been calculated using atoms in molecules (AIM) method.[26] The MP2/6-31+G* geometries and G2MP2 energies are employed in the discussion unless otherwise specifically mentioned.

5. Conclusions

Ab initio molecular orbital calculations on sulfonamide $HS(O)_2NH_2$ at the G2MP2 level showed that the S–N rotational barrier is 6.74 kcal/mol and N-inversion barrier is 0.64 kcal/mol. The short S–N distances observed in these molecules can be attributed to the electrostatic attractions between S (2.17) N (−1.174) but not due to any π character between S and N. The high rotational barrier however can be attributed to the intramolecular lone pair repulsions rather than to the anomeric π interactions, because anomeric interactions in the rotational transition structure are found to be stronger than those in the minima. The three dimensional anomeric delocalisation of lone pair electron density in the $O_2S–N$ unit of sulfonamides and the strong charge localization on S and N are the basic strengths of S–N interactions in sulfonamides. Substituent effects studied using CH_3, Cl and F substituents also support the above observations.

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