



Conformational analysis, vibrational and NMR spectroscopic study of the methanesulfonamide-N,N'-1,2-ethanediylbis

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ABSTRACT

A conformational analysis of the methanesulfonamide-N,N'-1,2-ethanediylbis (msen) was performed by using vibrational and NMR spectroscopies as well as theoretical computations. The possible stable conformers of msen on its potential energy surface were investigated by semi-empirical PM5 method and appropriate structures were defined with B3LYP hybrid density functional theory (DFT) method along with the basis sets of different size and type. Six different rotational isomers were found as the result of DFT calculation. The two isomer, called trans-trans-gauche⁺-eclipsed, synperiplanar (ttg⁺-e,bis) and trans-gauche⁺-gauche⁻-staggered, antiplanar (tg⁺g⁻-s,anti), were considered in the vibrational spectral analysis. The infrared (4000–30 cm⁻¹) and Raman (4000–60 cm⁻¹) spectra of msen were measured in solid state. For a complete assignment of the vibrational spectra, DFT calculations at B3LYP/6311-G(d,p) theory level combined with scaled quantum mechanics force field (SQMFF) methodology was performed. Furthermore, ¹³C and ¹H NMR analyses were performed for six conformers at B3LYP/6-311++G(d,p) level of theory and compared with the experimental findings. Results from experimental and theoretical data showed the ttg⁺-e,bis to be the most stable form of a msen molecule.

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1. Introduction

Sulfonamides are important bacteriostatic agents still commonly used in human and veterinary medicine. Sulfonamide derivatives are of considerable interest and have been used extensively as antimicrobial [1], antifungal [2], antimalarial [3], or antitumor activity [4,5], carbonic anhydrase inhibitors [6], diuretic or hypoglycaemic reagents [7,8] and also as pharmaceutical agents for the treatment of different diseases such as infections [9] Alzheimer's disease [10] or HIV [11]. Due to their significant pharmacology applications and widespread use in medicine, these compounds have gained importance in bio-inorganic and metal-based drug chemistry.

In our previous studies, we have reported conformational analysis and vibrational spectroscopic studies of the methanesulfonic acid hydrazide [12], methanesulfonic acid 1-methylhydrazide [13] and some methanesulfonyl hydrazone derivatives [14–16]. As a part of our ongoing studies, the aims of the present work is to

interpret the conformational behavior of methanesulfonamide-N,N'-1,2-ethanediylbis (msen), as well as its FT-IR, far-infrared, dispersive Raman and NMR spectra from experimental and theoretical viewpoints as a contribution to the understanding of the rational drug design of sulfonamide derivatives.

2. Experimental

2.1. Instrumentation

The elemental analyses (C, H, N and S) were performed by a Fisons EA-108 type elemental analyzer. The mass spectrum was recorded on Agilent 1100 LC/MS-APCI at 100 eV. Thin layer chromatography (TLC) was conducted on 0.25 mm silica gel plates (60F254, Merck). All NMR spectra of the compound were recorded on a Bruker WM-400 spectrometer at ambient probe temperature using DMSO-*d*₆ solutions with tetramethylsilane as internal reference. The FT-IR (4000–400 cm⁻¹) spectra between KBr pellet technique and far-infrared (600–30 cm⁻¹) spectra between polyethylene pellet technique of the sample were recorded using a Bruker Optics IFS66v/s FT-IR spectrometer with 2 cm⁻¹ resolution in vacuum. The dispersive Raman spectrum was recorded using

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a Bruker Senterra Dispersive Raman microscope spectrometer at 532 nm excitation from a doubled Nd/YAG laser having 3 cm^{-1} resolution between 3700 and 60 cm^{-1} spectral region.

2.2. Synthesis of msen

The chemicals were obtained from Sigma–Aldrich Co. and used without further purification. The msen compound was prepared in accordance with the procedure of Alyar et al. [17]. The nucleophilic substitution reaction of the ethylenediamine with methanesulfonyl chloride was carried out as follows:

Msen was prepared by adding dropwise of ethylenediamine (0.08 mol, 5.4 mL) to an ice-cold stirred solution of the methanesulfonyl chloride (0.04 mol, 3.1 mL) in tetrahydrofuran (25 mL) solution, maintaining the temperature between -5 and -10°C . The whole mixture was stirred around one day and then the solvent was evaporated. The obtained solid residue was crystallized from tetrahydrofuran mixture. The polycrystalline sample was dried in a vacuo and stored at tetrahydrofuran vapor.

The synthesized polycrystalline compound was firstly characterized by mass spectrometry and elemental analysis techniques. The experimental findings were given below:

Yield 2.6 g (91%); m.p. 116°C , APCI-MS (100 eV) m/z : 216 (M^+ , 100.0%; M^{1+} , 4.6%; M^{2+} 9.1%); Anal. for $C_4H_{12}S_2O_4N_2$ (calculated %/found %): C (60.22/59.46), H (5.05/5.01), N (16.21/15.89) and S (29.79/29.62).

3. Theoretical

Potential energy surfaces (PES) of the title molecule were primarily obtained in order to get the more stable conformers of msen. Therefore, PES were determined via MOPAC2002 geometry optimization by using semi-empirical PM5 Hamiltonian within Fujitsu CAChe WS Pro v.7.5.0 Windows software package [18] on a personal workstation for the possible stable structures of msen where the torsion angles around the free rotation bonds were iteratively changed by 10° . The appropriate structures were then selected by considering the heat of formation energy (ΔH) values were lower than -152.00 kcal/mol .

For the selected structures, local minima or transition states on the PES were then examined through geometric optimization and vibrational frequency analysis by using Becke's three-parameter exchange functional [19] in combination with the Lee–Yang–Parr correlation functional [20] (B3LYP) density functional theory (DFT) method. All conformers were initially examined with 6-31G(d) basis set and the stability of each conformers were also tested with 6-311G(d,p) and 6-311++G(d,p) basis sets at same theory level by using the Gaussian03W program package [21].

From our calculations, twelve conformers were obtained which were reduced to six using the mirror reflection symmetry operation (σ). The conformers were identified as five letters ($a^\pm b^\pm c^\pm$, $e, d^\pm$) by using Newman projection. The first three letters ($a^\pm b^\pm c^\pm$), t (trans) or $g^\pm$ (gauche $^\pm$), refer to the skeletal atom conformation relative to C_{12} – C_9 , C_{12} – N_{15} and C_9 – N_8 bonds on the ethylenediamine moiety of msen proposed by Kudoh et al. [22], where plus and minus signs in a superscript refer to opposite angles around relevant rotational axes. The fourth letter, eclipsed (e) or staggered (s), represents the oxygen atoms of sulfur dioxides and methyl groups in Newman projection corresponding to non-bonding S_{18} – S_1 axis and the last letter, synperiplanar (bis), antiplanar ($anti$), anticlinal $^\pm$ ($ac^\pm$) or synclinal $^\pm$ ($sc^\pm$) indicates the position of the methyl groups.

The vibrational spectrum combined with quantum chemical computations has been widely used for the conformational analysis of drug molecules or biological compounds during the last two decades. However, the assignment of vibrational spectral lines

Table 1

The scale factors used in the SQM FF methodology for internal coordinates at B3LYP/6-311G(d,p) theory level.

Scaling factors ^a	Value			
	Unscaled	Ref. [24]	Ref. [25]	In this study
C–C stretching	1.0000	0.9207	0.9271	0.9954
C–N stretching	1.0000	0.9207	0.9271	0.9954
C–S stretching	1.0000	0.9207	1.0332	1.0341
S–O stretching	1.0000	0.9207	1.0332	1.0341
S–N stretching	1.0000	0.9207	1.0332	1.0341
C–H stretching	1.0000	0.9164	0.9204	0.9162
N–H stretching	1.0000	0.9242	0.9242	0.8394
X–X–X bending	1.0000	1.0144	0.9909	0.9074
X–X–H bending	1.0000	0.9431	0.9497	0.9421
H–C–H bending	1.0000	0.9016	0.9016	0.9069
All torsions	1.0000	0.9523	0.9488	0.9811

^a X denotes any non-hydrogen atom such as carbon, oxygen, nitrogen or sulfur.

relevant of a specific molecular geometry often cannot be decided uniquely from the spectra alone. Corroborative chemical or other physical features such as relative energies, thermodynamic factors, NMR chemical shifts, intramolecular, intermolecular or weak hydrogen bonding, lone pair effect, including steric hindrance are necessary to understand conformational spectral features. For this reason, the relative energies of each conformer were taken into account with the purpose of getting the most stable form. To support this purpose, a population analyses were also made for the stable conformers due to their Gibbs free energy (ΔG) as in Ref. [23].

It is well-known that the vibrational wavenumbers obtained by DFT computations usually overestimate than their experimental counterpart. These discrepancies can be corrected either by computing anharmonic corrections or by introducing a scaled field. In order to compensate these systematic errors and also to get precise vibrational wavenumbers for msen in solid phase, we calibrated the vibrational wavenumbers by using a scale factor group for 11 individual primitive internal coordinates at B3LYP/6-311G(d,p) level of theory. The vibrational wavenumbers were scaled by using the scaling factors for primitive coordinates proposed by Baker et al. [24], Collier et al. [25] or by using the effective scaling frequency factors (ESFF) [26]. The scale factor values used in the scaled quantum mechanics force field (SQM FF) methodology for internal coordinates are given in Table 1. The assignments of each vibrational mode were defined from their potential energy distributions (PED) which were calculated by using SQM program [27].

The scaling factors were not applied to the infrared and Raman intensities. The relative Raman intensity (I^R), which simulates the measured Raman spectrum, was calculated by using the following relation derived from the intensity theory of Raman scattering [28,29];

$$I_i^R = \frac{f(\nu_0 - \nu_i)^4 S_i}{\nu_i [1 - \exp(-h\nu_i/kT)]} \quad (1)$$

where ν_0 is the exciting frequency ($18,798\text{ cm}^{-1}$), ν_i is the vibrational wavenumber of the i^{th} normal mode (in cm^{-1} units), S_i is the Raman scattering activity of the normal mode q_i , h , c , k are fundamental constants, $T = 298.15\text{ K}$ and $f(10^{-14})$ is a suitably chosen common normalization factor for all peaks. For the plots of simulated IR and Raman spectra, pure Lorentzian band shapes were used with a bandwidth of 10 cm^{-1} .

Nuclear magnetic resonance properties of the six conformers were calculated at B3LYP/6-311++G(d,p) theory level by using gauge including atomic orbital (GIAO) method [30,31] as implemented in Gaussian 03W program package. Isotropic shielding tensors of ^{13}C were changed into chemical shifts by using a linear relationship suggested by Blanco et al. [32]. A similar relationship

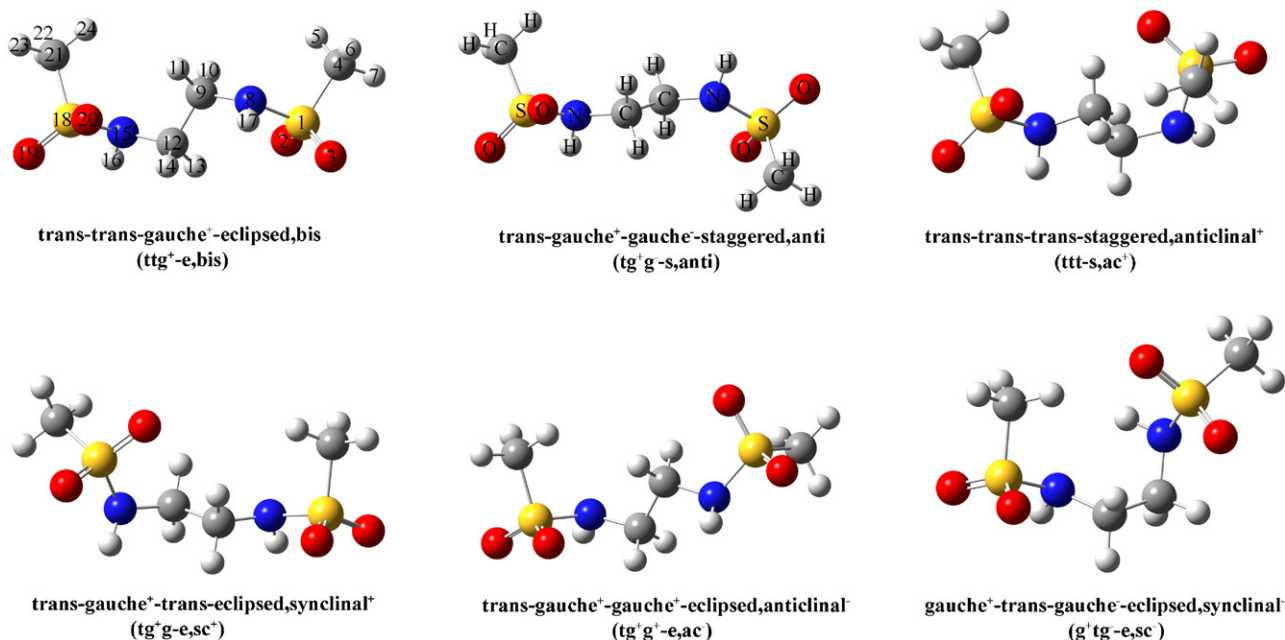


Fig. 1. The illustration of the six possible stable conformers of msen.

proposed by Silva et al. [33] was used to obtain chemical shifts for ¹H.

4. Results and discussion

4.1. Stability of the conformers

The results of the DFT computations have clearly demonstrated that msen has six possible stable conformers at room-temperature. The skeletal atomic conformations of each conformer were labeled according to Newman projection as given in the theoretical part of the manuscript (see Fig. 1). The calculated relative energies of these possible stable conformers at B3LYP/6-311++G(d,p) theory level is presented in Table 2 with respect to the zero point energy (ZPE), self-consistent field (SCF) and Gibbs free energy (ΔG) calculated for the conformer trans-trans-gauche⁺-eclipsed, synperiplanar (ttg⁺-e,bis) which was obtained as the most stable rotational isomer. As can be seen from Table S1 (Supporting Information), ZPE and SCF energies are not great and the stability order for the possible stable

conformers of the msen remains the same with the basis sets. On account of the relative energies and population analysis results, the ttg⁺-e,bis and tg⁺g⁺-s,anti rotational isomers were considered in the vibrational spectral analysis.

4.2. Vibrational spectral data

The msen consists of 24 atoms, so it has 66 normal vibrational modes and its all stable conformers belong to the point group C₁ with only identity (E) symmetry operation. It is difficult to offer an explanation for the vibrational assignments of title compound in the observed vibrational spectra due to its low symmetry. Hence, the proposed assignment of the vibrational bands of msen was made by taking into consideration the data reported in the literature for compounds which contain similar molecular groups [12–14,22,34–41]. Moreover, we made a direct comparison for the bond stretching force constants of ttg⁺-e,bis and tg⁺g⁺-s,anti isomers of msen and the literature data for some relevant compounds [12,35–38]. It is perhaps not completely appropriate because of

Table 2

The selected molecular properties of the possible stable conformers of msen molecule at DFT B3LYP method with 6-311++G(d,p) basis set.

Symmetry	ttg ⁺ -e,bis C ₁	ttt-s,ac ⁺ C ₁	tg ⁺ t-e,sc ⁺ C ₁	tg ⁺ g ⁺ -e,ac ⁺ C ₁	tg ⁺ g ⁺ -s,anti C ₁	g ⁺ tg ⁺ -e,sc ⁺ C ₁
μ_{TOTAL} (Debye)	5.80	1.68	5.99	4.75	1.80	8.27
E_{HUMO} (eV)	−0.67	−0.69	−0.75	−0.77	−0.79	−0.74
E_{LUMO} (eV)	−7.77	−7.56	−7.86	−7.97	−7.88	−7.89
$\Delta E_{\text{HUMO-LUMO}}$ (eV)	7.10	6.87	7.11	7.20	7.09	7.15
ΔZPE (kcal/mol)	–	0.21	0.35	1.00	1.07	1.83
ΔSCF (kcal/mol)	–	0.29	0.36	1.02	1.20	2.54
$\Delta \Delta G$ (kcal/mol)	–	0.36	0.57	0.74	0.11	0.83
N_i (%)	30.49	16.46	11.59	8.84	25.30	7.32
Dihedral angles (°)						
D(N ₁₅ C ₁₂ C ₉ N ₈)	177.98	171.22	−179.09	−179.71	179.69	55.19
D(C ₉ C ₁₂ N ₁₅ S ₁₈)	−88.03	73.76	166.58	−92.65	128.98	76.53
D(C ₁₂ C ₉ N ₈ S ₁)	76.81	73.76	78.87	167.26	−157.22	−152.87
D(C ₁₂ N ₁₅ S ₁₈ C ₂₁)	117.56	89.80	−90.80	109.88	−111.77	133.83
D(C ₉ N ₈ S ₁ C ₄)	104.20	89.80	103.29	−101.45	113.87	99.58
D(C ₂₁ S ₁₈ S ₁ C ₄)	8.76	121.91	73.45	−111.39	160.73	−67.63

The relative energies of the conformers were given in respect to the calculated self-consistent field (SCF), zero point energy (ZPE) and Gibbs free energy (ΔG) of the trans-trans-gauche⁺-eclipsed-bis (ttg⁺-e,bis) conformer.

Table 3The bond stretching force constants (mydne/Å) of $\text{ttg}^+\text{-e,bis}$ and $\text{tg}^+\text{g}^-\text{-s,anti}$ isomers calculated at B3LYP/6-311G(d,p) theory level.

Parameter	$\text{ttg}^+\text{-e,bis}$				Parameter	$\text{tg}^+\text{g}^-\text{-s,anti}$			
	Unscaled	Ref. [24]	Ref. [25]	In this study		Unscaled	Ref. [24]	Ref. [25]	In this study
S1—O2	9.056	8.338	9.357	9.365	S1—O2	9.262	8.528	9.570	9.578
S1—O3	9.260	8.526	9.568	9.576	S1—O3	9.180	8.452	9.485	9.493
S18—O19	9.223	8.492	9.529	9.538	S18—O19	9.243	8.510	9.550	9.559
S18—O20	9.115	8.392	9.417	9.425	S18—O20	9.204	8.474	9.509	9.518
N15—H16	7.036	6.503	6.476	5.906	N15—H16	6.957	6.429	6.403	5.839
N8—H17	7.007	6.476	6.449	5.881	N8—H17	7.070	6.534	6.507	5.935
C4—H5	5.409	4.957	4.979	4.956	C4—H5	5.434	4.980	5.002	4.979
C4—H6	5.441	4.986	5.008	4.985	C4—H6	5.419	4.966	4.987	4.965
C4—H7	5.394	4.943	4.964	4.942	C4—H7	5.394	4.943	4.965	4.942
C21—H22	5.428	4.974	4.996	4.973	C21—H22	5.442	4.987	5.009	4.986
C21—H23	5.389	4.939	4.960	4.937	C21—H23	5.394	4.943	4.964	4.942
C21—H24	5.431	4.977	4.999	4.976	C21—H24	5.414	4.961	4.983	4.960
C9—H10	5.282	4.840	4.861	4.839	C9—H10	5.271	4.831	4.852	4.830
C9—H11	5.214	4.778	4.799	4.777	C9—H11	5.143	4.713	4.734	4.712
C12—H13	5.339	4.893	4.914	4.892	C12—H13	5.091	4.665	4.686	4.664
C12—H14	5.143	4.713	4.733	4.712	C12—H14	5.295	4.852	4.873	4.851
C9—N8	4.912	4.523	4.544	4.890	C9—N8	4.911	4.521	4.553	4.888
C12—N15	4.792	4.412	4.442	4.770	C12—N15	4.814	4.433	4.463	4.792
C9—C12	4.203	3.870	3.897	4.184	C9—C12	4.244	3.907	3.935	4.225
S1—N8	3.956	3.642	4.087	4.091	S1—N8	3.909	3.599	4.038	4.042
S18—N15	3.775	3.476	3.901	3.904	S18—N15	3.791	3.491	3.917	3.921
C1—S4	3.023	2.783	3.123	3.126	C1—S4	3.032	2.791	3.132	3.135
C18—S21	3.017	2.778	3.117	3.120	C18—S21	3.025	2.785	3.126	3.128

the differently defined force fields. Nevertheless, the scaled bond stretching force constant values especially with respect to ESFF seem to be in the expected range in Table 3.

Before offering an explanation for the vibrational assignments of msen in solid state, FT-IR, far-infrared and dispersive Raman spectra of msen and comparison with calculated spectra of $\text{ttg}^+\text{-e,bis}$ and $\text{tg}^+\text{g}^-\text{-s,anti}$ isomers are given in Figs. 2–4. The vibrational data of this comparison is also tabulated in Table 4; see also Tables S2–S4 (Supporting Information) for the descriptions of all vibrational modes.

4.2.1. N–H vibrations

The N–H stretching vibration of secondary amine groups of some aliphatic sulfonamides occurs in the region $3300\text{--}3200\text{ cm}^{-1}$ [42]. Experimentally, the strong bands at 3261 cm^{-1} (IR) and 3259 cm^{-1} (Raman) are assigned to the N–H stretching mode of msen. The band corresponding to N–H in-plane bending vibration is expected near 1400 cm^{-1} [12,14,35,36,38,42]. Generally this band is masked by the band of CH_3 antisymmetric bending or the band of SO_2 antisymmetric stretching. However, very weak intense Raman active band observed at 1387 cm^{-1} is assigned to N–H in-plane bending vibration due to having 29% of PED value of mode 46. The band observed at 1418 cm^{-1} in the FT-IR and at 1416 cm^{-1} in the Raman spectra of msen are attributed to N–H in-plane bending mode, even though the corresponding band of both isomers is obscured by mode 48 or 49 (CH_3 antisymmetric bending mode) in the calculated vibrational spectra. The calculated PED contribution ($\gamma\text{N8-H}$; 25%) and infrared intensity of mode 22 suggest that the infrared active medium band at 539 cm^{-1} is the fundamental band of out-of-plane bending vibration of N–H. However, N–H out-of-plane bending band is observed above 600 cm^{-1} with respect to literature data [12,14,38]. The difference between experimental and calculated wavenumber of related band is around 26 cm^{-1} . These incompatibility offers that there may be inter- or intramolecular hydrogen bonding by the NH moiety of msen.

4.2.2. C–H vibrations

The C–H stretching vibrations of aliphatic compounds are observed slightly below 3000 cm^{-1} . The bands in the range of $3023\text{--}2856\text{ cm}^{-1}$ are due to C–H stretching modes of the methyl

CH_3 and methylene CH_2 groups of msen. In fact, the assignment of the vibrations of methylene group is very difficult because of the presence of the methyl group. However, the antisymmetric vibrations of CH_3 group have reported above 3000 cm^{-1}

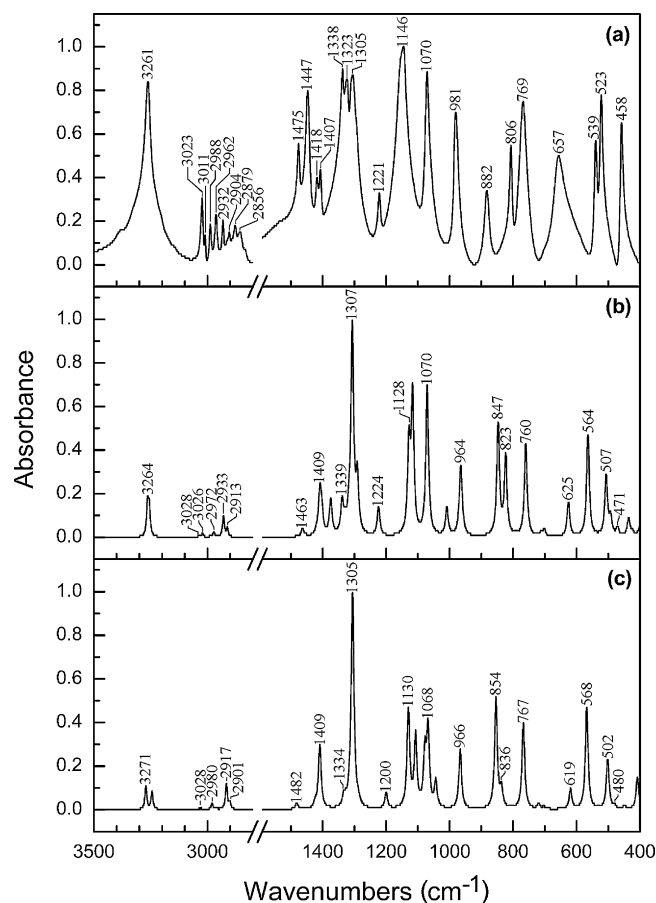


Fig. 2. The infrared spectra of msen molecule between 4000 and 400 cm^{-1} : (a) experimental FT-IR spectrum; (b) $\text{ttg}^+\text{-e,bis}$ isomer, calculated; (c) $\text{tg}^+\text{g}^-\text{-s,anti}$ isomer, calculated.

Table 4The vibrational assignments of the msen molecule and comparison with the calculated data of ttg⁺-e,bis and tg⁺g⁻-s,anti isomers at B3LYP/6-311G(d,p) theory level.

Mode	Experimental ^a			ttg ⁺ -e,bis			tg ⁺ g ⁻ -s,anti			PED (potential energy distributions) ^d
	Assignment	IR	R	ν^b	NI _{IR} ^c	NI _R ^c	ν^b	NI _{IR} ^c	NI _R ^c	
66	N–H stretch	3261 s	3259 s	3264	0.20	0.20	3271	0.11	0.15	ν N15H (100)
62	C–H ₃ stretch (asym.)	3023 m	3023 m	3028	0.01	0.49	3028	0.01	0.52	ν_{as} C21H ₃ (100)
61	C–H ₃ stretch (asym.)	3011 w	3011 w	3026	0.02		3027			ν_{as} C4H ₃ (98)
59	C–H ₂ stretch (asym.)	2988 w	2974 m	2972	0.02	0.22	2960	0.01	0.25	ν_{as} C9H ₂ (78) + ν C12H13 (21)
FR [2 × ν_{54} or C–H ₂ stretch (asym.)]	2962 w	2958 w								
58	C–H ₃ stretch (sym.)		2932 vs	2934		1.00	2934			ν_s C21H ₃ (100)
56	C–H ₃ stretch (sym.)	2932 w		2933	0.09		2917	0.13	0.23	ν_s C9H ₂ (94) + ν C12H14 (5)
55	C–H ₂ stretch (sym.)	2904 w	2906 w	2913	0.05	0.40	2901	0.04	0.54	ν_s C12H ₂ (95) + ν C9H10 (3)
FR [2 × ν_{53} or C–H ₂ stretch (sym.)]	2879 w	–								
$\nu_{53} + \nu_{52}$ or C–H ₂ stretch (sym.)	2856 w	–								
54	C–H ₂ scissor	1475 m	1462 m	1463	0.04	0.05	1482	0.03		sciCH ₂ (85)
53	C–H ₂ scissor	1447 s	1436 vw	1452		0.12	1471		0.19	sciCH ₂ (85)
52	N–H bend (ip.)	1418 m	1416 vw	1419			1423			δ NH (31) + δ C8,12C9H10 (15) + δ_{as} C4H ₃ (9)
49	C–H ₃ bend (asym.)		1402 w	1409		0.28	1409			δ_{as} C4H ₃ (86)
48	C–H ₃ bend (asym.)	1407 m		1409	0.25		1409	0.30		δ_{as} CH ₃ (58)
46	N–H bend (ip.)	–	1387 vw	1375	0.18	0.06	1380		0.04	δ N15H (29) + ν_{as} S18O ₂ (19) + δ C12,9C9,12H11,14 (10)
45	S–O ₂ stretch (asym.)	1338 s	–	1339	0.19	0.09	1334	0.09		ν_{as} SO ₂ (23) + δ C12C9H11 (21) + δ N8C9H11 (18)
44	S–O ₂ stretch (asym.)	1323 s	1322 w	1329	0.15		1328			ν_{as} S1O ₂ (63) + δ N8,15C9,12H10,14 (8) + δ C9C12H14 (4)
41	C–H ₃ bend (sym.)	1305 s	1299 w	1307	1.00		1305	1.00		umbCH ₃ (91)
39	C–H ₂ twist	1221 m	–	1224	0.14	0.03	1200	0.08	0.00	twC9H ₂ (66) + δ N8H (12)
37	S–O ₂ stretch (sym.)	1146 vs	1146 s	1128	0.53	0.11	1130	0.47	0.17	ν_s SO ₂ (87)
36	C–N stretch	–	1116 m	1117	0.71	0.26	1107	0.35	0.15	ν CN (41) + ν CC (29) + ν_s S1,18O2,20 (7)
34	C–N stretch	1070 s	1078 w	1070	0.70	0.05	1068	0.40	0.05	ν CN (79) + ν CC (3) + ν S1N8 (3)
31	C–H ₃ rock	981 s		964	0.34		966	0.28		ρ CH ₃ (81)
29	C–H ₃ rock		975 w	958		0.16	958		0.16	ρ C4H ₃ (76)
28	S–N stretch	882 m	896 w	847	0.55	0.04	854	0.51	0.08	ν SN (41) + ν C4S1 (9) + ν CC (7)
27	S–N stretch	806 m	–	823	0.39	0.12	836	0.13	0.25	ν SN (33) + ν CS (18) + δ_s O19S18N15 (11)
26	C–S stretch	769 s	764 m	760	0.44	0.05	767	0.39	0.03	ν CS (39) + ρ CH ₂ (27)
23	C–S stretch	657 m	–	625	0.15	0.33	619	0.10	0.19	ν C4S1 (45) + ν S1N8 (17)
22	N–H bend (op.)	539 m	–	564	0.48	0.06	568	0.45	0.03	γ N8H (25) + ν SN (15) + sciS1O ₂ (13) + ν C9N8 (6)
21	S–O ₂ scissor	523 s	525 m	507	0.30	0.19	502	0.22		sciSO ₂ (33) + wNH (18) + ν C4S1 (8) + γ_{as} CCN (7)
20	C–S–N bend (ip.)	–	504 w	493	0.13	0.24	496		0.35	δ_{as} C21S18N15 (56) + ν CS (19) + wS18O ₂ (7)
19	S–O ₂ wag	458 s	–	471	0.06	0.26	480	0.03	0.37	wSO ₂ (38) + γ NH (12) + ν C4–S1 (12)
15	C–S–N bend (op.)	–	357 w	338	0.01	0.07	322	0.02		γ_s CSN (53) + γ_s CCN (9)
13	C–S–N bend (op.)	–	324 w	308	0.03	0.15	288	0.02		γ_{as} CSN (80)
12	C–N–S bend (op.)	288 vw	–	287	0.02	0.19	280	0.02	0.12	γ_s CNS (53) + γ_{as} C9C12N15 (11) + γ_s C21S18N15 (6)
11	S–O ₂ twist	271 vw	–	264	0.01	0.07	270		0.14	twS18–O ₂ (45) + γ_s CNS (26) + τ C21–H ₃ (20)
10	S–O ₂ twist	–	240 w	251	0.01	0.16	244	0.00	0.26	twS1O ₂ (46) + τ C4H ₃ (23) + γ_s CCN (15) + γ_s C21S18N15 (13)
9	C–H ₃ torsion	197 w	–	216	0.01		218	0.00		τ CH ₃ (81)
6	C–S–N bend (ip.)	160 vw br	170 vw br	188	0.01	0.13	146	0.01	0.11	δ_{as} C4S1N8 (45) + γ_{as} C12C9N8 (25)
5	C–N–S torsion	78, 65 w	–	87	0.01	0.04	63	0.01	0.15	τ CNS (92)
3	S–N torsion	45 vw		45	0.04		42			τ SN (87)
2	C–C–N torsion	39 vw		35	0.02	0.12	25	0.02	0.08	τ CN (44) + τ CC (38)

^a vs: very strong, s: strong, m: medium, w: weak, vw: very weak, sh: shoulder, br: broad, asym.: antisymmetric, sym.: symmetric, ip.: in-plane, op.: out-of-plane and FR: Fermi resonance.^b Wavenumbers scaled by SQM FF methodology according to our scale factors (see the text).^c N: normalized to 1, I: intensity, IR: infrared and R: Raman. The relative intensities of the simulated spectra were obtained after using the pure Lorentzian band shapes with a band with 10 cm⁻¹.^d ν : bond stretching, δ : in-plane angle bending, γ : out-of-plane angle bending, umb: umbrella bending, sci: scissoring, tw: twisting, w: wagging, ρ : rocking, τ : torsion, as: antisymmetric and s: symmetric.

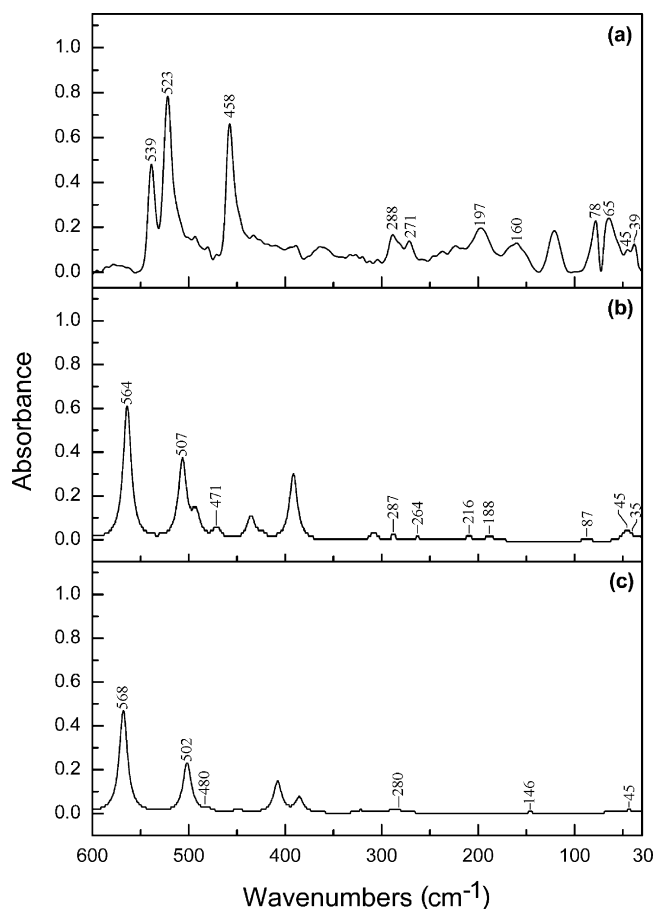


Fig. 3. The infrared spectra of msen molecule in the region of 600–30 cm^{-1} : (a) experimental FT-IR spectrum; (b) $\text{ttg}^+\text{-e,bis}$ isomer, calculated; (c) $\text{tg}^+\text{g}^-\text{-s,anti}$ isomer, calculated.

[12–14,38,42,43]. In accordance with the literature data, the bands observed at 3023 cm^{-1} and 3011 cm^{-1} (IR-Raman) are assigned antisymmetric $\nu(\text{CH}_3)$. The symmetric $\nu(\text{CH}_3)$ band is located at 2932 cm^{-1} (IR-Raman). The methylene CH_2 group stretching vibrations are observed between 2988 and 2879 cm^{-1} . The other fundamental CH_3 and CH_2 group vibrations which are CH_2 scissoring, antisymmetric or symmetric CH_3 bending, CH_2 twisting and CH_3 rocking modes appear in the expected wavenumber region of 1475–975 cm^{-1} . In the low wavenumber region, we have also observed a weak intense band at 197 cm^{-1} from far-infrared spectra is undoubtedly assigned CH_3 torsion according to PED result of mode 9.

The interaction of the methylene group with the lone pair on nitrogen produces the effect on the vibrational wavenumbers [22,40,41]. Therefore, the wavenumbers of CH_2 group are sensitive to conformational changes. As seen clearly from Table 4, the vibrational data of $\text{ttg}^+\text{-e,bis}$ form of msen is excellent agreement with the observed wavenumbers for the corresponding mode of CH_2 group vibrations than the $\text{tg}^+\text{g}^-\text{-s,anti}$ form.

4.2.3. S=O vibrations

The SO_2 antisymmetric and symmetric stretching vibrations appear in the range $1330 \pm 30 \text{ cm}^{-1}$ and $1160 \pm 30 \text{ cm}^{-1}$, both with strong intensity [44,45]. The strong bands at 1338 cm^{-1} and 1323 cm^{-1} in the FT-IR spectrum are assigned to νSO_2 antisymmetric modes and 1305 cm^{-1} are attributed to νSO_2 symmetric mode which are agree with the calculated wavenumbers ($\text{ttg}^+\text{-e,bis/tg}^+\text{g}^-\text{-s,anti}$) 1339/1334 cm^{-1} , 1329/1328 cm^{-1} and 1307/1305 cm^{-1} . The corresponding bands except the band at

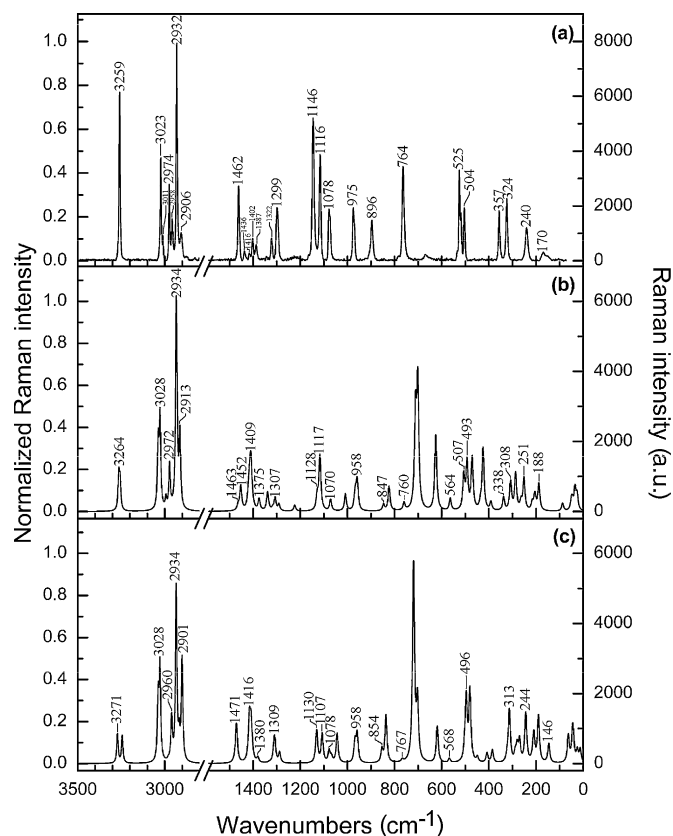


Fig. 4. The Raman spectra of msen molecule: (a) experimental dispersive-Raman spectrum; (b) $\text{ttg}^+\text{-e,bis}$ isomer, calculated; (c) $\text{tg}^+\text{g}^-\text{-s,anti}$ isomer, calculated.

1338 cm^{-1} (IR) are also observed in the Raman spectrum within weak intensity at 1322 cm^{-1} and 1299 cm^{-1} . The splitting of the νSO_2 antisymmetric bands could be attributed to solid-state effects [12,38]. The SO_2 scissoring and wagging vibrations occur in the range $570 \pm 60 \text{ cm}^{-1}$ and $520 \pm 40 \text{ cm}^{-1}$, both with medium or strong intensity and the two vibrations appear separately [44]. The corresponding bands are observed as strong peaks at 523 cm^{-1} and 458 cm^{-1} in FT-IR spectrum of msen, respectively. The infrared active band at 271 cm^{-1} and Raman active band at 240 cm^{-1} are attributed to the SO_2 twisting vibrations from the PED outcomes of modes 11 and 10.

4.2.4. S–N and C–S vibrations

The S–N stretching vibration exhibits a moderate band in the range $905 \pm 70 \text{ cm}^{-1}$ [44]. This vibration typically occurs in a medium band in the IR spectrum and a weak band in the Raman spectrum [44,45]. The vibrational wavenumbers of S–N stretching in some methanesulfonamide derivatives are also assigned in the region of 947–836 cm^{-1} [34]. The two bands appeared at 882 cm^{-1} (IR)–896 cm^{-1} (Raman) and 806 cm^{-1} (IR) are attributed to S–N stretching modes.

The assignment of C–S stretching vibration band in different compounds is difficult. However, νCS band of some methanesulfonamide derivatives in solid phase have been defined in the region of 760–780 cm^{-1} [34]. The strong band at 769 cm^{-1} in the FT-IR spectrum and the medium band at 764 cm^{-1} in the Raman spectrum of msen are attributed to the fundamental C–S stretching vibration. According to the PED result of mode 22, the medium intense infrared active band observed at 657 cm^{-1} is also attributed to νCS vibration owing to having more contribution than CH_2 rocking mode.

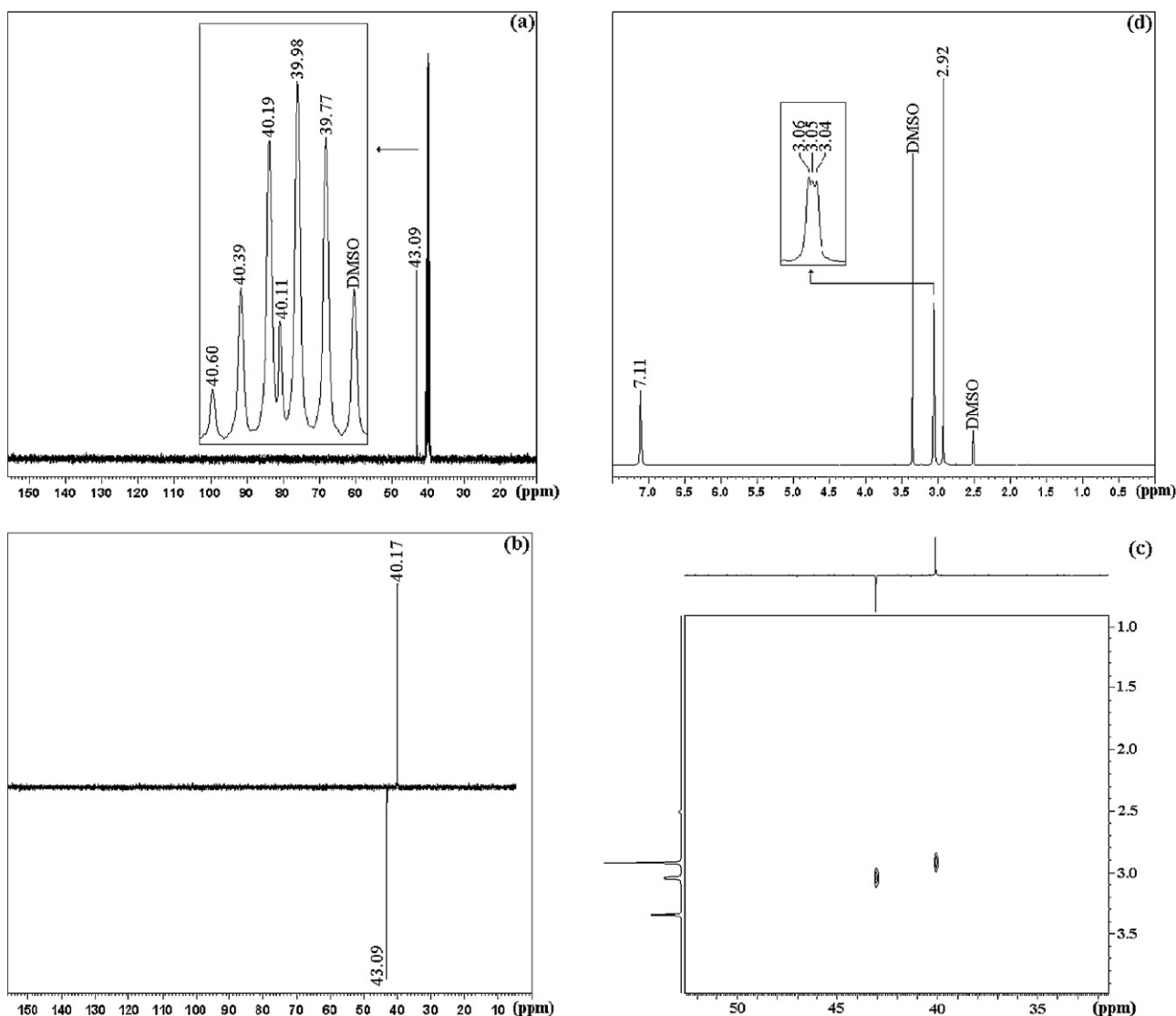


Fig. 5. The experimental NMR spectra of msen in DMSO- d_6 : (a) ^{13}C ; (b) DEPT-135; (c) 2D HETCOR; (d) ^1H .

4.2.5. C–N vibrations

The assignments of the CN stretching wavenumbers were made straightforwardly from analogy with 1,2-diaminoethane [22,40,41]. The vibrational results from pertinent references, the bands between 878 and 1100 cm^{-1} are commonly ascribed to the conformers of 1,2-diaminoethane displaying a gauche orientation around the NCCN dihedral angle [40,41]. However, Batista de Carvalho et al. [41] have been identified the band above 1100 cm^{-1} in the Raman spectrum of 1,2-diaminoethane (in solid phase) which confirms the trans skeletal arrangement around the C–C bond. Hence, the Raman active band was detected at 1116 cm^{-1} , confirming the existence of trans skeletal arrangement on 1,2-diaminoethane moiety of msen. The other bands at 1070 cm^{-1} (IR) and 1078 cm^{-1} (Raman) are attributed to the fundamental C–N stretching.

4.2.6. Skeletal vibrations

The low wavenumber region generally specifies the stable forms of the compounds in any physical state and it is particularly useful when performing conformational analysis [23,41]. The weak intense Raman active bands at 504, 357 and 324 cm^{-1} correspond to one C–S–N in-plane bending (mode 20) and two C–S–N out-of-plane bending (mode 15 and 13) vibrations, respectively. The

very weak infrared band at 288 cm^{-1} is also attributed to C–N–S out-of-plane bending vibration (mode 12). The torsional vibrations (modes 5–2) are only detected from the far-infrared spectra of msen between 78 and 39 cm^{-1} . Based on the calculated wavenumbers and intensities of modes 15, 13, 11, 9, 3 and 2 reflect the dominant feature of $\text{ttg}^+\text{-e,bis}$ form in solid phase. On the other hand, the weak infrared active band at 65 cm^{-1} is close to the $\text{tg}^+\text{g}^-\text{-s,anti}$ form.

4.3. NMR spectra

The experimental ^{13}C and ^1H NMR chemical shifts together within the calculated data for the stable conformers of msen are given in Table 5. ^{13}C , ^1H , DEPT-135 and 2D HETCOR NMR spectra of msen are given in Fig. 5. As in Fig. 5(a), the studied molecule shows two different carbon atoms. The characteristic feature of DEPT-135 spectrum is assisted to assign 40.17 ppm for C–H₂ and 43.09 ppm for C–H₃ (Fig. 5(b)). Likewise, two dimensional HETCOR spectrum in Fig. 5(c), cross peaks as triplet at 3.05 ppm and as singlet at 2.92 ppm are attributed to protons of H₂–C and H₃–C, respectively. The experimental N–H protons shift (7.11 ppm) showed poor correlation with the calculated proton shifts (4.33–4.66 ppm in DMSO- d_6 for all stable conformers) in Fig. 5(d). This suggests that

Table 5The experimental ^{13}C and ^1H NMR chemical shifts (ppm) together within the calculated data for the stable conformers of msen in DMSO- d_6 .

Nucleus	Experimental	B3LYP/6-311++G(d,p) ^a					
		ttg ⁺ -e,bis	tg ⁺ g ⁻ -s,anti	ttt-s,ac ⁺	tg ⁺ t-e,sc ⁺	tg ⁺ g ⁺ -e,ac ⁻	g ⁺ tg ⁻ -e,sc ⁻
C(9)	43.09	44.91	48.29	45.82	45.19	44.17	46.47
C(12)	43.09	44.76	42.28	45.82	44.22	41.95	43.61
C(21)	40.17	50.12	48.95	44.96	47.31	49.62	48.69
C(4)	40.17	47.48	48.95	44.96	44.68	46.58	46.75
H ₂ -N	7.11	4.50	4.43	4.51	4.33	4.41	4.66
H ₂ -C(12)	3.05	3.31	3.01	3.25	3.16	3.16	3.17
H ₂ -C(9)	3.05	2.91	3.22	3.25	3.03	2.85	3.03
H ₃ -C(21)	2.92	2.82	2.80	2.83	2.81	2.83	2.83
H ₃ -C(4)	2.92	2.79	2.79	2.83	2.80	2.79	3.06

^a σ transform into δ using equations given in Refs. [32,33]; $\delta^{13}\text{C} = 175.7 - 0.963 \sigma^{13}\text{C}$ and $\delta^1\text{H} = 31.0 - 0.970 \sigma^1\text{H}$.

NH protons should have both intra- and intermolecular hydrogen bonding.

The results given in Table 5 indicate that trans–trans–trans-staggered, anticlinal⁺ (ttt-s,ac⁺) form of the msen is more compatible with the experimental results than the other conformers due to the intra- and intermolecular hydrogen bonding from NH moiety of msen.

5. Conclusion

All the possible stable conformers of msen were investigated by a detailed conformational analysis. The conformational analysis results indicated that msen has six stable rotational isomers at room-temperature. The relative energies of the six isomers suggest that the most stable conformer is the ttg⁺-e,bis isomer. However, the population analysis showed that the tg⁺g⁻-s,anti isomer should be considered in the vibrational spectroscopic study.

In general, B3LYP method overestimates strongly all bond lengths around sulfur and nitrogen atoms as it includes electron correlation effects. Hence, the prediction of force constants and vibrational wavenumbers show great discrepancy in experimental results. In order to resolve this discrepancy, three different scale factor groups for eleven internal coordinates were considered. A complete vibrational analysis was performed in accordance with these scale factor groups within the SQM FF method based on DFT calculation at B3LYP/6-311G(d,p) level of theory. However, the great match between the experimental and calculated wavenumbers of the normal modes with respect to ESFF enables us to safely assign the fundamental bands observed in the experimental FT-IR, far-infrared and dispersive Raman spectra of solid msen. Some fundamental bands in the vibrational spectra such as N–H in-plane bending, SO₂ antisymmetric stretching, C–N stretching, S–N stretching, C–S stretching bands are split, which could be attributed to solid-state effects or to intermolecular hydrogen bonding between the N-hydrogen and the one of the sulfonyl oxygen (N–H...O). We could not comment on this feature in detail, because of the lack of crystal structure data for msen.

The fundamental bands of ttg⁺-e,bis and tg⁺g⁻-s,anti forms of the msen have nearly same wavenumbers in the region of 4000–400 cm⁻¹. On the other hand, in the low wavenumber region (400–30 cm⁻¹), the vibrational data corresponding to the ttg⁺-e,bis form is more compatible with the experimental findings. In the light of these results, the trans–trans–gauche⁺-eclipsed, synperiplanar (ttg⁺-e,bis) is the most stable form of the msen in solid state.

The comparison of the experimental and theoretical NMR results indicate that msen have a flexible side chain, hence could be showing different conformers depending on inter- or intramolecular hydrogen bonds in liquid state. In this study, the NMR analysis in DMSO- d_6 of msen has shown itself as trans–trans–trans-staggered, anticlinal⁺ (ttt-s,ac⁺) form.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.saa.2012.01.065.

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