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**GAS PHASE CONFORMATIONAL BEHAVIOR OF SELENOMETHIONINE:
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Selenium containing amino acids are known to play numerous key biological roles in various life-supporting processes. In the current theoretical investigation DFT(B3LYP) and MP2 methods are used to study the gas phase conformers of the selenomethionine molecule in view of their relative stabilities, theoretically predicted harmonic frequencies, HOMO-LUMO energy gaps, rotational constants, and dipole moments. The number and type of intramolecular H-bond interactions existing in the selenomethionine conformers, which play key roles in determining the energy of the conformers, are also analyzed. The predicted geometries as well as the relative stabilities of the conformers suggest that the structural aspects and energies of the conformers may depend on the level of theory and the size of the basis set used. A comparison of the vibrational frequencies furnished in this study with the previous experimental and theoretical results obtained at MP2/6-31++G(*d,p*) and B3LYP/6-311++G(*d,p*) levels promotes the interpretation of the vibrational spectroscopy data on biologically relevant molecules.

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The genetic code encodes only 22 amino acids (twenty canonical and two non-canonical or non-standard amino acids *viz.* pyrrolysine and selenocysteine) during the process of protein bio-synthesis, which adequately build up the proteins and enzymes necessary to support all the three kingdoms of life on the Earth. However, there are more than 140 naturally occurring amino acids whose incorporation into the protein structures are crucial for the proper functioning of chemical and bio-chemical machineries associated with living beings. Among these, selenium-containing amino acids are of special interest for amino acid biochemistry. Selenomethionine (Sem) is a naturally occurring α -amino acid in which a selenium atom replaces the sulfur atom of the methionine molecule. In cereals and forage crops Sem is incorporated into proteins in place of methionine (Met) since tRNA^{Met} cannot discriminate between Met and Sem. The L-isomer of Sem is a major natural food-form of selenium for both human and animals. Sem is known to protect human systems against oxidation, radiations, cancer, aging and related diseases [1—3]. Experimental studies have been carried out to understand the structural and vibrational spectroscopic behavior of the Cu(II) complex of L-selenomethionine [4]. Also, there have been efforts to study the palladium and platinum dihalide complexes of DL-selenomethionine [5] as well as the interactions between Sem and methylmercuric chloride regarding cellular uptake and selenium protection on methylmercuric chloride toxicity [6]. The experimental and gas

phase theoretical Raman spectral assignments of Met and Sem have also been well documented in the literature [7]. Structural features of dipeptides containing N-terminal selenomethionine have also been recently investigated theoretically [8]. However, a detailed account of the structural and molecular properties of Sem conformers is unavailable in the literature so far, which to a large extent may provide useful insights in the understanding of the dynamic properties and functional specificity of Sem-containing proteins and enzymes.

Amino acids are highly flexible molecules since they possess several rotatable single bonds. Even at room temperature an amino acid molecule may change form one conformation to another since the internal rotations around the single bonds require a very small amount of energy [9]. On many occasions it has been reported that the amino acid conformers having diverse structural motifs may differ in their thermodynamic stability by a narrow range of relative energy [10–12]. The structure-function relationships of proteins and polypeptides are known to be influenced by the conformational behavior of individual amino acid residues that constitute their primary structures. It is for this reason that solitary amino acids and their analogues have been extensively used as model systems for the computational studies concerning the structure of proteins and energies of protein folding. Atomic level structural information furnished by quantum chemical calculations regarding the structural and molecular properties of amino acids are crucial for the purpose of supporting or refuting the existing theories related to protein structure prediction. Such information collected at the level of a solitary amino acid structure are also potentially important for building up accurate geometrical force field parameters for semi-empirical or molecular mechanics simulations of proteins and other biological macromolecules [13–15]. The understanding of the conformational flexibility of amino acids is also important since it can influence their chemical reactivity and thus may have different functional aspects in biochemical processes [16–18]. A detailed knowledge of the conformational behavior of canonical amino acids and their derivatives is also becoming the need of the hour in the field of the rational design of metalloproteins and in expanding the spectrum of properties of the engineered or de novo designed metalloproteins [19–23].

Gas phase computational studies on the conformational behavior of neutral (non-zwitterionic) amino acids [10, 11, 24–29] have been performed with a view toward acquiring the atomic level structural information which is critical to the understanding of various chemical and biochemical processes taking place in the macromolecular context of real life systems. Such gas phase studies can provide us the opportunity to understand their intrinsic properties free from the solvent or crystal phase effects. Amino acids are known to exist in non-ionic forms in the gas phase and as zwitterions in solvent and solid phases [12, 30]. The gas phase conformers of a given amino acid are generally stabilized by a delicate interplay between the stabilizing intramolecular H-bond interactions and destabilizing repulsive forces arising either from the lone pair-lone pair electronic repulsion or steric effects [31, 32]. On the other hand, experimental studies on the neutral gaseous amino acids are limited due to the low thermal stability and low vapor pressure of amino acids [33, 34].

This theoretical study is aimed at studying the conformational space of a non-ionized Sem molecule about its five structurally significant internal backbone torsion angles in the gas phase. We also aim to analyze the relative stabilities of 13 different conformers of Sem on the energy surface, and to report theoretical results regarding rotational constants, dipole moments, HOMO-LUMO energies and their energy gaps as well as harmonic vibrational frequencies which may be helpful for future experimentalists as preliminary guidelines to characterize the gas phase conformers of the Sem molecule. Attempts are made to provide a detailed analysis of the number and type of intramolecular H-bond interactions existing in the Sem conformers, which may play key roles in determining the energies of the conformers.

Fig. 1 schematically represents seven internal rotatable bonds of the Sem molecule. To facilitate a clear representation of the intra-

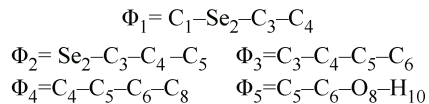


Fig. 1. Depiction of five rotatable internal backbone torsion angles in the Sem molecule

molecular hydrogen bond (H-bond) interactions present in the Sem conformers some of the hydrogen atoms are named H_a or H_b. This gas phase quantum chemical conformational analysis of an isolated Sem molecule (in its unbound state), apart from external factors such as pH effects, counterions, proteins, water etc., would provide the opportunity to know its intrinsic conformational properties at an atomic level, which in turn may help us to understand the fundamental nature of Sem interactions with other various bioactive chemical species as well as the dynamic properties and functional specificity of proteins and enzymes.

COMPUTATIONAL METHODOLOGY

In order to carry out the conformational search for the five internal backbone torsion angles, the molecular geometry of the neutral gaseous Sem molecule was subjected to full geometry optimization and vibrational frequency calculations using the B3LYP/6-311++G(*d,p*) level of theory [35, 36]. The absence of imaginary frequencies in the vibrational frequency calculations proved the optimized geometry of the Sem molecule to be the true minimum. To determine the other possible minimum/minima on the conformational potential energy surfaces (PESs) corresponding to the five rotatable internal backbone torsion angles of the Sem molecule, relaxed potential energy surface (PES) scans were performed at the B3LYP/6-31G(*d,p*) level by rotating the five dihedral angles (Φ_1 — Φ_5) from 0° to 360° at 20° intervals. Ten stable molecular geometries (minima) detected from the PES exploration along with other three conformers generated by considering some of the possible combinations of rotations about the five internal backbone torsion angles of the Sem molecule were then subjected to full geometry optimization and vibrational frequency calculations at B3LYP/6-311++G(*d,p*) and MP2/6-31++G(*d,p*) levels releasing the constraints on the torsion angles. The optimized geometries of all the conformers were characterized as true minima by the absence of imaginary frequency values in their vibrational frequency calculations. Zero-point energy (ZPE) corrections were applied to the total energies of all stable conformers using correction factors of 0.97 and 0.9877 for 6-31++G(*d,p*) and 6-311++G(*d,p*) levels respectively [10, 37—39]. The calculated harmonic vibrational frequencies were also scaled using the appropriate correction factors. For the MP2/6-31++G(*d,p*) level the frequency values below 1800 cm⁻¹ were scaled with a correction factor of 0.977 while those above 1800 cm⁻¹ were scaled with 0.955 [37, 38]. Whereas, for the B3LYP/6-311++G(*d,p*) method the vibrational frequencies below 1800 cm⁻¹ were scaled with 1.01 and for those above 1800 cm⁻¹ a correction factor of 0.9679 was used [37, 39]. The use of diffuse functions is important in order to take into account the relative diffuseness of the lone pair present in the molecule under investigation [40] whereas polarization functions are useful in conformational studies where stereoelectronic effects play an important role [41]. All the calculations were performed using the Gaussian 09 program [42].

RESULTS AND DISCUSSION

The PESs corresponding to the five internal backbone torsion angles of the Sem molecule, namely Φ_1 , Φ_2 , Φ_3 , Φ_4 , and Φ_5 are depicted in Fig. 2. It is apparent from them that in the plots for Φ_2 and Φ_4 torsion angles, the energies which correspond to 0° and 360° angles have different values in contrast to the plots for the Φ_1 , Φ_3 , and Φ_5 dihedrals. It seems to be that while scanning the Φ_2 and Φ_4 dihedrals, the molecule jumps from one energy well to another, and consequently the final conformation at $\Phi_2 = 360^\circ$ (at $\Phi_4 = 360^\circ$ in the case of rotation about Φ_4) is not the same as the initial conformation at $\Phi_2 = 0^\circ$ (at $\Phi_4 = 0^\circ$ for Φ_4 rotation). For Φ_2 and Φ_4 dihedrals these shifts seem to occur at angles of ~220° and ~100° respectively (Fig. 2). A close inspection reveals that the orientations of two H atoms of the amino group change when the molecule moves from $\Phi_2 = 220^\circ$ to $\Phi_2 = 240^\circ$ (or $\Phi_4 = 100^\circ$ to $\Phi_4 = 120^\circ$ for Φ_4), which makes the molecule jump from one energy well to another. As listed in Table 1, the conformational analysis at the B3LYP/6-31G(*d,p*) level reveals that a total of 162 different conformers of the Sem molecule would result if all the possible combinations of rotations about the five internal backbone torsion angles are considered, *i.e.* (i) threefold rotamers for Φ_1 around the Se₂—C₃ bond (73.41°, 176.75°, and -73.33°), (ii) threefold rotamers for Φ_2 around the C₃—C₄ bond (65.11°, 173.76°, and -69.94°), (iii) threefold rotamers for Φ_3 around the C₄—C₅ bond (70.82°,

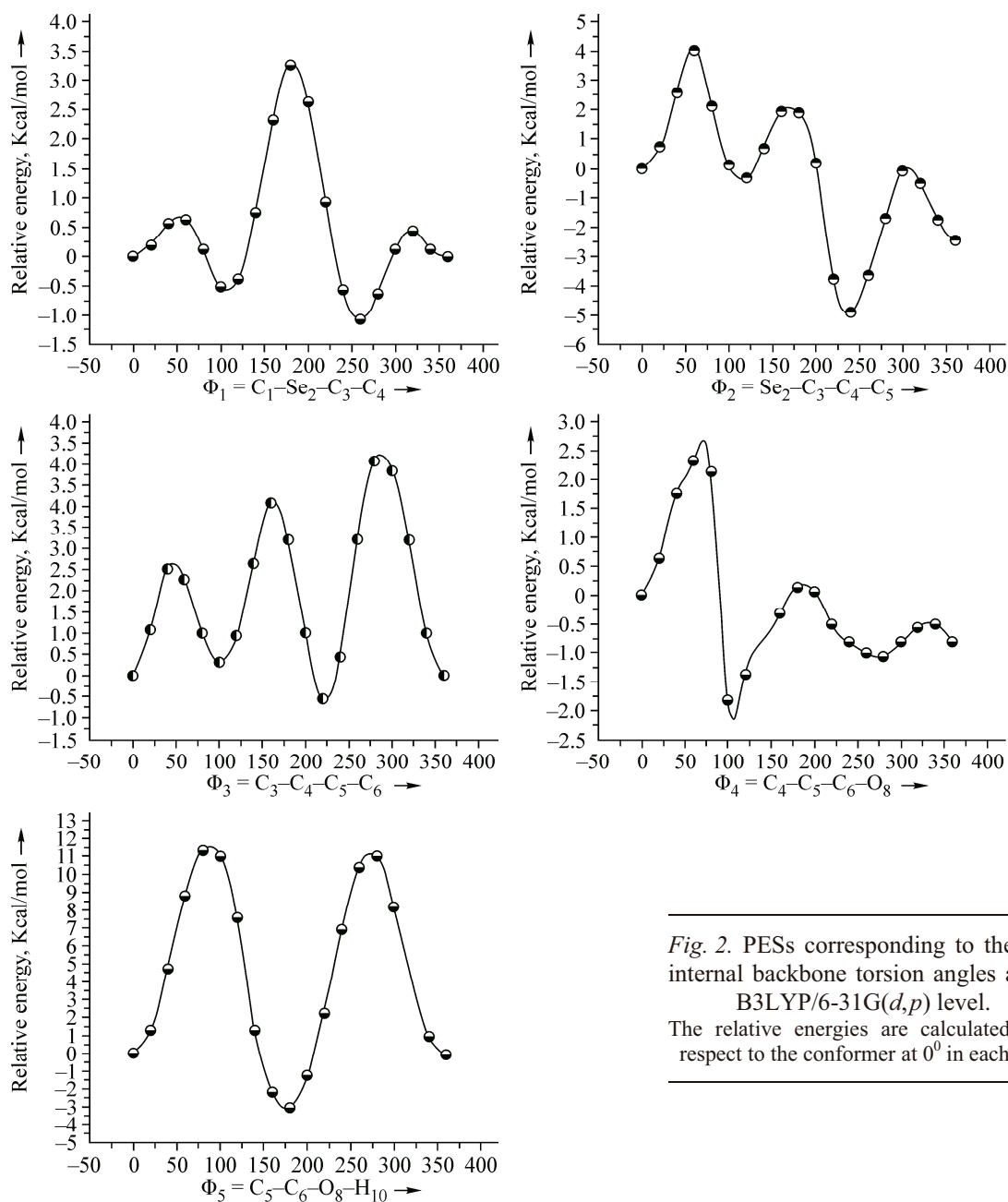


Fig. 2. PESs corresponding to the five internal backbone torsion angles at the B3LYP/6-31G(*d,p*) level. The relative energies are calculated with respect to the conformer at 0° in each plot

Table 1

Data generated from the DFT conformational analysis at the B3LYP/6-31G(*d,p*) level of theory about the five internal backbone torsion angles^a (in deg.) of the Sem molecule

Torsion angles	Definition	No. of fold	Value of torsion angles
Φ_1	C ₁ —Se ₂ —C ₃ —C ₄	3 fold	73.41, 176.75 and -73.33
Φ_2	Se ₂ —C ₃ —C ₄ —C ₅	3 fold	65.11, 173.76 and -69.94
Φ_3	C ₃ —C ₄ —C ₅ —C ₆	3 fold	70.82, 172.55 and -65.68
Φ_4	C ₄ —C ₅ —C ₆ —O ₈	3 fold	66.99, 176.55 and -98.79
Φ_5	C ₅ —C ₆ —O ₈ —H ₁₀	2 fold	-2.68 and -178.94

^a Torsion angle values are collected from the fully optimized conformers at the B3LYP/6-311++G(*d,p*) level.

Table 2

Dihedral angles (in deg.) about the five internal backbone torsion angles of the Sem conformers after the full geometry optimization at the MP2 and B3LYP levels. The B3LYP values are listed in parentheses

Conformers	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5
Sem ^A	— (176.75)	— (173.76)	— (70.82)	— (176.55)	— (-178.94)
Sem ^B	-86.47 (-73.33)	170.62 (176.61)	61.66 (71.00)	-169.51 (175.78)	-175.68 (-179.09)
Sem ^C	90.33 (73.41)	-178.12 (177.39)	69.09 (71.63)	-176.79 (178.08)	-177.39 (-178.65)
Sem ^D	104.28 (103.71)	-62.63 (-69.94)	76.73 (77.47)	48.70 (53.73)	-179.56 (-179.72)
Sem ^E	84.72 (71.37)	63.14 (65.11)	54.98 (68.80)	-90.08 (-87.35)	178.33 (178.72)
Sem ^F	-165.46 (-176.71)	-171.13 (-175.07)	179.42 (172.55)	168.10 (163.13)	179.36 (178.57)
Sem ^G	161.56 (178.74)	179.01 (-173.83)	-63.49 (-65.68)	150.40 (158.80)	176.71 (177.36)
Sem ^H	168.67 (177.37)	167.91 (175.26)	50.64 (61.11)	-99.18 (-98.79)	177.30 (178.85)
Sem ^I	169.60 (179.72)	169.91 (178.38)	49.62 (58.27)	67.70 (66.99)	-179.96 (179.19)
Sem ^J	165.63 (171.53)	165.17 (173.57)	50.14 (69.06)	93.56 (140.73)	7.86 (-2.68)
Sem ^K	161.57 (173.51)	170.06 (174.33)	52.69 (59.46)	-98.08 (-95.63)	-4.28 (-2.32)
Sem ^L	-89.89 (-175.31)	179.00 (179.17)	171.51 (172.21)	-77.72 (-75.29)	-3.68 (-2.14)
Sem ^M	172.07 (179.50)	-177.03 (-176.24)	-53.31 (-59.08)	-51.42 (-49.80)	3.29 (3.29)

The Sem^A conformer could not be characterized at the MP2/6-31++G(*d,p*) level.

172.55°, and -65.68°), (iv) threefold rotamers for Φ_4 around the C₅—C₆ bond (66.99°, 176.55°, and -98.79°), and (v) twofold rotamers for Φ_5 around the C₆—O₈ bond (-2.68° and -178.94°) since the Sem carboxyl group can possess *syn*- or *anti*-periplanar conformations corresponding to 0° and 180° torsions around the C₆—C₈ bond. The Sem^A—Sem^J conformers (listed in Table 2) correspond to ten minima detected from the PES exploration, whereas the other three conformers (Sem^K to Sem^M) were generated by considering some of the possible combinations of rotations about the five internal backbone torsion angles of the Sem molecule. Thus, for the Sem^K conformer the Φ_4 and Φ_5 dihedral angles were set as -98.79° and -2.68° respectively, for Sem^L the Φ_3 , Φ_4 and Φ_5 angles were set as 172.55°, -98.79°, and -2.68° respectively, while the Sem^M conformer was obtained by setting the Φ_3 , Φ_4 , and Φ_5 angles as -65.68°, -98.79°, and -2.68° respectively. It is interesting to note that though the B3LYP/6-311++G(*d,p*) level predicts the Sem^A conformer to be a true minimum (the number of imaginary frequency values is zero), this conformer is not stable at the MP2/6-31++G(*d,p*) level and converts back to Sem^C after the full geometry optimization.

The optimized geometries of the 13 conformers are depicted in Fig. 3, while the backbone torsion angle values of all the conformers are listed in Table 2. Table 3 presents the gas phase data on relative energies, rotational constants, dipole moments, and HOMO-LUMO energy gaps of the conformers calculated at the MP2 and B3LYP levels. The zero-point vibrational energies (ZPVE), total electron energies (*E*) as well as the ZPVE corrected values of the total electron energies (*E*_{corr}) of the conformers are listed in Table S1 of the Supplementary Information (SI). The gas phase HOMO-LUMO energies of the conformers calculated at the MP2 and B3LYP levels are listed in Table S2. The 3D plots of the frontier orbitals, HOMO and LUMO for the most stable Sem^E conformer are shown in Fig. 4. Some of the structurally significant intramolecular H bonds that play crucial roles in stabilizing the Sem conformers are listed in Table 4. Table 5 gathers the characteristic frequency values of the 13 conformers calculated at the MP2 and B3LYP levels. Table 5 also lists some gas phase experimental and theoretical frequency values (calculated at the B3LYP/6-31G(*d,p*) level of theory) available from the literature [43].

The dihedral angle values of the conformers calculated at the MP2 and B3LYP levels, listed in Table 2, reveal that most of the internal torsional rotations are independent of each other, *i.e.* the rotation around one dihedral angle does not alter the conformation of the other part of the Sem molecule. However, in the cases of Sem^D and Sem^E conformers, changes in the Φ_2 values from 173.76° to about -69.94° and 65.11° respectively alter the Φ_1 and Φ_4 values to about 103.71° and 53.73° respectively in

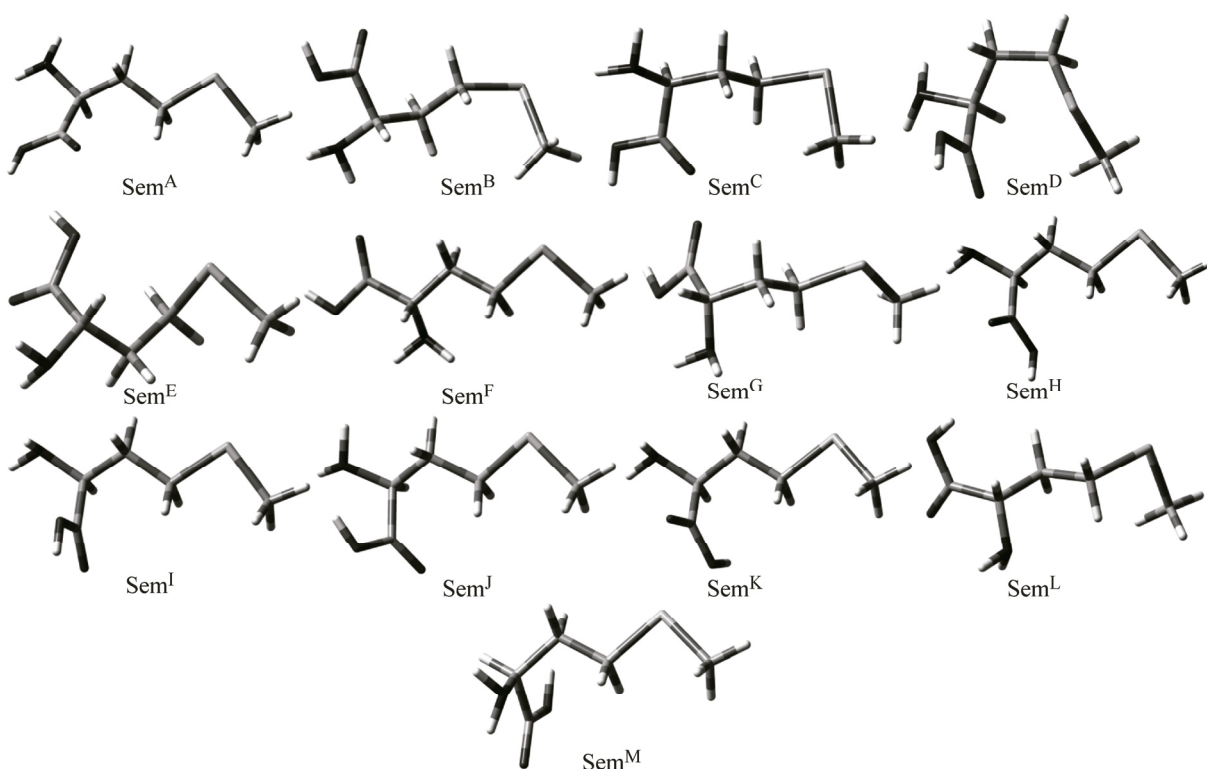


Fig. 3. Optimized structures of the Sem conformers at the MP2 level (B3LYP structure for Sem^A)

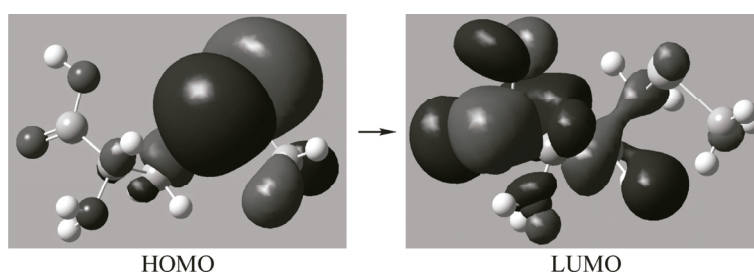


Fig. 4. 3D plots of the HOMO and LUMO of the Sem^E conformer at the B3LYP level

Sem^D and to about 71.37° and -87.35° respectively in the case of the Sem^E conformer at both levels. Similar situations are also observed in two more cases: (i) a change in the Φ_5 value to about -2.68° in Sem^J from the usual value of 180° changes the Φ_4 value to 140.73° at the B3LYP level and to 93.56° at the MP2 level, and (ii) in Sem^L when three (Φ_3 , Φ_4 , and Φ_5) dihedral angles are set at about 172.55° , -98.79° , and -2.68° . The value of the Φ_1 dihedral angle changes to -89.89° at the MP2 level while no such change has been observed at the B3LYP level. The relative energies of the 13 Sem conformers listed in Table 3 are determined relative to the energy of Sem^E, which is predicted to be the most stable conformer at both MP2 and B3LYP levels of theory. On the other hand, Sem^K is the least stable one in the stability order of the Sem conformers whose relative energy differs by a magnitude of $7.92 \text{ kcal}\cdot\text{mol}^{-1}$ at the MP2 level and $5.77 \text{ kcal}\cdot\text{mol}^{-1}$ at the B3LYP level as compared to that of Sem^E. As is recognized in several previous studies [10, 32], the data furnished by this theoretical study on the energies of the Sem conformers also points to the fact that though many of the Sem conformers differ from one another by small energy differences (for example, Sem^D and Sem^F conformers differ by only $0.03 \text{ kcal}\cdot\text{mol}^{-1}$ at the MP2 level while Sem^J differs from Sem^I by $0.09 \text{ kcal}\cdot\text{mol}^{-1}$ at the B3LYP level), their conformational aspects are significantly different. Thus, the predicted geometries as well as the relative stability orders furnished at the B3LYP/6-311++G(*d,p*) and MP2/6-31++G(*d,p*)

Table 3

The relative energies^a (kcal·mol⁻¹), theoretical rotational data (GHz), dipole moments (D), and HOMO-LUMO energy gaps (eV) of the Sem conformers at the MP2 and B3LYP levels. The B3LYP values are presented in parentheses

Conformers	Relative energies		Rotational constants			Dipole moments	HOMO-LUMO Energy gaps
	ΔE_1	ΔE_2	A	B	C		
Sem ^E	0	0	2.150 (2.150)	0.550 (0.550)	0.486 (0.486)	1.031 (0.656)	7.605 (5.422)
Sem ^H	1.98	0.36	2.160 (2.204)	0.476 (0.446)	0.420 (0.401)	2.885 (2.731)	7.675 (5.220)
Sem ^I	2.27	0.68	2.174 (2.214)	0.472 (0.444)	0.422 (0.406)	1.971 (1.310)	7.653 (5.215)
Sem ^J	2.52	0.59	2.313 (2.658)	0.465 (0.417)	0.411 (0.373)	4.055 (4.255)	7.890 (4.950)
Sem ^A	—	1.99	— (2.654)	— (0.415)	— (0.377)	— (3.161)	— (4.965)
Sem ^C	2.87	1.32	2.426 (2.464)	0.460 (0.433)	0.414 (0.400)	2.891 (2.480)	7.539 (4.986)
Sem ^G	3.28	1.65	2.333 (2.470)	0.454 (0.429)	0.438 (0.412)	3.596 (2.821)	7.410 (4.827)
Sem ^B	3.42	1.84	2.501 (2.602)	0.436 (0.425)	0.402 (0.380)	4.470 (3.782)	7.692 (4.997)
Sem ^D	4.58	4.96	1.755 (1.756)	0.770 (0.706)	0.675 (0.618)	2.779 (2.209)	7.707 (5.281)
Sem ^F	4.61	1.97	3.214 (3.185)	0.384 (0.377)	0.349 (0.344)	4.165 (3.644)	7.703 (5.044)
Sem ^L	6.84	4.65	2.492 (2.795)	0.407 (0.384)	0.382 (0.360)	3.007 (4.068)	7.954 (5.105)
Sem ^M	7.48	5.55	2.150 (2.222)	0.471 (0.445)	0.458 (0.431)	3.226 (2.750)	7.856 (4.980)
Sem ^K	7.92	5.77	2.148 (2.193)	0.476 (0.449)	0.4209 (0.402)	3.383 (3.438)	8.009 (5.126)

^a Relative energies: ΔE_1 = at the MP2/6-31++G(d,p) level; ΔE_2 = at the B3LYP/6-311++G(d,p) level.

levels in this study reveal that the structural aspects and relative energies of the conformers may depend on the level of theory and the size of the basis set used. Such disagreements are however not uncommon and have been encountered in several previous theoretical investigations concerning the structural and molecular properties of the genetically encoded amino acids [28]. It is well known that the intramolecular basis set superposition error (BSSE) can be quite significant in the case of the wave function based methods, such as the MP2 level, especially when smaller basis sets are used. On the other hand, though the DFT level is less sensitive to BSSE owing to its inherent architecture, the most commonly used B3LYP hybrid functional of the density functional theory suffers from the inability to describe dispersion effects. Nonetheless, except for the cases of Sem^A, Sem^J and Sem^L conformers, the DFT(B3LYP) and MP2 levels unanimously produce the same minima for all the other ten conformers of the Sem molecule and therefore it is reasonable to assume that these conformers should in fact exist and their predicted geometries are reliable.

It is evident from Table 3, which lists the total dipole moments of the conformers, that most of the Sem conformers exhibit larger values of total dipole moments in the gas phase; up to 4.470 D for the Sem^B conformer at the MP2 level and 4.255 D for Sem^J at the B3LYP level of theory. This indicates that the Sem conformers possess a greater polar character and greater affinity to polar solvents. It has been widely accepted that large dipole moments often lead to an extra stabilization in an aqueous solution. The large dipole moment values may also be useful in detecting the Sem conformers in the microwave spectrum since the microwave transition intensities are proportional to the square of the dipole moments [24]. On the other hand, the reliability of DFT and MP2 methods in predicting the rotational constants of biologically important molecules has been well discussed in the literature [44, 45]. In the absence of any experimental data on rotational constants the theoretically predicted gas phase values may assist experimentalists in determining the Sem conformers using the rotational spectroscopy. Table 3 also assembles data on the energy gaps between the HOMO and LUMO energies for the Sem conformers calculated at the MP2 and B3LYP levels in the gas phase. The predicted energy gaps of the Sem conformers at the MP2 level range from 7.410 eV to 8.009 eV while those at the B3LYP level range from 4.827 eV to 5.422 eV.

It is well known that the number of intramolecular H bonds and the strength of these interactions are the two important factors that may influence the relative energies of the various conformers of an amino acid. The H bond strength is assessed by considering two geometric criteria: (a) the shorter the

H-bond distances^a (Å) of the intramolecular H-bond interactions observed in the Sem conformers in the gas phase. The B3LYP values are given in parentheses

H-bonds	Sem ^A	Sem ^B	Sem ^C	Sem ^D	Sem ^E	Sem ^F	Sem ^G	Sem ^H	Sem ^I	Sem ^J	Sem ^K	Sem ^L	Sem ^M
O ₈ ...H _b —N ₇	— (2.41)	2.59 (2.41)	2.49 (2.43)	abs (abs)	abs (abs)	2.29 (2.29)	2.30 (2.30)	abs (abs)	2.58 (2.61)	abs (abs)	abs (abs)	abs (abs)	abs (abs)
O ₉ ...H _b —C ₃	— (2.56)	2.43 (2.55)	2.47 (2.58)	abs (abs)	abs (abs)	abs (abs)	2.67 (2.74)	abs (abs)	abs (abs)	2.66 (2.66)	abs (abs)	abs (abs)	abs (abs)
O ₉ ...H ₁₀ —O ₈	— (2.29)	2.30 (2.29)	2.31 (2.30)	2.30 (2.29)	2.31 (2.29)	2.30 (2.29)	2.30 (2.29)	2.31 (2.30)	2.31 (2.30)	abs (abs)	abs (abs)	abs (abs)	abs (abs)
O ₉ ...H _b —C ₄	— (2.74)	2.76 (2.75)	2.68 (2.71)	abs (abs)	abs (abs)	2.66 (2.56)	2.64 (2.67)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)
N ₇ ...H _a —C ₄	— (2.58)	2.68 (2.57)	2.63 (2.59)	2.53 (2.52)	2.62 (2.52)	abs (abs)	2.70 (2.71)	2.67 (2.58)	2.67 (2.60)	2.74 (2.74)	2.65 (2.67)	abs (abs)	2.62 (2.67)
N ₇ ...H _b —C ₄	— (2.75)	2.67 (2.76)	2.73 (2.75)	2.76 (2.78)	2.63 (2.76)	abs (abs)	abs (abs)	2.62 (2.69)	2.64 (2.70)	2.58 (2.58)	2.62 (2.59)	2.65 (2.69)	abs (abs)
O ₈ ...H—C ₅	— (2.63)	2.52 (2.64)	2.57 (2.62)	abs (abs)	2.45 (2.48)	2.71 (2.75)	abs (abs)	2.42 (2.43)	abs (abs)	abs (abs)	2.56 (2.56)	2.61 (2.62)	2.72 (2.72)
O ₉ ...H—C ₅	— (abs)	abs (abs)	abs (abs)	2.51 (2.49)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	2.53 (2.52)	2.58 (2.58)	abs (abs)	abs (abs)	abs (abs)
O ₉ ...H—C ₁	— (abs)	abs (abs)	abs (abs)	2.56 (2.50)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)
O ₈ ...H _b —C ₄	— (abs)	abs (abs)	abs (abs)	2.50 (2.56)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	2.75 (2.73)	abs (abs)	abs (abs)	abs (abs)	abs (abs)
O ₉ ...H _b —N ₇	— (abs)	abs (abs)	abs (abs)	abs (abs)	2.58 (2.59)	abs (abs)	abs (abs)	2.63 (2.64)	abs (abs)	abs (abs)	2.60 (2.61)	2.49 (2.56)	2.23 (2.21)
N ₇ ...H _a —C ₃	— (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	2.60 (2.67)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	2.62 (2.70)
N ₇ ...H _b —C ₃	— (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	2.68 (2.80)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	2.60 (2.68)	abs (abs)
N ₇ ...H ₁₀ —O ₈	— (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	1.96 (1.96)	abs (abs)	abs (abs)	abs (abs)
O ₈ ...H _a —C ₃	— (abs)	abs (abs)	abs (abs)	abs (abs)	2.54 (2.58)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (2.84)	abs (abs)	2.73 (abs)
Se ₂ ...H—C ₅	— (abs)	abs (abs)	abs (abs)	abs (abs)	2.97 (3.00)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)	abs (abs)

^a Only the (B...H) distances are listed, where B is H bond acceptor; abs = absent.

A—H...B distance, the stronger the H-bond and (b) the closer the A—H...B angle to 180° the stronger the H-bond; where A—H is the H bond donor and B is the H bond acceptor [11, 46]. The lowering in the vibrational frequency values corresponding to the presence of intramolecular H bond interactions in various biomolecular systems has been well documented in the literature [10, 39]. Table 4 collects the B...H distances of the intramolecular H bonds existing in the Sem conformers. It is evident from these data that the amino and carboxyl groups as well as the Se atom of the Sem molecule participate actively in the intramolecular H bond formation stabilizing the various conformers. The A—H...B angle of all the intramolecular H bond interactions reported in this study are greater than 85°, while their H...B distances span up to a maximum value of 2.76 Å [11]. However, in the Se₂...H—C₅ interaction, the H...B distances may range up to 3.00 Å because of the large atomic size of the selenium atom as compared to that of oxygen or nitrogen atoms. The H bond combinations in the Sem conformers are complex, and various types of intramolecular H bonds can coexist in one conformer. A thorough analysis reveals that six types of intramolecular H bonds, namely O...H—O, O...H—N, N...H—O, O...H—C, N...H—C, and Se...H—C, are present in the conformers. All these H bonds play key roles in determining the energies of the conformers. It is interesting to note that the weak H bond interactions such as O...H—C and N...H—C are predicted to occur regularly in the gas

phase conformers of the Sem molecule. The importance of the O...H—C type of intramolecular H bonds in various biological systems has been well documented in the literature [47]. On the other hand, some of the H bonds such as O₉...H—C₁, O₈...H_b—C₄, N₇...H_a—C₃, N₇...H₁₀—O₈, and Se₂...H—C₅ have been found to occur only in the Sem^D, Sem^E, Sem^G, Sem^I, Sem^J, and Sem^M conformers that uniquely shape their structure, stability and vibrational spectroscopic aspects.

The theoretical vibrational spectra of all the Sem conformers are calculated at the MP2/6-31++G(*d,p*) and B3LYP/6-311++G(*d,p*) levels of theories in the gas phase. The calculated harmonic frequencies are known to be usually larger than their corresponding experimental values [48], and such discrepancies have been attributed to the neglect of anharmonicity effects in theoretical treatments, incomplete incorporation of electron correlation, and the use of finite basis sets. Nevertheless, the predicted vibrational data of the Sem conformers listed in Table 5 provide the valuable information regarding the existence and nature of the various types of intramolecular H bond interactions in the conformers as well as their structural and molecular properties. The accuracy of the B3LYP functional in reproducing the experimental vibrational modes has been well discussed in the literature [34, 49, 50]. It has also been recognized that the B3LYP level performs better in predicting the vibrational frequencies as compared to the MP2 level [51, 52]. It is expected that the theoretical vibrational frequencies furnished in this study may be useful to give a preliminary guideline concerning the gas phase conformational behavior of the Sem molecule. Each conformer of the gaseous Sem molecule

Table 5

Vibrational frequencies^a (cm⁻¹) of various vibrational modes^b of the Sem conformers calculated at the MP2 and B3LYP (given in parentheses) levels in the gas phase. The experimental and theoretical (given in parentheses) frequency values are collected from the gas phase IR spectra of methionine [43]

	Sem ^A	Sem ^B	Sem ^C	Sem ^D	Sem ^E	Sem ^F	Sem ^G	Sem ^H	Sem ^I	Sem ^J	Sem ^K	Sem ^L	Sem ^M	Expt. (Theo.)
$\nu(\text{O}_8\text{—H})$	— (3636)	3610 (3637)	3613 (3636)	3617 (3643)	3595 (3619)	3614 (3639)	3611 (3637)	3595 (3618)	3613 (3639)	3395 (3356)	3669 (3682)	3663 (3678)	3665 (3678)	3572 (3568)
$\nu(\text{C}_6=\text{O}_9)$	— (1762)	1776 (1761)	1772 (1760)	1747 (1808)	1757 (1744)	1773 (1759)	1728 (1755)	1760 (1748)	1757 (1745)	1781 (1769)	1741 (1779)	1740 (1779)	1745 (1777)	1777 (1775)
$\nu_{\text{as}}(\text{N}_7\text{—H})$	— (3474)	3504 (3473)	3603 (3473)	3498 (3462)	3499 (3455)	3512 (3482)	3513 (3480)	3499 (3458)	3508 (3468)	3505 (3475)	3495 (3454)	3490 (3454)	3523 (3490)	— (3403)
$\nu_s(\text{N}_7\text{—H})$	— (3396)	3400 (3395)	3403 (3394)	3394 (3384)	3398 (3382)	3413 (3407)	3408 (3400)	3397 (3382)	3403 (3390)	3411 (3392)	3395 (3380)	3394 (3382)	3414 (3403)	— (3327)
$\nu(\text{C}_5\text{—H})$	— (2831)	2909 (2827)	2903 (2831)	2931 (2890)	3024 (2909)	2880 (2809)	2891 (2817)	3015 (2969)	3018 (2973)	2984 (2935)	2963 (2911)	2956 (2908)	2899 (2841)	
$\nu_{\text{as}}(\text{C}_3\text{—H})$	— (3026)	3072 (3024)	3058 (3022)	3053 (3010)	3057 (3018)	3031 (2985)	3067 (3030)	3034 (3009)	3032 (3007)	3063 (3046)	3030 (3003)	3063 (3026)	3060 (3026)	
$\nu_s(\text{C}_3\text{—H})$	— (2951)	2976 (2951)	2990 (2955)	2978 (2957)	2997 (2966)	2964 (2939)	2998 (2974)	2976 (2954)	2974 (2953)	2999 (2952)	2965 (2933)	2989 (2952)	2985 (2964)	
$\nu_{\text{as}}(\text{C}_4\text{—H})$	— (2988)	3045 (2996)	3040 (2992)	3041 (2989)	3035 (2981)	3058 (3007)	3040 (2985)	3051 (2982)	3051 (2984)	3020 (2962)	3050 (2981)	3027 (2965)	3021 (2954)	
$\nu_s(\text{C}_4\text{—H})$	— (2927)	2971 (2936)	2979 (2941)	2953 (2900)	2953 (2973)	2993 (2955)	2979 (2929)	2982 (2934)	2984 (2937)	2960 (2917)	2984 (2944)	2971 (2927)	2955 (2905)	
$\nu_{\text{as}}(\text{C}_1\text{—H})$	— (3041)	3104 (3034)	3091 (3045)	3110 (3052)	3098 (3037)	3104 (3040)	3093 (3040)	3102 (3041)	3103 (3041)	3105 (3038)	3103 (3042)	3100 (3042)	3107 (3043)	
$\nu_s(\text{C}_1\text{—H})$	— (2948)	2989 (2948)	2993 (2953)	2990 (2951)	2989 (2950)	2987 (2948)	2988 (2949)	2987 (2949)	2988 (2949)	2989 (2951)	2988 (2950)	2992 (2949)	2991 (2951)	
$\gamma(\text{N}_7\text{—H})$	— (1668)	1642 (1668)	1642 (1668)	1651 (1678)	1657 (1687)	1647 (1671)	1641 (1668)	1655 (1684)	1653 (1680)	1648 (1674)	1656 (1687)	1657 (1689)	1625 (1655)	
$\nu(\text{C}_6\text{—O}_8)$	— (1316)	1284 (1318)	1286 (1316)	1353 (1380)	1267 (1294)	1288 (1320)	1422 (1331)	1263 (1298)	1324 (1345)	1210 (1216)	1252 (1287)	1247 (1286)	1270 (1297)	

^a Frequencies are scaled using the appropriate correction factors as mentioned in the text.

^b Vibrational modes: ν = stretching; γ = scissoring; s = symmetric; as = asymmetric.

has a total of 54 normal vibrational modes. It is evident from Table 5 that the frequency values of certain vibrational modes such as asymmetric and symmetric stretching modes of the methyl group ($\nu_{as}(C_1-H)$ and $\nu_s(C_1-H)$ respectively) remain basically unaltered along with a change in the conformation, while some are very sensitive to even small changes in the configuration of the conformers and consequently leave noticeable signatures in their IR spectra. For example, in Sem^J the $\nu(O_8-H)$ stretching occurs at about 3395 cm^{-1} (3356 cm^{-1} at the B3LYP level) while for other 12 conformers its stretching frequencies range from 3595 cm^{-1} to 3669 cm^{-1} at the MP2 level (3618 cm^{-1} to 3682 cm^{-1} at the B3LYP level). This is because the Sem^J conformer possesses a strong and unique $N_7\dots H_{10}-O_8$ H bond interaction (with a B...H distance of 1.96 \AA at both MP2 and B3LYP levels) due to the *anti*-periplanar conformation of the carboxyl group ($\Phi_5 = 7.86^\circ$ at the MP2 level). Similarly, the increase or lowering in the frequency values of the other vibrational modes of the Sem conformer can be explained based on the H bond combinations present in them. The relevant experimental and theoretical frequency values collected from the gas phase IR spectra of methionine [43] listed in Table 5, suggest that both MP2/6-31++G(*d,p*) and B3LYP/6-311++G(*d,p*) levels of theory perform well in reproducing the previous experimental and theoretical results. Thus, it is expected that the data listed in Table 5 would greatly aid future experimentalists in detecting the gas phase Sem conformers even though they differ by small energy differences from one another, for example, the Sem^J conformer can be distinguished from the others by simply referring to its $\nu(O_8-H)$ stretching frequency appearing at $3356-3395\text{ cm}^{-1}$.

CONCLUSIONS

A detailed gas phase conformational analysis of the non-ionized selenomethionine (Sem) molecule with regard to its five internal backbone torsion angles has been carried out using the B3LYP/6-31G(*d,p*) level of theory. A total of 13 conformers, selected based on the PES exploration corresponding to the five torsion angles, are then subjected to the full geometry optimization and vibrational frequency calculations at the MP2/6-31++G(*d,p*) and B3LYP/6-311++G(*d,p*) levels. Characteristic intramolecular hydrogen bonds present in each conformer, their relative energies, theoretically predicted vibrational spectra, HOMO-LUMO energy gaps, rotational constants and dipole moments are systematically reported and thoroughly analyzed, which can be helpful for the future experimentalists. The calculated relative energy range of the conformers at the MP2/6-31++G(*d,p*) level is $7.92\text{ kcal}\cdot\text{mol}^{-1}$ whereas the same obtained at the B3LYP/6-311++G(*d,p*) level is $5.77\text{ kcal}\cdot\text{mol}^{-1}$. The predicted geometries as well as the relative stability orders furnished in this study at the B3LYP/6-311++G(*d,p*) and MP2/6-31++G(*d,p*) levels reveal that the structural aspects and relative energies of the conformers may depend on the level of theory and the size of the basis set used. Six types of intramolecular H bonds, namely $O\dots H-O$, $O\dots H-N$, $N\dots H-O$, $O\dots H-C$, $N\dots H-C$, and $Se\dots H-C$, are found to exist in the Sem conformers, all of which seem to play crucial roles in imparting the observed conformations to the conformers as well as in determining their energies and vibrational spectroscopic data. The vibrational frequencies are found to shift invariably toward the lower side of the frequency scale, corresponding to the presence of intramolecular H-bond interactions in the conformers.

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