

# Theoretical Comparative Study of the Structure, Dynamics and Electronic Properties of Two Allyl Molecules: S-allyl cysteine (SAC) and S-allyl mercaptocysteine (SAMC)

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**ABSTRACT:** The structural, dynamic and electronic properties of two allyl molecules (S-allyl cysteine and S-allyl mercaptocysteine) have been investigated theoretically by performing semi-empirical molecular orbital (AM1 and PM3), ab initio (RHF) and density functional theory calculations. The geometry of the molecules have been optimized, the vibrational spectra and the electronic properties of the molecules have been calculated in their ground states in gas phase. For each of the two molecules, we found that the optimized geometries resulting from calculations based on the three levels of accuracy, to be very similar. However, we found that an accurate description of the vibrational properties of these molecules necessitates calculations at the ab initio level. We also found electronic structures of the molecules to be satisfactory when performed at the DFT level.

**Keywords:** S-allyl cysteine, S-allyl mercaptocysteine, antioxidant, garlic, semi-empirical method, ab initio calculation, density functional method.

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## Introduction

The nature and origin of onion and garlic flavour compounds, have been studied since the 1940s. S-allyl cysteine (SAC) and S-allyl mercaptocysteine (SAMC) are bioavailable water-soluble organosulfur compounds from aged garlic extract (AGE). Other hydrophilic cysteine-containing compounds naturally formed in onion and garlic are: N-Acetyl cysteine (NAC), S-ethyl cysteine (SEC), S-methyl cysteine (SMC) and S-propyl cysteine (SPC). Once the plant tissue is damaged, comparatively stable flavour precursors are cleaved to give a series of biologically active, volatile sulphur compounds that undergo further vapour-phase chemical transformations. Information about the biosynthesis of cysteine, reactions in which glutathione participates, and the sources of alkyl

donors within other plants has been reviewed by Jones et al. [1] together with the primary pathways that have parallel routes with *Allium* flavour precursor biosynthesis. Work in their laboratory has shown that garlic has several cysteine synthase (CSs) enzymes, which vary in their tissue expression and ability to synthesize S-allyl cysteine. The allylthio group of allicin and other organosulfur compounds, isolated from garlic, is considered a pharmacophore, and a key structure component of the molecule, which affords biological activities.

AGE is aged garlic extract, containing antioxidant phytochemicals, which prevents oxidant damage. Oxidant damage is reactions such as oxidative modification of DNA, proteins and lipids which are caused by reactive oxygen species [2-4]. Although the five cysteine-containing compounds are structurally similar to cysteine, these compounds appear to have different biochemical activities. It is highly likely that the noncysteine part in

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each cysteine-containing molecule plays an important role in its antioxidant activity, and triglyceride- and cholesterol-reducing actions [2,5]. In brief, beneficial health effects attributed to AGE are: reducing the risk of cardiovascular disease, stroke, cancer and aging, including the oxidant-mediated brain cell damage that is implicated in Alzheimer's disease. Maldonado et al. [6] have shown SAC to prevent tubular and glomerular adverse effects induced by the antibiotic gentamicin due to antioxidant activities.

Several population based studies indicate that people in South East Asian countries have a much lower risk of acquiring colon, gastrointestinal, prostate, breast and other cancers when compared to their Western counterparts. It is very likely that constituents of their diet such as garlic, ginger, soy, curcumin, onion, tomatoes, cruciferous vegetables, chillies and green tea play an important role in their ability to avoid these cancers. Along this line diallyl sulfide, ajoene, S-allyl cysteine and alicin of garlic have been considered chemopreventive agents known to suppress tumorigenesis. These dietary agents are believed to suppress the transformative, hyperproliferative and inflammatory processes that initiate carcinogenesis. These inhibitory influences may ultimately suppress the final steps of carcinogenesis, namely angiogenesis and metastasis. These dietary agents have been classified as chemopreventive agents since they delay the onset of the carcinogenic process. They are considered pharmacologically safe since they are derived from natural sources [7].

Allicin, another organosulfur compound from garlic, was incubated with cysteine at physiological temperature and pH, under conditions mimicking those in the intestinal tract, and was found to react with cysteine in less than one minute, yielding two moles of SAMC per mol of allicin. Other garlic-derived compounds, including diallyl trisulfide, diallyl disulfide, and ajoene, were also transformed to SAMC in this *in vitro* model system. Furthermore, allicin can also react rapidly with glutathione-or thiol-containing proteins to produce SAMC. These results suggest that after the consumption of garlic, SAMC can be a major metabolic product in the intestinal tract and could, therefore, reach a high local concentration in the intestinal mucosa, thus enhancing its effects on colon cancer prevention. Xiao et al. [8] concluded that SAMC exerts antiproliferative effects by binding directly to tubulin and disrupting the MT assembly, thus arresting cells in mitosis and triggering JNK1 and caspase-3 signaling pathways that lead to

apoptosis. Their proposed mechanism of action was by forming disulfide bonds with thiol-containing amino acids (such as cysteine residues) in tubulin. Alicin, was shown to inhibit the proliferation of human breast, endometrial, and colon cancer cells. It is rapidly metabolized, both *in vitro* and *in vivo*. Therefore SAMC seems to be a bioavailable natural antitumor agent.

Disulfides such as ajoene, diallyl disulfide and imidazolyl disulfides have been studied for antitumor activity and shown to induce G<sub>2</sub>/M phase arrest leading to apoptosis in different cell lines. Griffiths et al. [9] have extended these studies and synthesized and tested a number of  $\alpha$ -sulfone disulfides. They found that the synthesized compounds also have significant promise as antileukaemic agents. Recently, a newly synthesized 3-alkoxy-6-allylthiopyridazine derivative, 3-methylthio-6-allylthiopyridazine (Thio-K6), one of the sulfur-substituted compounds, showed better chemopreventive activity on hepatocarcinoma cells [10]. Recently ajoene molecule has been investigated theoretically [11] and detailed calculations of other garlic molecules including allicin, methyl propyl disulfide and allyl methyl sulfide have been performed [12].

Our work is the first detailed calculation and provides additional scientific information on SAC and SAMC molecules to be used in structure-activity relationship approaches in the development of these organosulfur compounds as novel anticancer drugs. In this paper we describe the structural, vibrational and electronic properties of the two molecules mentioned above considering various levels of quantum chemical calculations, which have not been studied before.

## Theoretical Methods

In this study, isolated two molecules (in gas phase), namely, S-allyl cysteine (SAC) (C<sub>6</sub>H<sub>11</sub>SO<sub>2</sub>N) and S-allyl-mercaptocysteine (SAMC) (C<sub>6</sub>H<sub>11</sub>S<sub>2</sub>O<sub>2</sub>N), have been theoretically examined by performing successively semi-empirical molecular orbital, ab initio (Restricted- Hartree-Fock (RHF)) and density functional theory (DFT) calculations. The molecular-mechanics (MM) method [13] is used to get the pre-optimized structure using MM+ force field [14], in order to speed-up the structural optimization. The calculations were performed using the Hyperchem package [15]. Two levels of semi-empirical methods have been applied to calculate structural and dynamical properties of the systems studied here. The first one is the so called AM1 [16] within the RHF

approximation [17] and the second one is PM3 [18] within the same approximation RHF. The higher level of computation, ab initio (RHF) and DFT [19] were performed at the STO-3G [20] and 3-21G [21] basis sets with an exchange and correlation potentials B3LYP [22,23] for the DFT level. Geometry optimizations are carried out by using a conjugate gradient method (Polak-Ribiere algorithm [24]).

For the structural calculations, we used the STO-3G for DFT and both STO-3G and 3-21G for ab initio (RHF). In all cases (AM1, PM3, RHF and DFT), we found a convergence criterion of 0.001 kcal/mol/Å to be sufficient for structural optimization. However, for the calculations of the dynamics (vibrations), we found that a convergence criterion of 0.0001 kcal/mol/Å is needed to reduce the residual forces to less than 0.001 kcal/mol/Å in order to avoid modes with imaginary frequencies. For the RHF level, we found that the STO-3G basis set give a poor vibrational spectrum which is improved when the 3-21G basis set is used. For the molecules studied here, we found that the DFT with the STO-3G basis set to be unsuitable for the vibrational calculations. Calculations of the vibrational spectra using DFT and higher level basis sets were found to be prohibitive in computational time and were not attempted. Finally, the optimized structure is thus used at the DFT level with the 3-21G basis set to calculate the electronic structure of the systems.

## Results and Discussion

### Structural Information

#### A. S-allyl cysteine (SAC)

S-allyl cysteine (SAC) molecule ( $C_6H_{11}SO_2N$ ) contains 6 carbon atoms, 1 sulfur atom, 1 nitrogen atom, 2 oxygen atoms and 11 hydrogen atoms with a molecular point group C1. In Figure 1, we present the optimum structure of the SAC resulting from a geometry optimization using the DFT level of accuracy. In Figure 2, we show the bond length information between neighboring atoms for every step of our calculations (four different levels of computation). We note that semi-empirical, ab initio (RHF) and DFT calculations give molecular configurations that are close to each other, this behaviour is seen in our previous calculations of other garlic molecules including allicin, methyl propyl disulfide and allyl methyl sulfide [12]. The differences are of the order of a tenth of an angstrom. The carbon-carbon bond length is found around 1.5 Å which is found similar to the cases containing the other

molecules [12]. The C-C double bond, C-S bond and C-H bond length values are found respectively 1.3 Å, 1.8-1.9 Å and 1.1 Å which are found to be same as in the other molecules allicin, MPD and AMS. The bond lengths between C-N and C-O and C-O double bond lengths are calculated respectively as, 1.5 Å, 1.4 Å and 1.2 Å. Other structural information we present here is the angle between atoms in different parts of the molecule. We note that the angles between the 3 carbon atoms on the left and on the right side of the molecule (see Figure 2) are (4-5-6) 124° and (7-2-8) 109°.

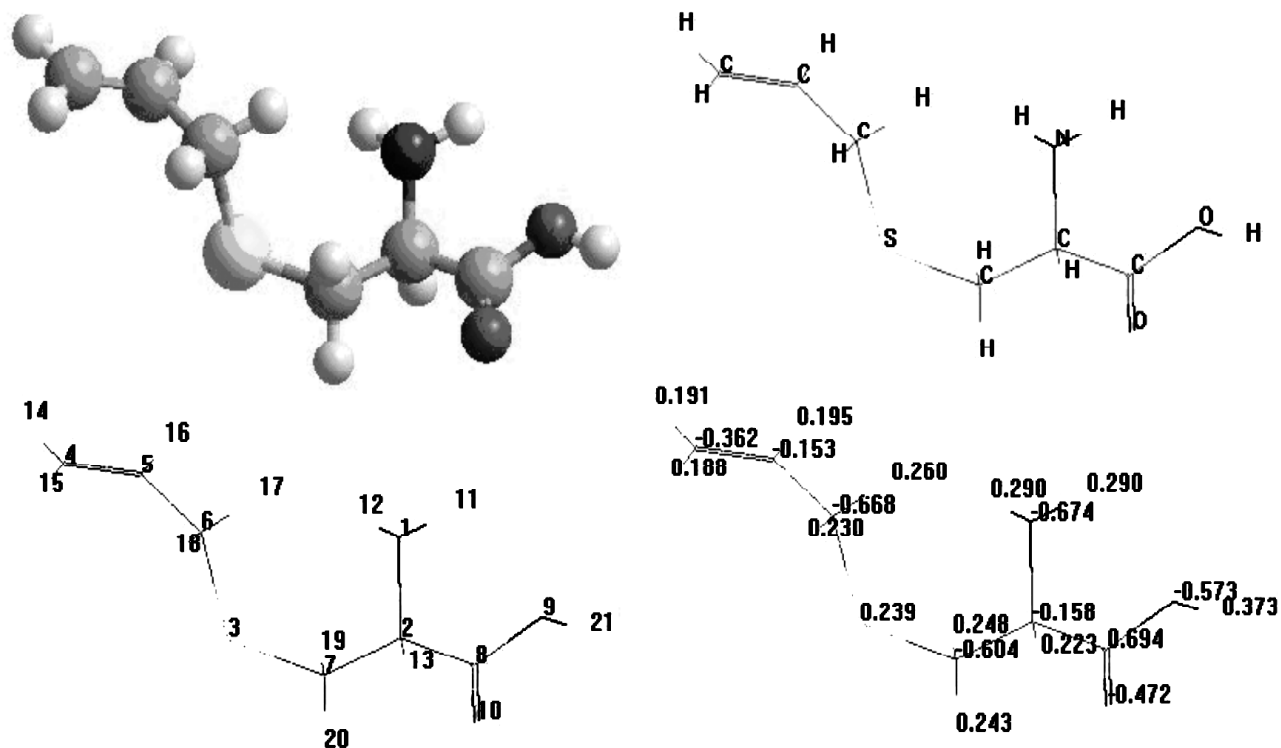
The angles between 2 carbon atoms and the sulfur atom on the left (5-6-3) and right side (3-7-2) are 109° and 112° respectively. The angles involving the nitrogen atom are found to be (7-2-1) 110° and (8-2-1) 108°. For the oxygen atom which sits almost perpendicular to the plane containing the two carbon atoms and the extra oxygen atom labeled 10. The angles including the oxygen atom are (2-8-10) 127° and (9-8-10) 122°. For completeness, we present the actual coordinates of all atoms of the molecule in Table 1.

#### B. S-allyl mercaptocysteine (SAMC)

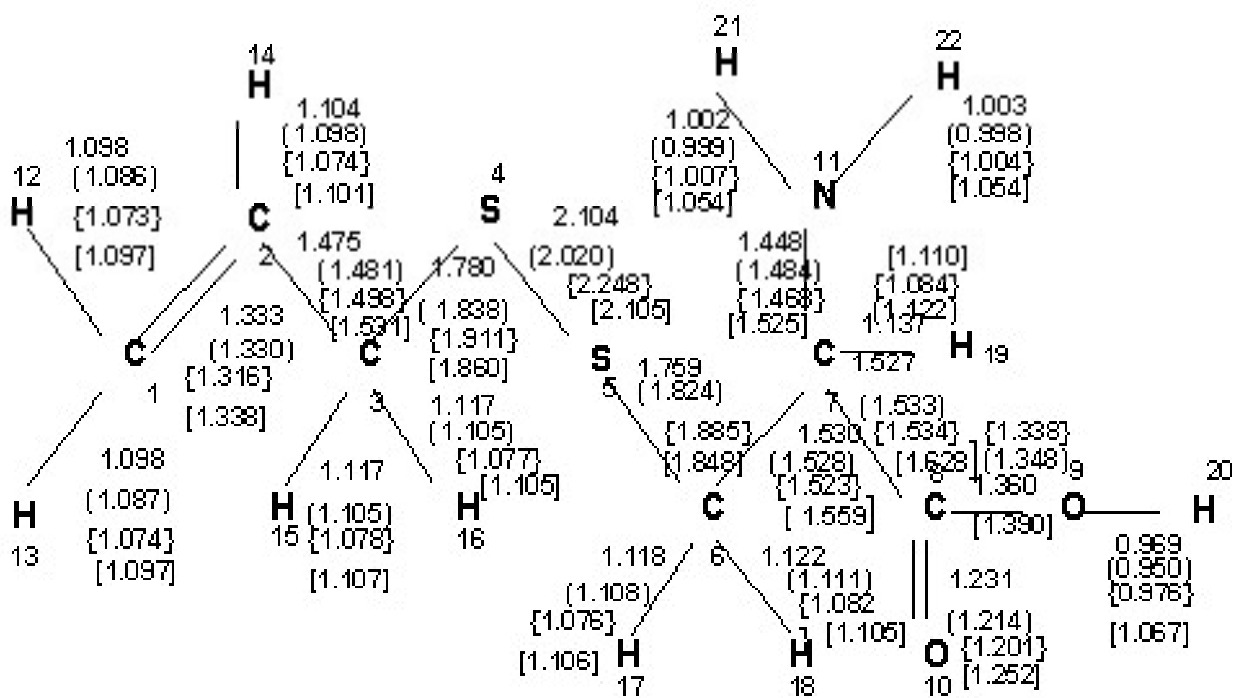
S-allyl mercaptocysteine ( $C_6H_{11}S_2O_2N$ ) molecule contains 6 carbon atoms, 2 sulfur, 2 oxygen, 1 nitrogen and 11 hydrogen atoms with the C1 molecular group. We present the optimized structure of SAMC from a geometrical optimization using DFT in Figure 3. In Figure 4, we show the bond length information between the atoms using different level of methods (semi-empirical, ab initio (RHF) and DFT). The first thing we can infer from the figure is that semi-empirical, RHF and DFT calculations give similar molecular configuration with what has been found in the case of the first molecule (SAC) which is studied here and also the molecules from our previous calculations [12].

The difference in the bond lengths in cases of the methods is again in the order of 0.1 Å. The C-C double bond length is found 1.3 Å, C-C bond length is 1.5 Å, C-S bond length 1.8-1.9 Å, C-N 1.5 Å, C-O double bond length is 1.2 and C-O single bond length is calculated as 1.3 Å. These specific bond lengths are similar to the ones calculated from the other molecules (allicin, MPD, SAC). The bond length between S-S is calculated as 2.1-2.2 Å for this molecule and it is found to be the same as in the cases of allicin and MPD molecules.

We get the information about the angles between the atoms from the optimized geometry. From Figure 4, the angles between three carbon atoms on the left and right



**Figure 1:** Optimized structure of SAC ( $C_6H_{11}SO_2N$ ) from DFT calculation. Bottom right panel shows the charge on the atoms of the molecule.



**Figure 2:** SAC molecule: Bond length (Å) information using semi-empirical (AM1, PM3), {ab initio (RHF)} and [DFT/B3LYP/STO-3G] calculations.

**Table 1**  
Atomic positions of SAC molecule (in Figure 1) from the optimized structure (DFT/B3LYP/STO-3G). Atom labels are as shown in Figure 2.

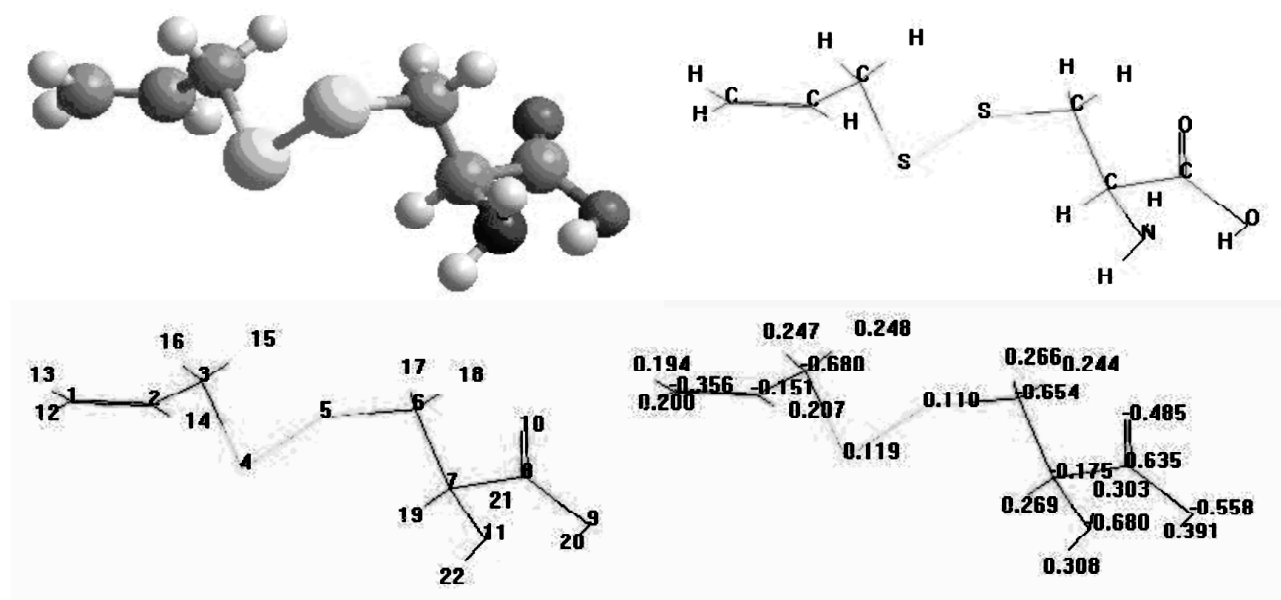
Atom Label	x	y	z
1	-0.49393333	1.16841134	0.40489382
2.	0.09954980	2.56174218	0.16928378
3.	-2.00589716	3.68515505	1.74528443
4.	-5.23480082	2.18430387	2.80687981
5.	-3.97134966	1.87566648	2.49397738
6.	-3.23712257	2.39270163	1.25601629
7.	-1.01737120	3.66533530	0.20054675
8.	0.82855508	2.55660488	-1.22797769
9.	1.62407231	1.37354642	-1.31581816
10.	0.77332001	3.40482516	-2.14373518
11.	0.25751389	0.52010534	0.02375129
12.	-0.41164824	1.02264128	1.45325038
13.	0.87241060	2.81230199	0.93314315
14.	-5.71696979	1.80183253	3.71438498
15.	-5.84800079	2.83250546	2.16820826
16.	-3.38390364	1.22857452	3.16327964
17.	-2.67861285	1.57309923	0.76141099
18.	-3.96444808	2.81065932	0.53619489
19.	-1.67450772	3.52962215	-0.67587420
20.	-0.52667072	4.64934791	0.09745525
21.	2.03003084	1.44543924	-2.25743162

side of the molecule are found to be respectively  $124^\circ$  and  $109^\circ$  which are found as same as for the ones in SAC molecule. The angles (2-3-4), (5-6-7) between the two carbon and one sulfur atoms are calculated as  $107.3^\circ$  and  $112.3^\circ$ , respectively. The angle (4-5-6) between the two sulfur and one carbon is found to be  $99^\circ$  which is found to be same as in allicin molecule [12].

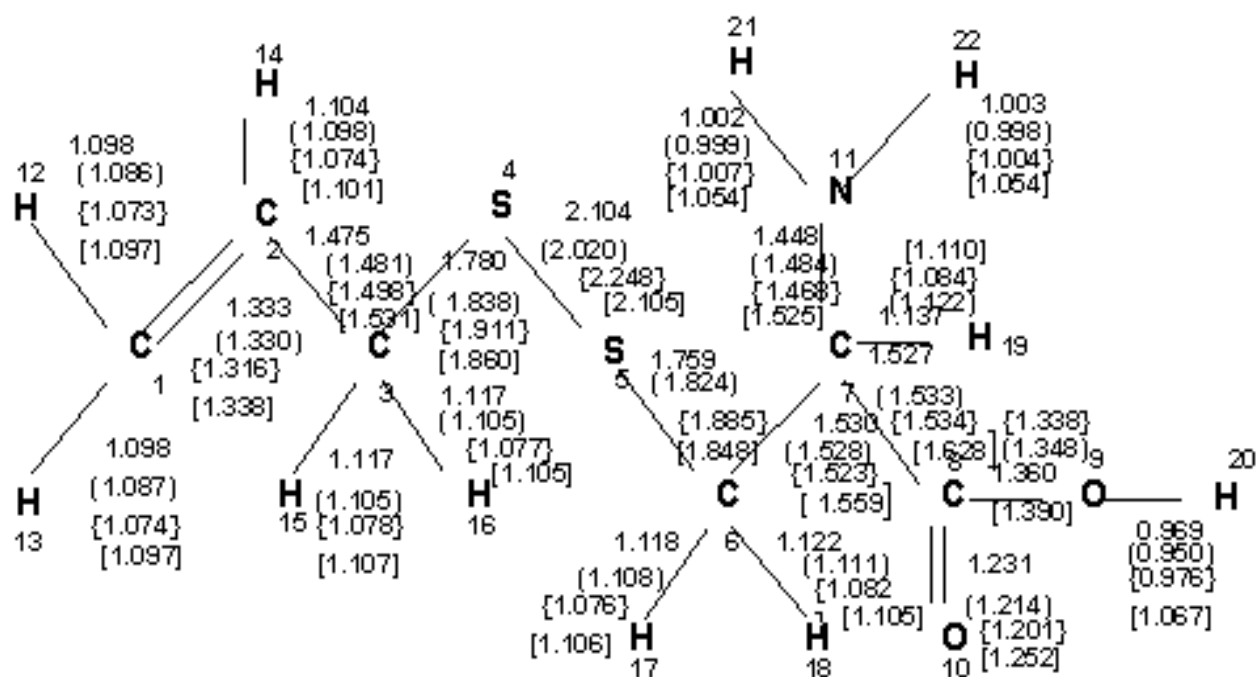
The angles involving the nitrogen atom are found to be (6-7-11)  $116^\circ$  and (8-7-11)  $108^\circ$  which are exactly the same as for SAC molecule. The angles including oxygen atom which makes the double bond with a carbon atom (labeled 10) is calculated as (7-8-10)  $123^\circ$ . The angle between the one carbon and two oxygen atoms is found to be (9-8-10)  $124^\circ$ .

#### Vibrational Properties of the molecules

The vibrational dynamics of the molecules are examined using two semi-empirical methods (AM1 and PM3) and by the RHF approximation using the 3-21G small basis set. The frequencies of the normal modes in the harmonic approximation for SAC molecule are given in Table 3. We note that here, in general, when comparing the calculated frequencies with those of measured by infrared (IR) spectroscopy, one rescales the calculated frequencies. The rescaling of the calculated frequencies is due to the fact that the measured frequencies are anharmonic, on the one hand, and the computational methods used here are implemented with finite basis sets. Scott and Radom [25] have investigated the difference



**Figure 3:** Optimized structure of SAMC ( $C_6H_{11}S_2O_2N$ ) from DFT calculation. Bottom right panel shows the charge on the atoms of the molecule.



**Figure 4:** SAMC molecule: Bond length (Å) information using semi-empirical (AM1, (PM3)), {ab initio (RHF)} and [DFT/B3LYP/STO-3G] calculations.

between the calculated and the measured frequencies for a variety of molecules and computational methods. They concluded that with a single scaling factor, one may achieve a relatively good agreement with the experimental observation. However, the scaling factor varies from one method to the other. The scaling factors for the methods used here are 0.9532 for AM1, 0.9761 for PM3 and 0.9085 for RHF/3-21G. Here after, we will present values of our calculations and will add between parentheses the scaled ones. The SAMC molecule contains 21 atoms and hence 57 normal modes. We examined again that the vibrational spectrum can be divided into two bands: a low frequency band containing 46 modes and a high frequency band with 11 modes. The low frequency band for the AM1 method runs from 20.27 (19.32)  $\text{cm}^{-1}$  to 2087.01 (1989.34)  $\text{cm}^{-1}$ , while the high frequency band starts at 2928.33 (2791.28)  $\text{cm}^{-1}$  and ends at 3453.28 (3291.66)  $\text{cm}^{-1}$ . For the PM3 method, these boundaries for the low band are 12.30 (12.01)  $\text{cm}^{-1}$  to 1980.35 (1933.02)  $\text{cm}^{-1}$  and for the high band are 2808.97 (2741.83)  $\text{cm}^{-1}$  to 3851.70 (3759.64)  $\text{cm}^{-1}$ . For the RHF/3-21G, we found that these limits for the low band starts at 39.21 (35.62)  $\text{cm}^{-1}$  to 1967.67 (1787.62)  $\text{cm}^{-1}$  and for high band from 3164.15 (2874.63)  $\text{cm}^{-1}$  to 3872.67 (3518.32)  $\text{cm}^{-1}$ . Although there is no available experimental IR spectra in the literature for the molecules considered, the calculated frequencies qualitatively agree

with available frequency values for particular vibrations in various molecular systems [26].

**Table 2**  
Atomic Positions of SAMC molecule (in Figure 3) from the Optimized Structure DFT/B3LYP/STO-3G).  
Atom labels are as shown in Figure 4

Atom label	x	y	z
1.	-0.04913043	-4.76383042	0.82856068
2.	-0.28368485	-3.45712380	0.66290473
3.	-1.09155625	-2.86772986	-0.49584652
4.	-2.74231448	-2.28849905	0.13621025
5.	-3.44803057	-1.25214674	-1.55445778
6.	-2.70363850	0.41099460	-1.24693052
7.	-3.17795402	1.10570996	0.06550893
8.	-3.24139284	3.49855996	0.68481223
9.	-3.24139284	3.49855996	0.68481223
10.	-1.10731416	2.57805186	0.30231007
11.	-4.63858286	1.54450503	0.06554655
12.	0.53020898	-5.14336924	1.67923508
13.	-0.42070416	-5.51484324	0.11975065
14.	0.10018720	-2.73058132	1.39530614
15.	-0.54355536	-2.01169052	-0.93367647
16.	-1.22876245	-3.62852374	-1.28525919
17.	-1.59925814	0.35789926	-1.20879197
18.	-2.96918204	1.04101136	-2.11509956
19.	-3.01926338	0.41347550	0.9187006
20.	-4.14585727	2.94849281	0.55216746
21.	-5.00403250	1.50558606	-0.922271735
22.	-5.22021450	0.85031431	0.60420188

The displacements of some particular modes of the SAC molecule are illustrated in Figure 5. From the Figure 5(a), the mode between the N-H bond (correspond to 3446.22  $\text{cm}^{-1}$  frequency) shows asymmetric stretching mode. The asymmetric mode here means displacement of H and N atoms are not equal for both N-H bonds. The mode between the H-C-H bond (3086.81  $\text{cm}^{-1}$ ) in Figure 5(b) shows the asymmetric stretching mode and again in the same figure, the C-H bond gives the stretching. In Figure 5(c), the mode (1787.61  $\text{cm}^{-1}$ ) between the C-O double bond shows stretching mode as it is seen in the SAMC molecule modes also. The mode between the C-S bond in Figure 5(d) gives the stretching mode also.

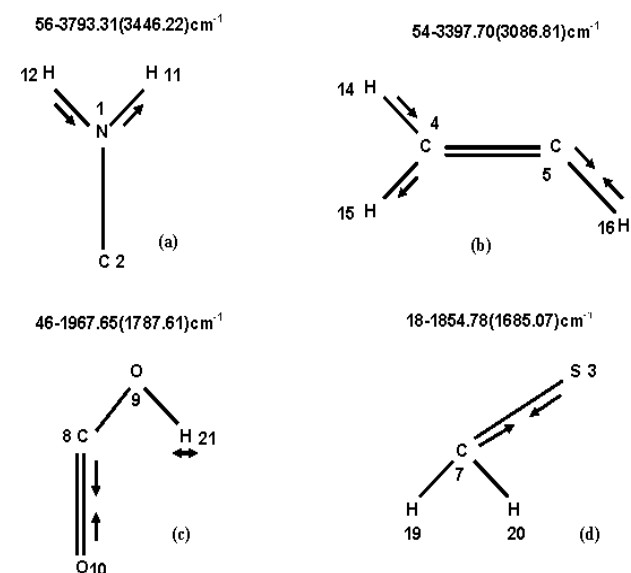
The S-allyl mercaptocysteine (SAMC) molecule contains 22 atoms and has 60 normal modes. For this molecule again the vibrational spectrum can be divided into two parts as low frequency and high frequency bands. The low frequency band contains 49 normal modes, and the high frequency band 11 modes.

**Table 3**  
Normal Mode Frequencies of Vibrations (in  $\text{cm}^{-1}$ ) and Integrated Infrared band Intensities (in  $\text{km/mol}$ ) (in Parenthesis) for the SAC Molecule for three Different levels of Computation

Mode #	AM1	AM3	ab initio (RHF)
1.	20.27(0.09890)	12.30(0.13863)	39.21(1.21608)
2.	30.73(0.48209)	26.01(1.12018)	49.70(0.55928)
3.	36.10(0.79413)	37.94(0.35477)	60.32(1.49930)
4.	51.24(0.11841)	47.26(0.15979)	92.04(0.40622)
5.	87.38(1.39222)	70.05(0.46565)	134.19(6.79272)
6.	153.01(1.55364)	154.56(1.13412)	181.04(3.85534)
7.	179.34(0.22169)	189.03(1.03026)	212.94(0.22777)
8.	217.96(1.40557)	193.55(23.63185)	262.74(1.18752)
9.	242.75(33.80293)	209.47(1.55624)	330.20(7.53729)
10.	303.02(0.70149)	280.39(1.86040)	345.37(38.96397)
11.	346.32(2.05022)	332.10(1.51332)	369.55(56.33691)
12.	395.40(0.59940)	360.40(2.76570)	427.92(5.27031)
13.	432.50(0.11124)	430.99(0.21850)	465.75(0.91418)
14.	518.87(10.84130)	471.60(9.84526)	521.64(18.74310)
15.	552.18(33.66503)	508.78(33.96803)	603.00(67.41998)
16.	574.65(11.13571)	525.29(26.52614)	619.80(23.42142)
17.	588.57(18.47851)	586.46(0.99299)	646.09(115.47615)
18.	724.75(23.76528)	696.09(15.26877)	758.54(110.46301)
19.	758.12(4.79237)	762.70(4.09430)	795.87(33.55247)
20.	798.96(3.93839)	777.67(4.14800)	813.86(12.81917)
21.	874.62(0.25516)	851.39(0.09917)	875.51(66.84328)
22.	892.58(4.32300)	866.89(0.34516)	893.04(126.34207)
23.	9.58.15(24.86274)	905.85(1.53379)	982.14(19.84485)
24.	964.44(10.40775)	931.86(19.64824)	989.79(1.02479)
25.	997.93(1.58407)	955.13(0.36853)	1004.36(2.90040)
26.	1018.88(11.40164)	1008.70(0.02682)	1073.29(7.54216)
27.	1058.15(20.82254)	1016.89(6.67361)	1118.59(78.12666)
28.	1084.25(0.60571)	1046.87(1.59804)	1162.00(0.04203)
29.	1099.98(2.04960)	1061.18(1.32725)	1199.82(69.13818)
30.	1150.14(3.68297)	1072.20(2.79115)	1202.66(19.05556)
31.	1206.80(4.97200)	1126.06(5.75963)	1217.00(303.48151)
32.	1237.17(1.90708)	1162.51(12.35175)	1319.59(1.63549)
33.	1252.73(2.96402)	1169.84(0.31036)	1359.61(2.92624)

34.	1259.06(1.43024)	1194.66(7.93072)	1366.62(18.66179)
35.	1271.45(2.35548)	1204.57(4.31189)	1394.04(24.71953)
36.	1317.36(0.84903)	1235.43(19.43651)	1413.06(7.17734)
37.	1372.62(6.02499)	1263.31(0.61019)	1454.06(33.88416)
38.	1386.43(22.99404)	1264.66(7.16170)	1469.06(0.39061)
39.	1392.38(0.76691)	1302.98(0.28741)	1490.63(9.32311)
40.	1423.69(11.46286)	1336.62(2.73786)	1539.30(30.64697)
41.	1432.89(1.47577)	1372.91(5.60723)	1612.43(9.29355)
42.	1453.61(9.44061)	1397.17(1.31726)	1618.07(9.29355)
43.	1538.65(62.48066)	1432.82(69.59943)	1658.18(3.46581)
44.	1707.99(1.53769)	1654.23(2.92814)	1830.50(65.58828)
45.	1855.97(0.58422)	1852.16(0.40270)	1854.78(3.34533)
46.	2087.01(124.36231)	1980.35(126.13953)	1967.67(250.35219)
47.	2928.33(0.14447)	2808.97(1.33680)	3164.15(26.70159)
48.	3027.93(4.38690)	2970.04(2.40824)	3267.95(11.62026)
49.	3035.23(15.02384)	2973.11(8.46200)	3287.45(7.00483)
50.	3099.05(2.61114)	3039.61(6.34504)	3318.25(8.87690)
51.	3105.78(7.13733)	3044.04(3.04440)	3331.15(1.11210)
52.	3153.52(4.19190)	3050.35(4.93572)	3344.49(5.84250)
53.	3179.91(8.99878)	3135.03(3.04379)	3348.80(1.53298)
54.	3213.26(16.76557)	3146.22(5.87754)	3397.71(17.50721)
55.	3411.31(15.52102)	3389.83(0.07947)	3692.84(8.62266)
56.	3425.33(65.05240)	3519.33(2.65931)	3793.31(18.99084)
57.	3453.28(9.85071)	3851.70(18.03686)	3872.67(96.97775)

The low frequency band for the AM1 method starts at 16.00 (15.25)  $\text{cm}^{-1}$  to 2070.03 (1973.15)  $\text{cm}^{-1}$ , for the high frequency band runs from 2949.35 (2811.32)  $\text{cm}^{-1}$  to 3455.97 (3294.23)  $\text{cm}^{-1}$ . For the PM3 method the low frequency band starting from 11.01 (10.74)  $\text{cm}^{-1}$  to 1977.87 (1930.59)  $\text{cm}^{-1}$ , while high frequency band 2819.17 (2751.79)  $\text{cm}^{-1}$  to 3870.14 (3777.64)  $\text{cm}^{-1}$ . The low frequency for the RHF/3-21G, we found to be starting from 24.65 (22.39)  $\text{cm}^{-1}$  to 1986.90 (1805.09)  $\text{cm}^{-1}$ , for high frequency band starts at 3245.42 (2948.46)  $\text{cm}^{-1}$  to 3768.23 (3423.44)  $\text{cm}^{-1}$ .



**Figure 5:** Some selected vibrational modes with the corresponding frequencies for the SAC molecule.

The vibrational modes of some specific modes of the SAMC molecule are given in Figure 6. In Figure 6(a), the mode between the C-O double bond (corresponding the frequency of  $1805.01 \text{ cm}^{-1}$ ) shows the stretching type mode. From the Figure 6(b), the mode between C-H (corresponding the frequency of  $3087.12 \text{ cm}^{-1}$ ) is so called C-H asymmetric stretching mode (type of stretching motion). While the N-H mode (see Figure 6(c)) is again is an example of asymmetric stretching mode, the double bond between the carbon atoms shows the stretching mode explicitly. The modes are examined for these specific bonds between the atoms are similar to those which are seen for the other small molecules [12].

### Electronic Structure

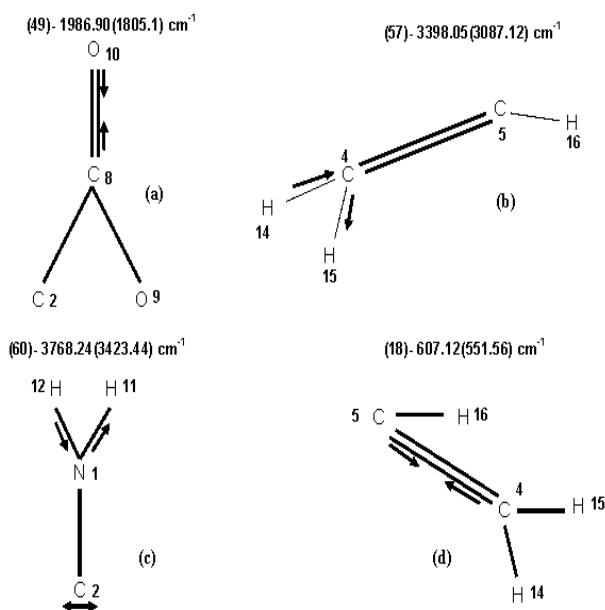
The electronic structures of the molecules studied were calculated with DFT using the 3-21G basis set with an exchange and correlation potentials B3LYP. We have performed a single point calculation on the previously optimized structure using a DFT calculation with an STO-3G basis set. In Figures 1 and 3, we present the excess charge on the atoms of the molecules. We note that the total charge of the molecules are zero (neutral). In Figure 1, for SAC molecule, the charges on the hydrogen atoms are all positive and the value is about 0.2 electron except the one (0.4 electron) which is neighbor of oxygen atom (9). While the carbon atoms (6-7) next to the sulfur atom having a large negative charge value of -0.6 electron, the carbon atom (8) which is neighbor of the two oxygen atoms has a large positive charge value (0.694 electron).

The charges on the oxygen atoms are found to be around -0.5, -0.6 electrons, and the sulfur atom has the charge of 0.3 electron.

The charges on the atoms of the SAMC molecule is given in Figure 3. From the figure, we can infer that, the hydrogen atoms have positive charge of 0.2-0.4 electrons as it is seen before for the other molecule studied (SAC). The only positively charged carbon atom (8) is found to be 0.6 electron. The other carbons which have the bond with sulfur atoms have negative values of -0.7 electron. The charge distribution of the atoms are seen similar to the SAC molecule. The difference only becomes significant for the sulfur atoms charge distribution is shared between two sulfur atoms (4-5).

**Table 4. Normal mode frequencies of vibrations (in  $\text{cm}^{-1}$ ) and integrated infrared band intensities (in  $\text{km/mol}$ ) (in parenthesis) for the SAMC molecule for three different levels of computation**

Mode #	AMI	PM3	ab initio (RHF)
1	16.00 (0.22218)	11.01 (0.06843)	24.65 (1.60894)
2	25.31 (1.67047)	24.82 (1.94436)	37.90 (6.00082)
3	31.54 (0.39833)	31.75 (0.98983)	52.55 (1.12925)
4	42.05 (1.10633)	39.45 (0.27022)	68.40 (3.48991)
5	45.96 (0.17700)	47.14 (0.87819)	77.36 (1.32824)
6	72.00 (1.38867)	83.93 (1.53559)	106.34 (2.66736)
7	116.69 (0.64400)	118.78 (1.17726)	128.57 (4.04901)
8	166.53 (4.09380)	175.98 (3.20816)	194.83 (12.76062)
9	186.87 (1.86695)	198.39 (2.16363)	228.79 (4.96135)
10	237.26 (15.65453)	243.95 (12.82039)	300.34 (3.23405)
11	259.38 (0.54253)	266.91 (0.78473)	311.13 (3.12508)
12	279.12 (2.23797)	274.71 (1.37661)	326.19 (17.64317)
13	353.08 (3.77018)	328.62 (0.94856)	385.77 (17.02167)
14	390.79 (0.86354)	402.65 (8.24323)	445.81 (3.34453)
15	413.37 (7.36655)	433.20 (0.33783)	462.84 (1.77158)
16	435.30 (0.28007)	454.80 (38.04403)	477.06 (1.97146)
17	466.07 (42.49999)	475.87 (1.48828)	552.49 (4.33981)
18	514.26 (2.19349)	514.46 (0.62287)	607.11 (4.05102)
19	574.38 (2.79693)	549.26 (7.61197)	643.80 (14.29951)
20	594.60 (10.37771)	583.49 (2.35286)	711.42 (11.78756)
21	710.54 (9.31791)	675.77 (4.34152)	807.91 (20.77764)
22	755.46 (8.38068)	760.22 (3.49802)	819.05 (54.67749)
23	789.52 (2.98512)	761.70 (2.55586)	863.39 (187.90100)
24	865.17 (6.35508)	833.38 (6.13848)	892.24 (4.75846)
25	873.05 (0.23385)	859.34 (0.11650)	917.45 (240.14729)
26	961.78 (15.93113)	875.99 (0.17026)	960.90 (61.24692)
27	971.25 (4.48645)	927.93 (19.61740)	969.73 (5.83514)



**Figure 6:** Some selected vibrational modes with the corresponding frequencies for the SAMC molecule.



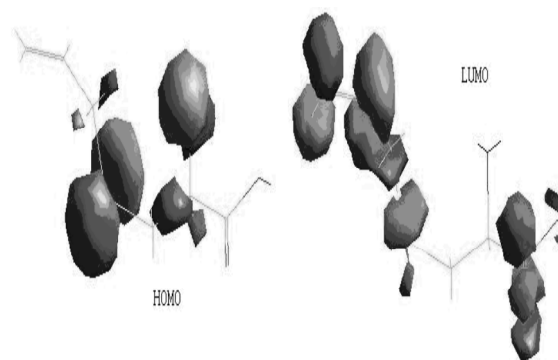
Mode #	AM1	PM3	ab initio (RHF)
28	991.57 (1.86368)	952.77 (0.43631)	997.58 (0.26109)
29	1020.14 (57.99967)	996.14 (5.30899)	1106.68 (79.93375)
30	1062.29 (19.28556)	1006.81 (4.56556)	1127.23 (76.58662)
31	1069.47 (1.36771)	1030.71 (0.34756)	1166.32 (0.57409)
32	1078.75 (0.92788)	1041.30 (4.93773)	1195.61 (0.92113)
33	1170.37 (2.91209)	1074.23 (6.45982)	1197.76 (9.41884)
34	1202.60 (0.14512)	1102.56 (12.25630)	1226.69 (14.35923)
35	1229.59 (3.83616)	1167.28 (1.02326)	1309.70 (7.56478)
36	1233.77 (5.15487)	1176.55 (1.47828)	1345.90 (0.44934)
37	1268.41 (1.43297)	1182.19 (13.35158)	1369.08 (17.69975)
38	1285.89 (4.03384)	1188.45 (4.01794)	1386.75 (67.03938)
39	1311.57 (0.31942)	1256.68 (2.24786)	1405.56 (5.43235)
40	1345.47 (3.90255)	1272.45 (10.95783)	1452.21 (400.03088)
41	1366.99 (8.84984)	1285.31 (5.14504)	1468.99 (2.83336)
42	1392.21 (2.19122)	1315.69 (21.13635)	1476.54 (279.76581)
43	1429.78 (1.38422)	1332.04 (2.83661)	1523.70 (5.44987)
44	1431.88 (4.17374)	1366.14 (9.86703)	1609.27 (6.81465)
45	1450.59 (11.15910)	1397.29 (1.77014)	1617.37 (13.12914)
46	1539.95 (151.49809)	1432.12 (113.96259)	1636.98 (8.70450)
47	1718.88 (2.93855)	1653.06 (6.16005)	1849.32 (47.60963)
48	1848.09 (3.66490)	1844.94 (3.00270)	1852.09 (1.51416)
49	2070.03 (117.93750)	1977.87(109.17891)	1986.90(267.54187)
50	2949.35(3.85055)	2819.17 (5.11108)	3245.42(3.98031)
51	3020.03 (22.86767)	2958.14 (13.73251)	3261.36 (1.67246)
52	3038.88 ( 4.56900)	2985.04 (2.25824)	3278.71 (9.60922)
53	3095.15 (17.00257)	3040.33 (7.52804)	3317.52 (5.93587)
54	3106.42 (2.34716)	3040.67 (12.20362)	3338.71 (3.21394)
55	3153.67 (4.36761)	3054.86 (2.46764)	3352.71 (0.23464)
56	3178.87 (11.59715)	3133.64 (3.75525)	3354.85 (2.78529)
57	3210.82 (20.68442)	3144.40 (6.73161)	3398.05 (12.52708)
58	3406.88 (13.53413)	3388.74 (0.28795)	3666.93 (14.81096)
59	3436.57 (53.83567)	3517.35 (4.32664)	3720.27 (208.33624)
60	3455.97 (9.36782)	3870.14 (15.80288)	3768.23 (14.86009)

The other informations we get from our calculations are the dipole moments, the quadrupole moments and the HOMO and LUMO energy levels and gaps for the molecules. The dipole moments for the molecules are calculated respectively, for SAC is (in Debye) 2.7611 (X: 1.3526, Y: -2.3588, Z: -0.4798), for SAMC molecule the dipole moment is (in Debye) 4.677 (X: - 2.0252, Y: -3.9942, Z: -1.2424). The different components of the quadrupole moments of the molecules are given in Table 5.

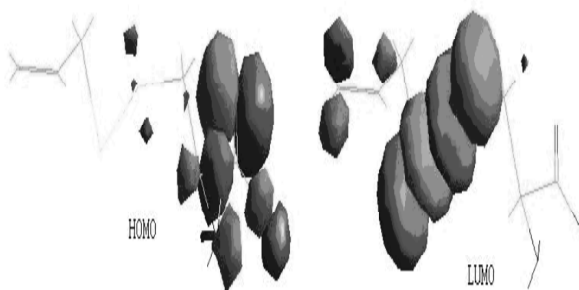
**Table 5**  
The different components of the quadrupole moments of the molecules (in Debye $\times\text{\AA}$ ).

Molecule	XX	YY	ZZ	XY	XZ	YZ
SAC	-60.1948	-81.2331	-68.4983	3.0668	-2.7167	-1.9770
SAMC	-66.4699	-94.5480	-79.5242	-4.4749	3.5284	-6.4403

The HOMO and LUMO energy levels of the molecules are calculated. In Figure 7, we show the 3D plots of HOMO and LUMO for SAC molecule. The HOMO energy level is -5.759 eV and the LUMO energy level is 0.216 eV giving rise to a gap of 5.543 eV. The HOMO energy level for the SAMC molecule is found to be -6.386 eV and the LUMO energy level is -1.424 eV (shown in Figure 8) yielding rise to a gap of 4.962 eV. HOMO of SAC is localized on sulfur and nitrogen atoms, whereas LUMO is localized on double bonded oxygen and carbon atoms and on carbon atoms on the left branch of the molecule (see Figure 7). On the other hand, HOMO of SAMC is localized on oxygen, nitrogen and carbon atoms bonded to them. However, LUMO of SAMC is localized mainly on sulfur atoms (see Figure 8).



**Figure 7:** 3D HOMO and LUMO plots on the SAC molecule, DFT/B3LYP/MP2/3-21G results.



**Figure 8:** 3D HOMO and LUMO plots on the SAMC molecule, DFT/B3LYP/MP2/3-21G results.

## Conclusions

Theoretical investigations will aid in the elucidation of antiplatelet aggregation and antioxidant activity and clarification of the uncertainty about the conditions under which biologically active sulfur-containing compound such as SAC and SAMC or other potential bioactive agents before they can be safely evaluated and commercially developed as beneficial therapeutic agents. The striking features of the molecules investigated in this treatise may be summarized as the following: The optimized structures of the molecules in gas phase are 3D; the carbon and sulfur containing skeleton of the molecules are not linear, they are bended (curved). Sulfur atom is playing an important role in this feature; bending usually takes place at sulfur positions. There is no experimental IR data for the molecules investigated. However, calculated IR spectra and vibrational modes agree qualitatively the general features of similar molecules [12]. From electronic properties point of view one of the remarkable features is that the frontier molecular orbital energy difference, namely the HOMO-LUMO difference, of the molecules studied are close to each other, SAC has a gap of about 5.5 eV, whereas SAMC has a gap value of about 5.0 eV. This (relatively) small difference in gaps should show similar features in the electronic spectra of these molecules. Dipole moment of SAMC (4.68 D) is relatively larger than that of SAC (2.76 D). Thus SAMC is expected to be more reactive in the aqueous environment of the cell than SAC. Another interesting point, which is worth to mention, is that double bonded oxygen atom in both molecules has relatively large negative excess charge (about -0.5 electron) and seems to be the most reactive part of these molecules and plays more important role in structure activity relationships, also in antioxidant properties of these molecules. It was experimentally shown that garlic extract and its major component SAC inhibited  $H_2O_2$  [27], and NO production and suppressed the production of hydroxyl radical [28] in cells, confirming their antioxidant activity. However, the molecular mechanism of garlic's pharmacological action has not been clearly elucidated. In the antioxidant activity of garlic extracts oxygen atom may play the major role.

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