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Investigation of fragmentation pattern of bis(trimethylsilyl) ester of 3-mercaptopropionic acid

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Abstract

The routes of fragmentation of the parent molecule resulting from electron impact ionization have been studied in a quadrupole ion trap using collision induced dissociation (CID) of fragments. Fragmentation of the parent molecular ion *m*/*z* 250 results in major ions 235, 178, 163, 135, 129, 75, 73, and 55. While some fragments are easily assigned according to literature—*m*/*z* 235 to $[M - CH_3]^+$, *m*/*z* 73 to $[Si(CH_3)_3]^+$, *m*/*z* 75 to $[Si(CH_3)_2OH]^+$, and *m*/*z* 55 to $[CH_2CHCO]^+$—other ions required CID to obtain their structure. Fragment *m*/*z* 178 was found to emerge from breaking of Si–S bond and hydrogen rearrangement in the molecular ion. Fragment *m*/*z* 163 is formed by elimination of CH_3 group from ion *m*/*z* 178. Elimination of H_2S from ion *m*/*z* 163 leads to formation of the ion *m*/*z* 129. Another route is elimination of molecule CO from ion *m*/*z* 163 to form ion *m*/*z* 135. Fragmentation of ion *m*/*z* 129 by elimination of neutral molecule CO_2 leads to emerging of ion *m*/*z* 85. For supporting the assumed structure of ions *m*/*z* 178, 163, 135, quantum chemical calculations were performed using methods PM3 and DFT. The calculations demonstrated that these ions have TMS group attached to the carboxyl group. The stability of the ions is associated with forming cyclic structures containing new bonds S–O (*m*/*z* 178), O–Si (*m*/*z* 163) and S–Si (*m*/*z* 129). Molecular dynamics calculations confirmed that these structures are the most stable conformations of the ions.

Keywords: Derivatization; Rearrangement; CID; Tandem mass spectrometry; TMS derivatives

1. Introduction

Trimethylsilyl (TMS) derivatives of organic compounds are widely used in gas chromatography. This technique is used for increasing thermal stability and volatility of unstable and highly polar compounds. These derivatives are of special interest for identification of unknown mixtures of non-volatile compounds by means of gas chromatography mass spectrometry (GC-MS) [1]. In contrast to liquid chromatography mass spectrometry, the GC-MS technique allows compiling libraries of mass spectra and identifying compounds from patterns of fragments of molecular ion. The clearly established fragmentation pathways dramatically facilitate identification of unknown compounds. Tandem mass spectrometry makes possible direct determination of the fragmentation of TMS-derivatives. The main goal of the present study was to trace fragmentation pathways of bis(trimethylsilyl) ester of 3-mercaptopropionic acid (bis(TMS)MPA) (Fig. 1A) using tandem mass spectrometry and support the proposed structure of the fragments by means of quantum chemical calculations. Fragmentation pathways of TMS-esters containing sulfur are poorly explored yet. Pathway information is useful for study of TMS-derivatives of other organic sulfur compounds, in particular products of catalytic oxidation [1]. The model compound bis(TMS)MPA has both thiol and carboxyl groups and, thus, simulates the products of partial oxidation of sulfur compounds.

The available information on fragmentation of TMS derivatives is briefly summarized below. The most abundant reactions of the molecular ion are elimination of methyl group, elimination of TMS group and various rearrangements. Rearrangements of TMS-esters often lead to elimination of neutral molecules. Diekman at al. [2] and Byun et al. [3] investigated the dissociation of 1,2-propandiol bis-TMS-ether (Fig. 1B) using electron bombardment. After formation of the $[M - CH_3]^+$ ion, TMS-groups at the

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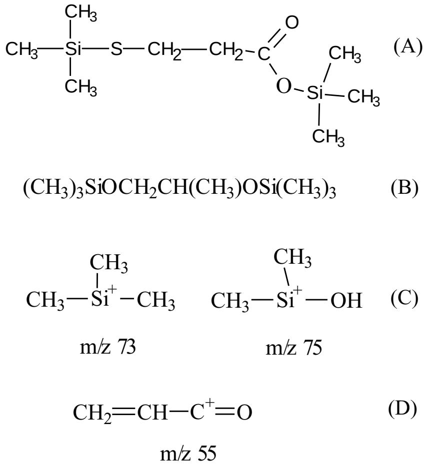


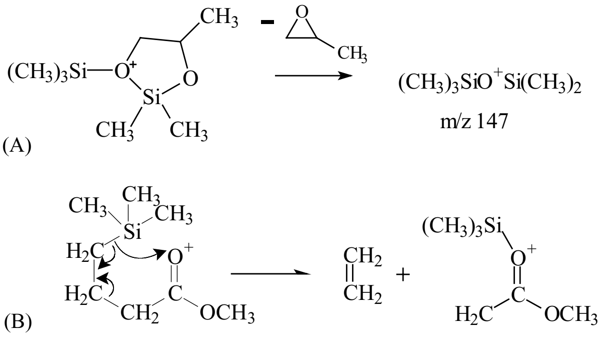
Fig. 1. Structure formulas: (A) bis(trimethylsilyl) ester of 3-mercaptopropionic acid; (B) 1,2-propandiol bis (TMS) ether; (C) ions m/z 73, 75; (D) ion m/z 55.

ends of the ion interact and the $[M - CH_3]^+$ ion collapses to cyclic oxonium ion. Then elimination (Scheme 1A) leads to formation of ion m/z 147 and propylene oxide.

The investigation of compounds with longer carbon chains was performed which also demonstrated similar rearrangements with formation of ion m/z 147 [3]. Ions m/z 73 and 75 (Fig. 1C) that are usually formed in fragmentation of TMS derivatives were also reported. The relative abundance of m/z 75 became higher with decreasing electron ionization energy.

It should be mentioned that interaction of TMS-groups is also possible even if they are separated by rigid parts of molecule [4]. It is typical for ions containing aliphatic, aromatic groups or triple bonds. It was determined that fragmentation of such ethers proceeds through the formation of either π- or σ-complex. In particular, this was found for fragmentation of bis-TMS-1,4-bis(hydroxymethyl) benzene shown in Scheme 2.

TMS groups have the ability to interact with other parts of ion. Experiments demonstrating interaction of TMS-group and carbonyl group for TMS-4-methylbutyrate were performed [3]. The observed rearrangement led to the elimination of ethylene (Scheme 1B).



Scheme 1. Fragmentation of some TMS-containing ions: (A) elimination of propylene oxide from cyclic oxonium ion resulting in the ion m/z 147; (B) elimination of ethylene from TMS-4-methylbutyrate.

Rearrangements in aromatic TMS ethers and carbonic acids have been explored in [5,6]. The elimination of stable fragment and neutral molecule takes place after formation of $[M - CH_3]^+$ ion. In case of TMS-benzoate, elimination of CO_2 takes place, in case of TMS-benzenealkyl ether—the elimination of aldehyde (Scheme 3).

In our work, we perform the investigation of fragmentation pathways of bis(TMS)MPA. Unlike the works mentioned above we did not find formation of ion m/z 147 as one could expect. Other previously reported rearrangements with elimination of neutral molecules were detected. Structures and energies of key fragments were calculated and we demonstrated that cyclic structures are often most appropriate.

2. Experimental

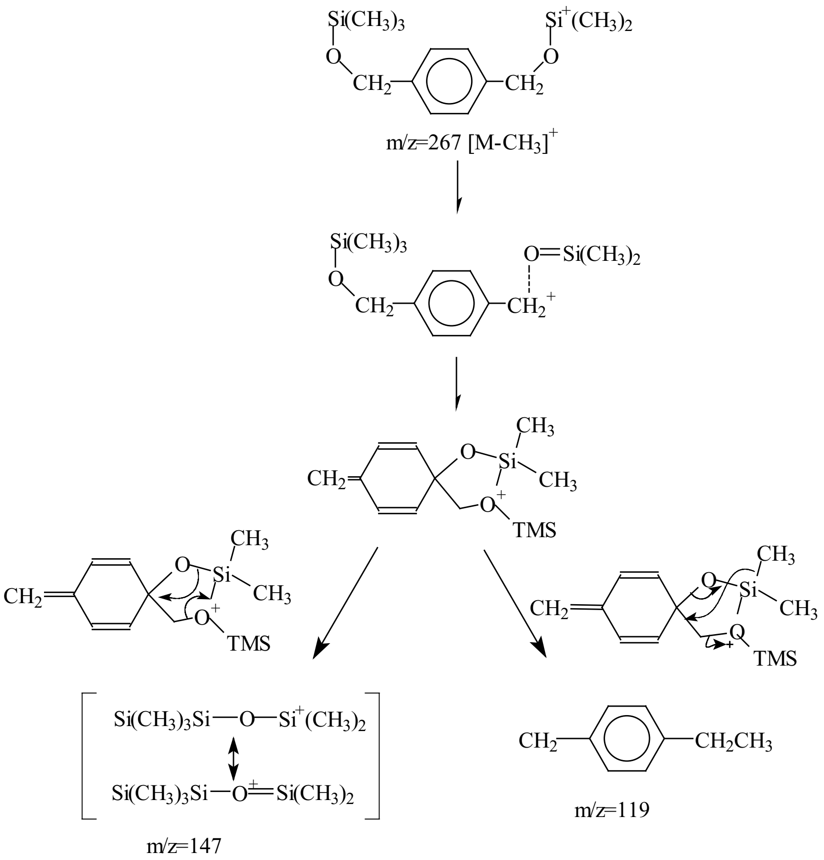
Reagent used for derivatization of 3-mercaptopropionic acid (Aldrich) was a mixture of bis(trimethylsilyl) trifluoroacetamide (BSTFA) 99% and trimethylchlorosilane (TMCS) 1% (Supelco). A 100-μL of the reagent was added to 20 μL of 3-mercaptopropionic acid. Temperature during derivatization was held at 60 °C, reaction was done in a closed 20 mL vial. Time of derivatization was 2 h. The resulting compound was bis-trimethylsilyl ester of 3-mercaptopropionic acid (Fig. 1A).

MS study was performed using Saturn 2000 gas chromatograph mass spectrometer (Varian, Walnut Creak, CA, USA). Mass spectrometric part of this instrument is based on a quadrupole ion trap. Besides single stage mass spectrometry, this instrument is capable of performing tandem mass spectrometry using resonant and non-resonant collision induced dissociation (CID). Detailed description of the ion trap was published elsewhere [7]. The energy of electrons for EI ionization in the trap was 50–80 eV.

Prior to the injection, 120 μL of mixture after performing derivatization was diluted in 6 mL of heptane. Heptane, BSTFA and bis(TMS)MPA have been well separated in a chromatographic column used, 30 m × 0.25 mm i.d. CP-Sil 8 CB (Varian). The GC injector temperature was 150 °C; this was sufficient for evaporating the probe. Column flow rate was 1 mL/min, column oven program: 50 °C held for 5 min, heating until 230 °C with rate 8 °C/min, then held for 10 min.

We used two methods of exciting ions for tandem mass spectrometry: resonant and non-resonant [7,8]. These both caused very similar collision induced dissociation pathways. The following settings were used for MS/MS: ejection amplitude 20 V, excitation time 20 ms, high edge amplitude 20 V.

All quantum chemical calculations have been performed using GAUSSIAN 94 program.



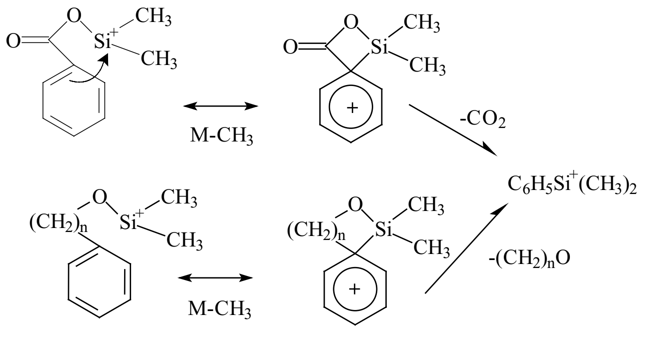
Scheme 2. Fragmentation of bis(TMS)-1,4-bis(hydroxymethyl) benzene.

3. Results and discussion

The mass spectrum of bis(TMS)MPA obtained by electron impact ionization is presented in Fig. 2. The prominent feature of this spectrum is the absence of molecular ion peak *m/z* 250. The heaviest ion detected was *m/z* 235 that is attributable to $[M - \mathrm{CH_3}]^+$.

The peaks at masses of *m/z* 73, 75, and 55 have high intensity. It is obvious that ions which abundance is higher are more stable than others. In other words, destruction of the compound follows the path of more stable ions formation. In fact the ion stability depends upon relative magnitudes of unimolecular rate constants but these magnitudes correlate with thermodynamical stability of the ion.

The ion *m/z* 55 corresponds to the stable ion shown in Fig. 1D. The stability of this ion can be explained as influence of extended electron π-system. This causes high bonding energy, so the ion is more stable. The stable ions *m/z* 75 and 73 (Fig. 1C) were mentioned earlier as highly expected in spectra of TMS derivatives [5,6]. The structure of other major ions seen in EI spectrum of bis(TMS)MPA is not so easily attributable. Thus, tandem mass spectrometry and quantum chemical calculations were employed for complete disentangling of their nature.



Scheme 3. Fragmentation of trimethylsylil benzoate and benzenealkyltrimethylsilyl ether.

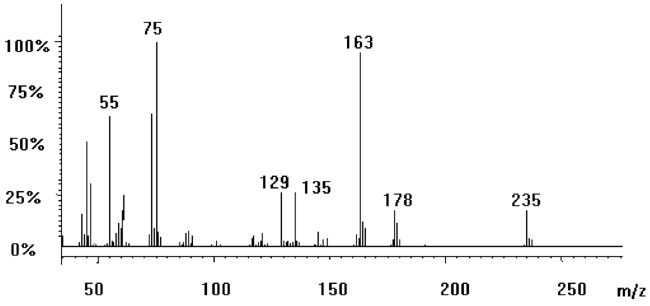


Fig. 2. Mass spectrum of bis(trimethylsilyl) ester of 3-mercaptopropionic acid.

Table 1
Parent ions and fragments detected after CID

Parent ion	Detected fragments and optimal excitation voltage (resonant, non-resonant)
178	163 (0.2 V, 30 V), 129 (0.4 V, 30 V), 75
163	129 (0.4 V, 30 V), 135 (0.4 V, 30 V), 75
135	75 (0.6 V, 30 V)
129	85 (0.6 V, 40 V), 75

3.1. Tandem mass spectrometry

Tandem mass spectrometry (MS/MS) was used for determination of the structure of ions *m*/*z* 178, 163, 135, and 129. Resonant and non-resonant methods were used for activating collision induced dissociation. We expected qualitative difference of spectra in both cases because of different accelerations of the ions [8]. Therefore, the effects of high energy decomposition paths non-resonant CID were expected, but they were not observed.

Product ion mass spectra are presented in Table 1. This table does not contain relative abundance of the ions because the relative abundance depends on excitation voltage. MS/MS spectra for different starting ions required using different excitation voltage. Table 1 contains all detected fragments at all different voltages used. For each daughter ion, there is an optimum excitation voltage to produce the highest yield of this ion. The example of such dependence of relative abundance of ions on excitation voltage is presented for parent ion *m*/*z* 135 in Fig. 3A and B for non-resonant and resonant excitation, respectively. At small excitation voltage no dissociation takes place. Higher voltage causes formation of ion *m*/*z* 75. Further decrease of *m*/*z* 75 is connected with dissociation of *m*/*z* 75 into smaller fragments that cannot be detected because of ion trap storage threshold limitation. One can see that both resonant and non-resonant CID delivered almost the same dependence on excitation voltage but relative intensity of the fragment *m*/*z* 75 was higher for resonant excitation. For non-resonant excitation, higher-energy channels are engaged because excitation time for non-resonant method is smaller then for resonant. This means that fewer ions lose their kinetic energy during excitation. We suppose that high-energy ions decompose into smaller fragments, which are not detected because of trap storage threshold limitation. Similar dependencies were obtained for other parent ions. Analogous dependencies on excitation voltage were also described in literature [8–10].

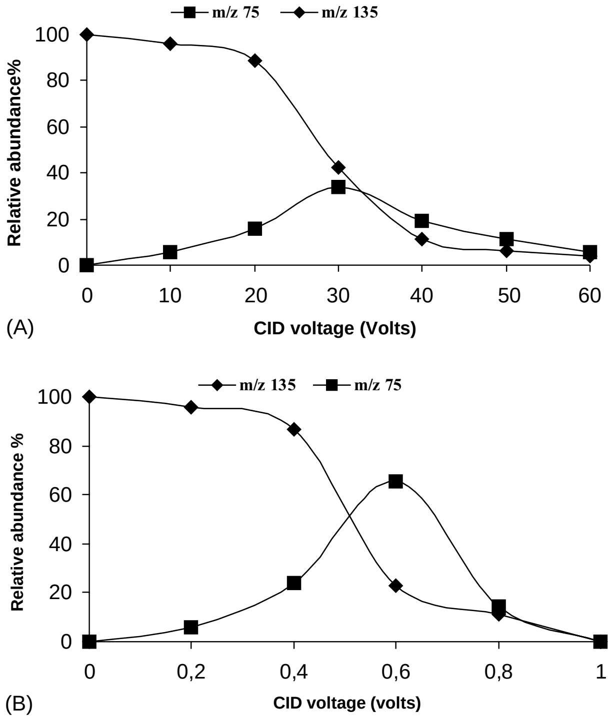


Fig. 3. (A) Breakdown curves for non-resonant excitation of ion *m*/*z* 135; (B) breakdown curves for resonant excitation of ion *m*/*z* 135.

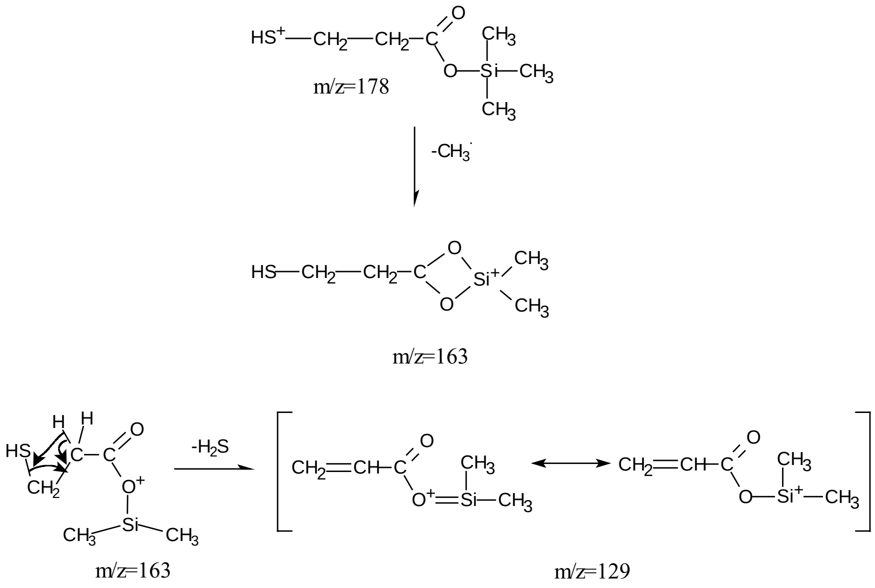
3.2. MS/MS fragmentation

The suggested pathways of fragmentation for bis(TMS)-MPA and its EI fragments are discussed here. Ion *m*/*z* 178 (=250 − 73 + 1) can be formed via the elimination of one TMS group with hydrogen rearrangement. The MS/MS spectrum of this ion consists of *m*/*z* 163, 129, and 75 (Table 1). Ion *m*/*z* 55 was supposed to be found also but it could not be detected. Quadrupole ion trap has the feature to make ion trajectories unstable during MS/MS procedure for ions with mass below some value. The lowest storage level for fragments of ion *m*/*z* 178 is 70.

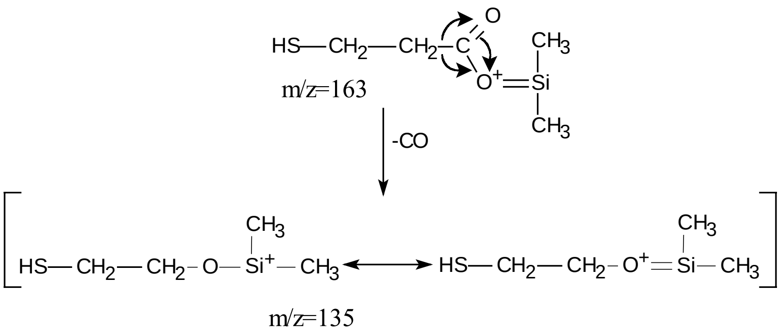
There are two main possible paths to form ion *m*/*z* 178. The first is breaking bond of TMS group with the oxygen atom, the second is breaking bond of TMS with the sulfur atom. In case of breaking from oxygen, *m*/*z* 91 resulting by cleavage of S–C bond should be expected in MS/MS spectra. The structure of ion *m*/*z* 91 is similar to *m*/*z* 75, but oxygen is replaced by sulfur atom. But MS/MS spectra of *m*/*z* 178 does not contain any remarkable amount of *m*/*z* 91, besides *m*/*z* 75 was found which signifies that breaking goes most probably from sulfur atom. The ion *m*/*z* 75 can appear only if TMS group is attached to oxygen atom or easily rearranges to form a bond with the oxygen atom.

On the base of MS/MS experiment results we propose the following mechanism of MS/MS fragmentation of *m*/*z* 178 (Scheme 4). Elimination of one methyl group from ion *m*/*z* 178 results in ion *m*/*z* 163. It is obvious that elimination of such group can take place at TMS group only. Therefore, the group $OSi(CH_3)_2$ must be present in the ion *m*/*z* 163. Ions with such group were detected in works cited above [2–6]. Its high stability is backed by resonant delocalization of charge between oxygen and silicon. Ion *m*/*z* 129 forms via elimination of H_2S molecule from ion *m*/*z* 163. The ion *m*/*z* 129 possesses an extensive π-system that determines its high stability.

MS/MS spectrum of the ion *m*/*z* 163 consists of ions with *m*/*z* 129, 75, and 135. Formation of ions *m*/*z* 129, 75 was



Scheme 4. Fragmentation of ion *m*/*z* 178.



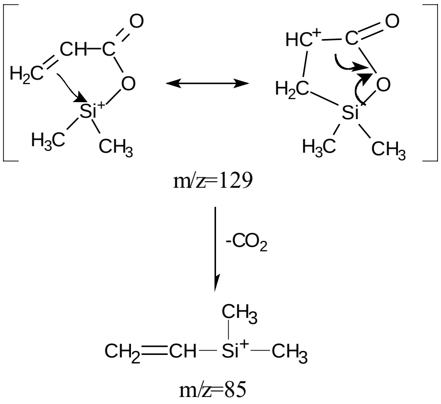
Scheme 5. Fragmentation of ion *m*/*z* 163.

described just above. Elimination of neutral molecule CO leads to formation of ion *m*/*z* 135 (Scheme 5). Such type of rearrangements was reported for some acids [11]. Ion *m*/*z* 135 was not found in ion *m*/*z* 178 MS/MS spectrum in contrast to *m*/*z* 163. Possible explanation is that ion *m*/*z* 163 looses energy and channel corresponding to formation of ion *m*/*z* 135 is not activated.

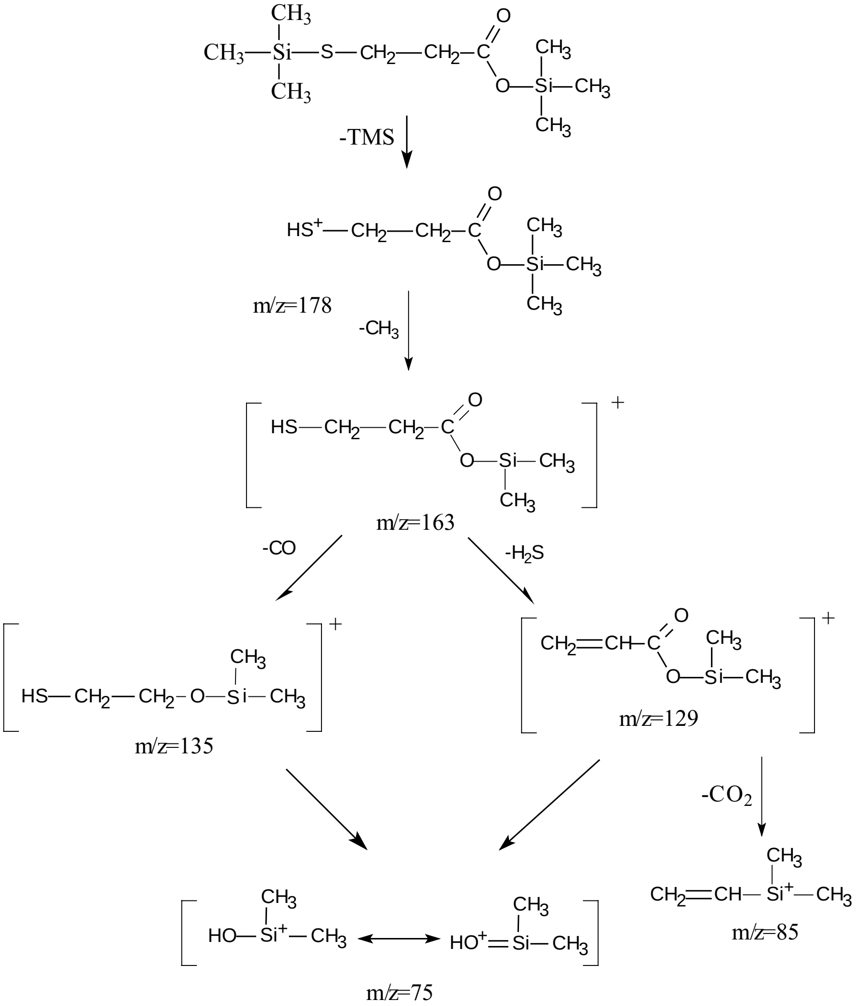
Only one peak *m*/*z* 75 (Fig. 1C) was detected in MS/MS spectrum for ion *m*/*z* 135.

MS/MS spectrum of ion *m*/*z* 129 consists of peaks at *m*/*z* 75 and 85 (Scheme 6). But in mass-spectrum of bis(TMS)MPA relative abundance of ion *m*/*z* 85 is negligible. In this case elimination of neutral molecule CO_2 from ion *m*/*z* 129 leads to rearrangement producing ion *m*/*z* 85 with charge delocalized by extensive π-system. This type of rearrangement was reported previously by Diekman et al. [5].

All ions detected in MS/MS experiments except ion *m*/*z* 85 $CH_2CHSi(CH_3)_2$, have one of the following parts: (1) CH_2CHCHO and (2) $OSi(CH_3)_2$. Stability of such fragments is due to charge delocalization by electron π- or σ-system. Scheme 7 summarizes all the results of MS/MS experiments and demonstrates the fragmentation path of the molecular ion of bis(trimethylsylil) ester of 3-mercaptopropionic acid.



Scheme 6. Fragmentation of ion *m*/*z* 129.



Scheme 7. Fragmentation pathways of bis(trimethylsilyl) ester of 3-mercaptopropionic acid

3.3. Computation of ion energies

Though MS/MS spectra of ions *m*/*z* 178, 163, 135 do not contain ion *m*/*z* 91 corresponding to the group $HS–Si(CH_3)_2^+$, still there is a possibility that TMS group is attached to sulfur atom in these ions. Additional support for the suggested ion structures can be obtained via quantum chemical computations of ion energies. We carried out calculations for ions *m*/*z* 178, 163, 135 with TMS group at sulfur and carboxyl group. At first, geometry of the ions was optimized using semi-empirical method PM3. This method was well developed and usually delivers good results for elements of the first three rows of the periodic table. Then, the optimized geometry was taken for DFT-calculation using functional B3LYP with basis set 6-31g(d) as well as PM3 calculation of ion energy (heat of formation). The results of energy calculations are presented in Table 2.

For obtaining the precise energy, vibration energies should be included. Calculations of frequencies were carried out using B3LYP functional with 6-31g(d,p) basis set. The number of vibrational degrees of freedom is equal for both structures of each of the ions *m*/*z* 135, 163, and 178; besides the frequencies are close to each other. The calculated correction due to vibrations for structures of the *m*/*z* 135 is only 0.02 eV. This correction is negligible for our consideration of the most stable structure of this ion. For the ion *m*/*z* 163 vibrational correction is 0.06 eV.

One can see that ions with TMS-group attached to oxygen atom have lower energy compared to those with TMS group attached to sulfur. The difference in energy is 1.5

Table 2
Calculated stabilization of O-TMS ions relatively to S-TMS ions

Ions	Energy of S-TMS minus energy of O-TMS ions (eV)	
	Method PM3	Method DFT (B3LYP) (vibrational correction)
178	1.80	1.45
163	0.17	0.06 (+0.06)
135	0.94	0.88 (+0.02)

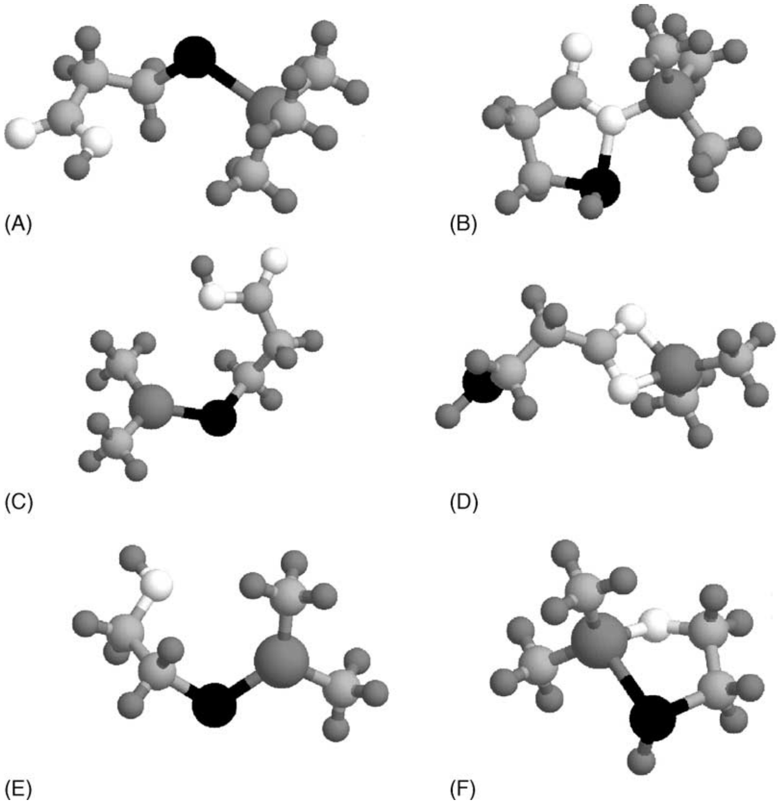


Fig. 4. Optimized geometries of ions: (A) ion *m*/*z* 178 with TMS-group attached to sulfur atom; (B) ion *m*/*z* 178 with TMS-group attached to oxygen atom; (C) ion *m*/*z* 163 with TMS-group attached to sulfur atom; (D) ion *m*/*z* 163 with TMS-group attached to oxygen atom; (E) ion *m*/*z* 135 with TMS-group attached to sulfur atom; (F) ion *m*/*z* 135 with TMS-group attached to oxygen atom. Black ball: sulfur; white: oxygen; large gray: silicon; medium gray: carbon; small gray: hydrogen.

and 1 eV for ions *m*/*z* 178 and 135 but is only about 0.1 eV for the ion *m*/*z* 163. Therefore, there is a chance that some quantity of the ion *m*/*z* 163 is represented by structures with TMS-S bond. However, in order to be formed, such ions requires rearrangement of TMS group of the parent ion 178 or simultaneous elimination of TMS and methyl group from the molecular ion of bis(TMS)MPA. Both processes are not of high probability. Thus, ions *m*/*z* 163 should be predominantly represented by structures with TMS attached to the carboxyl group.

Optimization of geometry of the ions with PM3 method provides structures with energy corresponding to a local minimum. It is possible that there are other local minima and the absolute minimum of energy does not correspond to the found conformation. The lowest energy conformations for the ions with TMS group attached to sulfur and oxygen might have different energy relative to each other. In order to obtain the absolute minimum energy conformations, molecular dynamics calculations were performed according to the following procedure. The PM3 geometry optimization gives the geometry corresponding to the 0 K temperature. Next step is raising the internal energy of the molecule. This leads to the movement of the point corresponding to the geometry on the adiabatic surface. We check for the magnitude of potential energy during movement so it is possible to reveal another minimum of energy. Finally, cooling is used to get the exact geometry at the final temperature.

Following settings for molecular dynamics were used: heat time, 10 ps; run time, 50 ps; cool time, 10 ps; step size, 0.001 ps. Calculations were performed at simulation temperature 500 K, starting temperature 0 K and final temperature 300 K. Temperature step was 1 K. Calculation method was PM3. Results showed that ions do not have another potential minimum.

The optimized geometry is presented in Fig. 4 for ions *m*/*z* 178, 163, and 135. One can see that the most stable conformations of ions possess cyclic structures. The bond length between sulfur atom and oxygen in ion *m*/*z* 178 is 1.82 Å (Fig. 4B). The bond length between sulfur atom and silicon atom in ion *m*/*z* 135 is 2.46 Å (Fig. 4F). In the case of ion *m*/*z* 178, there are two stable cyclic conformations with deep minima of energy—with sulfur close to terminal carbonyl oxygen and sulfur close to etheric conjunctive oxygen; the last conformation is shown in Fig. 4B. Relative energies of these two conformations were calculated by methods PM3, DFT (B3/LYP), and ab initio HF (MP2, basis set 6-31g(d,p)). While PM3 assigned lower energy to conformation with sulfur at carbonyl oxygen, the two other methods testified to lower energy of conformation in Fig. 4B. Therefore, this conformation is likely to be most stable for ion *m*/*z* 178.

4. Conclusions

Fragmentation scheme of bis(TMS) ester of 3-mercaptopropionic acid has been determined. Fragmentation proceeds via removal of TMS group from sulfur atom and rearrangements with elimination of neutral molecules. Fragmentation pattern found in this work can be used for identification of sulfur-containing TMS ethers. Calculated geometries of fragments provide insight into structures of ions of sulfur-containing TMS derivatives.

Acknowledgements

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