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Synthesis, identification and chemical features of high-purity trimethylselenonium iodide

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High-purity (99.8% ± 1.1) trimethylselenonium iodide (TMSeI) was synthesized from dimethyl selenide and methyl iodide. Its chemical structure was confirmed using the spectroscopic methods of nuclear magnetic resonance, Fourier transform infrared and electrospray ionization-mass spectrometry. Some thermodynamic properties of the pure TMSeI were studied with differential scanning calorimetry, and its decomposition point and entropy were determined to be 157.7 °C and 100.7 kJ mol^{-1}, respectively. The chromatographic and UV absorption behavior of the trimethylselenonium cation was also studied and the photochemical and chemical stability of $TMSe^+$ and its decomposition products under varying microwave digestion conditions were examined. Some peculiar, yet interesting chemical properties on the stability of the compound were revealed. This is the first time that the chemical properties of this compound are comprehensively studied by various techniques and from different angles. The high purity of the synthesized compound allows it to be used as a primary standard compound in analytical method development and in basic and environmentally related studies.

Keywords: trimethylselenonium iodide synthesis; NMR; FTIR; ESI-MS; DSC; microwave digestion

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1. Introduction

More than 50 years ago, Schwarz and Foltz (*1*) reported that Se was an essential trace element in biological systems. Later, many more studies confirmed that the deficiency of Se can cause several serious epidemic diseases to human and animals, such as the Keshan (*2*) and white muscle diseases. Other health-related problems, such as an impaired immune system, could also be induced by an insufficient intake of Se (*3*, *4*). However, diets high in Se concentration can provoke Se intoxication (*5–7*), and yet the Se concentrations range between safe and toxic is very narrow. Interestingly, it

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has also been observed that the presence of Se in aquatic systems can significantly reduce mercury methylation and bioaccumulation in the aquatic food web (*8–10*).

Like sulfur, Se presents in glutathione peroxidase, thioredoxin reductase and thyroid hormone deiodinase. It is actively involved in redox and metabolic reactions (*11, 12*). The trimethylselenonium ($TMSe^+$) ion, an analog of trimethylsulfonium (TMS^+), has been reported as an important metabolite and it has been found in the urine of rats fed with sodium selenite dissolved in water (*13–17*). Its existence was also analytically confirmed in some recent studies (*18–20*). The excreted $TMSe^+$ has been considered as a metabolite of Se detoxification and a metabolic pathway of Se compounds has been proposed based on these findings (*12, 21*). However, there is a controversy on the validity of some of the published data. In a recent review, Francesconi and Pannier (*22*) criticized the historic lack of necessary precautions and precision in the characterization of isolated $TMSe^+$ and in the quantization of synthesized compound in past reports. They questioned the very existence of $TMSe^+$ as a biological metabolite and proposed that selenosugars would be more likely urinary metabolites. In fact, until now, we still know little about the chemical and physical properties of this compound.

One of the important reasons for this problem originates from the unavailability of a commercial source of a high-purity $TMSe^+$ compound. The majority of the research studies that have used $TMSe^+$ relied either on a product synthesized in house or on a donation from other laboratories. In both situations, there is a serious lack of detailed synthetic protocol and comprehensive identification of this compound. The across citation is a common practice. For instance, several groups (*16, 23, 24*) synthesized their sample using the protocol of Palmer *et al*. (*14*) who in turn applied the Bird and Challenger protocol in their $TMSe^+$ synthesis (*25*). In one study, Gammelgaard *et al*. (*19*) synthesized $TMSe^+$ using the Foster and Ganther procedure (*26*), which was based on Hashimoto *et al*.'s work (*27*). In the Foster and Ganther procedure (*26*), labeled $TMSe^+$ was synthesized from ^{75}Se-methyl-selenocystine and methyl iodide in formic acid for 7 days without special precaution taken to exclude atmospheric oxygen. Considering the reactive nature of CH_3I, one can seriously question the purity of the synthesized compound. In a subsequent study by the same group (*17*), sodium borohydride was used to react with sodium selenite and the authors produced the $TMSe^+$ ionic compound without detailed explanation.

Bird and Challenger (*25*) were among the first researchers to synthesize alkyl derivatives of Se. This work has been cited by several researchers (*14, 27, 28*) in their individual $TMSe^+$ synthesis work. However, in this early study (*25*), there is no information directly related to the synthetic procedure of $TMSe^+$, but only a brief mention which states that in the preparation of dimethyl/ethyl selenides from powdered Se and in order to avoid the formation of trialkyl selenonium iodide, methyl or ethyl iodide should be added slowly to a mixture of sodium formaldehyde sulfoxylate, sodium hydroxide and water. The methods used in (*14, 27*) were based on the reaction between dimethyl selenide and an excess of methyl iodide. Unfortunately, both of them failed to provide a detailed protocol, product identification and quantitative measurement on the purity of the compound.

As concerning to the chemical stability of $TMSe^+$, several authors in earlier studies (*29, 30*) had expressed concerns on the difficulty of breaking down $TMSe^+$ in biological samples during digestion, despite the fact that there was not much experimental evidence. D'Ulivo *et al*. (*31, 32*) are the only few researchers who have presented some analytical data to demonstrate that the presence of Br^- can facilitate the breakdown of trimethyl selenide. A chemical reaction mechanism of nucleophilic attack was proposed (*32*).

In this paper, we propose a well-defined and simple protocol for the synthesis of high-purity trimethylselenonium iodide (TMSeI). Much of the careful investigation has been done in order to provide researchers with new information on the physical, chemical and photochemical properties of this interesting compound.

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2. Results and discussion

2.1. *Purity of the synthesized TMSeI*

The purity of the synthesized product was determined by measuring Se in a solution containing an exactly known mass of TMSeI. The Se in the solution was measured by three different analytical methods without any prior treatment (Section 4.5). Triplicate analysis was carried out with each technique and the average purity and analytical precision obtained from three analytical methods techniques was $99.8 \pm 1.1\%$ ($n = 9$). The high purity of the synthesized $(CH_3)_3SeI$ allows it to be used as a primary standard material in any analytical method development, basic chemistry and environmentally related research.

2.2. *Characterization of TMSeI by IR, NMR and HPLC–ESI-MS*

Several techniques were used to characterize the synthesized compound. The Fourier transform infrared (FTIR) spectrum of the product (Figure 1) demonstrates very strong bands at 2988 and 3005 cm^{-1}, characteristic bands of the C^3_{sp}–H stretching vibration of the $–CH_3$ groups. The bands at 1412, 1300 and 1265 cm^{-1} are consistent with C–H bending vibrations, which are also observed in the spectra for both dimethyl diselenide (1258.4 cm^{-1}, our own standard) and dimethyl selenide (1423.9, 1263.9 cm^{-1}) (*13, 14*). The large band found at 988 cm^{-1} is possibly assigned to the C–Se rocking mode, which has been earlier identified (*33*). Similar IR absorption bands have been observed at 957 and 912.3 cm^{-1} for dimethyl selenide (*13, 14*) and at 892 cm^{-1} for dimethyl diselenide (our own standard). The nuclear magnetic resonance (NMR) spectrum of the product is characterized by a singlet at a chemical shift of 2.76 ppm, indicating that all protons situated in three methyl groups of $TMSe^+$ in the compound are chemically equivalent. This is consistent with the NMR data reported for TMSeI (*34*).

The high-performance liquid chromatography (HPLC)-UV-electrospray ionization-mass spectrometry (ESI-MS) spectra of the synthesized product are presented in Figure 2. A species with a retention time of 2.54 min was detected by the photodiode array detector (PDAD) (Figure 2(a)), but this peak was not detected by mass spectrometry. It was only at a retention time of 5.47 min

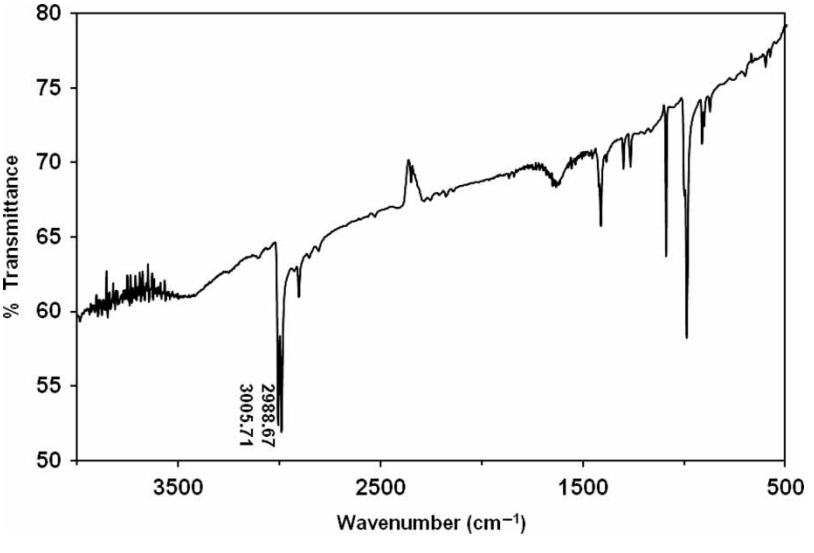

Figure 1. FTIR spectrum of the synthesized TMSeI.

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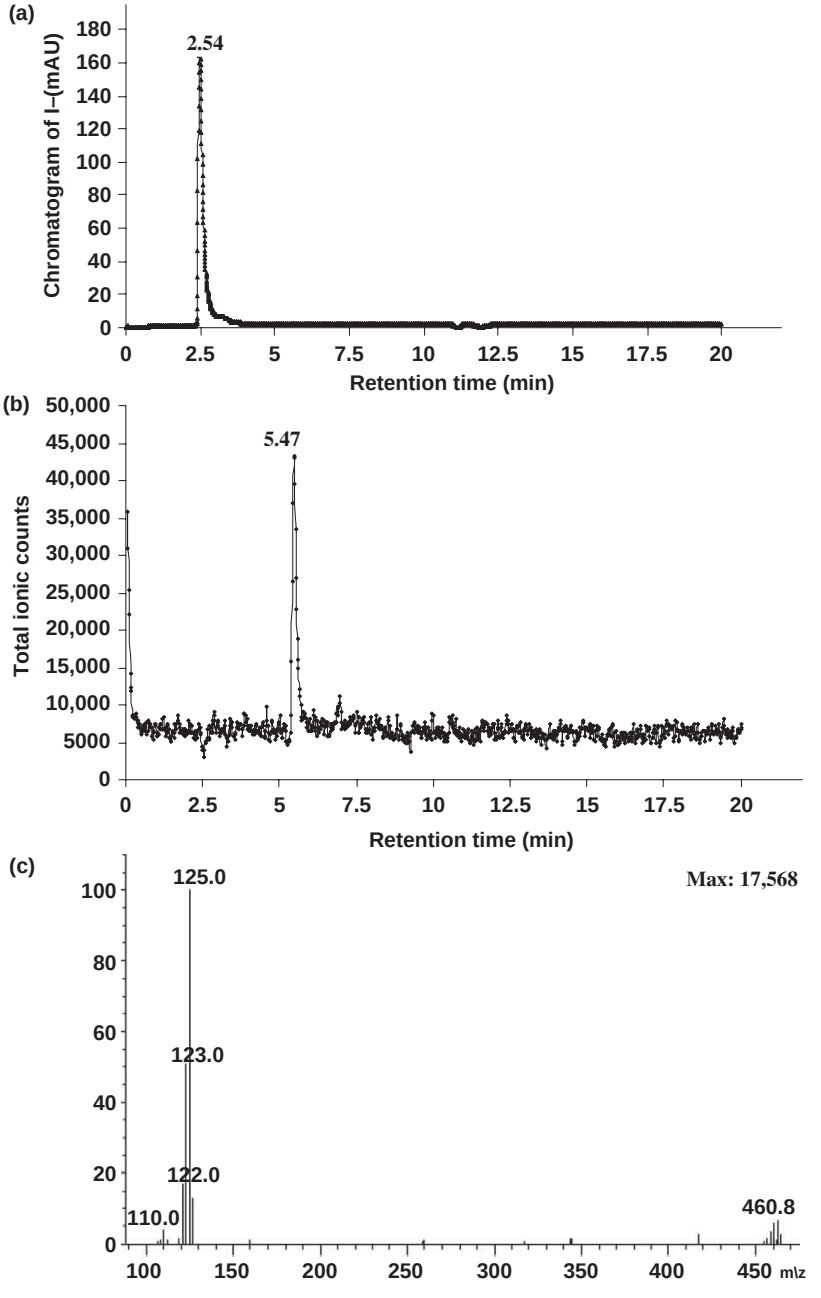

Figure 2. Chromatograms obtained from HPLC coupled with photodiode array detector-electrospray ionization-mass spectrometer. Column: Pursuit XRs C18 250 × 4.6 mm, particle size: 3 μm; mobile phase: 0.01% TFA/0.01% HFBA/5% methanol (pH 2.8); flow rate: 1.0 mL min^{-1}. Fragmentation voltage: 70 V; sample injection volume: 50 μL; TMSeI solution concentration solution: ∼100 μM. (a) HPLC chromatogram of I^- (UV wavelength 226 nm); (b) the total ionic chromatogram of $(CH_3)_3Se^+$ (positive mode) and (c) mass spectrum of the peak (ESI set at positive mode).

that an intense peak corresponding to positively charged ions was found by the mass detector (Figure 2(b)). The mass spectrum (Figure 2(c)) shows a cluster of ions with m/z of 125.0, 123.0 and 122.0 amu, respectively. These have been assigned to the isotopomers of $TMSe^+$, *i.e.* $TM^{80}Se^+$ (natural abundance (NA) of $^{80}Se = 49.8\%$), $TM^{78}Se^+$ (NA of $^{78}Se = 23.5\%$) and $TM^{77}Se^+$ (NA

of $^{77}Se = 7.6\%$). A similar ESI-MS spectrum was also obtained by Wrobel *et al*. (*35*) from their synthesized TMSeI compound.

2.3. *UV absorption properties of TMSeI*

The fact that the species with a retention time of 2.54 min was not detected by the mass detector was further studied. A series of standard potassium iodide solutions were prepared and injected into the HPLC column under the same chromatographic and detection conditions. Iodide (I^-) was eluted from the column and detected by PDAD at 226 nm at the same retention time of 2.54 min. The intensity of absorption corresponded linearly to the concentration of I^- at least from 1.0 to 100 μM. This confirms that the peak at retention time 2.54 min in Figure 2(a) corresponds to the I^- ion UV absorption resulting from a charge-transfer-to-solvent state (*36*). This phenomenon has been used to determine iodide in sea water by ionic chromatography with the UV detector (*37*). The negatively charged I^- was not seen because the detection mode of the MS was set at positive. Since there is no UV absorption peak at the retention time of 5.47 min, the UV absorption property of TMSeI was further checked using a freshly prepared TMSeI solution (~40 μM). There was no molecular absorption from 190 to 1100 nm, except for some sharp line peaks in the range of 190–250 nm, which were probably produced by I^- UV absorption. This confirms that $TMSe^+$ does not absorb UV/visible light, thus this peak was not detected by PDAD when it was eluted out at 5.47 min. It is thus important that the UV signal produced by I^- not be mistakenly regarded as that of $TMSe^+$.

2.4. *Thermodynamic properties of TMSeI*

Information on the chemical and physical properties of TMSeI is scarce. Hashimoto *et al*. (*27*) interchangeably used "fusion" and "decomposition" points of this compound at 162–163 °C in their paper. Furthermore, due to the lack of measurement of the purity of their compound, the exact "fusion" or "decomposition" point reported in their work remains questionable. Using a simple melting point apparatus, we observed that the colorless crystal TMSeI was gradually transformed to a white solid and its crystallinity seemed to deteriorate with increasing temperature. At about 149 °C, the sample was losing its mass rapidly which was accompanied with an evolving gas with the characteristic odor of $(CH_3)_2Se$. When the temperature reached 153–154 °C, the solid sample had completely disappeared. Therefore, we can now confirm that $(CH_3)_3SeI$ possesses the "decomposition temperature" rather than the "fusion temperature". A more precise measurement was made with a differential scanning calorimeter (DSC). The measurement shows that, at a temperature of 122.8 °C, the compound underwent a phase transition in which an enthalpy of 4.3 kJ mol^{-1} was involved. This agrees well with our earlier observation where a white amorphous precipitate appeared before its crystallization. The decomposition point of this compound was measured at 157.7 °C and the enthalpy of the decomposition reaction was 100.7 kJ mol^{-1} (Figure 3). Again, the characteristic smell of the decomposed $(CH_3)_2Se$ gas was detected at the decomposition temperature. No residue was found after the measurement, which confirmed the formation of gaseous compounds during the decomposition. Based on the above experiments, the following reactions are suggested:

$$(CH_3)_3SeI_{(crystal)} \underset{\text{low temp.}}{\overset{122.8^\circ C}{\rightleftharpoons}} (CH_3)_3SeI_{(amorphous)}, \quad \Delta H = 4.3 \text{ kJ mol}^{-1} \tag{1}$$

$$(CH_3)_3SeI_{(amorphous)} \underset{\text{low temp.; anoxic conditions}}{\overset{157.7^\circ C}{\rightleftharpoons}} (CH_3)_2Se_{(g)} + CH_3I_{(g)}, \quad \Delta H = 100.7 \text{ kJ mol}^{-1}. \tag{2}$$

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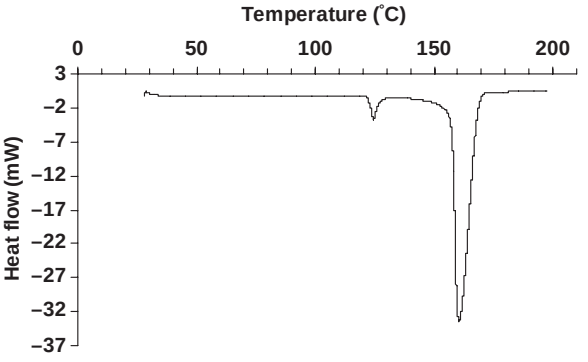

Figure 3. Decomposition of TMSeI measured with differential scanning calorimeter (DSC).

The same quantities of heat should be released when the reversed reactions occur. This also explains why it is preferred to carry this synthesis under a low temperature.

The amount of dimethyl selenide used in the reaction was 6.5 mmol, and the final amount of TMSeI obtained was 3.63 mmol (0.908 g) for a yield of around 56%. The low yield could be probably due, in part, to the high volatility of $(CH_3)_2Se$ (b.p. 42–43 °C) and to the incompleteness of the reaction. The results of the supernatant showed that only 0.045 mmol of Se was found in the aqueous solution, which represents approximately 0.7% of the $(CH_3)_2Se$ initially added for the synthesis. This suggests that a significant amount of dimethyl selenide was lost probably through the evaporation during the several steps of manipulation.

2.5. *The stability studies of $TMSe^+$*

Although $TMSe^+$ has been reported as a difficult compound to breakdown during acid digestion, there is little experimental evidence in the literature to demonstrate it. This is partially due to the fact that pure $TMSe^+$ is not easily available; therefore, very few people have conducted systematic studies on its properties. Still we know even less in what form(s) Se would be present under UV irradiation and different chemical attacks, if it does break down. Hydride generation-atomic fluorescence spectrometry (HG-AFS) is not only a very sensitive analytical method for several hydride-forming elements (Se, As, Sb, Sn, etc.), but it also possesses an advantage to identify the formation of different Se species in an aqueous digestion system. The understanding of the forms of final products of $TMSe^+$ breakdown is crucial for developing an on-line detection of $TMSe^+$ with the HPLC–HG-AFS system.

2.5.1. *The stability of $TMSe^+$ under UV irradiation*

The stability of $TMSe^+$ under UV irradiation was first studied. It was found that, unlike many other organo-selenium compounds (*38, 39*), the chemical bonds between Se and C in $TMSe^+$ become very stable once it is dissolved in water. It was shown that after 2.5 h of UV irradiation (300 nm), neither Se (IV) nor Se (VI) – two possible decomposition products by UV cleavage – was formed, indicating that no Se–C bond had been broken under a strong UV attack with a total output power of 336 W. A close to 100% recovery of Se in this solution as measured by graphite furnace-atomic absorption spectrometry (GF-AAS) suggests that there should be no significant loss in Se by the formation of any volatile selenium compounds, such as dimethyl selenide, during UV treatment (Table 1). The same phenomenon was observed both in 1.0% (v/v) HNO_3–2% (v/v) HCl and in pure water.

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Table 1. Study on the stability of $TMSe^+$ in different matrices under a UV (300 nm) irradiation of 336 W for 2.5 h ($n = 3$).

	Direct analyses (Se (IV), HG-AFS (i))	Pre-reduction (Se (IV)–Se (VI), HG-AFS (ii))	Direct analyses (total Se, GF-AAS (iii))
		1% HNO_3 (v/v)–2% HCl (v/v)	
Se detected ($\mu g\ L^{-1}$)	<Detection limit	1.6	105.3
SD ($\mu g\ L^{-1}$)	n.a	1.0	0.9
RSD (%)	n.a	62.5	0.9
Recovery (%)[a]	0.0	1.6	102.2
		Deionized water	
Se detected ($\mu g\ L^{-1}$)	4.8	7.5	104.0
SD ($\mu g\ L^{-1}$)	0.7	0.8	0.004
RSD (%)	13.6	10.2	0.004
Recovery (%)[a]	4.6	7.3	100.9

Note: [a]Recovery % is the measured Se in each treatment compared with total Se introduced before the digestion treatment.

Se can be present in four different chemical oxidation states. However, in a strong oxic environment, $(CH_3)_3Se^+$ could only be either intact or oxidized to Se (0), Se (IV) or Se (VI). The formation of Se (0) was excluded, as there was no formation of characteristic reddish elemental Se in any of the tested solutions, even at a concentration as high as 10.3 mg L^{-1}. Based on the previously established knowledge in the studied matrices, the formation of any other non-hydride-forming Se species, other than Se (IV) and Se (VI), is quite unlikely. Considering the chemical nature of this compound and our previous results, we hypothesize that all $(CH_3)_3Se^+$ in these solutions remained intact after a strong UV irradiation treatment.

2.5.2. *The stability of $TMSe^+$ under chemical attacks*

The stability of $TMSe^+$ in different chemical reagents was investigated in a microwave digestion system using two types of Teflon digestion vials: 100 or 6 mL (*38*). The obtained results (Table 2) are not in agreement with those obtained by D'Ulivo *et al*. (*31, 32*). In the tests carried in 100 mL vials, the average Se (IV) found after digestion was 29%, 23% and 30% of the initial $TMSe^+$ for digestion system (A), (B) and (C), respectively. A significantly smaller percentage of Se (VI) was found in these digestion systems, representing only 5–7% of the initial TMSe. The total Se

Table 2. Percentage of Se (IV), Se (VI) measured by HG-AFS compared with total Se by GF-AAS after microwave digestion (100 mL vial).

Replicate	(A): 7.0 mL 15.0 M HNO_3–1.0 mL 30% H_2O_2			(B): 8.0 mL 15.0 M HNO_3–0.2 mL 18.4 M H_2SO_4			(C): 7.0 mL 15.0 M HNO_3–0.5 mL Br solution[a]		
analysis	Se (IV)	Se (VI)	Total Se	Se (IV)	Se (VI)	Total Se	Se (IV)	Se (VI)	Total Se
1	52.0	9.9	97.0	18.1	4.8	142.2	8.3	7.9	100.3
2	24.5	7.2	98.3	6.3	4.6	159.5	6.4	4.8	97.8
3	40.5	6.0	100.0	15.4	5.9	146.3	2.1	2.4	96.9
4	25.8	7.6	97.9	35.9	7.7	130.0	60.1	5.8	106.5
5	20.8	4.6	98.7	39.3	4.4	116.5	69.8	2.1	103.4
6	13.2	5.7	97.5	23.0	n.a	n.a.	32.3	8.5	101.8
Average (%)	29.5	6.8	98.3	23.0	5.5	138.9	29.8	5.3	101.1
SD (%)	14.2	1.9	1.1	14.1	1.4	16.3	29.4	2.7	3.6
RSD %	48.2	27.5	1.1	61.1	25.4	11.8	98.3	50.7	3.5

Note: [a]Br solution is 1.1 M KBr–0.22 M $KBrO_3$ saturated solution.

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Table 3. Percentage of Se (IV) and Se (VI) measured by HG-AFS after the microwave digestion (6 mL vial).

Vial number	(I): 1.0 mL 15.0 M HNO_3–0.20 mL 30% H_2O_2		(II): 1.0 mL 15.0 M HNO_3–0.10 mL 18.4 M H_2SO_4		(III): 0.7 mL 15.0 M HNO_3–0.15 mL Br solution[a]	
	Se (IV)	Se (VI)	Se (IV)	Se (VI)	Se (IV)	Se (VI)
1	89.8	8.2	52.9	9.5	10.0	52.3
2	85.8	9.0	50.2	10.6	9.2	55.5
3	67.3	8.2	11.8	3.5	5.5	24.1
4	62.7	10.1	9.9	2.9	2.7	24.0
5	90.4	6.5	17.3	8.9	1.2	75.0
6	92.1	2.3	17.1	13.2	0.9	73.5
Average (%)	81.4	7.4	26.5	8.1	4.9	50.8
SD (%)	12.9	2.8	19.6	4.1	4.0	22.6
RSD (%)	15.9	37.4	73.8	50.1	81.6	44.6

Note: [a]Br solution is 1.1 M KBr–0.22 M $KBrO_3$ saturated solution.

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in the digested solutions (A) and (C), measured by GF-AAS, was closed to 100% of the initial $TMSe^+$, whereas for system (B), the recovery of Se was significantly higher, probably due to interference from H_2SO_4 in the sample (Table 2). A 100% recovery of Se by GF-AAS indicates that there was no loss of Se in forms of volatile Se during the microwave digestion. Similarly, these results indicate that even under a temperature of 210 °C and in the presence of large quantities of strong chemicals, only a small percentage of $(CH_3)_3Se^+$ was broken down and most of the compound remained stable. The reagent blanks for digestion systems (A), (B) and (C) were all negligible.

The $TMSe^+$ stability was also examined using 6 mL vials using the same chemical reagents but in much smaller volumes (Table 3). Since there is no formation of volatile Se compound $(CH_3)_2Se$ (based on the data from Table 2) and since the formation of other Se species, apart from Se (IV) and Se (VI), is quite unlikely in the investigated chemical digestion systems, the difference between the Se added and the sum of Se (IV) and Se (VI) measured in digested solutions can be attributed to the remaining $(CH_3)_3Se^+$. It was noticed that, with group (I) tests, although chemical reagents (HNO_3–H_2O_2) were the same as those used with 100 mL vial trial (Table 2, (A)), an average of 81% of $TMSe^+$ was converted to Se (IV) in 6 mL vials compared with less than 30% in 100 mL vials. In addition, a remarkable difference between 6 and 100 mL vial digestions was observed in group (III) in Table 3 and group (C) in Table 2. In the 6 mL vials after digestion, about 50% of $TMSe^+$ was converted to Se (VI) and 5% in Se (IV), whereas in 100 mL vials these values were somewhat reversed, with 5% and 30% for Se (VI) and Se (IV) present, respectively. This suggests that the chemical environment between these two types of digestion vials was not the same. This difference can be explained by the difference in temperature measurement and chemical environment created in the two types of vials. When using 100 mL vials, the temperature probe was set directly in the reagent solution, whereas in 6 mL vials, it was set in the deionized water placed between two sets of digestion vials; therefore, the temperature inside the 6 mL vials may differ from that in 100 mL vials. The presence of deionized water in the digestion system and smaller quantity of digestion reagents in the small vials also produce different chemical conditions in the 6 mL vials digestion system.

Despite these differences, data in Tables 2 and 3 have a remarkable common feature – the large variations in results related to Se (IV) and Se (VI) in the same chemical treatment group. To check this variation, the experimental work was repeated several times and they all showed the same trend. It is also important to mention that in the 6 mL vials, although the percentage of Se (IV) and Se (VI) varied largely within the same digestion system (Table 3), the variations were much smaller between the samples located in the same 100 mL vial, remembering that vials 1

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and 2, 3 and 4 and 5 and 6 were grouped into three individual 100 mL vials. This phenomenon suggests that the small vials inserted in the same 100 mL vial were subjected to the same digestion conditions, whereas the digestion conditions varied from one to another 100 mL vial. The reagent blank in each group was negligible, indicating that no spill had occurred during the digestion. The large variation in the results strongly suggests heterogeneity in the distribution of the microwave energy. It is also clear that a larger quantity of chemical reagents added in 100 mL vials did not promote the breakdown of $TMSe^+$, but rather the opposite result.

Our study with a chemical system containing Br^-/BrO_3^- did not show a significant advantage in breaking down $TMSe^+$ over the other types of chemical systems. This could be explained as below. In the acidic solution and in the coexistence of Br^- and BrO_3^-, the comproportionation reaction occurs:

$$BrO_3^- + 5Br^- + 6H^+ \longrightarrow 3Br_2 + 3H_2O.$$

Br_2 possesses a strong oxidative power. As the bromine solution was prepared in 1.1 M KBr – 0.22 M $KBrO_3$, a 5:1 molar ratio, therefore, no Br^- (nucleophilic reagent) remained after the above reaction. Unlike the open digestion system (*31*, *32*), the usage of a large quantity of the HBr reagent was carefully avoided to prevent high pressures generated during the digestion in a closed digestion system. The discrepancy in observation between our study and that of D'Ulivo *et al*. (*31*, *32*) may be due to these differences in digestion systems, open *vs.* closed vials and large *vs.* restricted quantity of HBr.

2.6. *Other observed properties related to $(CH)_3SeI$*

It was observed that soon after the synthesis of TMSeI, the aqueous solutions in both the glove box and the refrigerator were heavily contaminated for Se determination with HG-AFS, possibly due to the dissolution of $(CH_3)_2Se$ into these solutions. By flushing the glove box with abundant N_2 gas and evacuation of air in the refrigerator, the false AFS signals produced in such a way were all eliminated. Therefore, it is recommended to safeguard sample solutions if they are to be analyzed by HG-AFS. Apparently, $(CH_3)_2Se$ emits a very strong fluorescent signal which overlaps with that of atomic fluorescence signal produced by Se atoms after the H_2Se breakdown in the flame.

3. Conclusion

This work presents a detailed protocol to synthesize TMSeI with a high purity, which makes it qualified as a primary standard substance (99.8 ± 1.1%). The synthesis is simple, straightforward and affordable. Differential scanning calorimetric analysis shows that a phase transition occurred at 122.8 °C with an enthalpy of 4.3 kJ mol^{-1}, and decomposition of $(CH_3)_3Se^+$ happened at 157.7 °C with an enthalpy of 100.7 kJ mol^{-1}. Once it is dissolved in water, $TMSe^+$ becomes very stable under strong UV irradiation. Under harsh chemical attacks at a high temperature (210 °C) and a high pressure in a microwave digestion system, this compound also appeared quite stable as indicated by relatively small percentage of broken down products such as Se (IV) and Se (VI) species in most digested solutions. The poor reproducibility in results is possibly produced by the heterogeneity of microwave energy; the inadequate amount of Br^- and reagent combination, therefore, needs to be further studied.

TMSeI is stable when stored under frozen conditions. No structure modification was found after 1 year of storage. The chemical structure of $TMSe^+$ in an aqueous solution remained unchanged 4 months after storage at 4 °C.

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4. Experimental

4.1. *Instrumentation*

The synthesis was carried in a controlled atmosphere chamber (Vacuum Atmospheres Company, Omni-Lab System) in which high-purity nitrogen gas was flushed to maintain the chamber oxygen level at around 400 ppmv (parts per million in volume) prior to synthesis. The compound was characterized with the aid of a Varian Gemini 2000 NMR spectrometer, an FTIR spectrometer (MB102, BOMEM Hartman & Braun, Inc.), a HPLC–ESI-MS (Agilent 1100 series, Agilent 6120 quadrupole LC/MS) in the positive mode of detection. The decomposition point and decomposition enthalpy of TMSeI were studied with a melting point apparatus (MEL-TEMP®, Electrothermal) and a DSC Q20, TA Instrument calibrated with indium (m.p. 156.6 °C). The UV–visible spectrum of the synthesized product and that of sodium iodide were recorded on an Ultraspec 3000 UV–visible spectrometer (Pharmacia Biotech).

The purity of the synthesized product was determined with three different analytical techniques: inductively coupled plasma mass spectrometry (ICP-MS; ELAN DRC-e, Perkin Elmer), GF-AAS (Perkin Elmer, AAnalyst 600) and flame atomic absorption spectrometry (FAAS; Perkin Elmer, AAnalyst 400).

In the studies of photochemical stability of $TMSe^+$, a Rayonet photochemical chamber reactor (RPR-100, Southern New England Ultraviolet Company) equipped with 16 lamps of 300 nm wavelength (21 W each) was employed. The chemical stability of $TMSe^+$ under strong digestion conditions was examined with a microwave Labstation (Milestone Ethos 1600 URM, HPR 1000/10 system, Bergamo, Italy) equipped with 100 or 6 mL Teflon digestion vials. HG-AFS (PSA 10.055 Millennium Excalibur) was also used in the studies to identify the formation of Se (IV) and Se (VI) species under different chemical digestion systems. A five-digit microbalance (Mettler Toledo, Switzerland) was employed when a small sample size was required.

4.2. *Reagents and standards*

Dimethylselenide (>99%), methyl iodide (99%) and *n*-hexane (99%) were purchased from Sigma-Aldrich and used for synthesizing TMSeI. Water used in all studies was purified using an NANO Pure Diamond™ Water Purification System (Barnstead, NH, USA). The primary standard Se (IV) solution of 1000 mg L^{-1} (as Se) was prepared in 3.0 M HCl from SeO_2 (99.8% Aldrich) and stored at 4 °C. This solution is stable for at least 12 months. Trifluoroacetic acid (TFA) (>99.5%, Fisher) and heptafluorobutyric acid (HFBA) (>99.5%, Fisher) were employed in HPLC as eluents for $TMSe^+$. All other chemicals used in this work are at least of analytical purity.

4.3. *Protocol for synthesis*

The synthesis was conducted in a controlled atmosphere chamber kept at an oxygen level of ~400 ppmv. The reaction vessel was a 15 mL conical bottom-graded Pyrex glass centrifuge tube with a ground glass stopper. Mixture I (1.0 mL of CH_3I and 1.0 mL of *n*-hexane) and mixture II (0.5 mL of dimethyl selenide and 0.75 mL of hexane) were both prepared in the pre-cleaned and dried Pyrex glass centrifuge tubes and placed in an ice-water bath to reduce the rapid evaporation of the solvents and moved into the glove box. The solvent of mixture II was added into mixture I dropwise with a gentle stirring until it was all added and the stopper was tightened. Within a few minutes after mixing the two solutions, a white amorphous precipitate was formed. The reaction vessel together with the icy bath was withdrawn from the glove box and placed in a refrigerator overnight, and at this point, the amorphous precipitate was transformed into colorless crystals.

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By then, the supernatant was evaporated to dryness. It is important to close the tubes tight and perform the mixture (II) addition as swift as possible, due to the low boiling points of methyl iodide (42.5 °C), dimethyl selenide (42–43 °C) and *n*-hexane (69 °C).

The solid was washed with ∼1 mL of *n*−hexane and recrystallized in ∼1 mL of methanol (100%). The dried crystals were then transferred into a clean conical bottom-graded Pyrex glass centrifuge tube; a small and just sufficient volume of hot methanol (HPLC grade) was introduced to dissolve the crystals and then added another aliquot of hot methanol of about 10% of existing volume. The sample was left at 4 °C overnight. The crystals were then filtered through a #1 Whatman filter paper under vacuum to remove the solvent and dried at 50 °C for 2 h in an oven. The resulting transparent crystals (0.908 g, yield 56%) were stored at −23 °C.

In laboratories with no access to a sophisticated commercial glove box, a simple plastic glove box can be used providing that a thorough removal of the air and a 2 h N_2 flush is performed prior to the synthesis. The inert atmospheric conditions prevent a fast oxidation of CH_3I, and the formation of I_2 thus increases the purity of the synthesized compound.

4.4. *Characterization of the synthesized TMSeI*

To obtain NMR spectroscopic information, a solution containing 10 mg of synthesized TMSeI was dissolved in 0.50 mL of D_2O. For FTIR analysis, 2.0 mg of the product was mixed and ground with 0.20 g of KBr and pressed into a disc. The chromatographic behavior and mass spectroscopic data were collected by HPLC–ESI-MS. A solution of synthesized TMSeI (∼80 μM), prepared with pure water, was injected (20 μL) on the column (Pursuit XRS – C18, 250 × 4.6 mm, A6001250 × 046, Varian) and the chromatographic peaks detected with a 6120 Quadrupole MS.

4.5. *Investigation of the purity of $TMSe^+$*

To determine the purity of the synthesized TMSeI, the compound was assumed as 100% pure. A known amount of the synthesized product (32.8 mg) was weighed precisely and dissolved in 10.00 mL of ultra-pure water to obtain a solution with a concentration of 1030.5 mg L^{-1} as Se. The above solution was sequentially diluted to a final concentration of 10.3 mg L^{-1}, 103.1 μg L^{-1} and 25.7 μg L^{-1} as Se for FAAS, GF-AAS and ICP–MS determination, respectively. A wavelength of 196.03 nm and a Se electrodeless discharge lamp were employed in Se determination by FAAS and GF-AAS. The graphite furnace program comprised five steps: drying at 110 °C (ramp 1, hold 30 s) and at 130 °C (ramp 15, hold 30 s), ashing at 1300 °C (ramp 10, hold 20 s), atomization at 1900 °C (ramp 0, hold 5 s) and cleaning at 2100 °C (ramp 1, hold 2 s). The addition of 6 μL $MgNO_3$ (1000 mg L^{-1})–Pd (1500 mg L^{-1}) matrix modifier is necessary to avoid the loss of $TMSe^+$. The determination by ICP-MS was done with both Se^{78} and Se^{82}. In each method, at least three individual analyses were carried and the overall average of measured Se in the synthesized TMSeI was derived.

4.6. *Stability studies of $TMSe^+$*

4.6.1. *$TMSe^+$ stability studies under UV irradiation*

In the studies on the effect of UV radiation on the stability of $TMSe^+$, two aliquots of 10.00 mL of the 103.1 μg L^{-1} TMSeI solution (as Se) were prepared, one in deionized water and another one in 1.0% (v/v) HNO_3–2.0% (v/v) HCl. They were subjected to UV irradiation (300 nm) for 2.5 h (*40*). The UV irradiation studies were performed as below: (i) direct determination of Se (IV) by HG-AFS without any treatment in order to check the possible formation of Se (IV) after

UV irradiation; (ii) pre-reduction of Se (VI) in 3.0 M HCl in a microwave oven (temperature arising from 20 to 110 °C within 10.0 min, then hold at 110 °C for 15.0 min, venting for 20 min in a sealed 100 mL digestion bomb) and determination of the sum of Se (IV) and Se (VI) with HG-AFS, in case there is any Se (VI) formed in the solution during irradiation. The difference in Se between (ii) and (i) should be the concentration of Se (VI) formed under UV radiation. (iii) Direct determination of Se in the UV-irradiated solution by GF-AAS to investigate whether there was any loss of Se in form of volatile Se compound such as $(CH_3)_2Se$ during the UV irradiation.

4.6.2. *$TMSe^+$ stability studies under chemical attacks*

The chemical stability of $TMSe^+$ under a variety of strong digestion systems was studied using a microwave oven digestion system with 100 or 6mL Teflon digestion vials. The microwave program consists: (1) room temperature → 85 °C in 4 min; (2) 85 °C → 145 °C in 10 min; (3) 145 °C → 210 °C in 6 min; (4) maintained at 210 °C for 10 min and (5) vent (210 °C → 170 °C) in 20 min. A standard TMSeI solution of 10.3 mg L^{-1} as Se was prepared. Three tested chemical systems were (A) 7.0 mL 15 M HNO_3–1.0 mL 30% (w/w) H_2O_2; (B) 8.0 mL 15.0 M HNO_3–0.2 mL 18.4 M H_2SO_4 and (C) 7.0 mL 15.0 M HNO_3 – 0.5 mL of bromine solution (1.1 M KBr–0.22 M $KBrO_3$ in saturation). HG-AFS was used to examine the possible formation of Se (IV) and Se (VI) during the digestion. GF-AAS was used to determine the total Se that remained in the microwave digested solutions. To avoid the possible matrix effect in GF-AAS determination, the Se concentration was obtained based on a three point – spike, standard and addition – method for all measurements.

For the studies of chemical attacks using 6 mL vials, the microwave digestion program was identical as for 100 mL vials. The chemical attack system was (I) 1.0 mL 15.0 M HNO_3–0.2 mL 30% (w/w) H_2O_2; (II) 1.0 mL 15.0 M HNO_3–0.10 mL 18.4 M H_2SO_4; (III) 0.7 mL 15.0 M HNO_3–0.15 mL Br solution (1.1 M KBr–0.22 M $KBrO_3$ in saturation). Vial numbers 1 and 2, 3 and 4 and 5 and 6 were installed in three different 100 mL vials, and a reagent blank vial was included in each group. The detailed description for low-volume digestion is provided in (*39*).

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