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Mass spectral study of the CWC-related S-alkyl methylphosphonochloridothioites/S,S′-dialkyl (alkyl′)methylphosphonodithioites under gas chromatography–mass spectrometry conditions

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ABSTRACT

A class of S-alkyl methylphosphonochloridothioites **3** (11 compounds), S,S′-dialkyl methylphosphonodithioites **4** (12 compounds) and S-alkyl S′-alkyl′ methylphosphonodithioites **5** (9 compounds) were synthesized and were analyzed using gas chromatography–electron ionization mass spectrometer (GC–EIMS). Generalized fragmentation pathways under experimental condition for synthesized compounds are proposed based on analysis of fragment ions of deuterated analogs and density functional theory (DFT) calculations. Results of the study were undertaken with a view to enrich the Organization for the Prohibition of Chemical Weapons (OPCW) Central Analytical Database (OCAD), which may be used for detection and identification of Chemical Weapons Convention (CWC)-related chemicals during on-site inspection and/or off-site analysis, such as OPCW proficiency tests.

1. Introduction

Among chemical weapons, Organophosphorus nerve agents (OPNA) constitute the greatest concern due to their high toxic effects on humans; even low levels of exposure can cause muscle twitching, miosis, hyperglycemia, and ultrasecretions, convulsions, seizures, and death of the individual [1]. The high toxicity of these agents can be attributed to the excessive cholinergic stimulation caused by inhibition of acetylcholinesterase (AChE) [2]. One AChE molecule can efficiently hydrolyze around 25,000 molecules of ACh per second. It is not present in very large amounts in the human body, so blocking of the enzyme quickly leads to fatal consequences. The OPNAs, such as sarin, soman, VX, and tabun, were used for the first time during the Iran–Iraq war and subsequently in some terrorist attacks in Japan [3]. Chemical warfare agents are still a threat, and based on CWC, the international community should work to achieve a world free of such weapons of mass destruction.

Chemical warfare agents analysis is an important part of verification activities according to CWC [4]. The Organization for the Prohibition of Chemical Weapons (OPCW) maintains a network of designated laboratories in order to provide off-site analytical services [5]. A great deal of attention has been focused on the development of analytical techniques for the rapid and unambiguous identification of chemical warfare agents (CWAs), their precursors, reaction, and degradation products. Gas chromatograph (GC) coupled with mass spectrometer (MS) is widely used for the analysis of CWAs, because most CWAs are volatile and nonpolar compounds [6–10]. On the other hand, GC–MS instrument has been extensively used due to its high sensitivity, reliability, and versatility [11]. GC–MS analysis is generally performed using electron ionization (EI). This system provides extensive structural hints about the chemical through its characteristic fragmentation pathways. On the other hand, EI mass spectra of many CWC-related chemicals are available in the OPCW Central Analytical Database (OCAD) [12]. For unequivocal identification of CWC-related compounds in real samples or OPCW proficiency tests, the availability of mass spectra and interpretation skills are essential requirements. Millions of chemicals are listed in CWC annex of chemicals in three distinct schedules.

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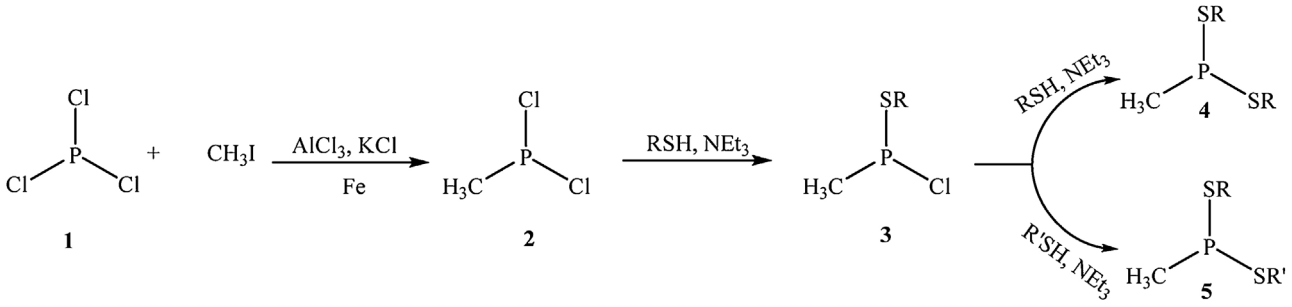

Scheme 1. Microsynthesis route of the studied compounds **3**, **4**, and **5**.

It is impossible to have a complete collection of GC–MS data for all CWC-related compounds due to millions of possibilities. S-alkyl methylphosphonochloridothioites **3**, S,S′-dialkyl methylphosphonodithioites **4**, and S-alkyl S′-alkyl′ methylphosphonodithioites **5** are covered under CWC schedule 2.B.04, as well as other compounds with phosphorus bonded to methyl, ethyl, isopropyl, or propyl moieties. Currently, there is no mass spectrum for such chemicals in commercial databases and OCAD. Therefore, we have focused on the EI mass spectral characterization of them through possible fragmentation pathways based on data from analysis of fragment ions of deuterated analogs, and energy calculations.

2. Experimental

2.1. Reagents and chemicals

All chemicals required for the microsynthesis of S-alkyl methylphosphonochloridothioites **3**, S,S′-dialkyl methylphosphonodithioites **4**, and S-alkyl S′-alkyl′ methylphosphonodithioites **5** were purchased from Sigma–Aldrich (St. Louis, MO, USA), Fluka (Neu-Ulm, Germany), and Merck (Darmstadt, Germany), and were used as received. Methylphosphine dichloride **2** was synthesized using existing method (Scheme 1) [13].

2.2. GC–MS analyses

The GC–MS analyses were performed using an Agilent 6890N gas chromatograph coupled to a 5973 Mass Selective Detector, a HP-5MS capillary column (30 m, 320 μm i.d. and 0.25 μm film thickness), and helium as carrier gas at constant flow at 1.8 mL min^{-1}. The oven's temperature was set at 40 °C for 3 min and then it was increased to 280 °C with ramp of 10 °C/min and held at 280 °C for 6 min. The samples were injected in splitless mode at an injection temperature of 250 °C. The temperatures of the EI source and analyzer were kept at 230 and 150 °C, respectively. The scan range was *m/z* 35–500. Automated mass spectral deconvolution and identification system (AMDIS) software [14] was used to calculate retention indices of the synthesized compounds. An alkane mixture [octane (C_8) to tetracosane (C_{24})] was used for the retention index calculation [15].

2.3. Computational details

Geometry optimizations and frequency calculations for all species were carried out using the Gaussian 03 program [16]. DFT with the Becke three parameters hybrid functional (DFT-B3LYP) calculations were performed with a 6-311++G (2d, 2p) basis set for all atoms. Vibrational frequencies were calculated at the same level to ensure that each stationary point was a real minimum. Harmonic-oscillator approximation was also used for the thermodynamic partition functions. After geometry optimization and frequency calculations, zero-point energies (ZPEs) and thermal corrections were obtained at 298 K.

2.4. General procedure for microsynthesis of S-alkyl methylphosphonochloridothioites 3, S,S′-dialkyl methylphosphonodithioites 4, and S-alkyl S′-alkyl′ methylphosphonodithioites 5

The corresponding S-alkyl methylphosphonochloridothioites **3** were synthesized by the controlled addition of RSH to methylphosphine dichloride solution. The appropriate thiol (0.30 mmol) and triethylamine or pyridine (0.65 mmol) in dichloromethane (200 μL) were added slowly into the solution of methylphosphine dichloride (0.25 mmol) in dichloromethane (500 μL), while stirring at 0–5 °C. After 15 min, the resulting precipitate was filtered off and the solution was analyzed using GC–MS (Scheme 1).

The more addition of RSH (R′SH) to the solution of S-alkyl methylphosphonochloridothioites **3** was afforded the desired products of S,S′-dialkyl methylphosphonodithioites **4** and S-alkyl S′-alkyl′ methylphosphonodithioites **5**. Solution RSH or R′SH (0.30 mmol) in dichloromethane (200 μL) was slowly added into the S-alkyl methylphosphonochloridothioites **3** solution and the resulted mixture was allowed to stir at 0–5 °C for 1 h. Any precipitate was filtered off and the solutions were analyzed using GC–MS, as required (Scheme 1).

It should be noted that the separation and purification of CWC-related chemicals, due to the extreme toxicity of these materials, are very difficult and, therefore, should be handled only by a trained professional in an efficient fume cupboard equipped with active charcoal filtration system.

3. Results and discussion

3.1. Synthesis

The microsynthesis of products **4** and **5** generally involves two steps: the initial addition of the corresponding thiol to methyldichlorophosphine **2** in the presence of triethylamine or pyridine, to form S-alkyl methylphosphonochloridothioites **3**, and subsequently, more addition of RSH (R′SH) to the solution of S-alkyl methylphosphonochloridothioites **3** to yield desired products **4** and **5**. Using CD_3I instead of CH_3I in Scheme 1 afforded deuterated analogs of **3**, **4**, and **5** (Tables 1–3).

It should be noted that the corresponding methylphosphinothioates or methylphosphonodithioates as by-products are also observed with low yields in the crude of the reaction, while all attempts for the synthesis of corresponding O-O′-dialkyl methylphosphonites were failed and often produced O-alkyl methylphosphinates and methylphosphonates as main products [17]. High affinity of O-O′-dialkyl methylphosphonites to oxidation can be described by symbiosis effect. The term "*symbiosis*" is

Table 1
GC/MS data of S-alkyl methylphosphonochloridothioites **3**.

Entry	R	Retention index (RI)	$M^{+\bullet}$	Fragment ions (% relative abundances)								
				[A]	[B]	[C]	[D]	[E]	[F]	[G]	[H]	[I]
1	Et	957	142 (100)	127 (16)	114 (97)	113 (43)	107 (36)	79 (26)	81 (14)	99 (23)	127 (16)	127 (16)
			144 (36)	129 (6)	116 (35)	115 (18)	109 (2)	81 (14)	83 (4)	101 (9)	129 (6)	129 (6)
2[a]	Et	952	145 (100)	127 (12)	117 (93)	116 (43)	110 (38)	82 (20)	84 (14)	99 (21)	130 (1)	130 (1)
			147 (36)	129 (6)	119 (34)	118 (17)	112 (2)	84 (14)	86 (4)	101 (8)	132 (–)	132 (–)
3	*n*-Pr	1055	156 (49)	141 (1)	114 (100)	113 (13)	121 (23)	79 (31)	81 (13)	99 (9)	127 (2)	141 (1)
			158 (18)	143 (–)	116 (37)	115 (36)	123 (1)	81 (13)	83 (4)	101 (3)	129 (1)	143 (–)
4	*i*-Pr	999	156 (52)	141 (1)	114 (100)	113 (7)	121 (19)	79 (27)	81 (7)	99 (9)	–	141 (1)
			158 (19)	143 (–)	116 (37)	115 (9)	123 (1)	81 (7)	83 (2)	101 (3)		143 (–)
5[a]	*i*-Pr	886	159 (51)	144 (1)	117 (100)	116 (8)	124 (20)	82 (26)	84 (7)	99 (9)	–	144 (1)
			161 (20)	147 (–)	119 (35)	118 (9)	126 (1)	84 (7)	86 (2)	101 (3)		146 (–)
6	*n*-Bu	1156	170 (27)	155 (1)	114 (100)	113 (16)	135 (22)	79 (17)	81 (14)	99 (6)	127 (3)	155 (1)
			172 (10)	157 (–)	116 (37)	115 (58)	137 (1)	81 (14)	83 (4)	101 (5)	129 (1)	157 (–)
7	*sec*-Bu	1107	170 (54)	155 (1)	114 (100)	113 (10)	135 (16)	79 (21)	81 (9)	99 (5)	–	155 (1)
			172 (20)	157 (–)	116 (37)	115 (42)	137 (1)	81 (9)	83 (3)	101 (6)		157 (–)
8[a]	*sec*-Bu	1102	173 (51)	158 (1)	117 (100)	116 (112)	138 (19)	82 (20)	84 (10)	102 (1)	–	158 (5)
			172 (19)	159 (–)	119 (38)	118 (44)	140 (1)	84 (10)	86 (3)	14 (5)		160 (–)
9	*n*-Pen	1253	184 (3)	–	114 (87)	113 (18)	149 (23)	79 (12)	81 (17)	99 (5)	127 (4)	169 (–)
			186 (1)		116 (33)	115 (58)	151 (1)	81 (17)	83 (5)	101 (2)	129 (2)	171 (–)
10[a]	*n*-Pen	1250	187 (3)	–	117 (86)	116 (18)	152 (25)	82 (11)	84 (18)	99 (4)	130 (5)	172 (–)
			189 (1)		119 (33)	118 (59)	154 (1)	84 (17)	86 (6)	101 (2)	132 (2)	173 (–)
11	*n*-Hex	1360	198 (1)	–	114 (51)	113 (11)	163 (12)	79 (6)	81 (10)	99 (2)	127 (2)	183 (–)
			200 (1)		116 (100)	115 (45)	165 (1)	81 (10)	83 (1)	101 (7)	129 (1)	185 (–)

[a] S-alkyl methyl(d_3)phosphonochloridothioites **3**.

Table 2
GC/MS data of S,S′-dialkyl methylphosphonodithioites **4**.

Entry	R	Retention index (RI)	$M^{+\bullet}$	Fragment ions (% relative abundances)						
				[A]	[B]	[C]	[D]	[E]	[F]	[G]
1	Et	1200	168 (86)	153 (15)	139 (61)	140 (43)	125 (7)	111 (100)	112 (14)	107 (10)
2[a]	Et	1197	171 (91)	153 (15)	142 (62)	143 (45)	125 (6)	114 (100)	115 (15)	110 (10)
3	*n*-Pr	1380	196 (65)	181 (8)	153 (19)	154 (78)	139 (17)	111 (100)	112 (79)	121 (10)
4[a]	*n*-Pr	1378	199 (59)	181 (7)	156 (17)	157 (73)	139 (16)	114 (100)	115 (84)	124 (10)
5	*i*-Pr	1271	196 (71)	181 (2)	153 (29)	154 (36)	139 (5)	111 (100)	112 (69)	121 (5)
6	*n*-Bu	1572	224 (59)	209 (5)	167 (16)	168 (50)	153 (12)	111 (85)	112 (100)	135 (13)
7[a]	*n*-Bu	1464	227 (42)	209 (<1)	170 (12)	171 (43)	153 (2)	114 (68)	115 (100)	138 (4)
8	*sec*-Bu	1467	224 (45)	209 (1)	167 (13)	168 (45)	153 (3)	111 (66)	112 (100)	135 (4)
9[a]	*sec*-Bu	1463	227 (44)	209 (1)	170 (13)	171 (43)	153 (2)	114 (67)	115 (100)	138 (4)
10	*n*-Pen	1782	252 (21)	237 (2)	181 (8)	182 (7)	167 (5)	111 (40)	112 (56)	149 (12)
11[a]	*n*-Pen	1769	255 (20)	237 (2)	184 (7)	185 (7)	167 (5)	114 (38)	115 (55)	152 (12)
12	*n*-Hex	1973	280 (11)	265 (1)	195 (5)	196 (3)	182 (1)	111 (18)	112 (38)	164 (2)

[a] S,S′-dialkyl methyl(d_3)phosphonodithioites **4**.

applied to explain the phenomenon of maximum flocking of either hard or soft substitutions in the same molecules [18].

3.2. GC–MS analyses

Major EI fragment ions of S-alkyl methylphosphonochloridothioites **3**, as well as their retention indices (RI), are given in Table 1, and the plausible fragmentation routes of **3** are shown in Fig. 1.

As expected, RI of compounds containing branched alkyl groups were less than those of compounds containing normal alkyl groups. Deuterosubstitution can affect analyte evaporation, diffusion, and partition properties, affecting molecular interactions with the GC stationary phase. In general, compounds **3**, **4**, and **5** have higher RI than their corresponding deuterated analogs (Tables 1–3).

The molecular ion ($M^{+\bullet}$) of S-alkyl methylphosphonochloridothioites **3** is observed in their EI–MS spectra with relative good to moderate abundance. The base peak in EI–MS of chemicals bearing

Table 3
GC/MS data of S-alkyl S′-alkyl′ methylphosphonodithioites **5**.

Entry	R	R′	Retention index (RI)	$M^{+\bullet}$	Fragment ions (% relative abundances)						
					[A]	[B]/[B′]	[C]/[C′]	[D]/[D′]	[E]	[F]	[G]/[G′]
1	Et	*n*-Pr	1287	182 (63)	167 (8)	139 (22)/153 (10)	140 (69)/154 (4)	125 (21)/138 (–)	111 (100)	112 (41)	107 (9)/121 (4)
2[a]	Et	*n*-Pr	1283	185 (70)	167 (9)	142 (23)/156 (10)	143 (76)/157 (4)	125 (20)/138 (–)	114 (100)	115 (45)	110 (8)/124 (4)
3	Et	*sec-Bu*	1330	196 (73)	181 (1)	139 (280)/167 (2)	140 (89)/168 (2)	125 (21)/153 (–)	111 (85)	112 (100)	107 (22)/135 (2)
4[a]	Et	*n*-Bu	1327	199 (69)	181 (1)	142 (27)/170 (2)	143 (84)/171 (2)	125 (18)/153 (–)	114 (84)	115 (100)	110 (22)/138 (–)
5	Et	*n*-Pen	1498	210 (41)	195 (7)	139 (33)/181 (7)	140 (72)/182 (1)	125 (26)/167 (–)	111 (100)	112 (84)	107 (18)/149 (7)
6[a]	Et	*n*-Pen	1492	213 (43)	195 (6)	142 (32)/184 (7)	143 (75)/185 (1)	125 (24)/167 (–)	114 (100)	115 (88)	110 (17)/152 (7)
7	*n*-Pr	*sec*-Bu	1424	210 (38)	195 (<1)	153 (11)/167 (2)	154 (32)/168 (15)	139 (8)/153 (11)	111 (61)	112 (100)	121 (6)/135 (2)
8[a]	*n*-Pr	*sec*-Bu	1421	213 (45)	195 (–)	156 (12)/170 (2)	157 (34)/171 (16)	139 (8)/153 (–)	114 (61)	115 (100)	124 (6)/138 (2)
9	*n*-Pr	*n*-Pen	1581	224 (36)	209 (5)	153 (12)/181 (5)	154 (32)/182 (7)	139 (12)/167 (2)	111 (81)	112 (100)	121 (8)/149 (7)

[a] S-alkyl S′-alkyl′ methyl(d_3)phosphonodithioites **5**.

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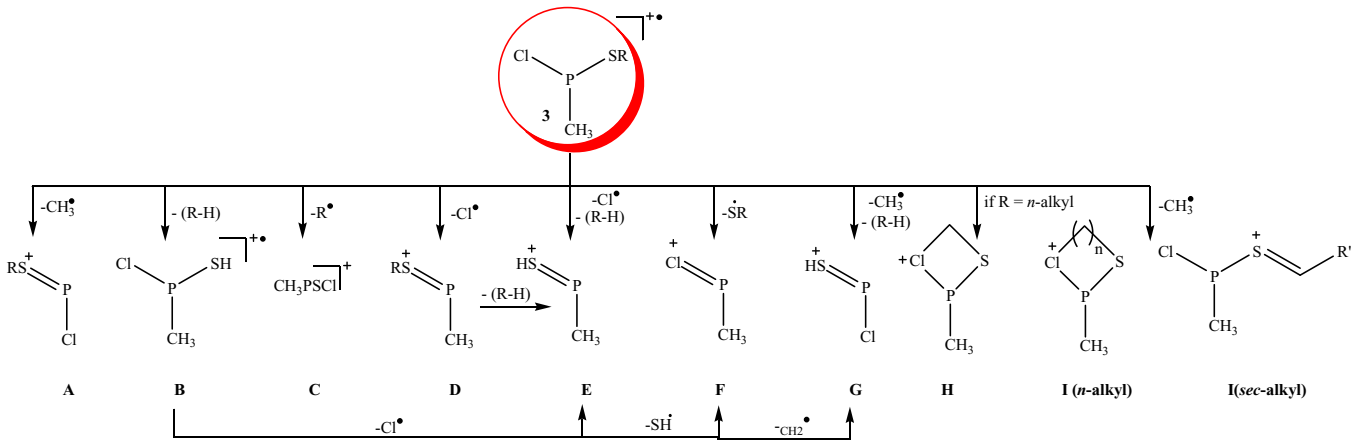

Fig. 1. Proposed fragmentation routes for S-alkyl methylphosphonochloridothioites **3**.

ethyl substitution on sulfur atom is $M^{+\bullet}$ (Table 1, entry 1 and 2). When the *S*-alkyl chain length increases, the $M^{+\bullet}$ signal decreases in intensity. Expected isotopic ratios of chlorine and sulfur containing fragments were observed, as is evident from the relative abundances listed in Table 1.

Fragment ion [A] is formed through α-cleavage of CH_3—P bond. The ion at *m/z* 127 in the EI mass spectrum of deuterated analog of S-ethyl methyl(d_3)phosphonochloridothioites (Table 1, entry 2) is the result of elimination of CD_3 from $M^{+\bullet}$ via α-cleavage. Ion [B] as the base peak or the second highest peak in the EI–MS spectra of **3** resulted from loss of an alkene molecule from $M^{+\bullet}$ through 1,3 C-S hydrogen shift as depicted in Scheme 2. Analysis of mass spectra of deuterated analogs also supported this point (Fig. 2).

Direct expulsion of alkyl on sulfur from $M^{+\bullet}$ led to the formation of fragment ion [C] at *m/z* 113. Spectra of deuterated analogs (Table 1, entry 2, 5, 8, and 10) revealed the ion corresponding to this fragmentation at *m/z* 116. It should be noted that ion [C] could be related to three possible structures (Scheme 3). The DFT calculated

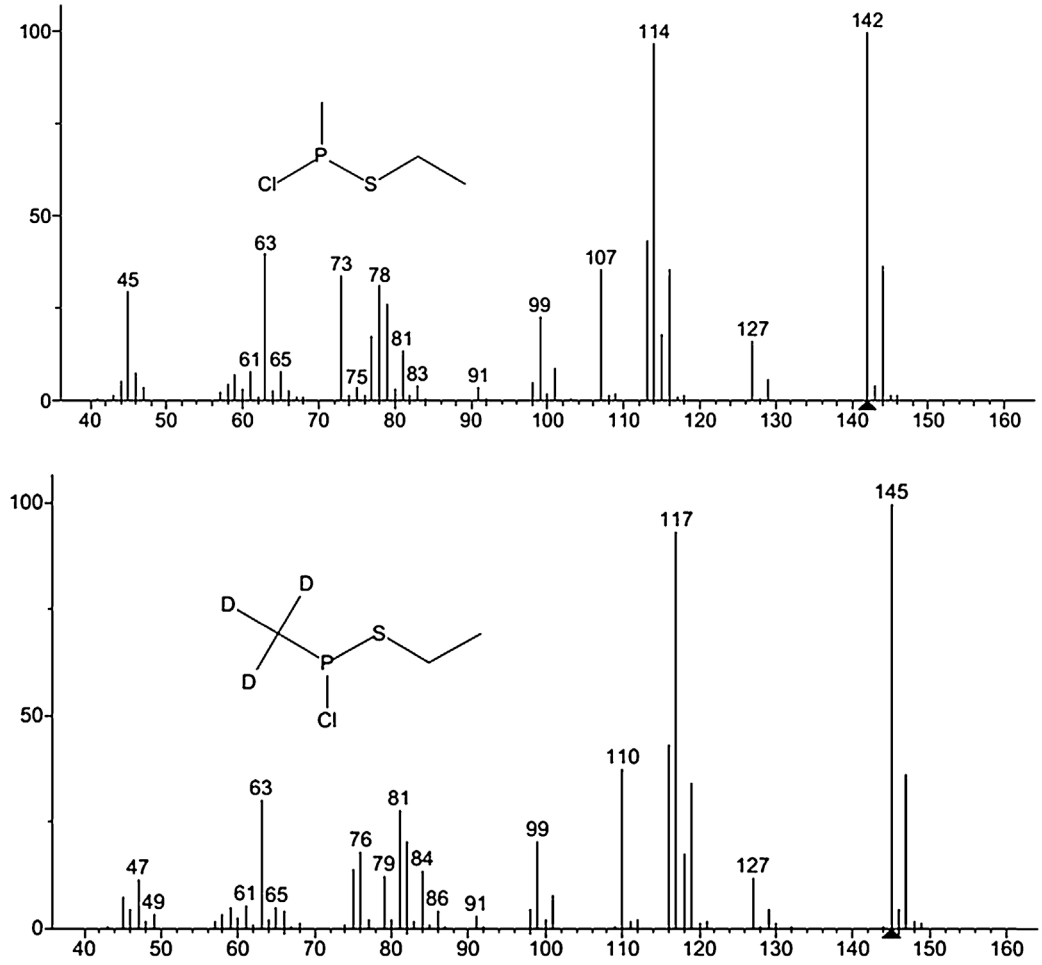

Fig. 2. Representative EI–MS mass spectra of **3** and its deuterated analog.

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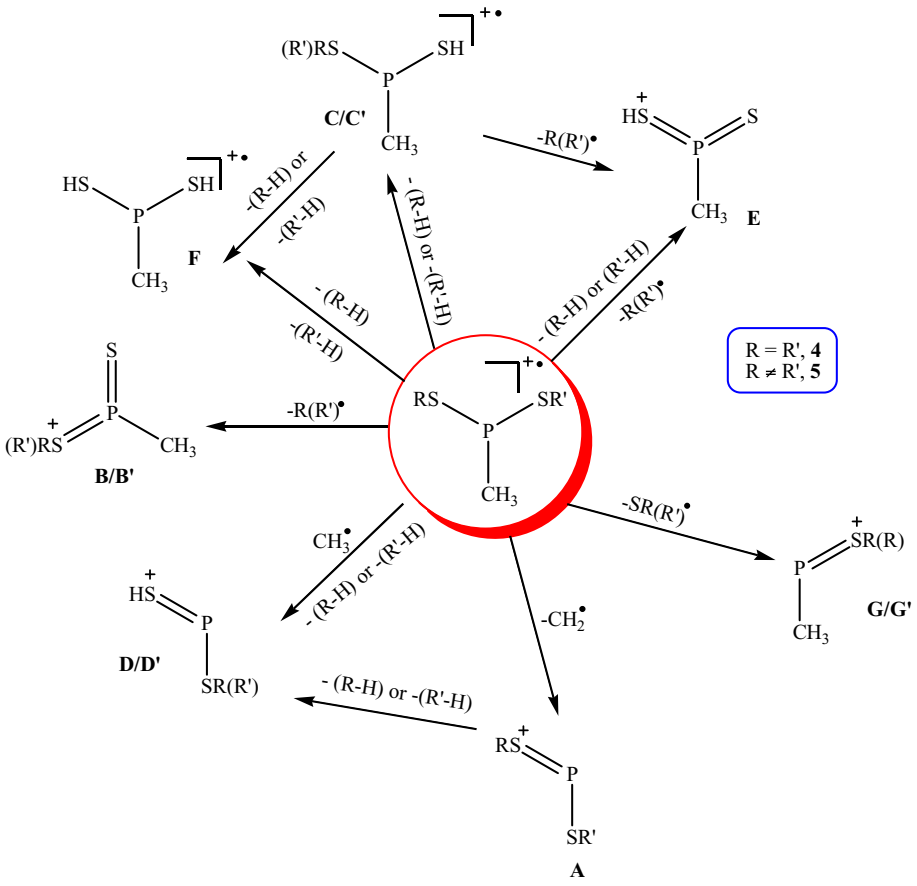
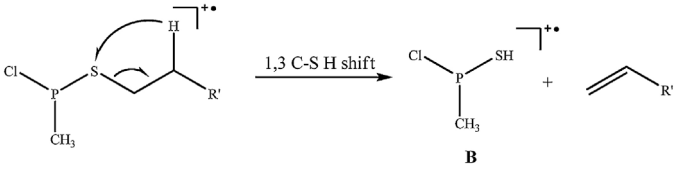


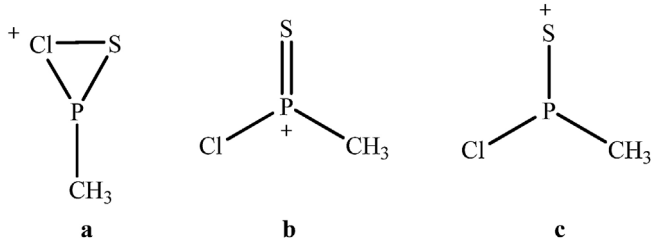
Fig. 3. Proposed fragmentation routes for S,S′-dialkyl methylphosphonodithioites **4** and S-alkyl S′-alkyl′ methylphosphonodithioites **5**.



Scheme 2. Proposed fragmentation pathway for formation of [B].

free energy of the structures (**b**) and (**c**) are equal. Free energy of the structure (**a**) was calculated to be 151 kJ mol^{-1} higher than the structures (**b**) and (**c**). Fragment ion (**a**) is an unstable ion due to its angel strain [19]. This indicated that the cleavage of the S—R bond initiated from chlorine (**a**) is not preferred over that the process initiated from phosphorous (**b**) or sulfur (**c**).

Elimination of chlorine radical and RS• from EI–MS of **3** led to the formation of fragment ions [D] and [F], respectively with relative moderate abundance. Concerted or step-wise expulsion of chlorine and alkene from M$^{+\bullet}$ resulted in a fragment ion at *m/z* 79 as [E]. When the *S*-alkyl chain length increases, the [E] signal decreases in intensity. Fragment ion [G] was observed in EI–MS of all S-alkyl methylphosphonochloridothioites **3** with relative low intensity. The characteristic ion [H] was observed in EI–MS spectrum of chemical **3** that is bearing *n*-alkyl group on sulfur. Loss of R_{n-1}• as an alkyl radical from *S*-(*n*-alkyl) chain gave rise to fragment [H]. This peak can be used for unambiguous distinction of *n*-alkyl from *sec*-alkyl group in such compounds. It is interesting to note that the leaving of a methyl radical from alkyl on sulfur atom led to the formation of fragment ion [M$^{+\bullet}$−15] as [I] with relative low intensity. In case of *sec*-alkyl, structure of the ion [I] is a sulfonium fragment, while in case of *n*-alkyl, it is a cyclic chloronium fragment. The corresponding fragment ions [I] in EI–MS spectra of deuterated analogs are also observed.



Scheme 3. Three possible structures of [C].

It is noteworthy that in EI–MS spectra of chemicals bearing large alkyl ($R \geq 4$) on sulfur atom, elimination of this alkyl as a thioaldehyde or thioketone by hydrogen migration and direct elimination of RS• from fragment ion [M$^{+\bullet}$] resulted in characteristic fragment ions with relative high intensity, in some cases as the base peak. These ions are good hints to discriminate between large ($R \geq 4$) and small alkyl ($R \leq 3$) group on **3**. Details of these fragmentations will be discussed with the chemicals in the following section.

With these encouraging results, attention was focused on the spectra of S,S′-dialkyl methylphosphonodithioites **4** and S-alkyl S′-alkyl′ methylphosphonodithioites **5**. Major EI fragment ions of **4** and **5**, as well as their retention indices (RI), are given in Tables 2 and 3. The plausible fragmentation routes for them are illustrated in Fig. 3.

EI–MS spectra of structural isomers of **4**, bearing *n*-alkyl and *sec*-alkyl on sulfur atom, show a great deal of similarity, as shown in Fig. 4. As a result, misidentification may occur. Retention index

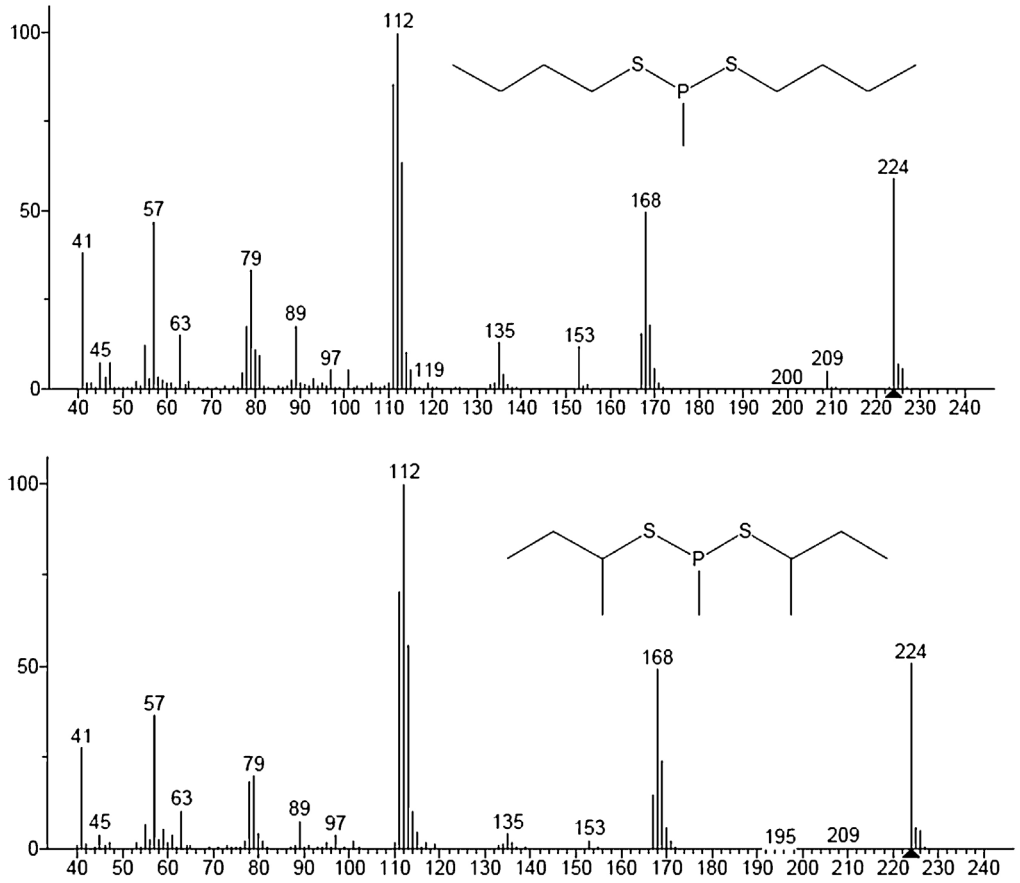


Fig. 4. Representative EI–MS mass spectra of **4**.

is a very good hint to discriminate between them. As expected, RI of compounds containing *sec*-alkyl groups were less than those of compounds containing *n*-alkyl groups (Table 2).

Ion [A] is formed via cleavage of P—CH_3 bond from $M^{+\bullet}$, which is observed in all the spectra of **4** and **5**. Support for this route is provided by the analysis of mass spectra of deuterated analogs (Tables 2 and 3). It should be mentioned that such a fragmentation route is not observed in the spectra of S-alkyl methylphosphonochloridothioites **3**, except chemicals bearing ethyl group on sulfur. Cleavage of P—CH_3 bond from $M^{+\bullet}$ in all EI–MS spectra of **4** and **5** should be dictated by symbiotic effect [18]. Expulsion of a methyl radical from $M^{+\bullet}$ of **4** and **5** increases the symbiotic effect of sulfur atoms in the ion [A]. Elimination of alkyl on sulfur as alkyl radical or as an alkene molecule from $M^{+\bullet}$ through 1,3 C-S hydrogen shift gave fragments [B] and [C] with relative moderate abundance, respectively. Fragment ion [D] can be generated presumably from the ion [A] by expulsion of an alkene or from $M^{+\bullet}$ by step-wise cleavage of CH_3—P bond and elimination of alkyl as an alkene. Deuterium labeling analysis confirmed this fragmentation pathway. EI–MS spectra of **4** and **5** showed a strong ion at *m/z* 111 as [E], resulting with loss of both alkyl groups on sulfur atoms as alkyl radical and alkene molecule. It should be noted that the ion [E] is the base peak in chemicals **4**, bearing $R \leq 4$ on sulfur atoms. When the *S*-alkyl chain length increases, the [E] signal decreases in intensity. Formation of ion [F] ($M^{+\bullet}$-2(R-H)) by the loss of two alkene molecules from $M^{+\bullet}$ and hydrogen rearrangements was also observed in EI–MS spectra of all chemicals **4**. The base peak in EI–MS spectra of chemicals bearing $R \geq 5$ (Table 2, entry 10, 11, and 12) is a diagnostic fragment at *m/z* 103, which will be discussed in the following section.

As mentioned above, in the EI spectra of **3**, bearing large alkyl ($R \geq 4$), elimination of methyl phosphinchloride and chloromethylphosphanyl radical gave rise to two distinctive fragment ions, which can be used for the identification of alkyl moiety on such chemicals. In case of $R = n$-pentyl or *n*-hexyl, these ions appeared in *m/z* 102 and 103, respectively (Fig. 5).

At the first, it can be considered that the proposed mechanism for the formation of ions with *m/z* 102 in MS ion source for S-*n*-pentyl methylphosphonochloridothioite (Fig. 5) and S,S′-di-*n*-pentyl methylphosphonodithioite (Fig. 6) is a concerted 1,3 C-P hydrogen migration process (Scheme 4).

According to the proposed mechanisms, the intensity ratio of these ions should be the same in EI–MS spectra of both chemicals. Intensity of ion at *m/z* 102 is higher than for the ion at *m/z* 103 in EI–MS of S-*n*-pentyl methylphosphonochloridothioite (Fig. 5). Surprisingly the intensity ratio of them in EI–MS spectra of S,S′-di-*n*-pentyl methylphosphonodithioite (Fig. 6) is vice versa. This may suggest step-wise mechanisms for the formation of ion at *m/z* 102, not concerted process.

As shown in Scheme 5, direct cleavage P—SR bond initiated from chlorine atom results in a radical-cation complex. Subsequently, hydrogen radical transfer from cation to the radical gave rise to form fragment ion at *m/z* 102.

In chloromethylphosphanyl radical ($CH_3PCl^{\bullet}$), attachment of chlorine to phosphorous atom increases its affinity for the abstraction of $H^{\bullet}$. This conclusion is based on the hard and soft acids and bases (HSAB) concept [18]. Therefore, the relative intensity of the ion at *m/z* 102 is higher than the ion at *m/z* 103 in EI–MS spectra of *S*-*n*-pentyl methylphosphonochloridothioite, while in *S*-ethyl methylphosphanyl radical ($CH_3PSEt^{\bullet}$), attachment of

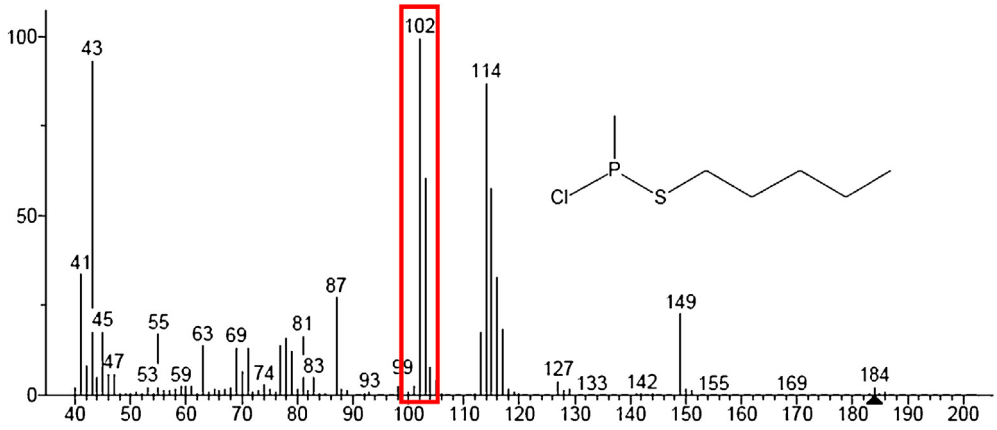


Fig. 5. EI–MS spectrum of S-*n*-pentyl methylphosphonochloridothioite.

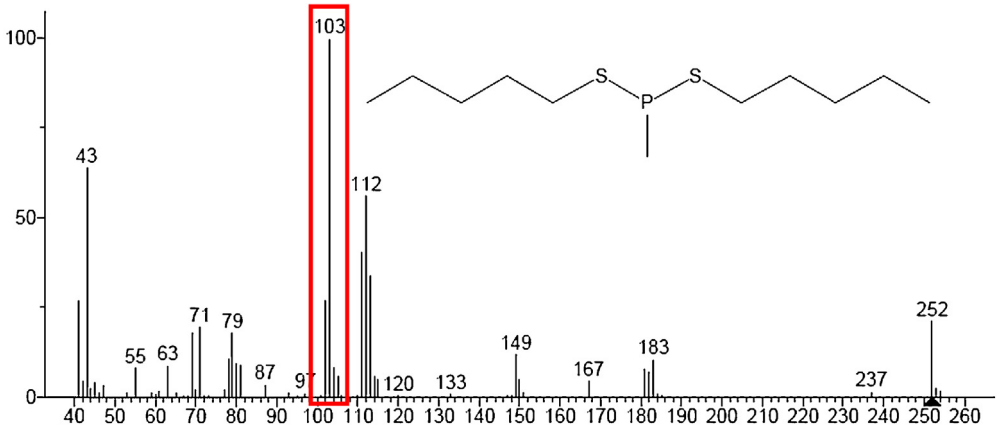
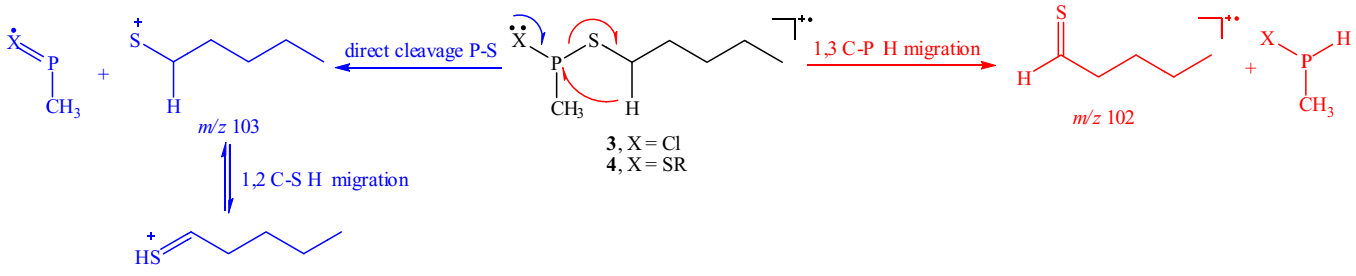


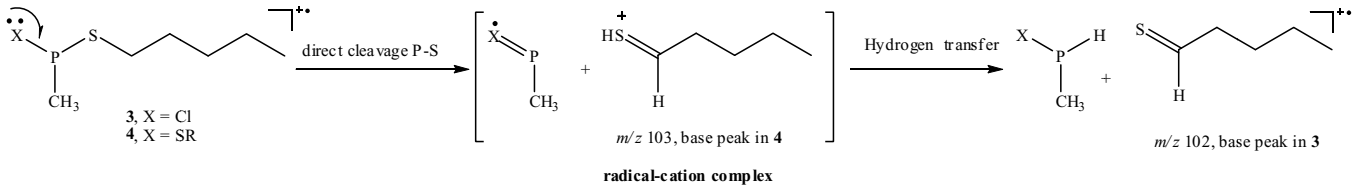
Fig. 6. EI–MS spectrum of S,S′-di-*n*-pentyl methylphosphonodithioate.



Scheme 4. Primary proposed mechanism for the formation of ions at *m/z* 102 and 103 in EI–MS of **3** and **4**.

sulfur to phosphorous atom causes a decrease in its affinity for the abstraction of H•; thus, the relative intensity of the ion at *m/z* 103 is higher than the ion at *m/z* 102 in EI–MS of S,S′-di-*n*-pentyl methylphosphonodithioate. Energy calculations also confirmed this observation. It shows that the formation energies of methyl phosphinchloride and S-ethyl methylphosphonodithioate are 408 and 387 kcal/mol, respectively (Scheme 6).

Some studied chemicals, **4** and **5**, are isomeric pairs. The isomerism among them is exclusively due to the size and structure of alkyl substitutions attached to sulfur atoms. Fig. 7 shows representative EI–MS mass spectra of an isomeric pair of **4** and **5**. Overall spectra of this pair look similar. The notable difference between the mass spectra of them is the ratio of the fragment ion [E] to [F]. The ion [E] is dominant in compounds bearing two small alkyl groups ($R \leq 3$),



Scheme 5. Step-wise mechanism for the formation of ion at *m/z* 102 in EI–MS spectra of **3** and **4**.

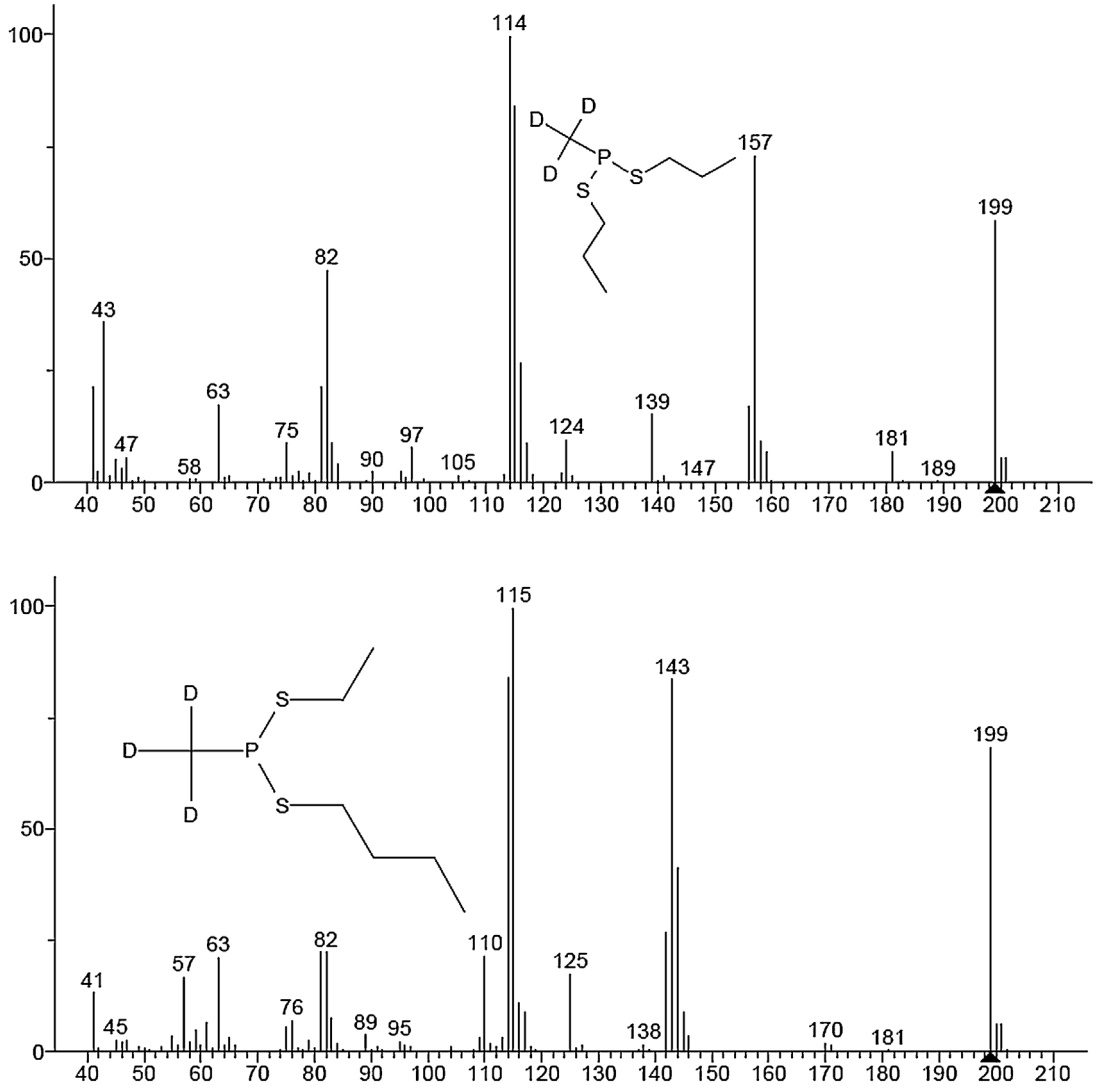
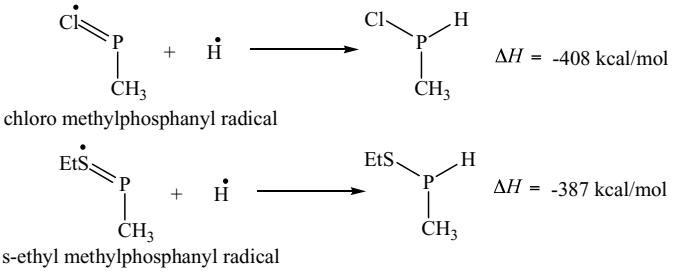


Fig. 7. Representative EI–MS mass spectra of an isomeric pair of **4** and **5**.



Scheme 6. Formation energies of methylphosphinchloride and S-ethyl methylphosphonodithioite.

and in the case of one large alkyl ($R \geq 4$), the ion [F] is dominant. In addition, the $[M\text{-}CH_3\text{-}(R\text{-}H)]^+$ ions as the ion [D] at *m/z* 125 and 139 in EI–MS spectra of **4** and **5**, respectively, are good hints for the identification of small alkyl on sulfur atom.

4. Conclusions

EI–MS spectra of the S-alkyl methylphosphonochloridothioites **3** (11 compounds), S,S′-dialkyl methylphosphonodithioites **4** (12 compounds), and S-alkyl S′-alkyl′ methylphosphonodithioites **5** (9 compounds) were collected and investigated with the aim of enriching OCAD, which may be used in OPCW verification activities, on/off site analysis, and to improve MS interpretation knowledge. Fragmentation processes were mostly dominated by hydrogen rearrangement, alkene, and thiol elimination. Energy calculations of fragment ions revealed their relative probability of formation during ionization.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijms.2015.12.004.

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