International Journal of Mass Spectrometry xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Mass Spectrometry

journal homepage: www.elsevier.com/locate/ijms

Fragmentation mechanisms in mass spectrometry of Chemical Weapons Convention related spiro alkylphosphonates and alkyldioxaphosphinane oxides

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ARTICLE INFO

Article history:
Received 23 February 2014
Received in revised form 25 May 2014
Accepted 2 June 2014
Available online xxx

Keywords:
Mass spectrometry
Spiro alkylphoshonates
McLafferty rearrangements
Cycloaddition
Microsynthesis
Chemical Weapons Convention

ABSTRACT

The availability of mass spectra and interpretation skills are essential for unambiguous identification of the Chemical Weapons Convention (CWC)-related compounds. This paper examines electron ionization (EI) and electrospray ionization (ESI) mass spectral fragmentation routes of spiro alkylphosphonates I and 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II as compounds which are covered under CWC schedule 2.B.4. Mass spectrometric studies revealed some fragmentation pathways, such as elimination of alkyl(oxo)phosphane oxide (RPO_2), chlorine, chloromethylene, alkene, HCl, and H_2O, α-cleavage and McLafferty-type and hydrogen rearrangements. The proposed fragmentation processes include some new fragmentation patterns, such as isomerization of cations to stabilized carbocations and oxocarbocations, and elimination of formaldehyde and alkoxy through concerted retro [2+2] cycloaddition reaction and 1,2 P—O alkyl shift. Structures of fragments were confirmed using EI-MS and MS/MS analysis of the deuterated analogs. The results will make a contribution to the Organization for the Prohibition of Chemical Weapons (OPCW) Central Analytical Database (OCAD) which may be used for the detection and identification of CWC-related compounds during on-site inspection and OPCW proficiency tests.

1. Introduction

All activities related to the production, development, stockpiling and use of chemical weapons are forbidden by the Chemical Weapons Convention (CWC), which came into force on 29 April 1997. Chemical warfare agents (CWAs) were used during World War I, the Iran–Iraq war and subsequently in some terrorist attacks in Japan. Recently sarin, as nerve agent, was used during the Syria conflict. These tragic events show that monitoring and analysis of CWAs, their precursors and degradation/reaction products is an important part of verification activities in support of CWC. The state parties to CWC have established the Organization for the Prohibition of Chemical Weapons (OPCW) to achieve the objective and purpose of CWC. It is interesting to note that OPCW received the Nobel peace prize for its extensive efforts to eliminate chemical weapons in 2013. Mass spectrometry coupled with gas chromatography (GC/MS) provides a key analytical technique for the unambiguous identification of scheduled chemicals during proficiency tests (PTs) and off- and/or on-site analyses [1]. For unequivocal identification of CWC-related compounds in real samples or PTs, the availability of mass spectra and interpretation skills are essential requirements. Due to the extreme toxicity of CWC-related compounds, there is limited number of research on such compounds. In recent years, some research results have been reported which contains microsynthesis and interpretation of mass spectra of CWC-related compounds [2–7], but to our knowledge there is no mass spectral fragmentation study for spiro alkylphosphonate compounds I and 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II. These compounds are covered under CWC schedule 2.B.4 as well as all compounds with phosphorus bonded to a methyl, ethyl, isopropyl, or propyl moieties. The studied compounds are the reaction products of alkylphosphonic dichlorides with pentaerythritol. Mass spectra of such compounds might be of interest to OPCW. It should be mentioned that pentaerythritol is a versatile building block for the

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http://dx.doi.org/10.1016/j.ijms.2014.06.003
1387-3806/

preparation of many polyfunctionalized compounds such as the explosive pentaerythritol tetranitrate and pentaerythritol tetraacrylate [8]. As continuation of our mass spectral fragmentations studies on CWC-related compounds [9–12], it was concluded that detailed studies on a class of spiro alkylphosphonate I and 5,5-bis (chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II were necessary. This paper describes a study on a general microsynthesis procedure for a few title compounds (Scheme 1). Subsequently, electron ionization (EI) and electrospray ionization (ESI) mass spectra of these compounds, with possible fragmentation routes, were investigated via analysis of fragment ions of deuterated analogs and MS–MS experiments.

2. Experimental

2.1. Reagents and chemicals

All chemicals required for the microsynthesis of spiro alkylphosphonates were purchased from Sigma–Aldrich (St. Louis, MO, USA), Fluka (Neu-Ulm, Germany), and Merck (Darmstadt, Germany), and were used as received. Alkylphosphonic dichlorides were synthesized by use of a method described elsewhere [13,14].

2.2. GC/MS and GC/MS–MS analysis

GC/MS analyses were performed using an Agilent 6890 N gas chromatograph equipped with a 5973 quadrupole mass selective detector, MSD, (Agilent Technologies, Inc., Santa Clara, CA, USA), a HP-5MS (5% phenyl, 95% dimethylpolysiloxane, Agilent's J&W Scientific) capillary column of (30 m, 320 μm i.d. and 0.25 μm film thickness), and helium as carrier gas at constant flow of 1.8 mL min^{-1}. The oven temperature was set at 40 °C for 3 min and then 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. GC/MS–MS analyses were performed using an Agilent 7890 N gas chromatograph interfaced to a 7000 A triple quadruple mass spectrometer (Agilent Technologies, Inc., Wilmington, DE, USA). GC conditions were as noted above. The ionization energy was set at 70 eV in both MS spectrometers. MS–MS analyses were carried out using nitrogen as collision gas, at collision energy of 10 eV and source temperature of 230 °C. CI-MS experiments also were done on 5973 MSD using isobutane as reagent gas. The scan range was set at m/z > 70–500. Other instrumental conditions were as EI experiments. Automated mass spectral deconvolution and identification system (AMDIS) software (NIST, Gaithersburg, MD, USA) were used to calculate retention indices of the synthesized compounds. An alkane mixture [octane (C_8) to tetracosane (C_{24})] was used for retention indices calculations.

2.3. ESI-MS and ESI-MS–MS analysis

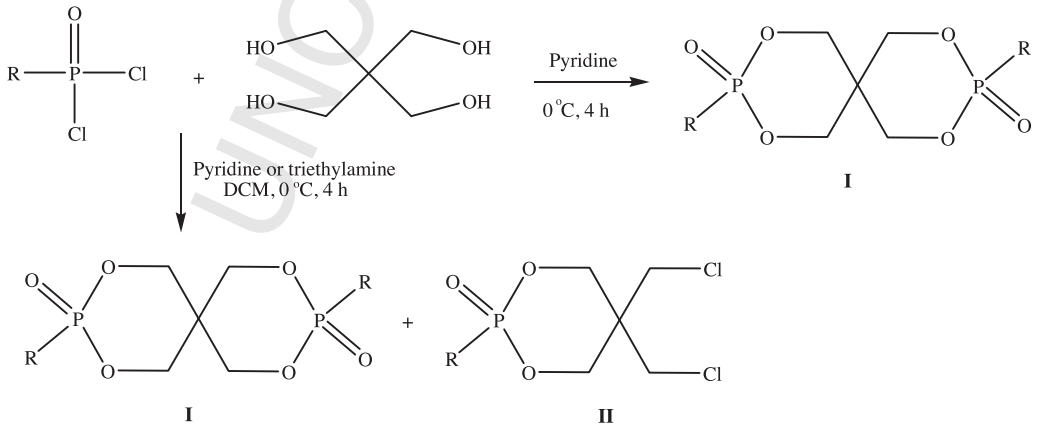
LC/MS analysis was performed on an Agilent 1200 LC system (Agilent Technologies, Inc., Waldbronn, Germany) equipped with Agilent 6410 triple quadrupole tandem mass spectrometer and managed by a Mass Hunter workstation (Agilent Technologies Inc., CA, Santa Clara, USA). The column used for separation was an Agilent rapid resolution HT zorbax SB-C18 (3 × 150 mm, 3.5 μm) (Agilent Technologies Inc., Santa Clara, CA, USA). The column temperature was set at 25 °C. A gradient mobile phase of (A) water plus 20 mM formic acid and (B) acetonitrile plus 20 mM formic acid was used. The initial condition was set at 5% of B. The following solvent gradient was applied: from 95% A and 5% B to 5% A and 95% B within 20 min, hold for 10 min. Flow rate was set at 0.25 mL $min^{-1}$and 4 μL of samples were injected using ALS autosampler (Agilent Technologies, Inc., Waldbronn, Germany). The electrospray ionization (ESI) and fragmentor voltages were set at 4000 and 60 V, respectively. The ultra-high pure nitrogen was used as the nebulizer, drying and collision gas. The heated capillary temperature was maintained at 300 °C. The drying gas flow rate and nebulizer gas pressure were 10 L min^{-1} and 40 psi, respectively. Mass spectra were obtained by scanning from m/z > 80 to 1000 with 0.5 s scan time.

2.4. NMR analysis

A Bruker (Avance DRX-250 MHz, Germany) NMR instrument was employed for ^{1}H, ^{31}P and ^{13}C NMR experiments. All spectra were recorded at ambient temperature using $CDCl_3$ as a solvent.

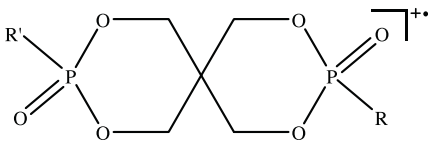
2. 5. General procedure for microsynthesis of spiro alkylphosphonates I

Pentaerythritol (0.30 mmol) and triethylamine or pyridine (0.65 mmol) in 500 μL CH_2Cl_2 or pyridine were added dropwise, with stirring, to a solution of 0.60 mmol alkylphosphonic dichloride, in 500 μL CH_2Cl_2 at 0–5 °C. The reaction mixture was stirred for 4 h. The resulting precipitate was removed by filtration and the solution analyzed by GC/MS or GC/MS–MS as required. For separation of spiro methylphosphonate 1a (entry 1a, Table 1) from mixture, after completion of the reaction, the mixture was poured into ice cold H_2O and stirred for 15 min, then the mixture was saturated with brine. Subsequently, extraction



Scheme 1. Microsynthesis route of spiro alkylphosphonates I and 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II.

Table 1
GC/EI–MS data of spiro alkylphosphonates I.



Entry	R	R′	$M^{+\bullet}$	Fragment ions (% relative abundances)														
				[A]	[B]	[C]	[D]	[E]	[F]	[G]	[H]	[I]	[J]	[K]	[L]	[M]	[N]	[O]	[P]
1a	Me	Me	256	241 (7)	225 (1)	242 (–)	178 (12)	187 (10)	175 (18)	157 (78)	148 (49)	97 (37)	79 (44)	119 (8)	160 (100)	131 (10)	181 (2)	211 (12)	159 (11)
1b	Me (d_3)	Me (d_3)	262	244 (2)	228 (–)	246 (–)	181 (17)	193 (5)	181 (17)	163 (100)	151 (31)	100 (24)	82 (53)	122 (3)	163 (100)	134 (7)	184 (–)	214 (6)	162 (7)
1c	Et	Et	284	255 (8)	239 (1)	256 (5)	192 (17)	215 (7)	203 (26)	185 (61)	162 (34)	111 (53)	93 (32)	133 (12)	174 (100)	145 (13)	195 (1)	225 (32)	173 (16)
1d	Et (d_5)	Et (d_5)	294	260 (3)	244 (1)	262 (2)	197 (15)	225 (7)	213 (24)	195 (54)	167 (29)	116 (39)	98 (27)	138 (3)	179 (100)	150 (10)	200 (1)	230 (27)	178 (10)
1e	*n*-Pr	*n*-Pr	312	269 (30)	253 (4)	270 (77)	206 (36)	243 (5)	231 (35)	213 (46)	176 (18)	125 (81)	107 (30)	147 (17)	188 (100)	159 (13)	209 (1)	244 (1)	187 (18)
1f	Me	Et	270	241, 255 (11), (4)	225, 239 (20), (7)	242, 256 (22), (–)	178, 181 (18), (–)	201 (–)	189 (–)	171 (4)	148, 162 (24), (39)	97, 111 (40), (37)	79, 93 (24), (24)	119, 133 (4), (14)	160, 174 (100), (57)	131, 145 (9), (8)	181, 195 (–), (4)	211, 225 (–), (20)	159, 173 (12), (13)
1g	Me	*n*-Pr	284	241, 269 (13), (7)	225, 253 (21), (–)	242, 270 (22), (–)	178, 206 (17), (4)	215 (8)	203 (38)	185 (79)	148, 176 (24), (12)	97, 125 (40), (37)	79, 107 (24), (9)	119, 147 (4), (19)	160, 188 (100), (57)	131, 159 (9), (12)	181, 209 (–), (–)	211, 244 (–), (–)	159, 187 (12), (5)
1h	Et	*n*-Pr	298	255, 269 (13), (7)	239, 253 (17), (2)	256, 270 (36), (10)	192, 206 (22), (9)	229 (6)	217 (31)	199 (54)	162, 176 (19), (32)	111, 125 (46), (27)	93, 107 (30), (14)	133, 147 (11), (10)	174, 188 (100), (28)	145, 149 (13), (5)	195, 209 (–), (–)	225, 244 (8), (–)	173, 187 (11), (10)

with acetonitrile (5 × 1 mL) then dry the organic phase with Na_2SO_4 and concentration under vacuum, afforded the desired spiro methylphosphonate 1a with 89% yield with up 97% purity as indicated by GC/MS and NMR analysis.

It should be mentioned that in this reaction 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II are also formed as indicated by the GC/MS results. These compounds are also covered under CWC schedule 2.B.4. Therefore, EI-MS compounds with possible fragmentation routes were also investigated. It is interesting to note that reaction of pentaerythritol with alkylphosphonic dichlorides in pyridine as base and solvent yielded only spiro alkylphosphonates I with high yield (upto 80–90%). In the case of methylphosphonic dichlorides (entry 1a, Table 1), spiro methylphosphonate 1a was separated from reaction mixture and was fully characterized by ^1H, ^{13}C and ^{31}P NMR and chemical ionization (CI)-MS analysis.

The ^1H, ^{13}C and ^{31}P NMR spectra of 1a clearly indicated the formation of spiro methylphosphonate (Fig. 1). The ^1H NMR spectrum of 1a consisted of a doublet (J_{HP} = 17.5 Hz) for the methyl protons at δ = 1.56–1.63 ppm, and a multiplet peak (δ = 4.01–4.54 ppm) for the methylene protons, which are diastereotopic and would exhibit different peak in the ^1H spectrum. ^1H-decoupled ^{13}C NMR spectrum of 1a showed 3 distinct resonances in agreement with the proposed structure, at δ = 8.63–10.86 ppm a doublet resonance ($^1J_{CP}$ = 139.40 Hz) for carbon of methyl moieties, a triplet resonance ($^3J_{CP}$ = 4.83 Hz) for spiro carbon (quaternary carbon) between δ = 37.33–37.49 ppm and a doublet resonance ($^2J_{CP}$ = 6.17 Hz) at δ = 66.49–66.59 ppm for carbon of methylene. The ^{31}P NMR of 1a showed a distinct resonance at δ = 27.93. CI-MS mass spectrum of 1a clearly showed the presence of ion $[M+H]^+$, m/z > 257.

3. Results and discussion

3.1. Mass spectrometric analyses

3.1.1. 1. GC/MS and GC/MS–MS analyses of spiro alkylphoshonates I

Major EI fragment ions of spiro alkylphosphonates I are given in Scheme 2 and Table 1. The molecular ions ($M^{+\bullet}$) of spiro alkylphosphonates I are not observed in their mass spectra (Fig. 2). CI-MS of spiro alkylphosphonates I was performed to the proposed structures (Supplementary material).

Ion [A], the result of direct elimination of an alkyl (R or R′) radical from $M^{+\bullet}$, was observed for all these compounds (Table 1), with relative abundance <30%. Spectra of deuterated analogs (1b, and 1d) and spiro alkylphosphonates bearing different alkyl (R and R′, 1f–1h) clearly show the ions corresponding to this fragment. Interesting fragment ion [B] can arise through two possible fragmentation pathways. (1) Elimination of oxygen atom from [A] or (2) 1,2 P—O alkyl (R or R′) shift then elimination of R(R′)O$^\bullet$ from $M^{+\bullet}$ (Scheme 3) [15,16].

Expulsion of the alkyl group (R or R′) on phosphorus atom as an alkene gave ion [C] with relative abundance in the range 2–77%. Formation of [C] in mass spectral of compounds bearing R = *n*-Pr take place through the McLafferty-type rearrangement. McLafferty rearrangement is a skeletal rearrangement, meaning formation of an allylic group is not possible for R = CH_3 analogs [17]. Consequently, spectra for these compounds are distinct from the other spiro alkylphosphonates. As ethyl analogs can not form allylic radicals, formation of ion [C] from ethyl analogs is not possible via the McLafferty-type rearrangement. Instead, neutral loss of ethylene is possible from ethyl analogs via a hydrogen migration (1,4C—O H shift) to the oxygen-bearing cation radical site.

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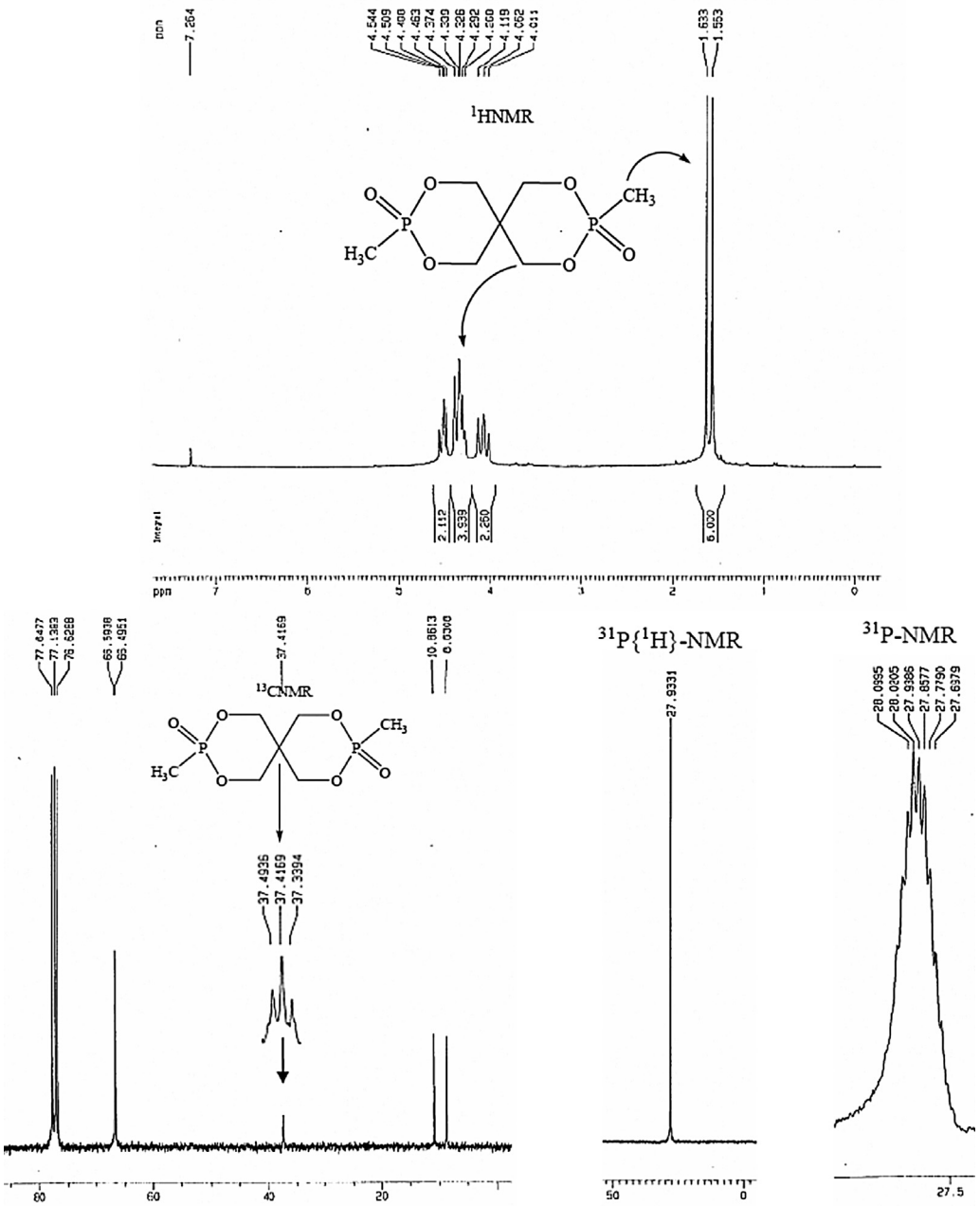

Fig. 1. ^{1}H, ^{13}C and ^{31}P NMR spectra of spiro methylphosphonate 1a.

Fragment ion [D] is attributed to oxetane spiro ion by the elimination of a neutral alkyl(oxo)phosphane oxide (RPO_2) from $M^{+\bullet}$ (Scheme 4). The peak of this ion is visible in the deuterated spiro alkylphosphonates I EI-MS spectra.

Ions [E] and [F] were generated from $M^{+\bullet}$ by some hydrogen rearrangements. The loss of H_2O from [F] gave rise to ion [G] with relative high abundances >46%. The product ion scan of [G] for spiro methylphosphonate 1a revealed further fragmentation to [J] with $m/z > 79$. The product ion spectrum of [G] at $m/z > 163$ in spiro methyl(d3) phosphonate 1b mass spectrum, supports the structural assignment for [G] and [J] (Supplementary material, Fig. 28S and 29 S). Proposed fragmentation for the formation high intensity ion [H] involves two steps: elimination of a neutral alkyl(oxo) phosphane oxide (RPO_2) from $M^{+\bullet}$ which gave ion [D] then expulsion of formaldehyde from [D] via a concerted retro [2 + 2] cycloaddition reaction (Scheme 5) [18]. Fragmentation of ion [H] for 1a ($m/z > 148$) leads to product ions $m/z > 42$, 70, 97, 119 and 133 (Scheme 5). The proposed structural assignments in Scheme 5 are supported by deuterium-labeling studies, which show the formation of corresponding ions to these fragments. The product ion scan of $m/z > 151$ in mass spectrum of 1b revealed further disintegration to product ions $m/z > 42$, 70, 100, 121 and 133 (Fig. 3). All EI-MS spectra of I show fragment ion at $m/z > 133$.

Fragment ion [K] was formed by expulsion of formyl (CHO) radical from [H]. As shown in Scheme 6, elimination formyl radical from [H] can be explained by hydrogen migration from carbon to oxygen of P═O group.

Fragment ion at $m/z > 133$ was formed by cleavage of the P—R bond in ion [H] which is observable in all mass spectra of spiro alkylphosphonates I. It should be mentioned that the fragment

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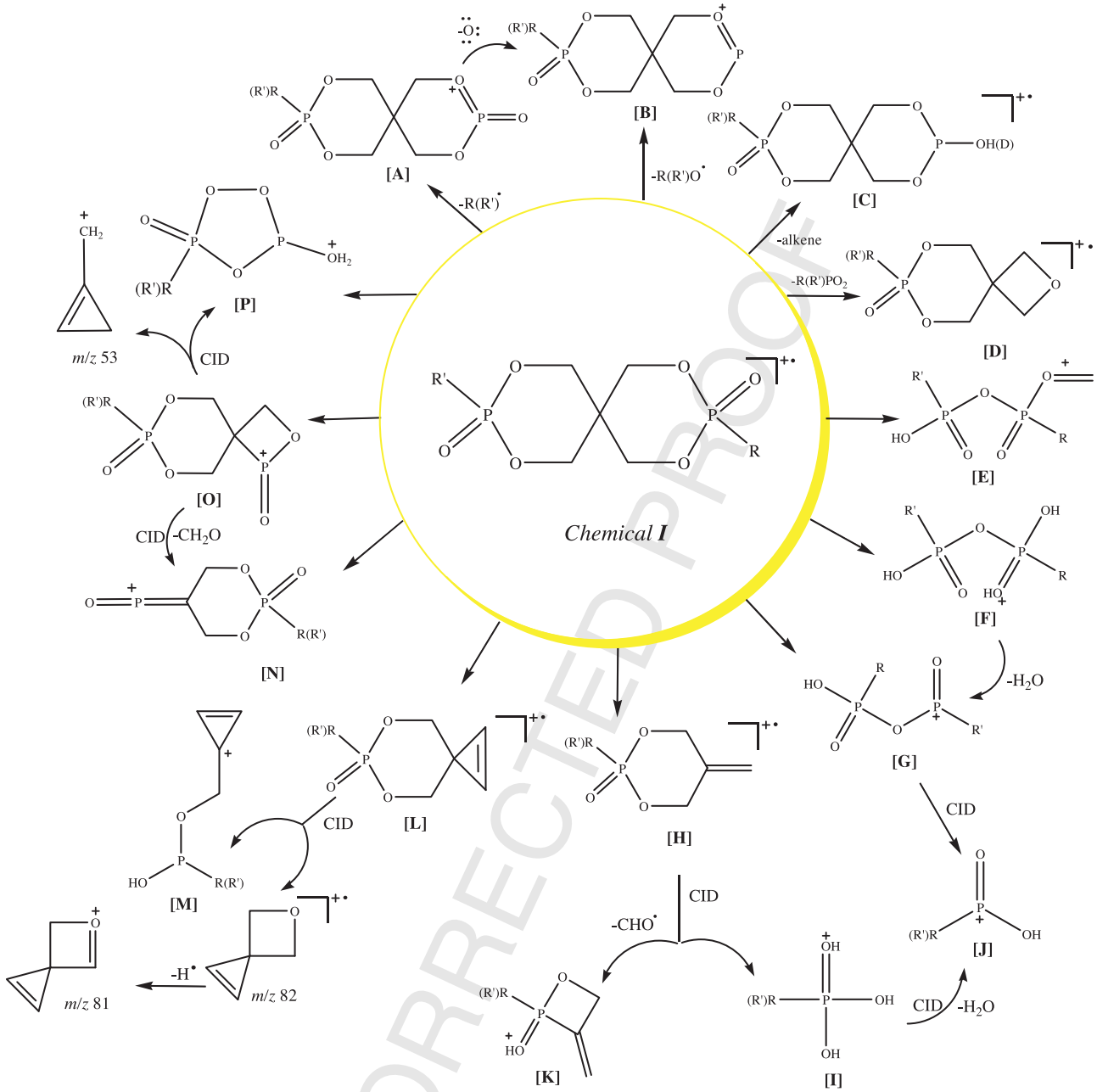


Scheme 2. Proposed EI-MS fragmentation routes for spiro alkylphosphonates I.

ions at $m/z > 42$ and 70 are also present in mass spectrum of pentaerythritol (Supplementary material, Fig. 27S). Elimination of an alkylphosphonic acid molecule from the molecular ion of spiro alkylphosphonates gave rise to ion [L] as base peak in all EI mass spectra of I. Further fragmentation of [L] in mass spectrum of 1a and 1b at $m/z > 160$ and 163, respectively showed product ions at $m/z > 81$, 82 and ion [M] (Supplementary material, Fig. 30S). Stability of cation cyclopropyl due to aromaticity is driving force for formation of ion [M]. Mass spectra of deuterated analogs (1b and 1d) clearly show the corresponding ions to [L] and [M]. Loss of formaldehyde from fragment ion [A] can result in an interesting fragment [O] [19]. The product ion scan of ion [O] at $m/z > 211$ in mass spectrum of 1a revealed further fragmentation to product ions at $m/z > 181$, 159, 133, 79 and 53 (Fig. 4). Elimination of formaldehyde from [O] yielded fragment ion [N] at $m/z > 181$ for 1a and $m/z > 184$ for 1b. Ion [P] was also observed in product ion scan of ion $m/z > 214$ in mass spectrum of 1b. Fragment ion at $m/z > 53$ is stable cation. The stabilization of carbocation at $m/z > 53$ by cyclopropyl substituent, is a result of the interaction of electrons in the cyclopropyl C—C bonds with the positive carbon [18].

3.1.2. LC/MS and LC/MS–MS analyses of spiro alkylphoshonates I

The sipro methylphosphonate 1a formed relative moderate intensity $[M+H]^+$ under positive ion ESI conditions. The most abundant ions in ESI-MS are observed at $m/z > 279$ as ion $[M+Na]^+$ and at $m/z > 535$ as $[2M+Na]^+$. Tandem mass spectrum of the $[M+H]^+$ ion ($m/z > 257$) is shown in Fig. 5. The most abundant product ion is observed at $m/z > 83$. The general fragmentation pathway of the $[M+H]^+$ of 1a is summarized in Scheme 7. ESI fragmentation pattern is similar to EI fragmentation pattern. Elimination of a neutral methyl(oxo)phosphane oxide (CH_3PO_2) and a methylphosphonic acid molecule from $[M+H]^+$ result in an ion at $m/z > 179$ and 161 corresponding to ions [D] and [L] in EI-MS of 1a, respectively. Formation of the ion at $m/z > 149$ can be

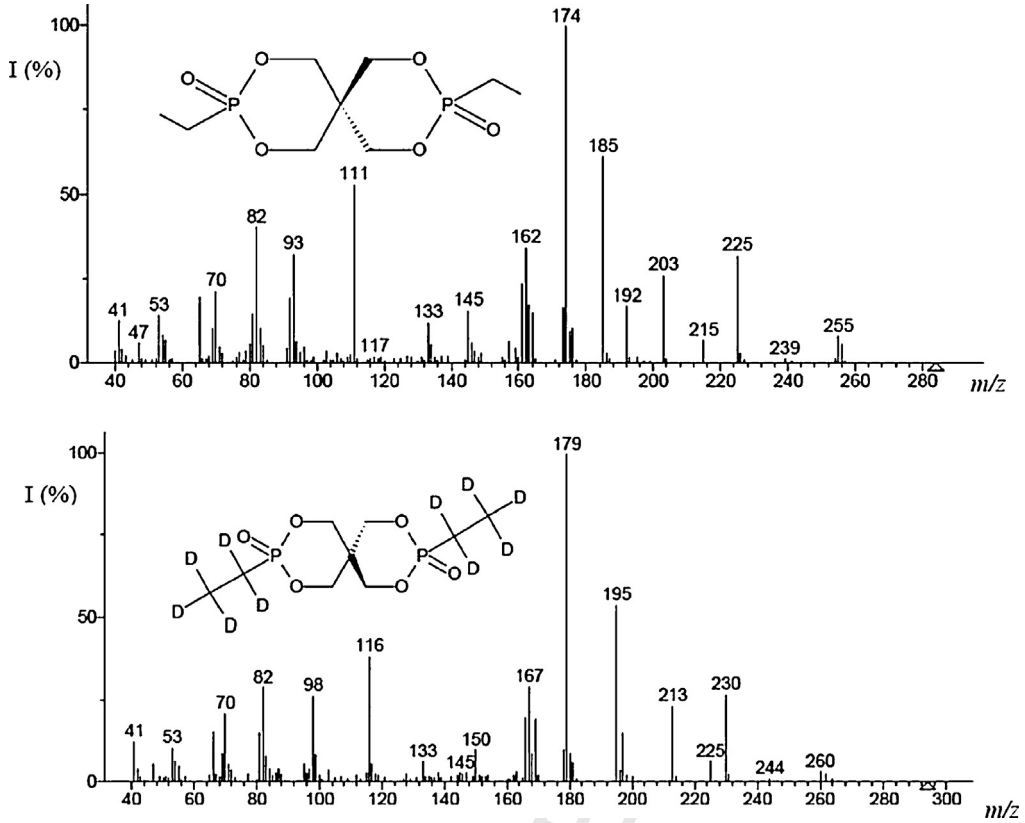
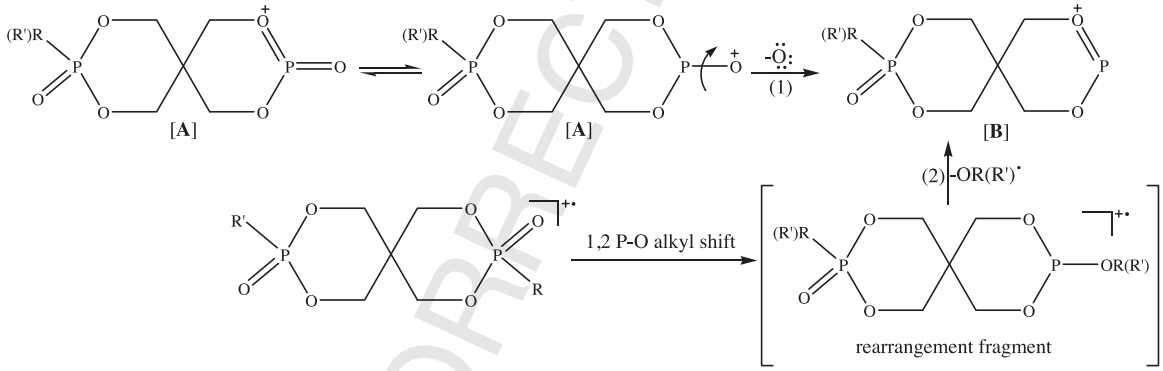
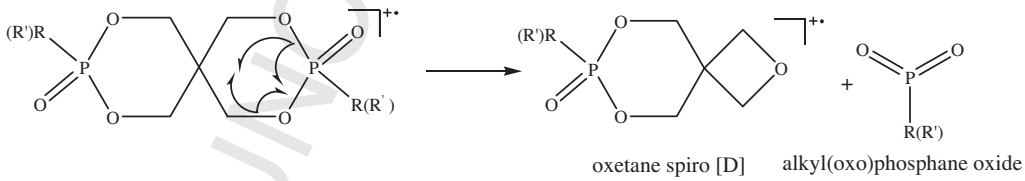


Fig. 2. Representative EI mass spectra of spiro ethylphosphonate 1c and deuterated analog 1d.



Scheme 3. Proposed mechanisms for formation of ion [B].

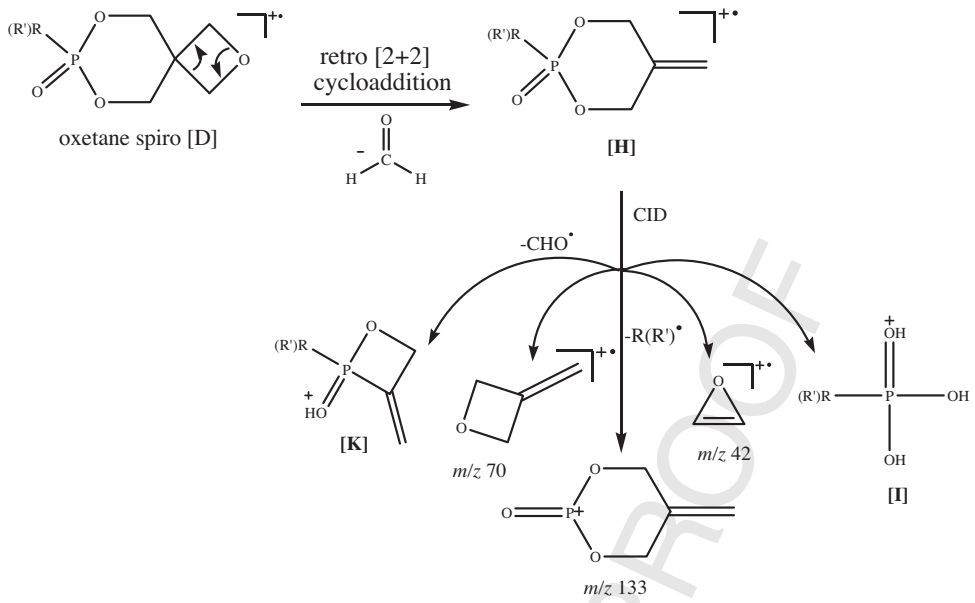


Scheme 4. Fragmentation mechanism for formation of ion [D].

explained by direct elimination of formaldehyde from ion at *m/z* > 179 by a concerted process. This proposed mechanism is similar to that envisaged to explain the formation of ion [H] in EI fragmentation of spiro alkylphosphonates. The proposed fragmentation pathways of the $[M+H]^+$ of 1a in Scheme 7 are supported by analysis of ESI mass spectrum of the deuterated analog 1b (Fig. 5)

3.1.3. GC/MS and GC/MS–MS analyses of 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II

Prominent EI fragment ions of 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II are listed in Table 2 and their corresponding structures are shown in Scheme 8. Expected



Scheme 5. Proposed fragmentation pathways of ion [H] for the spiro alkylphosphonates.

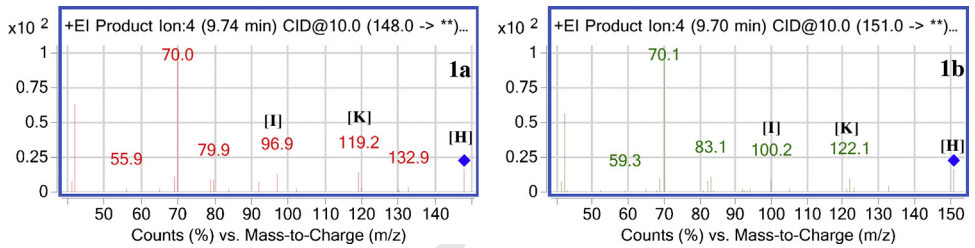
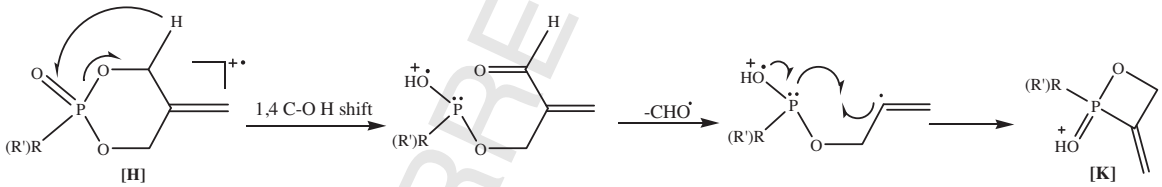


Fig. 3. Product ion spectra of *m*/*z* 148 and 151 from 1a and deuterated analog 1b, respectively.



Scheme 6. Proposed mechanism for formation of ion [K] from [H].

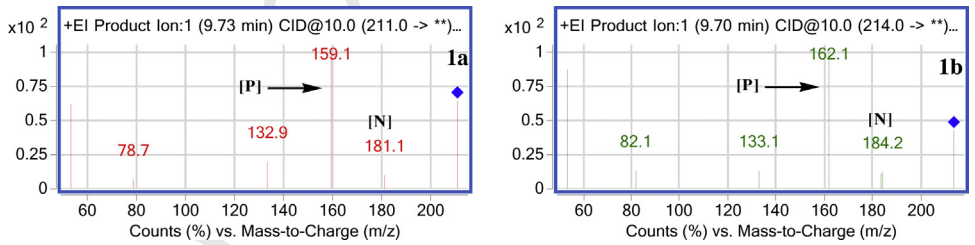


Fig. 4. Product ion spectra of *m*/*z* 211 and 214 from 1a and deuterated analog 1b, respectively.

isotopic ratios of chlorine containing fragments were observed, as is evident from the relative abundances listed in Table 2. Loss of a chlorine radical from $M^{+\bullet}$ gave rise to ion [A] as base peak in all compounds II, except the compound bearing *n*-Pr moiety (entry 2d, Table 2)

Product ion scan of chloronium ion [A] in spectra of ethyl(d_5) derivatives (entry 2c, Table 2) at *m*/*z* > 216 revealed high relative abundance product ions [B, C, D, J, K] and product ions at *m*/*z* > 83 and 101. Elimination of formaldehyde as a neutral molecule from ion [A] yielded ion [C] as base peak in molecular ion spectrum of 2c (Fig. 6). Formation of interesting ion [D] from $M^{+\bullet}$ and/or ion [A] can be explained in the proposed mechanism shown in Scheme 9. This assignment is base on the observation of ion [D] in all mass spectra of II along with 2c, the presence of expected isotopic ratio of chlorine for [D] in all mass spectra and CID spectrum of ion [D] from 2c. The CID spectrum of ion [D] at *m*/*z* > 134 for 2c includes the

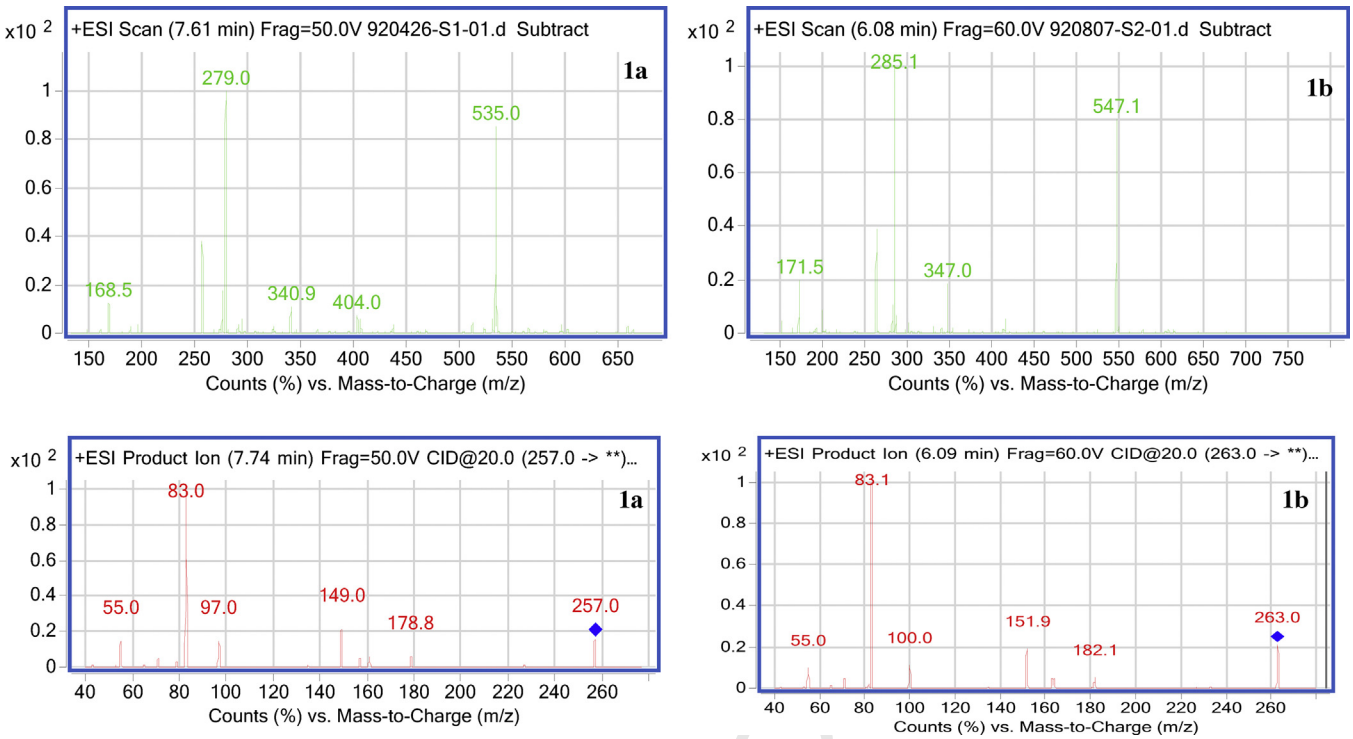
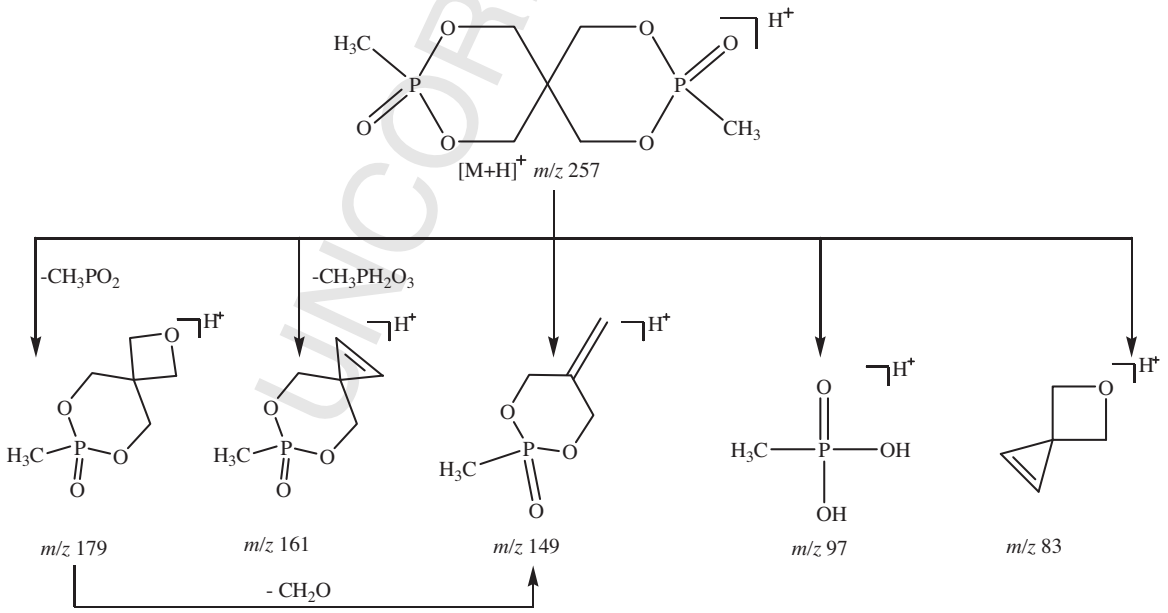


Fig. 5. ESI-MS and ESI-MS/MS spectra of protonated spiro methylphosphonate 1a and deuterated analog 1b.

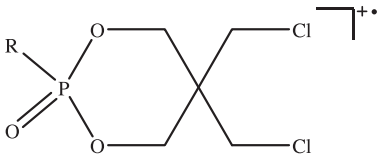
product ions at $m/z > 116$ and 98 corresponding to exclusion of H_2O and HCl from ion [D], respectively (Fig. 6). The first step in the proposed mechanism for formation of [D] is involved, a rearrangement process which afford the intermediate 1 as a stabilized cyclic oxocarbocation. Stability of 1 is the major driving force for this rearrangement. Then a cation and neutral alkylphosphonochloridic acid (ion-neutral complex) [20] are produced by McLafferty rearrangement. Migration of a hydrogen atom to the neutral alkylphosphonochloridic acid resulted in fragment ion [D] (Fig. 7).

Ion [E] (Scheme 8) as a chloronium ion was formed by the loss of chloromethylene radical from $M^{+\bullet}$. It appears relatively in high abundance in the range of 46–77%. This peak is the base peak or the second highest peak in EI-MS of compounds bearing Et or *n*-Pr substitutes (Table 2). Elimination of HCl from [E] yielded ion [F] with moderate relative abundance. Spectrum of deuterated analog also (entry 2c, Table 2) shows the ions corresponding to [E] and [F]. The proposed assignment is further supported by CID spectra of [E] from 2a and 2c at $m/z > 183$ and 202 (Supplementary material, Fig. 31S).

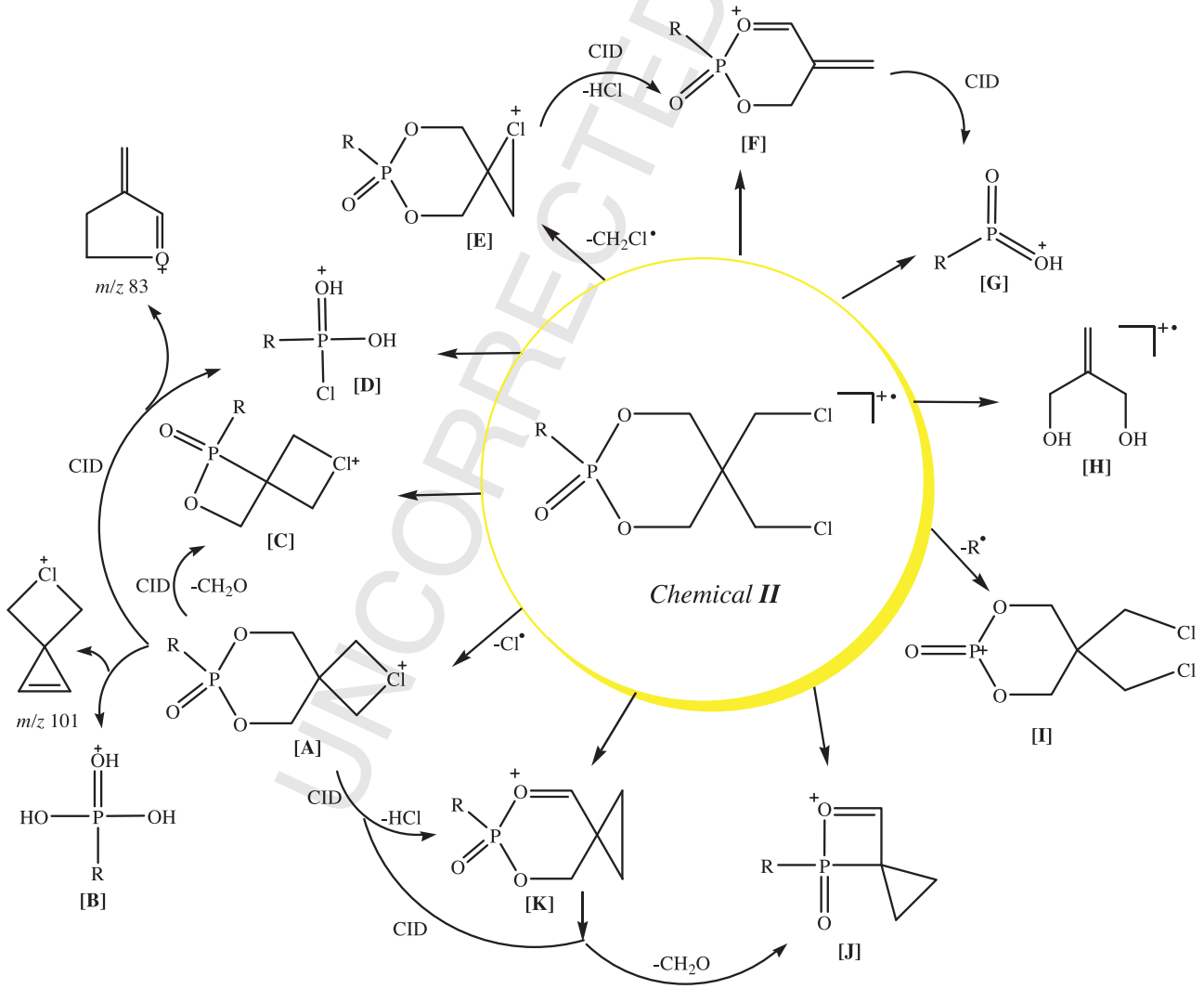


Scheme 7. General fragmentation pattern of $[M+H]^+$ of spiro methylphosphonate 1a.

Table 2
GC/MS data of 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II.



Entry	R	Fragment ions (% relative abundances)										
		[A]	[B]	[C]	[D]	[E]	[F]	[G]	[H]	[I]	[J]	[K]
2a	Me	197, 199 (100), (32)	97 (18)	167, 169 (25), (8)	115, 117 (13), (5)	183, 185 (46), (16)	147 (34)	79 (51)	88 (26)	217 –	131 (9)	161 (11)
2b	Et	211, 213 (100), (33)	111 (18)	181, 183 (38), (15)	129, 131 (17), (6)	197, 199 (94), (31)	161 (60)	93 (50)	88 (23)	217 (1)	145 (8)	175 (13)
2c	Et(d_5)	216, 218 (100), (33)	116 (6)	186, 188 (41), (13)	134, 136 (21), (10)	202, 204 (94), (30)	166 (60)	98 (53)	88 (22)	217 (9)	150 (9)	180 (12)
2d	*n*-Pr	225, 227 (74), (24)	125 –	195, 197 (23), (20)	143, 145 (12), (4)	211, 213 (100), (33)	175 (27)	107 –	88 (18)	217 (2)	159 (3)	189 (7)



Scheme 8. Proposed EI-MS fragmentation routes for 5,5-bis(chloromethyl)-2-alkyl-1,3,2-dioxaphosphinane 2-oxides II.

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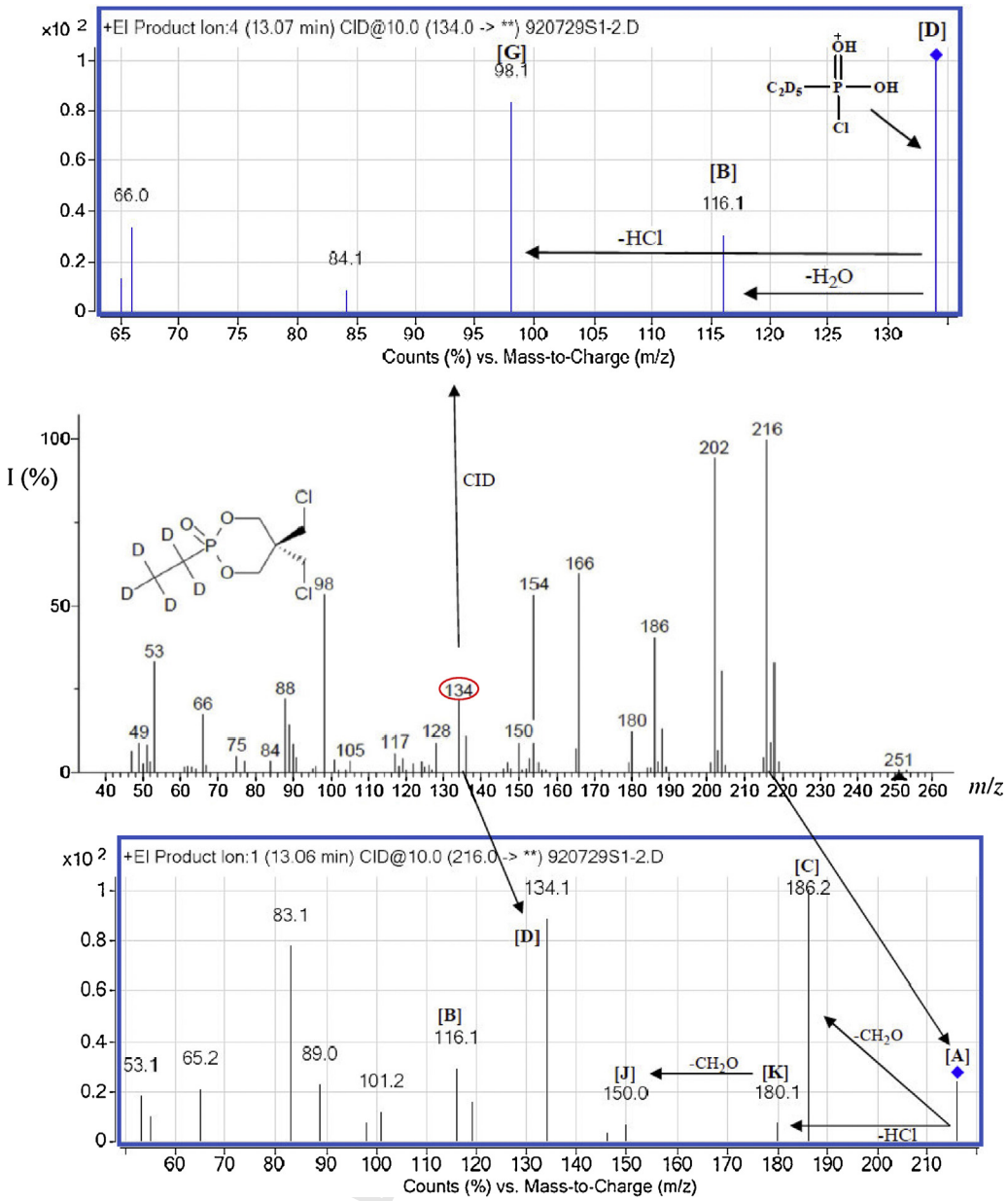

Fig. 6. EI-MS and product ion spectra of the ions at *m/z* 216 and 134 from 2c.

The ion [F] fragmented to ion [G], as shown by CID spectra of [F] from 2a and 2c at *m/z* > 147 and 166, respectively (Supplementary material, Fig. 32S and 33S). Cation-radical ion [H] as 2-methyl-idenepropane-1,3-diol were present in all compounds II. It should be noted that this fragment is not observable in EI-MS of spiro alkylphosphonates I. On the other hand, EI-MS of pentaerythritol also show the ion [H] (Supplementary material, Fig. 27S). Direct elimination of alkyl ($R^{\bullet}$) radical by α-cleavage from $M^{+\bullet}$ gave rise to ion [I] in relative low abundance <10. When the alkyl group is methyl, $M^{+\bullet}$ was not disintegrated to ion [I] (entry 2a, Table 2). Formation of ion [K] from $M^{+\bullet}$ can be explained by a step-wise mechanism involving loss of a chlorine radical then elimination of HCl. The proposed step-wise fragmentation is further supported from CID spectra of ion [A] from 2a and 2c (Fig. 6). It is interesting to note that fragment ion [K] is a very stable fragment. It can be isomerized to stabilized carbocation ion [K′] (Scheme 10). There is a favorable orbital overlap between the filled cyclopropane bent bonds and the empty p-orbital in [K′] [18].

4. Conclusion

This investigation reported the microsynthesis and NMR, EI-MS and ESI-MS analyses of some spiro alkylphosphonates I and alkyldioxaphosphinane oxides II. Important fragmentations and disintegrations that rationalized the formation of most of the characteristic fragment ions were McLafferty-type rearrangements, alkyl and hydrogen shifts, HCl, chlorine and formaldehyde eliminations and α-cleavage. Fragmentation ion product structures were proved using MS/MS experiments and investigation of MS spectra of deuterated analogs.

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.2014.06.003.

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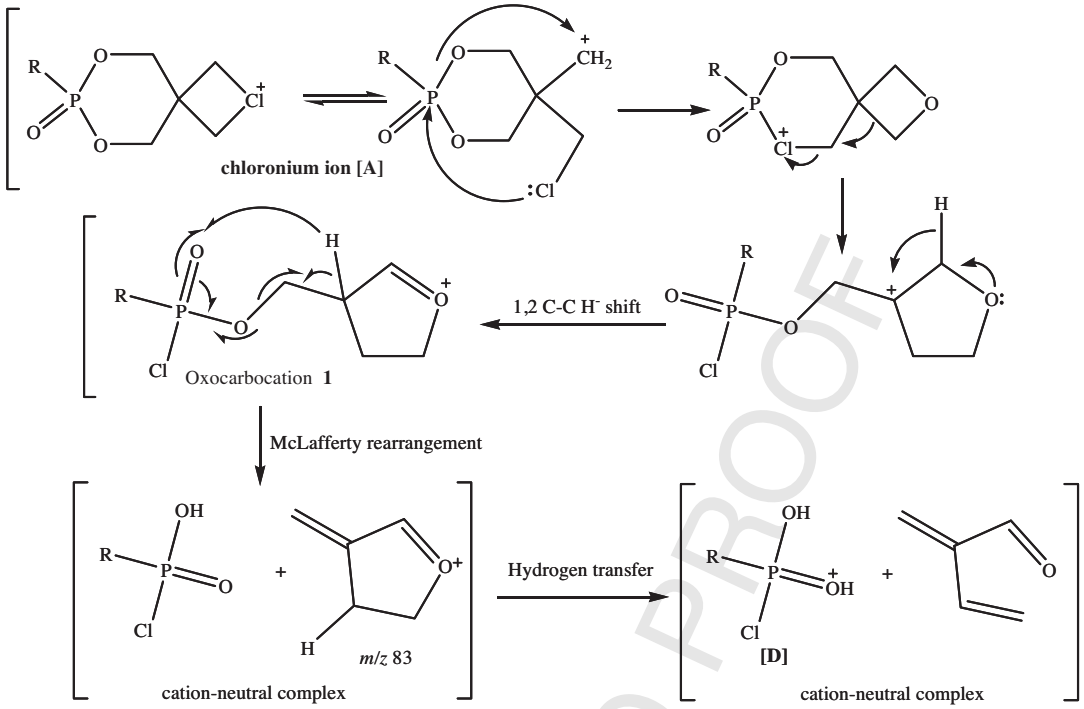


Scheme 9. Proposed mechanism for formation of ion [D] in EI-MS of II.

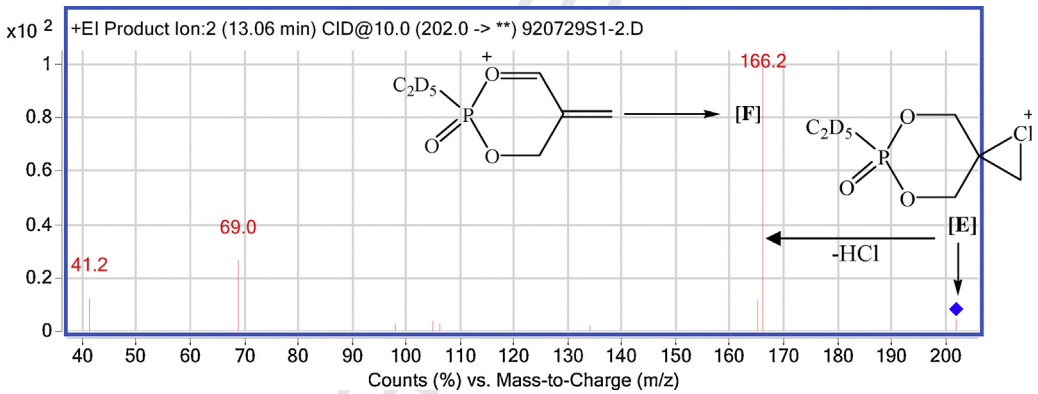
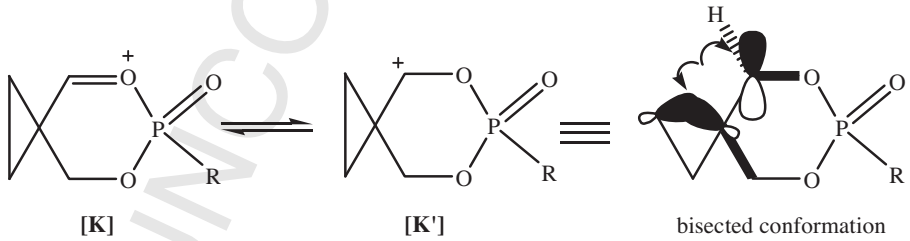


Fig. 7. Product ion spectrum of *m*/*z* 202 from 2c.



Scheme 10. Stabilization of ion [K] by favorable orbital overlap between the filled cyclopropane bent bonds and the empty p-orbital.

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