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Methanol chemical ionization quadrupole ion trap mass spectrometry of *O*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate (VX) and its degradation products

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Abstract

Mass spectrometric analysis of *O*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate (VX) degradation products by electron ionization produces extensive fragmentation with little or no molecular ion information making product identification difficult. Milder chemical ionization (CI) is commonly used to provide molecular mass and structure confirmation. In this study, methanol was used as a CI reagent in combination with an ion trap detector for detection and identification of over 30 compounds present in a thermally degraded sample of VX. The use of methanol provides superior results for this class of compounds with less fragmentation than commonly observed with gas reagents and offers logistical advantages for on-site analysis by being easier to transport and safer to use than gas cylinders. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Mass spectrometry; Chemical ionization, methanol; Warfare agents; VX

1. Introduction

Detection and identification of trace levels of chemical warfare (CW) agents and their degradation products in the environment is important for monitoring future destruction of chemical stockpiles, environmental clean-up of past storage sites, and allegations of CW agent use. Gas chromatography–mass spectrometry (GC–MS) analysis of the nerve agent *O*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate (VX) and its degradation products under standard electron ionization (EI) conditions often produces extensive fragmentation which limits sensitivity and makes product identification difficult. Milder chemical ionization (CI), typically using methane, isobutane or ammonia as reagent gases, is commonly used to provide molecular mass and structure confirmation. The applicability of methane CI for the identification of organophosphorus compounds [1–3] and VX [4] has been reported. The successful application of ammonia CI for identification of organophosphorus CW agents [5], impurities in munition grade tabun [6] and VX [7] has been demonstrated. Ammonia in general provides superior pseudomolecular ion formation with less fragmentation than methane for this class of compounds, but

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even under ammonia CI conditions the pseudo-molecular ions can be small (less than 20% of the base peak) for some of the higher-molecular-mass products.

The use of methanol as an alternative CI reagent for detection of VX degradation products has the potential to provide softer ionization than methane or ammonia to aid in the identification of higher-molecular-mass degradation products and also would be advantageous for analysis in the field because it is easier to transport and use than gas cylinders. Internal ionization ion trap detection is ideally suited to take advantage of the headspace vapor generated by liquid reagents because lower concentrations of reactant gas are required than with quadrupole or magnetic sector instruments. The use of methanol and acetonitrile as liquid reagents has recently been demonstrated for the detection of chemical agents and related compounds [8] and the use of methanol has been reported for the analysis of pesticides [9,10]. In this study, methanol was used as a CI reagent using an ion trap detector for the detection and identification of VX and 34 VX degradation products found in a thermally degraded VX sample.

2. Experimental

2.1. Materials

VX (lot VX-U-4308-CTF-N) was obtained from the Chemical Transfer Facility (CTF), Operations Directorate, US Army Edgewood Research, Development and Engineering Center. Thermally degraded VX was prepared by sealing 0.2 ml of the unstabilized VX in a 1-ml glass ampoule with an overlay of room air and heating the sealed ampoule at 150°C for 16 h. GC–MS characterization of the VX prior to thermal degradation revealed the composition was 92.3% VX, 2.7% 2-(diisopropylamino)ethanethiol, 1.5% *O*,*O*-diethyl dimethylpyrophosphonate, 1.3% bis[2-(diisopropylamino)ethyl] disulfide, 0.8% *O*-ethyl *S*-ethyl methylphosphonothioate, 0.7% bis[2-(diisopropylamino)ethyl] sulfide, 0.6% *O*-ethyl *O*-[2-(diisopropylamino)ethyl] methylphosphonate and 0.2% *O*,*O*-diethyl dimethylmonothionopyrophosphonate.

Methanol was purchased as 99.9+% A.C.S. HPLC grade (lot 04842BN) from Sigma–Aldrich (Milwaukee, WI, USA).

2.2. Instrumental

Electron and chemical ionization spectra were obtained on a Varian Saturn 4D ion trap detector equipped with a Varian Star 3400CX gas chromatograph (Varian Associates, Walnut Creek, CA, USA). The instrument was equipped with a 30 m×0.25 mm Rtx-1701 (14% cyanopropylphenyl, 86% dimethylpolysiloxane, 0.25 μm film) capillary column (Restek, Bellefonte, PA, USA). The column temperature was programmed from 60°C to 270°C at 15°C/min and held at 270°C for 8 min. Injection was in the split mode with a 50:1 split and an injection temperature of 250°C. The carrier gas was helium at a flow of 35 cm/s at 150°C. The manifold temperature was 170°C, the transfer line temperature was 240°C, the emission current was 20 μA, the axial modulation voltage was 4 V, the AGC gain control target current was 15 000 counts, the radio frequency (RF) dump value was 650 u and the mass range was scanned from 46 to 500 u (EI) or 60 to 500 u (CI) at 1 scan/s. For EI, the background mass was 45 m/z, the maximum ionization time 25 000 μs, the AGC prescan storage level 42 m/z, and the AGC prescan time 100 μs. All CI data were obtained in the selected ejection chemical ionization (SECI) mode. SECI-specific parameters used for methanol as reagent gas were ARC ionization time 100 μs, CI maximum ionization time 1000 μs, CI maximum reaction time 50 ms, CI ionization storage level 15 m/z, CI reagent ion eject amplitude 10.0 V, CI reaction storage level 15 m/z and CI background mass 45 m/z. The CI reagent gas pressure was adjusted until the spectrum shown in Fig. 1 was obtained.

3. Results and discussion

Fig. 2 illustrates a methanol CI total ion chromatogram obtained for a degraded VX sample using ion trap detection. Thirty-five compounds were detected. The chromatogram peak number, GC retention time (t_R), molecular mass (M_r), compound name, and

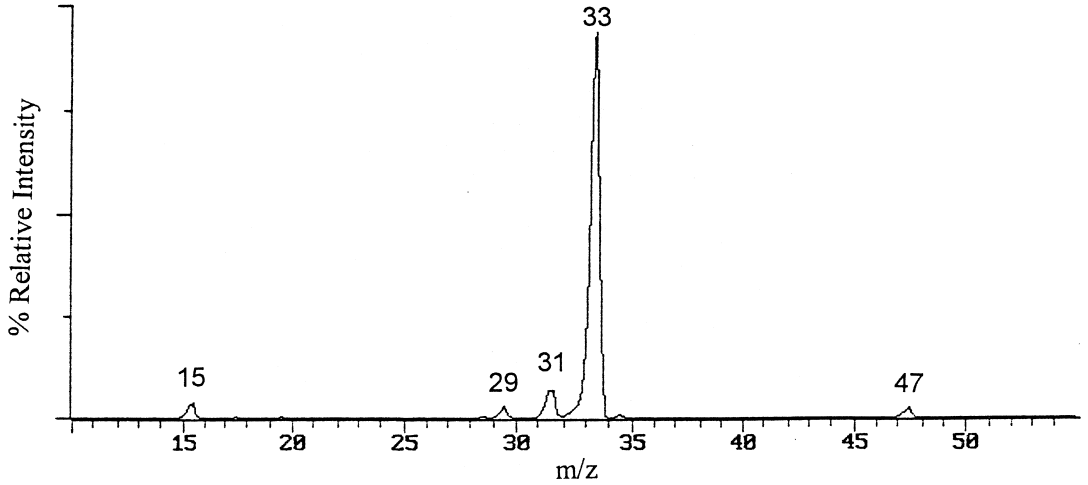


Fig. 1. Methanol CI tune spectrum.

compound structure for each compound detected are listed in Table 1.

Methanol CI mass spectra obtained for VX and selected degradation products are provided in Fig. 3. EI spectra for many of the degradation products [7] and structures of the most common EI and CI fragmentation ions observed for these compounds [4,7] have been previously reported.

The problems associated with the identification of VX degradation products based on EI mass spectra have been documented [4,7]. Any compound containing the diisopropylaminoethyl group fragments extensively under EI conditions. Spectra are dominated by an ion at m/z 114, $[\text{i-Pr}_2\text{N}{=}\text{CH}_2]^+$. Fragmentation to a less intense ion at m/z 72 $[\text{i-PrNH}{=}\text{CH}_2]^+$, also occurs. Similar spectra dominated by these ions are obtained for sulfide, disulfide and organophosphonate series containing the diisopropylaminoethyl group with little or no molecular ion information to aid in identification of the compounds.

The use of methane and ammonia as effective CI reagent gases for providing molecular ion information for VX degradation products has been demonstrated. The results of this study indicate methanol CI coupled with ion trap detection provides even

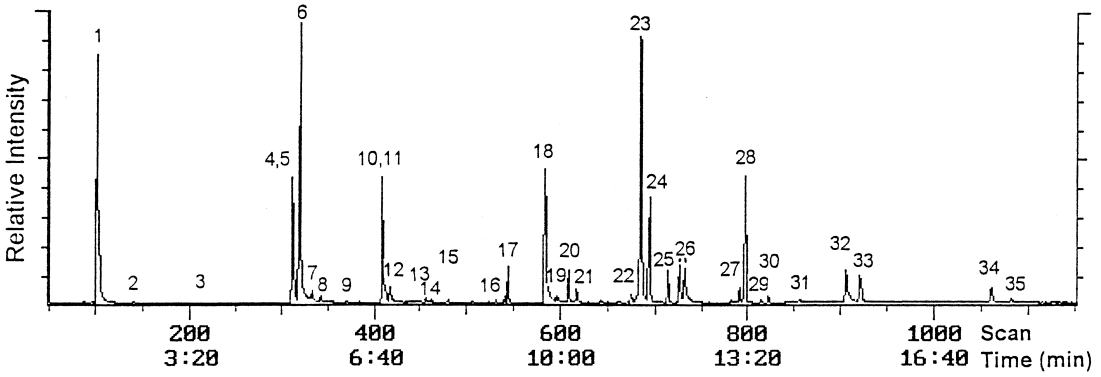


Fig. 2. GC–MS total ion chromatogram of thermally degraded VX.

Table 1
Products identified by methanol CI ion trap detection in degraded VX

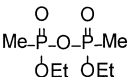
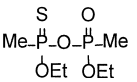
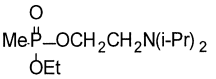
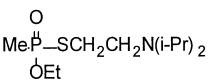
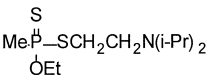
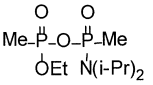
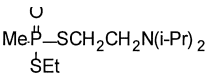
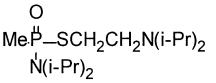
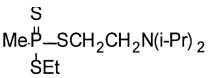
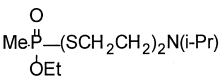
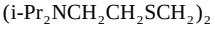
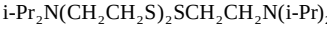
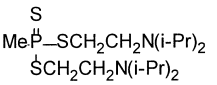
No.[a]	t_R[b] (mins)	M_r	Compound name (CAS registry No.)	Structure
1	1:43	101	Diisopropylamine[c] (108-18-9)	i-Pr_2NH
2	2:18	129	*N,N*-Diisopropylethylamine[c] (7087-68-5)	Et-N(i-Pr)$_2$
3	3:31	122	Diethyl disulfide[c] (110-81-6)	EtSSEt
4	5:13	152	*O,O*-Diethyl methylphosphonate[c] (683-08-9)	
5	5:14	168	*O,O*-Diethyl methylphosphonothioate[c] (6996-81-2)	
6	5:20	161	2-(Diisopropylamino)ethanethiol[c] (5842-07-6)	i-$Pr_2NCH_2CH_2SH$
7	5:34	159	2-(Diisopropylamino)ethanethial[e]	i-Pr_2NCH_2CH=S
8	5:44	129	Unknown	$C_8H_{19}N$
9	6:11	187	2-(Diisopropylamino)ethyl vinyl sulfide[e]	i-$Pr_2NCH_2CH_2SCH$=CH_2
10	6:51	168	*O,S*-Diethyl methylphosphonothioate[c]	
11	6:52	189	2-(Diisopropylamino)ethyl ethyl sulfide[d]	i-$Pr_2NCH_2CH_2SEt$
12	6:58	228	1,2-Bis(2-diisopropylamino)ethane[e]	i-$Pr_2NCH_2CH_2N$(i-Pr)$_2$
13	7:36	165	*O*-Ethyl *N*-isopropyl methylphosphonamidate[e]	
14	7:44	203	2-(Diisopropylamino)ethyl isopropyl sulfide[d]	i-$Pr_2NCH_2CH_2S$(i-Pr)
15	8:01	207	*O*-Ethyl *N,N*-diisopropyl methylphosphonamidate[e]	
16	9:01	184	*O,S*-Diethyl methylphosphonodithioate[e]	
17	9:05	221	2-(Diisopropylamino)ethyl ethyl disulfide[e]	i-$Pr_2NCH_2CH_2SSEt$
18	9:46	230	*O,O*-Diethyl dimethylpyrophosphonate[c] (32288-17-8)	
19	9:57	246	*O,O*-Diethyl dimethylmonothionopyrophosphonate[c]	
20	10:10	221	2-[2-(Diisopropylamino)ethylthio]ethanethiol[e]	i-$Pr_2NCH_2CH_2SCH_2CH_2SH$

Table 1. Continued

No.[a]	t_R[b] (min:s)	M_r	Compound name (CAS registry No.)	Structure
21	10:18	251	*O*-Ethyl *O*-[2-(diisopropylamino)ethyl] methylphosphonate[c] (71840-26-1)	
22	11:15	179	Unknown	Unknown
23	11:25	267	*O*-Ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate[c] (50782-69-9)	
24	11:35	288	Bis[2-(diisopropylamino)ethyl] sulfide[c]	
25	11:55	283	*O*-Ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonodithioate[e]	
26	12:07	285	*O*-Ethyl *N*,*N*-diisopropyl dimethylpyrophosphonamidate[e]	
27	13:11	283	*S*-Ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonodithioate[d]	
28	13:19	320	Bis[2-(diisopropylamino)ethyl] disulfide[c]	
29	13:35	322	*N*,*N*-Diisopropyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothioamidate[e]	
30	13:43	299	*S*-Ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonotrithioate[e]	
31	14:16	281	1-Diisopropylamino-3,6,7-trithianonane[e]	
32	15:07	327	*O*-Ethyl *S*-[2-(2-diisopropylaminoethylthio)ethyl] methylphosphonothioate[d]	
33	15:22	348	1,2-Bis[2-(diisopropylamino)ethylthio] ethane[d]	
34	17:42	380	1,9-Bis(diisopropylamino)-3,4,7-trithianonane[d]	
35	18:03	398	*S*,*S*-Bis[2-(diisopropylamino)ethyl] methylphosphonotrithioate[d]	

[a] Refer to chromatogram in Fig. 2.

[b] GC retention time (t_R) using a 30 m×0.25 mm Rtx-1701 capillary column (60–270°C at 15°C/min).

[c] Identification based on comparison of EI mass spectra and GC retention times with those previously obtained for authentic standards and/or reported in the literature for unambiguous identifications.

[d] Tentative identification based on EI and CI mass spectral interpretation and comparison of EI spectra to those previously reported in the literature for tentative identifications.

[e] Tentative identification based on EI and CI mass spectral interpretation.

i = Iso.

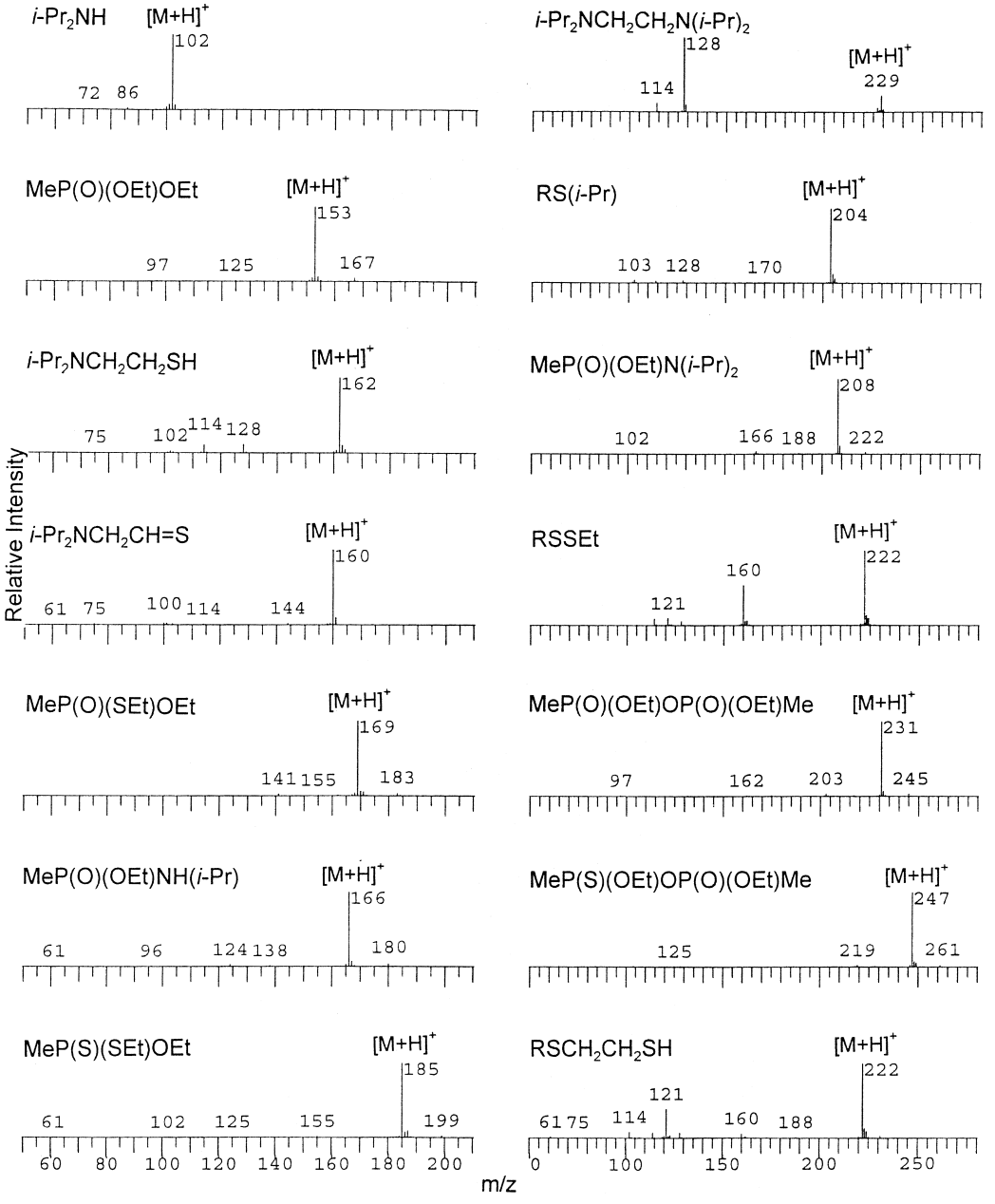


Fig. 3. Methanol CI mass spectra of VX degradation products (R = $-CH_2CH_2N[i\text{-}Pr]_2$).

more intense protonated molecular ion formation and less fragmentation than either methane or ammonia for most compounds. The protonated molecular ion dominates the spectra of 31 of the 35 compounds observed. The only exceptions were *O*-ethyl *O*-[2-(diisopropylamino)ethyl] methylphosphonate (66% of base peak), 1,2-bis(2-diisopropylamino)ethane (31% of base peak), 2-(diisopropylamino)ethyl vinyl

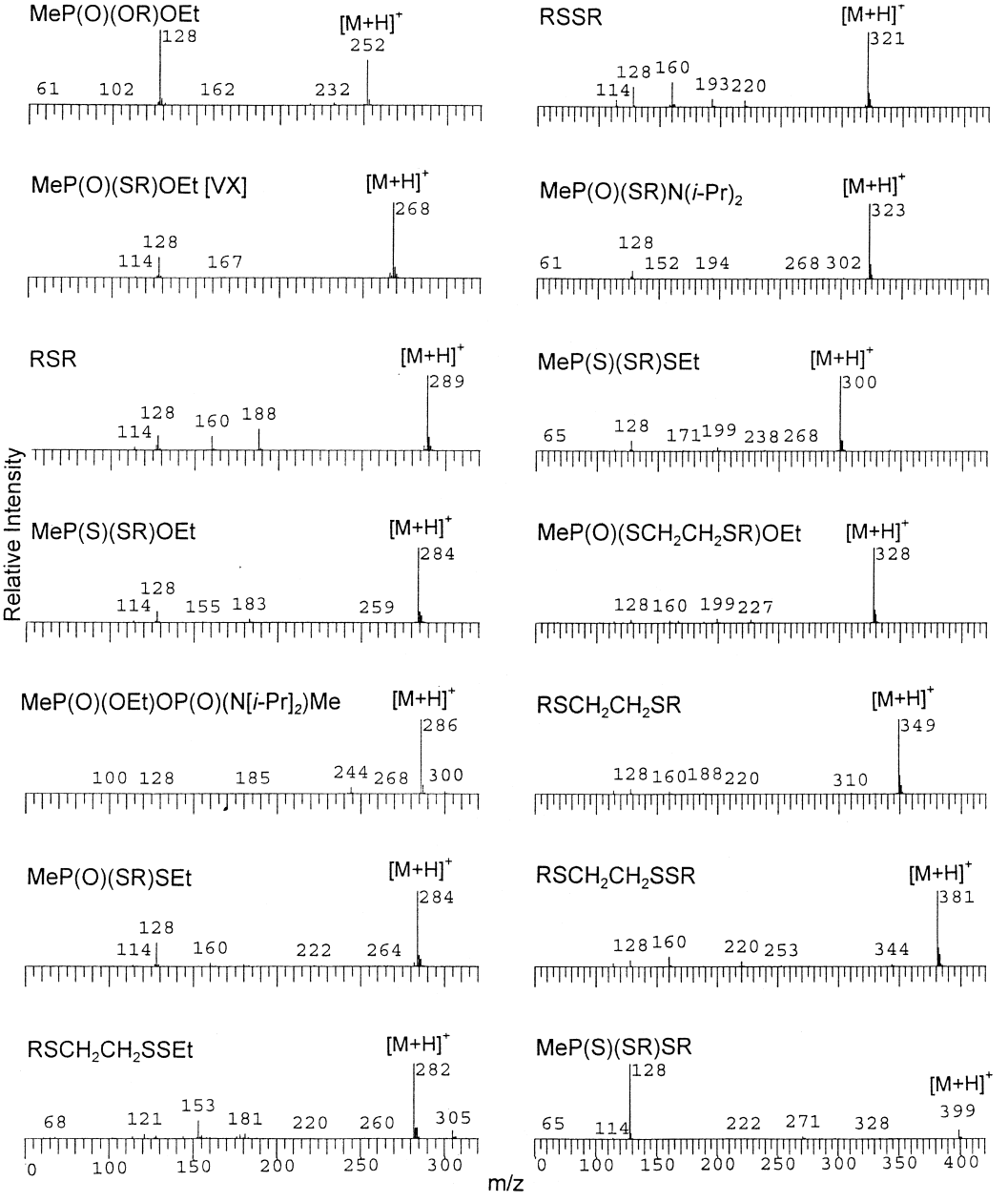


Fig. 3. (*continued*).

sulfide (92% of base peak) and *S*,*S*-bis[2-(diisopropylamino)ethyl] methylphosphonotrithioate (20% of base peak). As a comparison, typical protonated molecular ions are observed at approximately 100% (methanol), 75% (methane) and 50% (ammonia) of the base peak for VX and 100% (methanol), 60% (methane) and 15% (ammonia) of the base peak for bis[2-(diisopropylamino)ethyl] disulfide [4,7]. A comparison of mass spectra obtained for VX under EI, methane CI, and methanol CI ion trap conditions

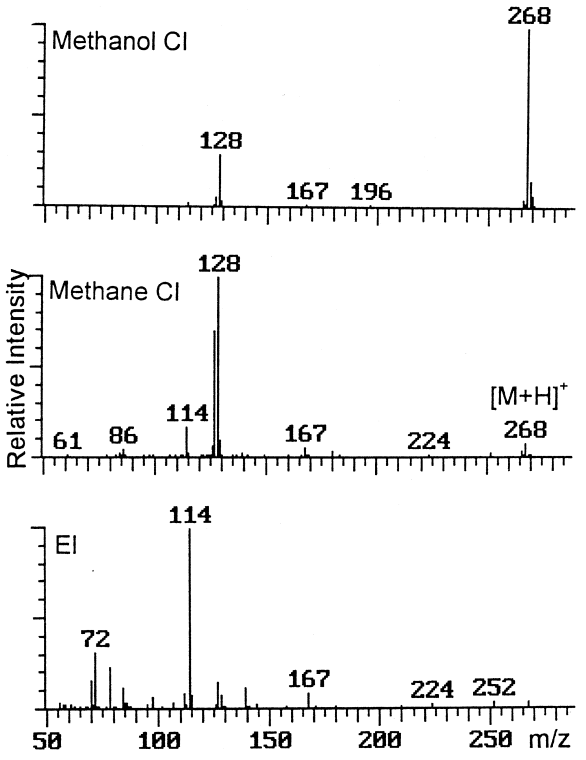


Fig. 4. Saturn 4D EI, methane CI and methanol CI mass spectra of VX.

is provided in Fig. 4. Because molecular ion intensity generally decreases with increasing molecular mass, the enhanced protonated molecular ion formation observed with methanol could play a significant role in the identification of higher-molecular-mass methylphosphononates, sulfides and disulfides observed in VX degradation products.

The enhanced protonated molecular ion formation and significantly reduced fragmentation noted for VX and other products under methanol CI conditions offers opportunities for increased sensitivity and selectivity for trace level detection. Concentration of the signal as the protonated molecular ion provides increased sensitivity through a stronger signal and reduced background and provides an ideal ion for the application of ion trap tandem mass spectrometry to further enhance selectivity.

Ion–molecule reactions to form adduct ions at masses greater than the molecular mass of the compound are sometimes observed during ion trap analysis of certain classes of chemical agents and their degradation products, particularly alkyl methylphosphonofluoridates and the trimethylsilyl derivatives of alkyl methylphosphonic acids [9,10]. Little adduct ion formation was observed for VX and the VX degradation products detected in this study.

4. Conclusions

Methanol CI using ion trap detection is an excellent technique for the detection and identification of VX degradation products, producing primarily the protonated molecular ion for VX and 34 VX degradation products. Reduced fragmentation was observed relative to the use of methane or ammonia as CI reagent gases. Little ion–molecule reaction was observed relative to that observed for other classes of compounds.

The use of methanol as a CI reagent offers potential logistical advantages for environmental field analysis by being cheaper, easier to transport and safer to use than traditional gas reagents which require the use of gas cylinders.

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