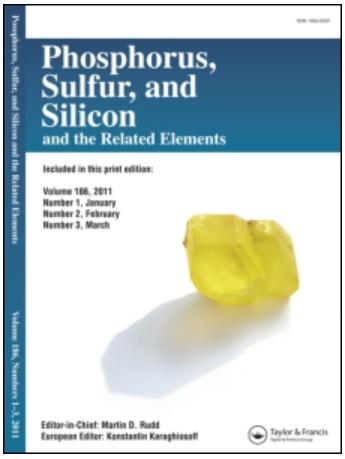

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ANALYSIS OF DIMETHYLPYROPHOSPHONATE DECOMPOSITION PRODUCTS OF VX BY GC-MS/MS AND ^{31}P NMR

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The detection and identification of decomposition products of chemical warfare agents can be used to investigate allegations of chemical warfare agent use, identify synthetic routes and trace sources of chemical warfare agents and their precursors. Compounds which contain a P—CH_3 bond are particularly important as these compounds can provide evidence for the presence or decomposition of organophosphorus nerve agents. Capillary column GC-MS analysis of a distillation fraction of O-ethyl S-[2-diisopropylamino)ethyl] methylphosphonothiolate (VX), a major phosphonothiolate nerve agent, indicated the presence of two additional components comprising about 10% of the total volatile organic content. These compounds were characterized and identified by GC-MS, GC-MS/MS and ^{31}P NMR as O,O-diethyl dimethylpyrophosphonate and O,O-diethyl dimethylmonothionopyrophosphonate. O,O-Diethyl dimethylmonothionopyrophosphonate presented a structural isomerism ambiguity whereby the position of the sulfur atom could not be defined by MS alone. Identification of the correct structure required spectrometric data from two different techniques, MS/MS and NMR, an important illustration of the use of complementary spectrometric techniques for unambiguous identification of chemicals for verification of the Chemical Weapons Convention.

Key words: Chemical warfare agents, verification, organophosphates, pyrophosphonates, VX, gas chromatography-mass spectrometry, tandem mass spectrometry, nuclear magnetic resonance, phosphorus NMR.

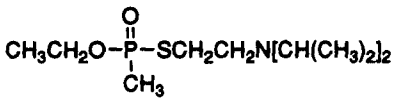
INTRODUCTION

Decomposition products or impurities of chemical warfare agents can provide an indication of chemical warfare agent use or act as tracers to follow synthetic routes and sources. Compounds which contain a P—CH_3 bond are particularly important as the detection of these compounds can provide strong evidence for the presence or prior presence of organophosphorus nerve agents.[1–5] Recently the identification of isopropyl methylphosphonic acid and methylphosphonic acid, decomposition products of the nerve agent isopropyl methylphosphonofluoridate (SARIN), have been reported in soils samples taken from bomb craters in Iraq years after the alleged attack.[6]

The *Convention on the Prohibition of the Development, Production, Stockpiling, and Use of Chemical Weapons and Their Destruction*, otherwise known as the Chemical Weapons Convention (CWC), is an international treaty which will potentially eliminate the world-wide threat of chemical warfare.[7] Key to the success of this treaty are its verification provisions which allow for on-site inspections and chemical sampling and analysis to ensure compliance and identify treaty violations. The Organization for the Prohibition of Chemical Weapons have placed a priority on identification and characterization of such compounds as these data may be

used to verify an allegation of use and support determinations of non-compliance with the Chemical Weapons Convention.

Chemical warfare agents used for research and development at the Defence Research Establishment Suffield are synthesized, redistilled, and analyzed for purity prior to use. During capillary column GC-MS analysis of a distillation fraction of O-ethyl S-[2-(diisopropylamino)ethyl] methylphosphonothiolate (VX, **1**), several



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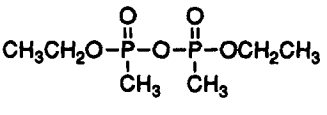
additional sample components, comprising about 10% of the volatile organic content, were observed. The characterization and identification of these compounds by GC-MS, GC-MS/MS and ^{31}P NMR was performed to obtain reference data that may be used for the identification of these VX decomposition products.

RESULTS AND DISCUSSION

The capillary column GC-MS chromatogram obtained under El conditions for the major distillation fraction of VX is shown in Figure 1. The major sample component, VX, comprised approximately 90% of the volatile organic content based on integration of the total-ion-current chromatogram. Similar purity was also found during capillary column GC analysis with flame ionization detection. O,O-Diethyl dimethylpyrophosphonate (**2**), a P—CH_3 containing pyrophosphonate, was con-



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firmed following comparison of acquired El and ammonia Cl mass spectral data with published data.[8]

A pair of incompletely resolved sample components with a retention time of about 12 minutes exhibited identical El and ammonia Cl mass spectra (Figures 2(a) and 2(b)). This suggested the presence of a pair of diastereomers for the unknown structure. The molecular ion at m/z 246 was confirmed by the presence of both $(M + H)^+$ and $(M + NH_4)^+$ pseudo-molecular ions during ammonia Cl-MS analysis. Sulfur content was suspected due to the presence of a significant El $(M + 2)^{+\cdot}$ ion at m/z 248. The higher mass El fragmentation ions at m/z 218, 202, 190 and 187 were likely due to the loss of C_2H_4, OC_2H_4, $[C_2H_4]_2$ and $[C_2H_4O + CH_3]$ from the molecular ion.

A structure similar to O,O-diethyl dimethylpyrophosphonate, where one of the oxygen atoms (P=O or P—OC_2H_5), was replaced by a sulfur atom, was postulated based on the interpretation of low resolution El and ammonia Cl data. Accurate

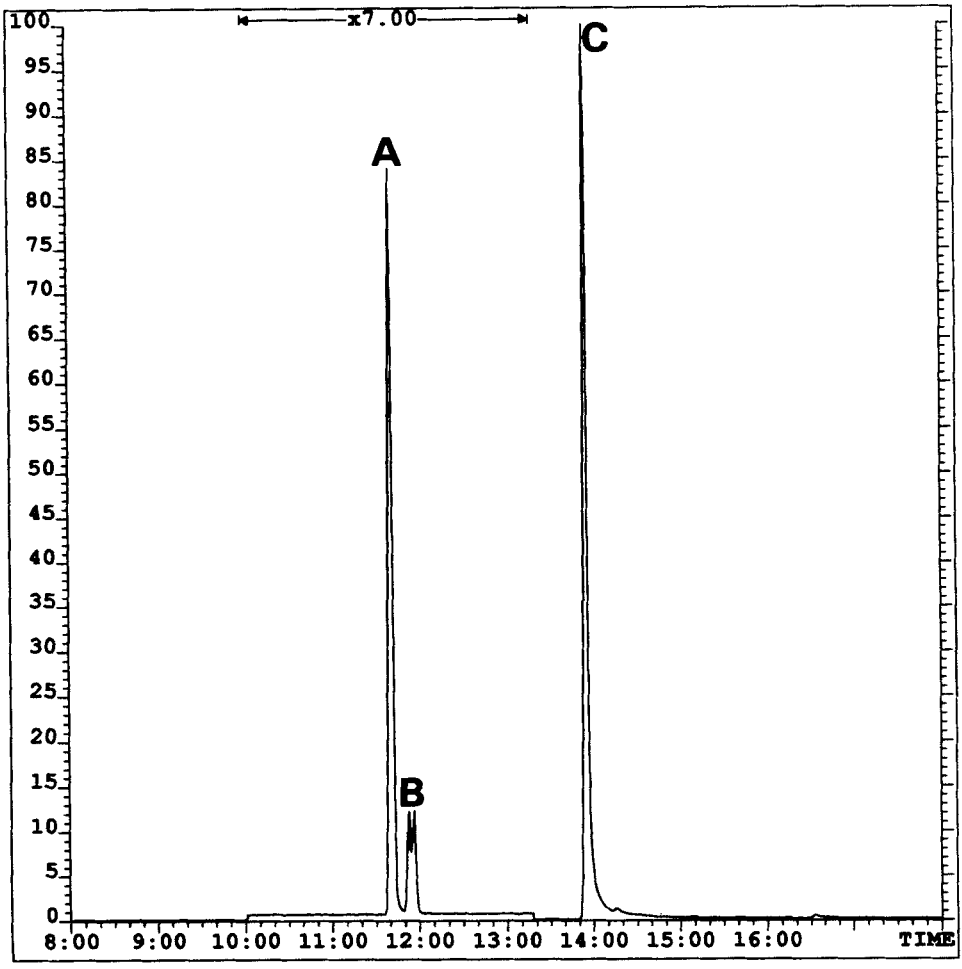
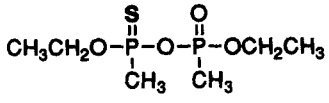


FIGURE 1 Capillary column GC-MS chromatogram of the distilled VX sample containing O,O-diethyl dimethylpyrophosphonate (A), the unknown pyrophosphonate (B), and VX (C).

mass measurement data, obtained at a resolution of 7000, confirmed the elemental composition of the molecular and fragmentation ions (Table I). The postulated structures for this pyrophosphonate, **3** and **4**, each contain two chiral centers at



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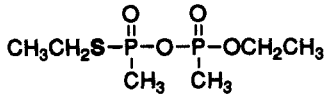

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the phosphorus atoms which would give rise to two chromatographic peaks due to diastereomeric pairs. However it was not possible to determine the location of the sulfur atom (P=S vs P—SC_2H_5) based on the interpretation of the acquired EI and ammonia CI mass spectral data.

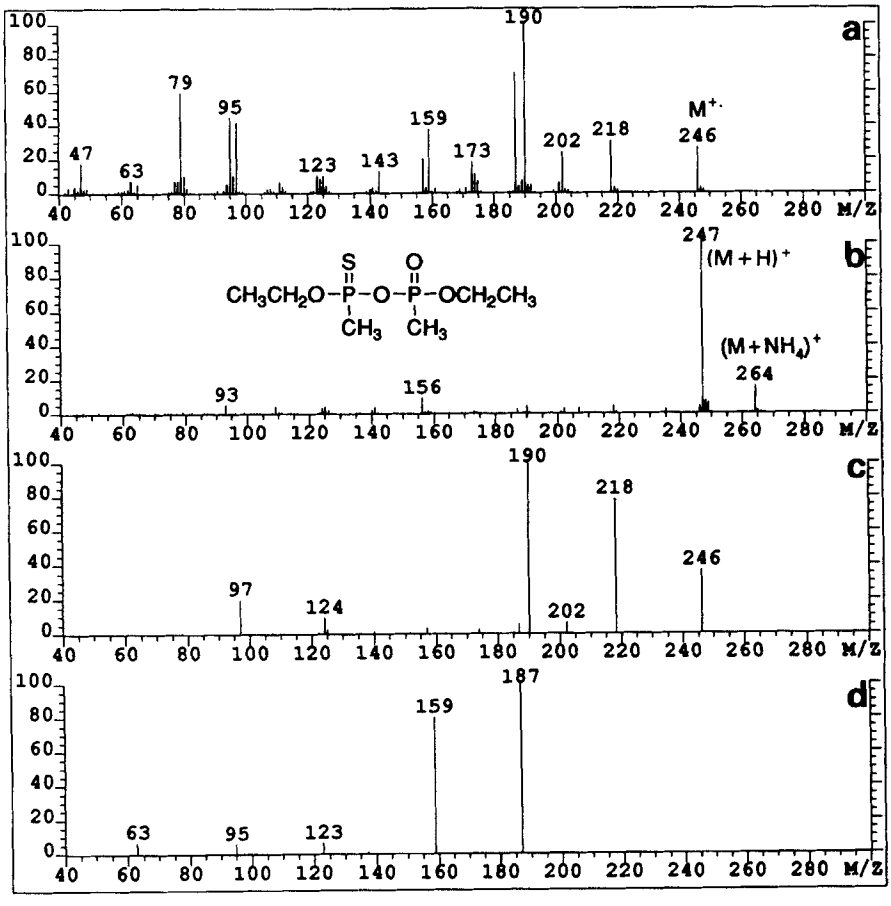


FIGURE 2 EI (a) and ammonia CI (b) spectra of the unknown pyrophosphonate, later identified as O,O-diethyl dimethylmonothionopyrophosphonate, and the daughter spectra (40 eV; 2×10^{-5} Torr argon) of the m/z 246 (c) and m/z 187 (d) ions.

TABLE I

High resolution data for EI ions (>20% relative abundance) of the unknown pyrophosphonate

Mass Observed	Elemental Composition	Error (mmu)
246.0216	$C_6H_{16}O_4P_2S_1$	-2.9
217.9907	$C_4H_{12}O_4P_2S_1$	-2.5
201.9955	$C_4H_{12}O_3P_2S_1$	-2.7
189.9608	$C_2H_8O_4P_2S_1$	-1.1
186.9739	$C_3H_9O_3P_2S_1$	-0.9
158.9446	$C_1H_5O_3P_2S_1$	+1.1
156.9824	$C_2H_7O_4P_2$	+0.4
97.0043	$C_1H_6O_3P_1$	-1.2
94.9705	$C_1H_4O_1P_1S_1$	-1.5
78.9979	$C_1H_4O_2P_1$	+3.0

As tandem mass spectrometry was previously successful in determining the location of a sulfur atom in a partially hydrolyzed longer chain sulfur vesicant,[9] the structure of the unknown pyrophosphonate was investigated by this technique. During prior analyses, a significant ion (approximately 50% relative abundance) due to loss of SC_2H_4 was observed for a compound of similar structure, O,S-diethyl methylphosphonothiolate.[8] Observation of a daughter ion due to loss of SC_2H_4 from the molecular ion or a fragmentation ion containing the SC_2H_5 substituent (analogous to the loss of OC_2H_4), would strongly suggest the presence of a compound with P—SC_2H_5 as opposed to P=S substitution. The best candidate ions for daughter analysis, based on the structures postulated from high resolution EI data, were m/z 246, 218, 202 and 187. These ions and m/z 190 were all investigated under daughter conditions. Although the loss of SC_4H_4 was not observed, which would suggest the presence of a P=S, this negative evidence alone was not sufficient for conclusive determination of the sulfur position.

Figures 2(c) and 2(d) illustrate two daughter spectra acquired during this investigation and Figure 3 illustrates probable daughter ion structures based on P=S

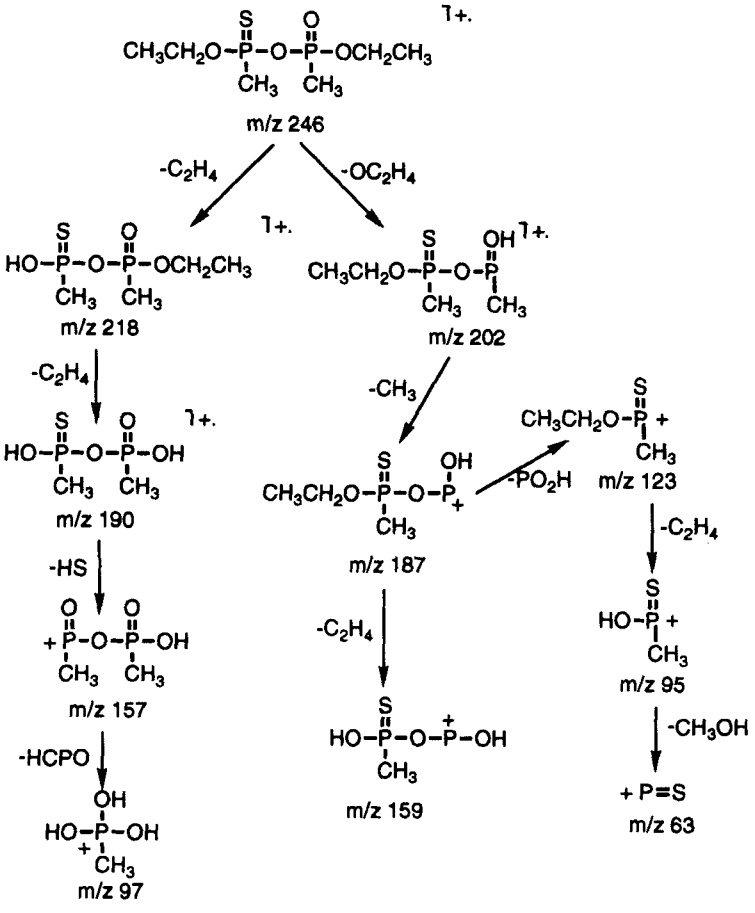
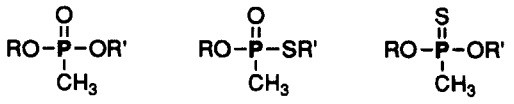


FIGURE 3 Possible structures and fragmentation pathways for the m/z 246, 218, 202, 190, and 187 ions observed during acquisition of O,O-diethyl dimethylmonothionopyrophosphonate (3) daughter spectra.

substitution. Exact mass data acquired during El-MS aided in the assignment of other possible structures with the same nominal mass.

The ^{31}P NMR spectrum of the distillation fraction showed, in addition to VX at δ 53.9 ppm, two other sets of signals (Figure 4). Downfield to VX there was an apparent doublet of doublets at approximately δ 86 ppm. The strong upfield doublet (δ 22.08 ppm) was assigned to O,O-diethyl dimethylpyrophosphonate (**2**) based on the El-MS data and correlation to the reported chemical shift value.[10]

The ^{31}P NMR spectrum of **2** overlaps a second doublet of doublets of similar intensity to those downfield of VX and comparison of the observed J values show that these doublets are coupled pairs (Figure 5). The chemical shifts of each of doublets are consistent with two differently substituted phosphorus nuclei in an asymmetrical pyrophosphonate. Methylphosphonates (**5**), methylphosphonothiolates (**6**), and methylthionophosphonates **7**, can be readily distinguished by differ-



5 **6** **7**

ences in their chemical shift values. Methylphosphonates have values typically between 24–30 ppm[11] whereas O-alkyl methylphosphonothiolates such as VX appear in the 50–55 ppm region. O,O-Diethyl methylthionophosphonate has a reported chemical shift value of δ 93.9 ppm.[12]

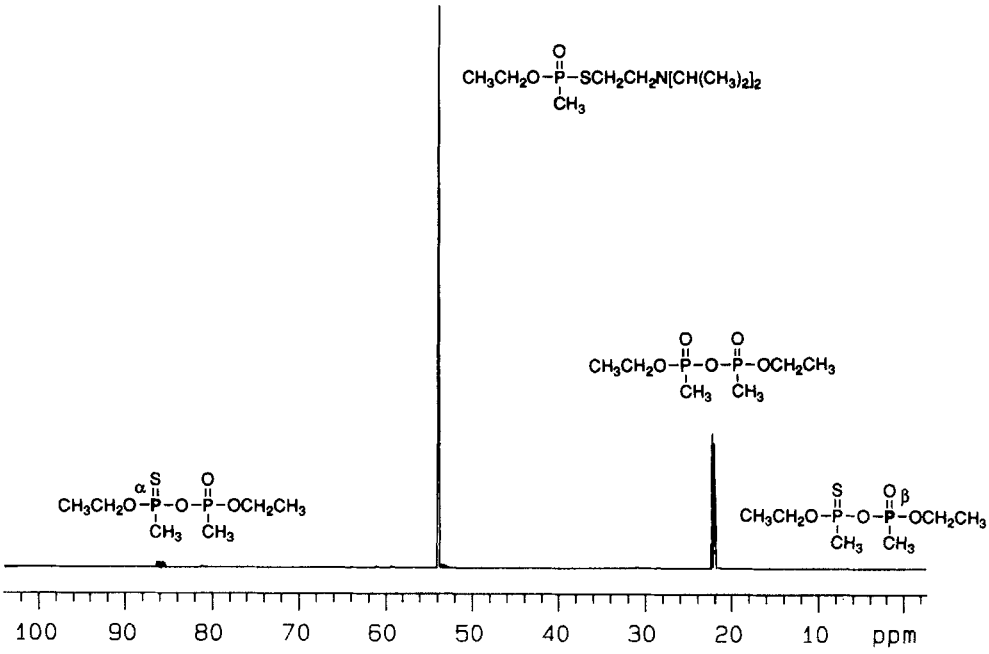


FIGURE 4 ^{31}P NMR spectrum of the distilled VX sample showing the major component VX and the dimethylpyrophosphonate impurities.

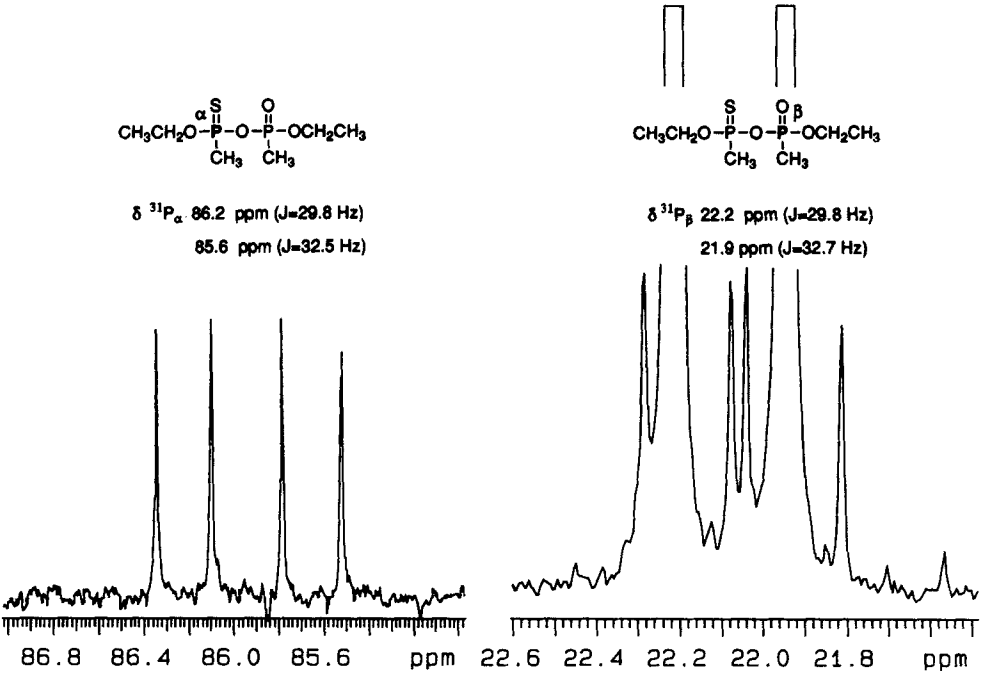


FIGURE 5 Expansions of the two ^{31}P NMR chemical shift regions showing the methylthionophosphonate α-phosphorus and methylphosphonate β-phosphorus of O,O-diethyl dimethylmonothionopyrophosphonate (**3**).

^{31}P NMR data established the structure of the unknown pyrophosphonate as O,O-diethyl dimethylmonothionopyrophosphonate (**3**). This compound contains two non-equivalent, chiral centers at phosphorus which gives rise to two pairs of diastereomers. The ^{31}P NMR chemical shifts of the two phosphorus centers in each set of diastereomers are quite different appearing at δ 86.22 and 85.65 ppm for the methylthionophosphonate α-phosphorus whereas the methylphosphonate β-phosphorus appear at 21.94 ppm (Figure 5). Although the synthesis[13] and ^{1}H NMR spectrum[14] of **3** have been previously reported, these papers do not report the MS or ^{31}P NMR data for this compound.

Samples of VX are known to contain a complex mixture of decomposition products including O,S-diethyl methylphosphonothiolate, O,O-diethyl methylthionophosphonate,[8] and their corresponding acids.[15] Symmetrical pyrophosphonates have been found in stored samples[8] of VX and are produced during the oxidative degradation of phosphonothiolates and phosphoramidothiolates.[10,16] Because **3** had not been previously observed in stored VX samples, it was likely formed during distillation by reaction of these decomposition products with VX or with themselves.

The identification of O,O-diethyl dimethylmonothionopyrophosphonate (**3**) by MS/MS and ^{31}P NMR illustrates the importance of using two or more spectrometric techniques for the unambiguous identification of CWC scheduled compounds. As defined by the analytical requirements of the CWC, a compound must be unambiguously identified before it can be reported. Identification is only considered unambiguous if the compound is identified on the basis of data from at least two

different spectrometric techniques.[17] Because chemicals subject to verification are organized according to schedules,[7] some compounds, such as O-alkyl S-dialkyl aminoethylalkylphosphonothiolates, are only listed as a class. It is therefore incumbent on the verification analysis to provide unambiguous identification that enables assignment of a compound to the CWC schedules.

This principle of unambiguous identification has been developed and evaluated in a series of international round robin analytical exercises and these requirements have been reported.[17–21] Although these exercises have demonstrated that it is possible to use analytical data to support verification of the CWC, no compounds used in those exercises presented a structural isomerism ambiguity as reported in this paper. Resolution of the ambiguity and identification of O,O-diethyl dimethylmonothionopyrophosphonate (**3**) by MS and NMR demonstrates the importance of the CWC principle of unambiguous identification by two independent spectrometric techniques.

CONCLUSIONS

The unambiguous identification of CWC relevant chemicals requires that the compound be identified on the basis of positive spectrometric data from at least two independent spectrometric methods, with one method including a chromatographic separation. The three primary analytical techniques used are GC-MS, GC-FTIR, and NMR. A number of international round robin analytical exercises have been conducted to test these criteria and various analytical methods to validate the analytical requirements of the CWC. In this paper, the analysis of VX results in the identification of a new decomposition product and validated the principle of unambiguous identification. The structural isomerism ambiguity of the sulfur atom in the dimethylpyrophosphonate required spectrometric data from two different techniques to confirm its structure. Identification of O,O-diethyl dimethylmonothionopyrophosphonate (**3**) as a decomposition product of VX is an important illustration of the principle of unambiguous identification.

EXPERIMENTAL

A stock supply of O-ethyl S-[2-(diisopropylamino)ethyl] methylphosphonothiolate (VX, **1**) which showed visible decomposition (yellowing) after prolonged storage (>12 months) at 5°C was purified by vacuum distillation. The sample was distilled to give a major fraction boiling at 100–103°C/0.05 mm Hg. An aliquot of this fraction was removed and a 1 mg/mL sample in dichloromethane and a 5 mg/mL sample in deuterated chloroform were prepared for GC-MS and NMR analysis, respectively.

The 1 mg/mL VX sample was analyzed by capillary column GC-MS and GC-MS/MS using an Autospec-Q hybrid tandem mass spectrometer (VG Analytical, Wythenshawe, U.K.) interfaced to a Hewlett Packard 5890 gas chromatograph under the following chromatographic conditions. All injections were on-column at 40°C onto a 15 m × 0.32 mm ID J&W DB-1701 (0.25 μm) capillary column with a 40°C (2 min) 10°C/min 280°C (5 min) temperature program. EI-MS operating conditions were as follows: accelerating voltage, 8 kV; emission, 0.1 mA; electron energy, 70 eV; source temperature, 200°C and source pressure, 3×10^{-6} Torr. Ammonia (Anhydrous-grade, 99.99%, Liquid Carbonic) CI-MS operating conditions were as follows: accelerating voltage, 8 kV, emission, 0.3 mA; electron energy, 50 eV; source temperature, 120°C and source pressure (near source), 1×10^{-4} Torr. The ratio of NH_4^+: $NH_3^{+\cdot}$, was approximately 15:1 in the VG Autospec EI/CI source. Full scanning EI and CI data were

collected over the 400 to 40 u mass range at 0.7 sec/decade. El-MS data were acquired at a resolution of 1000 or 7000 (10% valley definition) and ammonia Cl-MS data were acquired at a resolution of 1000.

Daughter spectra were obtained under low resolution El conditions (as defined previously) with a collisional activated dissociation (CAD) cell energy of 25 eV and an argon pressure of 8×10^{-6} Torr or a CAD cell energy of 40 eV and an argon pressure of 2×10^{-5} Torr. The first CAD cell condition represents a standard operating procedure[22] that reduces the intensity of the PFK ion at m/z 219 to 50% of that observed with residual air in the CAD cell. The second CAD cell condition, which results in an 80% reduction of the PFK ion at m/z 219, was used for several ions to increase daughter ion production. Daughter spectra of m/z 246, 218, 202, 190 and 187 were acquired during capillary column GC-MS/MS analyses with the quadrupole scanned from 260 to 50 u at 0.7 sec/scan (unit resolution).

The 5 mg/mL sample was analyzed by phosphorous NMR on a Varian VXR 300S NMR (Palo Alto, California) using the following conditions: ^{31}P frequency 121.421 Hz, acquisition time 2.8 s, relaxation delay 20 s, pulse width (90°) 15.9 μsec, 256 transients. Triethyl phosphate in deuterated chloroform (δ − 1.00 ppm) was used as an external standard.

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