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Verification of the Chemical Weapons Convention: Mass Spectrometry of Alkyl Methylphosphonofluoridates

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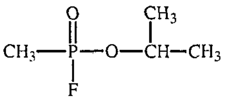
Abstract

Under the provisions of the United Nations Chemical Weapons Convention (CWC), certain parts of chemical industry will be monitored to verify compliance with the Convention. This will include analysis of samples from industrial sites to check for the presence or absence of chemical warfare related compounds. One of the problems in screening the chemicals to be monitored under the CWC is that certain classes of chemical warfare agents are represented as families of chemicals, with many of the individual chemicals having no analytical data available. One example is the alkyl methylphosphonofluoridate family with an alkyl ester substituent from CH_3 to $C_{10}H_{21}$. In this work, the mass spectra of 60 alkyl methylphosphonofluoridate family members have been studied to enable the development of rapid on-site screening methods for this family of chemicals.

Introduction

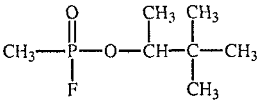
The Chemical Weapons Convention (CWC), which was signed by 130 nations in Paris on 13 January 1993, will prohibit the development, production, stockpiling and use of chemical weapons.[1] Stockpiled chemical weapons will be destroyed under the provisions of this treaty, and certain parts of the chemical industry will be monitored to verify that no chemical warfare agents are being produced.[2]

One of the problems in defining the chemicals to be monitored under the CWC is that certain classes of chemical warfare agents cannot be represented as a short list of individual chemicals. In order to overcome this problem, the schedules of chemicals to be monitored under the CWC contain both individual chemicals and families of chemicals. For example, the nerve agents sarin (1) and soman (2) and related chemicals in the alkyl methylphosphonofluoridate family



$$CH_3-\overset{\overset{O}{\|}}{\underset{\underset{F}{|}}{P}}-O-\overset{\overset{CH_3}{|}}{C}H-CH_3$$

(1)



$$CH_3-\overset{\overset{O}{\|}}{\underset{\underset{F}{|}}{P}}-O-\overset{\overset{CH_3}{|}}{C}H-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_3$$

(2)

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[1] Conference on Disarmament, The Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction, United Nations Document CD/1170, Geneva, August 1992.

[2] Mathews, R. J., 'Verification of Chemical Industry under the Chemical Weapons Convention', in Poole, J. B., and Guthrie, R., (Eds) 'Verification 1993: Peacekeeping, Arms Control and the Environment' (VERTIC: London 1993).

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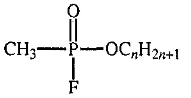
with an alkyl ester group up to $C_{10}H_{21}$ will be monitored under the CWC. There are 879 different chemicals represented in this family (Table 1). Other chemical warfare agents will also be covered within families of chemicals, resulting in several thousand chemicals to be monitored. For the majority of these chemicals, analytical data are not available. This raises the question of how to verify that these chemicals are not being produced by the chemical industry.

Table 1. Members in the alkyl methylphosphonofluoridate family



$CH_3\text{—}P(=O)(F)\text{—}OC_nH_{2n+1}$

$n = 1\text{–}10$

n	Molecular mass	No. in family[A]	n	Molecular mass	No. in family[A]
1	112	1	6	182	17
2	126	1	7	196	39
3	140	2	8	210	89
4	154	4	9	224	211
5	168	8	10	238	507

[A] Based on number of alcohols in $C_nH_{2n+1}OH$.[3]

In this paper, we have examined the problem of detection of family members, using the sarin family as an example. In particular, we have synthesized the alkyl methylphosphonofluoridates corresponding to 60 commercially available aliphatic alcohols (from C_2H_5OH to $C_{10}H_{21}OH$) and studied their mass spectra to identify the general features in the spectra that may assist in the development of a pattern classifier. We have used this information subsequently to develop a classification procedure that would be suitable for rapid on-site screening for this family of chemicals, and which would discriminate against unrelated chemicals.

Electron Ionization Mass Spectra of Alkyl Methylphosphonofluoridates

Previously Reported Results

The electron ionization (e.i.) mass spectra of sarin and soman have been reported by Sass and Fisher.[4] Neither compound gave a molecular ion, which is consistent with the electron ionization mass spectra of organophosphorus chemicals generally.[5] The highest ion observed in the mass spectrum of sarin was that of m/z 125 $[M-CH_3]^+$, with intensity of 25%, due to methyl cleavage with hydrogen rearrangement. The highest ion observed for soman was that of m/z 126 $[M-C_4H_8]^+$, with intensity 88%, as a result of alkyl rearrangement and subsequent loss of isobutene. For both sarin and soman the base peak of m/z 99 was due to the ion $[CH_5FO_2P]^+$.

The mass spectra of an additional nine alkyl methylphosphonofluoridates, ranging from $n = 1$ (that is, methyl ester) to $n = 7$ (heptyl ester) have also been

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[3] Henze, H. R., and Blair, C. M., *J. Am. Chem. Soc.*, 1931, **53**, 3042.

[4] Sass, S., and Fisher, T. L., *Org. Mass Spectrom.*, 1979, **14**, 257.

[5] Gillis, R. G., and Occolowitz J. L., 'Mass Spectrometry of Phosphorus Compounds', in Halman, M., (Ed.) 'Analytical Chemistry of Phosphorus Compounds' p. 295 (Interscience: New York 1972).

reported, without discussion.[6] The spectrum of the methyl ester exhibited a small molecular ion (m/z 112, 5%), a small $[M-CH_3]^+$ (m/z 97, 8%) and a base peak of m/z 82, due to $[CH_4FOP]^+$. The spectra of the other eight esters were characterized by a base peak of m/z 99 and by the absence of a molecular ion.

General Features of the E.I. Mass Spectra

The e.i. fragmentation of the alkyl methylphosphonofluoridates, $CH_3P(O)(F)OC_nH_{2n+1}$, where $n = 2$–10, are characterized by the absence of a molecular ion. The base peak is typically (but not always) of m/z 99, depending on the branching of the alkyl chain.

Depending on the value of n, and the degree and location of branching of the alkyl side chain, ions with m/z values greater than 99 are observed from one or more of the following ion series.

(A) m/z 111, 125, 139, 153, 167 corresponding to ions with the compositions $[C_2H_5FO_2P]^+$, $[C_3H_7FO_2P]^+$, $[C_4H_9FO_2P]^+$, $[C_5H_{11}FO_2P]^+$ and $[C_6H_{13}FO_2P]^+$.

(B) m/z 112, 126, 140, 154, 168 corresponding to ions with the compositions $[C_2H_6FO_2P]^+$, $[C_3H_8FO_2P]^+$, $[C_4H_{10}FO_2P]^+$, $[C_5H_{12}FO_2P]^+$ and $[C_6H_{14}FO_2P]^+$.

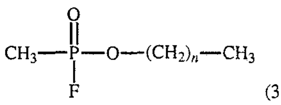
(C) m/z 112, 126 and 140 corresponding to alkene ions $[C_8H_{16}]^+$, $[C_9H_{18}]^+$ and $[C_{10}H_{20}]^+$, derived from the alkyl side chain of the alkyl methylphosphonofluoridate (for $n = 8$, 9 and 10 respectively), and related daughter ions of m/z 111 (resulting from loss of CH_3 from $[C_9H_{18}]^+$ ion and loss of C_2H_5 from $[C_{10}H_{20}]^+$) and m/z 125 (resulting from loss of CH_3 from $[C_{10}H_{20}]^+$).

As the alkyl group becomes larger, ions originating from the alkyl group (that is, containing only C and H) become a more dominating feature of the spectra. In general, as the chain becomes more branched, the intensities of the $[C_nH_{2n}]^+$ ion and associated daughter ions increase.

Preliminary examination of these mass spectra indicates that they may usefully be divided into sub-categories based on the branching of the C 1 and C 2 positions. In each sub-category (i)–(iii) discussed below, a typical spectrum is illustrated, and, where appropriate, a spectrum is also presented of a chemical in this sub-category that does not display these general features.

(i) *Primary C 1 Alkyl Methylphosphonofluoridates*

(A) *Alkyl (3).*—The mass spectra of these chemicals are characterized by the absence of a molecular ion, the presence of a base peak of m/z 99 and a weak ion of m/z 125 $[C_3H_7FO_2P]^+$. Other minor peaks are often observed at m/z 111 $[C_2H_5FO_2P]^+$, 112 $[C_2H_6FO_2P]^+$, 126 $[C_3H_8FO_2P]^+$ and 139 $[C_4H_9FO_2P]^+$, due to hydrogen rearrangement with loss of either alkane or alkene fragments from the side chain. These fragment ions all contain the P(O)F backbone structure characteristic of alkyl methylphosphonofluoridates. In addition, low mass ions



$$CH_3-\overset{\overset{O}{\|}}{\underset{\underset{F}{|}}{P}}-O-(CH_2)_n-CH_3$$

(3) $n = 0$–9

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[6] 'Identification of Potential Organophosphorus Warfare Agents' (The Ministry of Foreign Affairs of Finland: Helsinki 1979).

of *m/z* 41, 55, 69 and 83 associated with hydrocarbon ions are a feature of these spectra, particularly for the higher molecular weight homologues. A typical spectrum is the hexyl ester (3; $n = 5$) (Fig. 1). The ion of *m/z* 81 (due to CH_3FOP) becomes progressively less intense as the alkyl chain length increases (for example, ethyl ester, *m/z* 81, 50%; decyl ester, *m/z* 81, 10%).

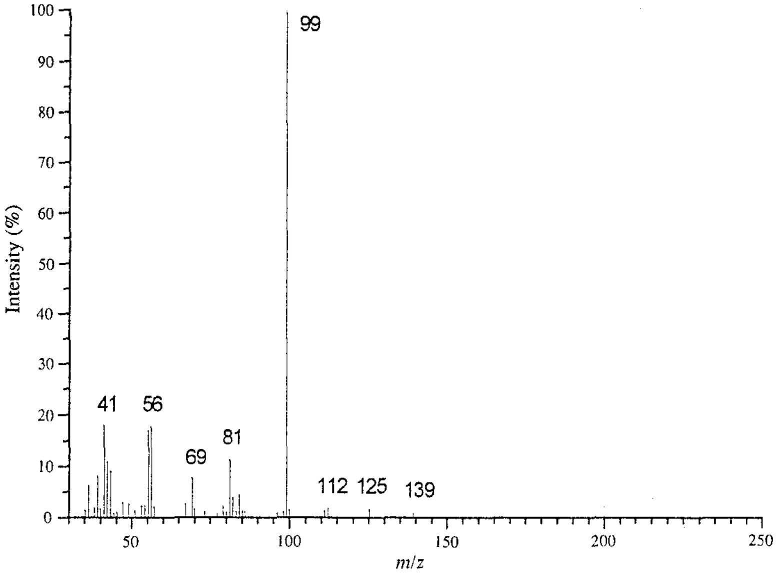
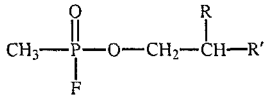


Fig. 1. E.i. mass spectrum of hexyl methylphosphonofluoridate (molecular mass 182 u).

(B) *Other primary C 1*.—The eight chemicals in this sub-category [see (4)] were all substituted at the ester C 2 position.


$$CH_3-\underset{F}{\overset{O}{\overset{\|}{P}}}-O-CH_2-\overset{R}{CH}-R'$$

(4)

The spectra of these chemicals are typically characterized by intense ions of *m/z* 99 and 112. A typical spectrum is that of the 2-ethylbutyl ester (Fig. 2). In this case the *m/z* 112 ion has the composition $[C_2H_6FO_2P]^+$ (determined by high resolution), due to cleavage of the bond between C 1 and C 2, with hydrogen rearrangement. In other cases, for example, the 2-propylpentyl ester, the peak also includes ions with the composition $[C_8H_{16}]^+$ (determined by high resolution to be in the ratio 5 : 1 for $[C_2H_6FO_2P]^+$ with respect to $[C_8H_{16}]^+$).

The *m/z* 112 ion varies in intensity, but for C_4–C_6 substituents it constitutes greater than 65% of the base peak intensity, with the highly branched 2,2-dimethylpropyl ester giving a base peak of *m/z* 112. The only spectrum of a chemical in this sub-category without an intense *m/z* 112 ion is the 2,4,4-trimethylpentyl ester, with an intensity of only 4% of the base peak. In this case, it appears that the branching at C 4 favours sequential losses of C_4H_9 and C_4H_6 to give an ion of *m/z* 99, and loss of CH_3 from $[C_8H_{16}]^+$ to give an intense ion of *m/z* 97.

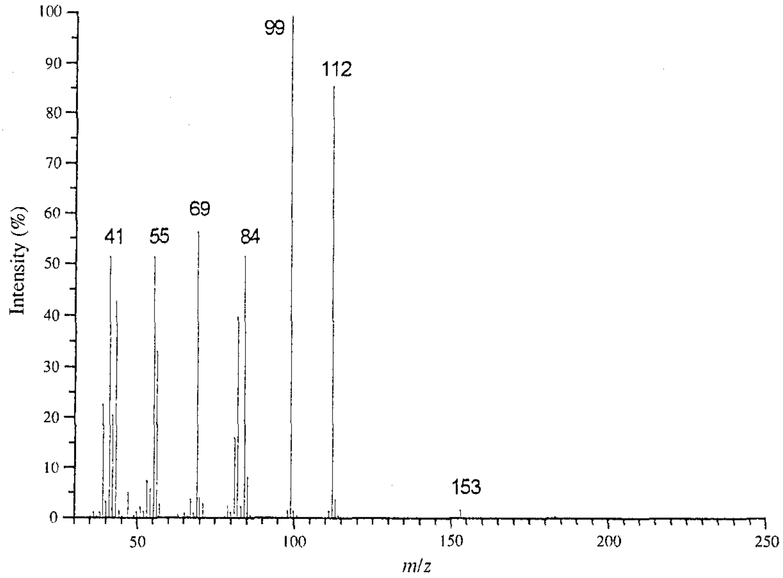
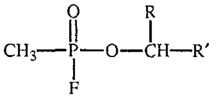


Fig. 2. E.i. mass spectrum of 2-ethylbutyl methylphosphonofluoridate (molecular mass 182 u).

(ii) *Secondary C1 Alkyl Methylphosphonofluoridates (5)*

The typical spectrum of these alkyl methylphosphonofluoridates with a single branch at C1 is the 1-methylpentyl ester (Fig. 3), which is characterized by an intense ion of m/z 125 (corresponding to rupture of the bond between C1 and C2), a base peak of m/z 99, and peaks due to $[C_nH_{2n}]^+$ and related daughter ions.



$CH_3-P(=O)(F)-O-CH(R)-R'$

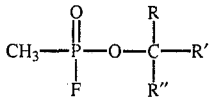
(5)

In some cases, additional branching along the carbon chain has very limited effect on the spectrum (for example, the 1,3-dimethylbutyl ester) other than enhancing the hydrocarbon peaks as a result of branch position stabilization.

However, in other cases, additional branching along the carbon chain can have a very significant effect. For example, in the spectrum of the 1,5-dimethylhexyl ester (Fig. 4), the intensity of the ion of m/z 99 is approximately 30% of the base peak, and the spectrum is dominated by hydrocarbon ions of m/z 41 $[C_3H_5]^+$, 55 $[C_4H_7]^+$, 56 $[C_4H_8]^+$, 69 $[C_5H_9]^+$, 70 $[C_5H_{10}]^+$, 84 $[C_6H_{12}]^+$ and 97 $[C_7H_{13}]^+$.

(iii) *Tertiary C1 Alkyl Methylphosphonofluoridates (6)*

The typical mass spectrum of this group of chemicals is characterized by the absence of a molecular ion, small peaks corresponding to the loss of alkyl



$CH_3-P(=O)(F)-O-C(R)(R'')-R'$

(6)

fragments from the molecular ion, and an intense ion (between 20% and base peak) of m/z 99. There are also prominent peaks due to the alkene rearrangement ion $[C_nH_{2n}]^+$ and $[C_nH_{2n+1}]^+$ which is formed by simple cleavage of the C–O bond (for example, the 1,1-dimethylpropyl ester, Fig. 5).

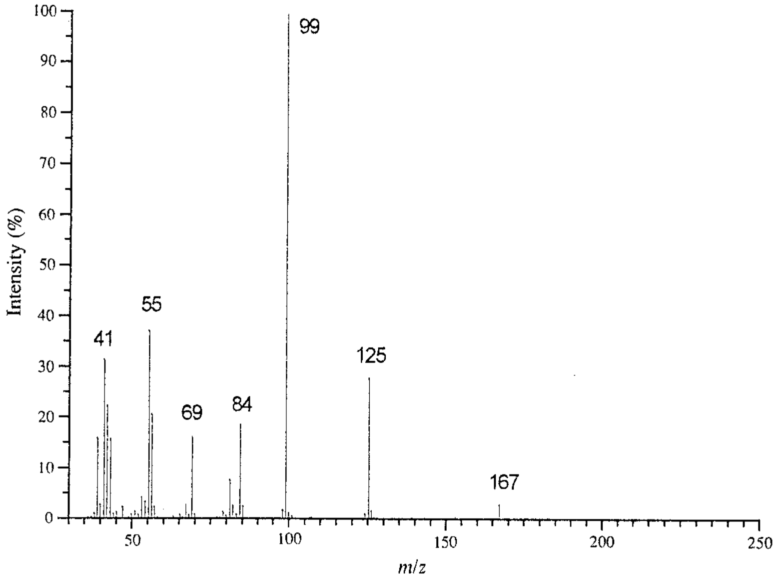


Fig. 3. E.i. mass spectrum of 1-methylpentyl methylphosphonofluoridate (molecular mass 182 u).

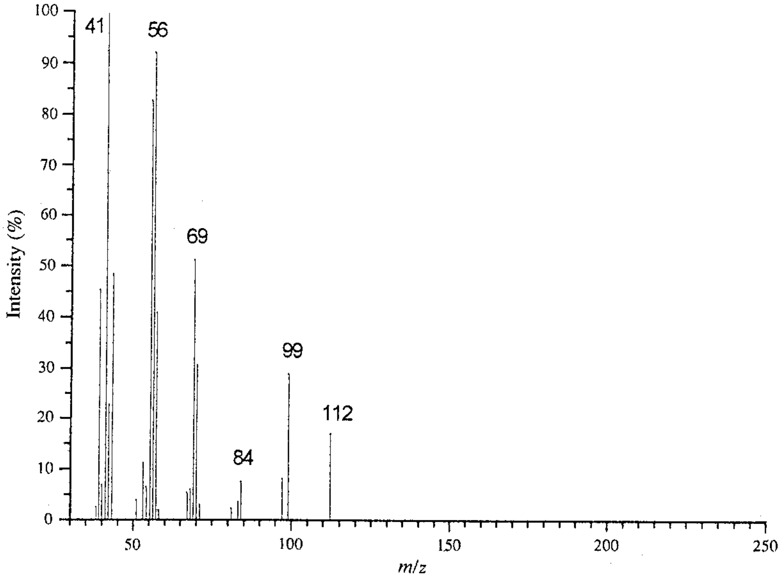


Fig. 4. E.i. mass spectrum of 1,5-dimethylhexyl methylphosphonofluoridate (molecular mass 210 u).

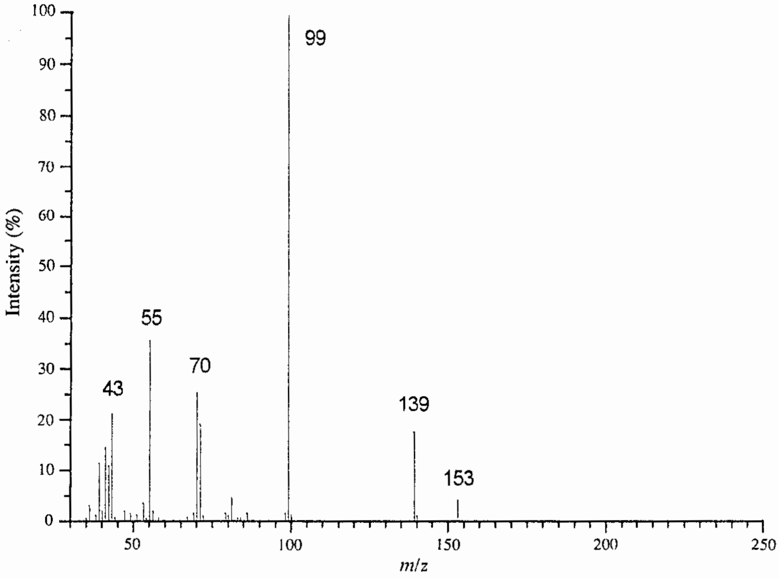


Fig. 5. E.i. mass spectrum of 1,1-dimethylpropyl methylphosphonofluoridate (molecular mass 168 u).

However, the spectra of this group are significantly affected by the extent of branching in the alkyl chain, as illustrated by the spectrum of the 1,1-diethyl-2,2-dimethylpropyl ester (Fig. 6), which has neither a $C_8H_{16}^+$ nor a $C_8H_{17}^+$ ion, but loses neutral hydrocarbon fragments to give intense ions of m/z 140 and 125

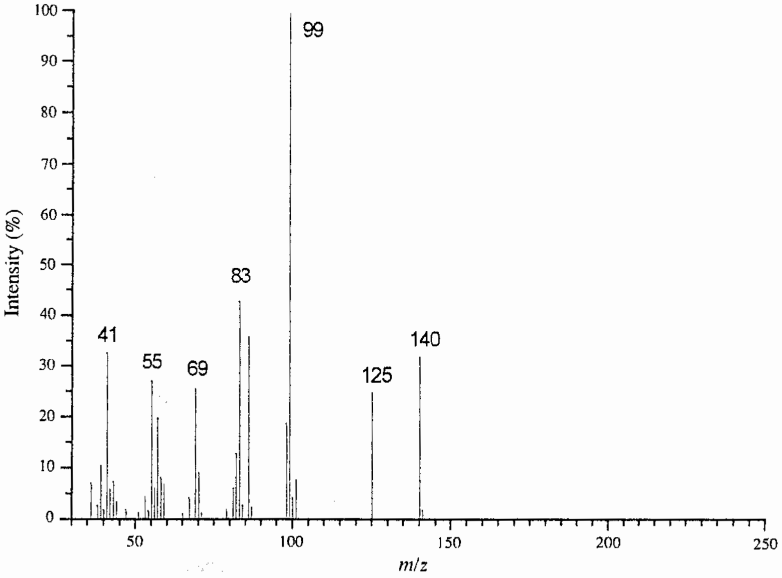


Fig. 6. E.i. mass spectrum of 1,1-diethyl-2,2-dimethylpropyl methylphosphonofluoridate (molecular mass 224 u).

with compositions $[C_4H_{10}FO_2P]^+$ and $[C_3H_7FO_2P]^+$ respectively, in addition to the base peak of *m/z* 99. Comparison of this spectrum with the spectrum of the 1-ethyl-1,5-dimethylhexyl ester (Fig. 7) provides a useful example of the care that is required when comparing apparent similarities in the mass spectra of alkyl methylphosphonofluoridates. In the latter case, the ion of *m/z* 140 has the composition $C_{10}H_{20}$.

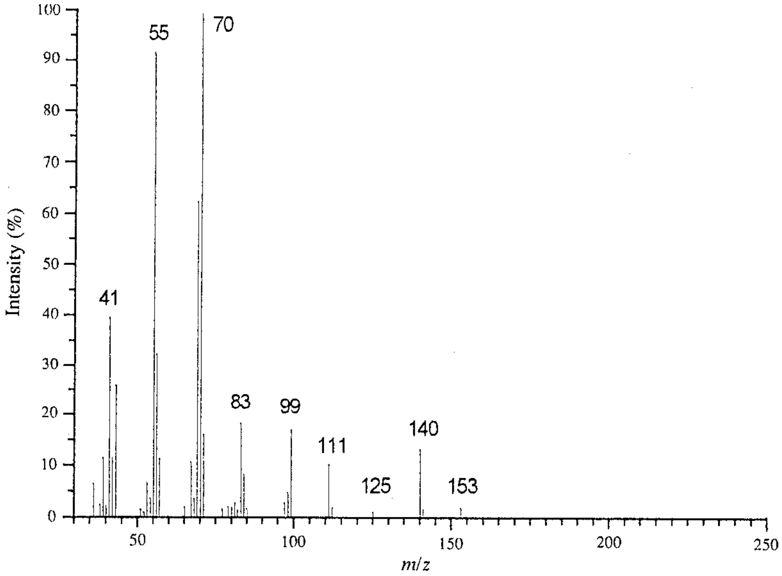


Fig. 7. E.i. mass spectrum of 1-ethyl-1,5-dimethylhexyl methylphosphonofluoridate (molecular mass 238 u).

Chemical Ionization Mass Spectra of Alkyl Methylphosphonofluoridates

In the chemical ionization (c.i.) mass spectra of sarin and soman, intense $[M+H]^+$ ions have been observed with isobutane reagent gas.[6] With ammonia c.i., the pseudomolecular ion $[M+H]^+$ and ammonium adduct ion $[M+NH_4]^+$ have been reported to be very intense in the sarin mass spectrum (base peak and 67% respectively) and less intense in the soman spectrum (10 and 20% respectively).[7]

The ammonia c.i. spectra obtained for the alkyl methylphosphonofluoridates synthesized in the current project all indicated formation of the $[M+NH_4]^+$ ion, with a base peak of $[M+NH_4]^+$ for all except the highly branched homologues. For these highly branched members, an ion of *m/z* 116 becomes more prominent, particularly where there is substitution on the α-carbon. The ion of *m/z* 116 is probably due to fragmentation of the $[M+NH_4]^+$ ion to give the ammonia adduct ion corresponding to the prominent *m/z* 99 ion observed in the e.i. mass spectra of these compounds.

[7] D'Agostino, P. A., and Provost, L. R., *Biomed. Environ. Mass Spectrom.*, 1986, **13**, 231.

Preliminary Classification System for the CWC Monitoring System

Two of the methods which have been suggested as suitable for on-site chemical analysis during CWC inspections are gas chromatography–mass spectrometry (g.c.–m.s.) with e.i. and c.i. capability, and gas chromatography equipped with a flame photometric detector (g.c.–f.p.d.) for the detection of phosphorus or sulfur-containing chemicals.[8]

Concerns have been expressed that, because analytical data are not available for the majority of chemicals in the families of chemicals covered by the CWC, 'the analyst would be faced with the horrendous task of identifying all compounds containing phosphorus, including intermediates, by-products, and impurities in order to decide whether or not they belonged to the families covered by the CWC'.[9] Industry personnel have also expressed concern at the potential loss of confidential information from such an intrusive analysis.[2]

We have previously developed reliable pattern classifiers for the presence of a number of structural features, based on application of various pattern recognition methods with low-resolution mass spectra.[10,11] We have now developed a preliminary rapid screening procedure of the 60 alkyl methylphosphonofluoridates based on g.c.–m.s. (e.i. and c.i.) and g.c.–f.p.d., which resulted in correct classification of each of the alkyl methylphosphonofluoridates synthesized in this project, without confusion with any of the chemicals represented in the 130000 spectra Wiley Library.[12]

We are currently extending this work, both in the further development and refinement of the alkyl methylphosphonofluoridate family classifier, and we are also extending this general approach to the classification of other families of chemicals that will be covered by the CWC.

Experimental

All 60 alkyl methylphosphonofluoridates were synthesized by a modified standard method for the synthesis of sarin.[13] An equimolar solution (1·00 ml) of methylphosphonyl difluoride ($MePOF_2$)/methylphosphonyl dichloride ($MePOCl_2$) (35% $MePOF_2$/35% $MePOCl_2$/30% dichloromethane by volume) was added to $1\cdot71\times10^{-3}$ mol of each high purity alcohol (>98%, Aldrich Chemical Company). A further 0·2 g (2×10^{-3} mol) of triethanolamine dissolved in 1·0 ml of dichloromethane was added to remove acid generated by the reaction mixture. This mixture was allowed to react under an atmosphere of nitrogen gas at ambient temperature for 7 days. Tertiary alcohol mixtures, as an exception, were refluxed for 2 h. Sufficient alkyl methylphosphonofluoridate product was formed in all cases to enable identification by g.c.–m.s. analysis of the crude reaction mixture. **Caution: sarin, soman and the alkyl methylphosphonofluoridate family are potent anticholinesterases and extreme care must be taken when working with them.**

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[8] Conference on Disarmament, Report of the Technical Group on Instrumentation, United Nations Document CD/CW/WP.272, Geneva, January 1990.

[9] 'Standard Operating Procedures for the Verification of Chemical Disarmament: D.2. Second Proposal for Procedures Supporting the Reference Database' (The Ministry of Foreign Affairs of Finland: Helsinki 1989).

[10] Mathews, R. J., *Aust. J. Chem.*, 1973, **26**, 1955.

[11] Mathews, R. J., *Int. J. Mass Spectrom. Ion Phys.*, 1975, **17**, 217.

[12] Borrett, V. T., Mathews, R. J., and Mattsson, E. R., Classification Scheme for On-site Screening of Families of Scheduled Chemicals, Proceedings of the U.S. Army Scientific Conference on Chemical Defense Research, Edgewood, Maryland, 16–19 November 1993.

[13] Bryant, P. J. R., Ford-Moore, A. H., Perry, B. J., Wardrop, A. W. H., and Watkins, T. F., *J. Chem. Soc.*, 1960, 1553.

G.c.–m.s. analyses were performed on a Varian 3700 gas chromatograph equipped with a 25 m 0·22 mm BP-5 (SGE Australia) capillary column, a Grob split/splitless injector and a direct capillary interface. The gas chromatograph injector and the g.c.–m.s. interface were maintained at 260°C. Temperature programming was achieved by using a 10°/min rate for 20 min from an initial temperature of 50°C. High purity helium, at a flow rate of 30 $\mathrm{cm}^3\ \mathrm{s}^{-1}$, was used as the carrier gas.

Mass spectra were obtained on a VG7035 (VG Analytical) EB double sector mass spectrometer by using exponential down scanning from 400 to 20 u at a rate of 0·2 s/decade with a 0·5 s interscan delay, accelerating voltage 4 kV, and a resolution of 450 (10% valley definition). Electron ionization conditions: electron energy 70 eV; emission current 100 μA; source temperature 180°C. Chemical ionization conditions: electron energy 100 eV; emission current 500 μA; source temperature 100–130°C. High-resolution data were acquired at a resolution of 4500 (10% valley definition) and by using scans of the accelerating voltage V and electrostatic voltage E at constant V/E ratio and constant magnetic field. Perfluorokerosene was used as the calibrant for peak matching. Data were acquired on a DEC PDP8/A computer.

Accessory Publication

A full set of data has been deposited. Copies are available from the Australian Journal of Chemistry, P.O. Box 89, East Melbourne, Vic. 3002.