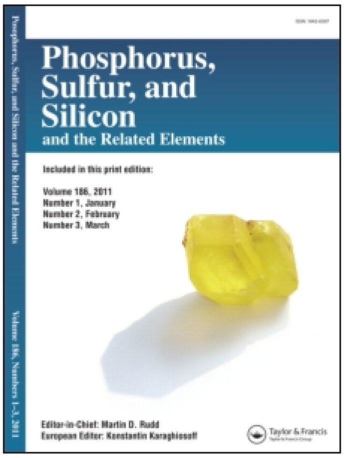

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ANALYSIS OF CHEMICAL NEUTRALIZATION PRODUCTS OF PHOSPHONOTHIOLATES BY GAS CHROMATOGRAPHY MASS SPECTROMETRY

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A series of phosphonothiolates, including the highly toxic O-Ethyl-S-(2-diisopropylamino) ethyl methylphosphonothioate (VX), have been subjected to chemical neutralization reaction with metallic sodium. The phosphonothiolates decompose to their respective phosphonic and phosphonothioic acids and this results in the detoxification of VX. GC/MS technique in both EI and CI mode has been applied for reaction monitoring and final identification of the neutralization products formed in this reaction.

Keywords: Chemical ionization; chemical neutralization; disulphide; electron ionization; GC/MS; phosphonic acid; phosphonothiolates; sodium; thiophosphonic acid; VX

Chemical warfare agents either can be destroyed by incineration or neutralized by chemical reaction to produce nonlethal or nontoxic products, which can be disposed of safely, or postprocessed.[1] O-Alkyl methylphosphonothiolates constitute one of the most lethal classes of "nerve agents" represented by O-ethyl S(2-diisopropylamino)ethyl methylphosphonothiolate commonly known as VX (**1**) which is a highly toxic chemical and can stop respiratory and nervous functions and can kill in minutes.[2]

VX can be neutralized effectively by the use of bleach at low pH, where VX readily dissolves in acidic solutions; on the other hand the solubility of VX is reduced significantly at higher pH. Hydrolysis catalyzed

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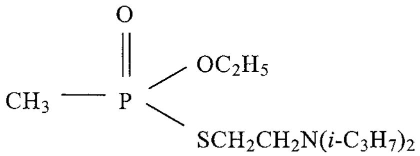
by base is one of the most widely used neutralization reaction for nerve agents. VX ($pK_a = 9$) dissolves in pure water to form a basic solution and the solubility of VX decreases significantly as the solution becomes more basic, leading to very slow rate of hydrolysis.[3] Another approach for the neutralization of VX is oxidation of the sulfur atom. But on oxidation, nitrogen present in VX is predominantly oxidized to the stable N-oxide, which is still toxic.[4] Thus, the neutralization of VX by oxidation is not the method of choice. Nano-size MgO, CaO, and Al_2O_3 also have been used for the neutralization of VX.[5–7] These reactions are analogous to their solution behavior,[3] with two exceptions: The first is that the corresponding nontoxic phosphonate products reside as surface bound complexes; the second, and most notable exception, is that toxic EA-2192 which forms under basic hydrolysis[8,9] is not observed in these reactions. VX also has been neutralized and decontaminated by using metal ions supported on zeolites. Silver and sodium exchanged zeolites have been used to enhance the rate of decomposition of VX and related compounds at ambient temperature.[10,11] Recently, desulfurization of alkyl and alkyl-aryl organ sulfur compounds with sodium was reported resulting in the formation of corresponding alkanes and small amounts of alkylmercaptans.[12] Our interest in detoxification of highly-toxic VX and related phosphonothiolates prompted us to apply this method for the chemical neutralization of these compounds. In this study we selected VX (**1**), and some structurally related phosphonothiolates as shown in Figure 1.

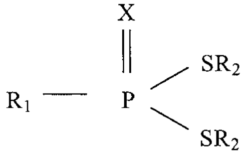
RESULTS AND DISCUSSION

The total chemical neutralization was achieved within 120 min. The chemical neutralization of VX (**1**) yielded nontoxic products namely N,N-diisoprylaminoethyl disulfide (**1a**), methylphosphonic acid (**1b**), O-ethyl methylphosphonic acid (**1c**), methylthiophosphonic acid (**1d**), and O-ethyl methylthiophosphonic acid (**1e**). All the phosphonic acids were identified as their trimethylsilyl derivatives both in EI and CI modes. **1a** was observed only while monitoring the neutralization reaction with GC/MS-EI, but after doing the work-up of the reaction mixture, **1a** could not be detected either in organic or aqueous layer. This may have been due to further desulfurization.

The neutralization of S,S-dialkyl alkylphosphonothiolates (**2–8**) produced their respective disulfides (**2a–8a**), alkylphosphonic acids (**2b–8b**), and alkylthiophosphonic acid (**2c–8c**). The acids were identified on the basis of EI and CI data of their silylated derivatives. In **5** we detected S-butyl isopropylthiophosphonic acid (**5d**) as its trimethylsilyl



VX (I)



	X	R1	R2
(2)	O	CH_3	n-C_4H_9
(3)	O	C_2H_5	n-C_4H_9
(4)	O	n-C_3H_7	n-C_4H_9
(5)	O	i-C_3H_7	n-C_4H_9
(6)	O	C_2H_5	n-C_3H_7
(7)	O	n-C_3H_7	n-C_3H_7
(8)	O	i-C_3H_7	n-C_3H_7
(9)	S	CH_3	n-C_3H_7

FIGURE 1 Structures of phosphonothiolates subjected to chemical neutralization reaction.

derivative which was formed most probably due to incomplete desulphurisation.

The neutralization reaction of S,S-dipropyl methylthiophosphonothiolate (**9**) yields not only its corresponding disulfide (**9a**) but also tri- and tetra-sulfides (**9b** and **9c**) respectively. The other neutralization products obtained from **9** were methylthiophosphonic acid (**9d**) and methyl phosphonic acid (**9e**) identified as their trimethylsilyl derivative by GC/MS.

In all these neutralization reactions, we observed disulfides only while monitoring the reaction products before work-up; however, after giving extended reaction time or after the addition of methanol, these disulfides disappear and only corresponding alkylphosphonic acids and alkylthiophosphonic acids were detected by GC/MS as their

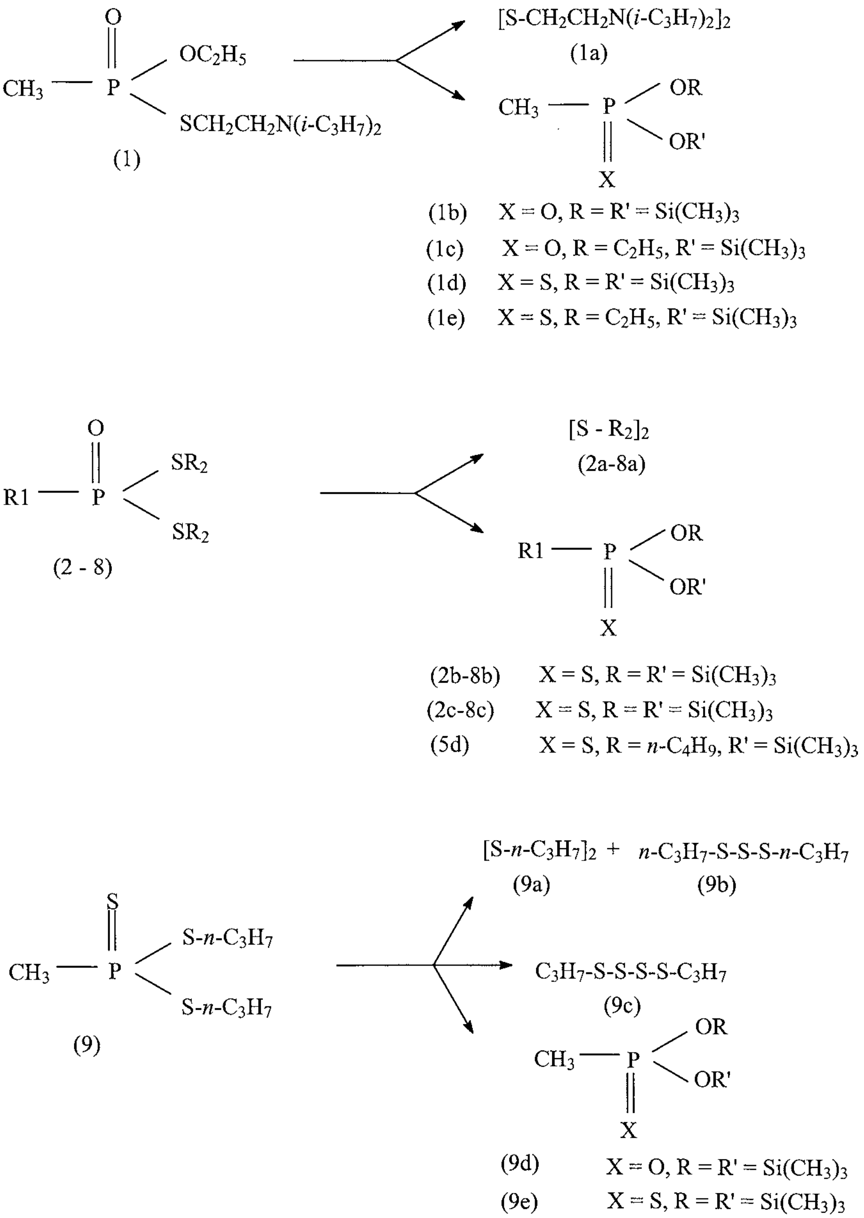


FIGURE 2 Products obtained on chemical neutralization reaction of **1–9** as confirmed by GC/MS.

TABLE I EI and CI MS Data of the Compounds Detected from Chemical Neutralization of **1–9**

Compd. no.	Molecular weight	EI mass spectrum (m/z)	CI MS $(M+H)^+$
1a	320	42, 72, 89, 114 (100%), 160, 174, 189, 285	321
1b, **2b**, **9d**	240	59, 73, 105, 133, 147, 181, 209, 225 (100%), 240 $(M^{+\cdot})$	241
1c	196	61, 75, 121, 137, 153 (100%), 169, 181, 196 $(M^{+\cdot})$	197
1d, **2c**, **9e**	256	73, 93, 113, 133, 147, 241 (100%), 256 $(M^{+\cdot})$	257
1e	212	56, 73, 121, 137, 153, 169 (100%), 197, 212 $(M^{+\cdot})$	213
2a, **3a**, **4a**, **5a**	178	57, 87, 122, 178 (100%), $(M^{+\cdot})$	179
6a, **7a**, **8a**, **9a**	150	66, 78, 108, 150 (100%) $(M^{+\cdot})$	151
3b, **6b**	254	73, 121, 135, 147, 195, 211, 226, 239 (100%), 254 $(M^{+\cdot})$	255
4b, **7b**	268	73, 135, 195, 211, 225, 237, 253 (100%), 268 $(M^{+\cdot})$	269
5b, **8b**	268	73, 135, 147, 195, 211, 226, 253 (100%), 268 $(M^{+\cdot})$	269
5d	284	73, 121, 133, 147, 209 (100%), 242, 269, 284 $(M^{+\cdot})$	285
9b	182	55, 64, 100, 111, 140, 182 (100%) $(M^{+\cdot})$	183
9c	214	65, 70, 104, 130, 142, 193, 214 (100%) $(M^{+\cdot})$	215

trimethylsilyl derivatives. The disulphides perhaps undergo further desulfurization to give alkenes, which were not detected. The EI and CI mass spectral data of various phosphonothiolates obtained from the neutralization reaction are presented in Table I.

Chemical neutralization with sodium metal may thus be a useful reaction for the complete decontamination of thiophosphonates including the highly toxic compounds such as VX. The mass spectral data in both EI and CI for various degradation products can be used for the detection of the compounds even in the reaction mixture.

EXPERIMENTAL

Synthesis of Phosphonothiolates

O-Ethyl-S- [2-(diisopropylamino) ethyl] methylphosphonothiolate (VX) was synthesized inhouse according to literature procedure[13] and the final structure and purity was checked by GC/MS and ^{1}H-NMR. (*Caution*: VX is synthesized in a special laboratory, built mainly for synthesis of highly-toxic compounds. Full body protection including breathing protection is worn when handling the agent, which includes both synthesis work and the neutralization reaction.)

Dialkyl alkylphosphonothiolates (**2–8**) and dialkyl alkylthiophosphonothiolate (**9**) were synthesized according to the literature procedure[14–16] and the final structure and purity were checked by GC/MS and ^{1}H-NMR.

Desulphurization Reaction

Sodium (0.1 mmol) and phosphonothiolates (0.01 mmol) were taken in a solvent (10 mL) [decane for **1**, **2**, **5** and dodecane for **3**, **4**, **6–9**] in a 50 mL two-necked, round-bottom flask fitted with a condenser. The reaction mixture, monitored by GC/MS in EI mode, was vigorously stirred and refluxed till the substrate was totally consumed. After cooling the reaction mixture to room temperature, unreacted sodium was destroyed with methanol at 0°C. Saturated aqueous NH_4Cl (50 mL) was added to the mixture.

Extraction and Derivatization

After the addition of saturated aqueous NH_4Cl solution, the aqueous and organic layers were separated using separating funnel. The organic layer was analyzed by GC/MS in both EI and CI modes as such while the aqueous layer was extracted with diethyl ether and analyzed after concentration. This layer was later silylated with BSTFA at 80°C for 120 min and subjected to GC/MS analysis.

One portion of the aqueous layer was evaporated to dryness on rotavapour followed by reconstitution with acidic methanol (HCl/methanol –0.5N). It was further evaporated to dryness and silylated for GC/MS analysis. Another portion of the aqueous layer after evaporation to dryness was reconstituted with alkaline methanol (1% triethylamine/methanol). It was further evaporated to dryness and silylated for GC/MS analysis.

GC/MS Analysis

The GC/MS analyses were performed by Varian 3400 GC coupled to a TSQ 7000 mass spectrometer (Finnigan Mat). GC operating conditions were as follows: injector temperature 250°C, transfer line temperature 280°C, column temperature programming 50°C (2 min)—@10°C/min-280°C (5 min), carrier gas helium at pressure of 10 psi. EI mass spectrometric operating conditions were as follows: ion source pressure 1.5×10^{-6} torr, source temperature 150°C, electron energy 70 eV, and emission current 400 μA. CI mass spectrometric operating conditions were as follows: ion source pressure with methane as the reagent gas 1.5×10^{-3} torr, source temperature 150°C, electron energy 100 eV, and emission current 300 μA.

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