Group 13 chelates in nerve gas agent and pesticide dealkylation†

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Received (in Durham, UK) 5th November 2007, Accepted 31st January 2008
First published as an Advance Article on the web 5th March 2008
DOI: 10.1039/b717041f

Schiff base boron and aluminium bromides have been used to cleave organophosphate nerve agents and pesticides and their simulants: salben(^{t}Bu)[BBr_2]$_2$ was very effective in cleaving the VX simulants EMPPT and DEPPT and nerve agent VX; salen(^{t}Bu)AlBr was effective in cleaving the nerve agents VX and Soman and the pesticide Diazinon.

Decontamination of nerve gases is required in battlefields, laboratories, storage and destruction sites. Organophosphate pesticides are the most widely used type of pesticide and have replaced the environmentally persistent organochlorine reagents. Despite their potential environmental problems the use of organophosphate pesticides has been increasing and is predicted to increase in the future because of the lack of suitable substitutes.[1] Long-lived pesticides pose a threat when they spread beyond their intended application.

Nerve gases can be destroyed by bleach through oxidation to less toxic inorganic phosphates, and alkali through hydrolysis of the P–O or P–S bond.[2,3] One disadvantage of using bleach is that a large excess is required. Also the active chlorine content of bleach solutions decreases with time. Moreover, bleach is indiscriminately corrosive to any surface or compound it comes into contact with. Base hydrolysis also has some limitations, such as the requirement for large quantities to maintain a high pH level. Also VX (*O*-ethyl-*S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate) has low solubility in alkaline solution and reacts with base very slowly. Catalytic hydrolyses involving metal ions (*e.g.*, Cu^{2+}, Ag^{+}, Hg^{2+}).[2,4–6] and enzymes (*e.g.*, organophosphorus acid anhydrases).[2,7–11] have been proposed but they have limitations too. For example, Cu(II) has limited capability for the hydrolysis of VX whereas Ag^{+} is too expensive and Hg^{2+} is too toxic to be used as a decontamination agent. The enzyme organophosphorus hydrolase (OPH) is highly efficient for the hydrolysis of organophosphorus pesticides but has much lower efficiency for the hydrolysis of VX (k_{cat} = 0.3 s^{-1}).[12]

Nanocrystalline metal oxides as catalysts for nerve agent destruction have also been investigated by various researchers,[13–15] and more recently, studies conducted at the US Army Edgewood Chemical and Biological Center at Aberdeen Proving Ground, Maryland, have shown aqueous solutions of aluminium sulfate and sodium aluminate buffered to pH 4 to be very promising for destroying large quantities of VX, GB and GD.[16] The search for alternative agents for decontamination of organophosphate nerve agents and pesticides still continues.

Many of the toxic nerve agents and pesticides possess a P–O–C linkage in their structure. Cleaving the P–O–C bond could be a means of deactivating these toxic agents.[2,3] This is convenient due to the nucleophilicity of the phosphorus and polar nature of the P–O and C–O bonds. Previously, it was shown that binuclear boron halide chelate compounds can dealkylate a wide range of phosphates at ambient temperature.[17–19] For example, salpen(^{t}Bu)[BBr_2]$_2$ dealkylates $(MeO)_3P(O)$ by 89% and $(^nBuO)_3P(O)$ by 99% in only 30 min.[17] This is significant considering the fact that BCl_3 or BBr_3 alone are ineffective for phosphate dealkylation. In the dealkylation reaction MeCl or MeBr is produced along with several potential phosphate-containing chelate compounds. The reaction can be monitored by comparing the ^{1}H NMR peak integration of methyl halide to that of the original phosphate. It was also shown that mononuclear Schiff base aluminium compounds such as salen(^{t}Bu)AlBr could dealkylate organophosphate esters under mild conditions.[20] Herein are reported the results obtained from dealkylation studies on actual nerve agents and pesticides and their simulants with boron and aluminium salen chelate compounds combined in a 1 : 1 stoichiometry.

Two Salen(^{t}Bu) compounds of boron and aluminium salben(^{t}Bu)[BBr_2]$_2$ (**1**) and salen(^{t}Bu)AlBr (**2**) (Fig. 1) were used to study the the P–O–C bond cleavage in a series of organophosphate nerve agents and pesticides and their simulants. The nerve agents used were VX, Sarin (*O*-isopropyl methylphosphonofluoridate, GB) and Soman (3,3-dimethyl-2-

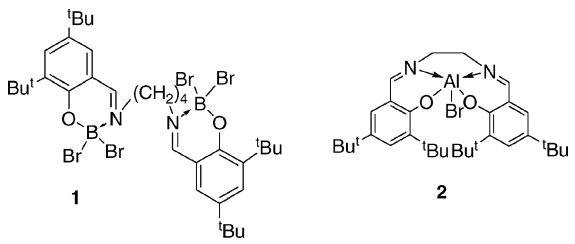

Fig. 1 The compounds used as dealkylating agents: salben(^{t}Bu)-[BBr_2]$_2$ (**1**) and salen(^{t}Bu)AlBr (**2**).

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† Dedicated to Jerry Atwood on the occasion of his 65th birthday.

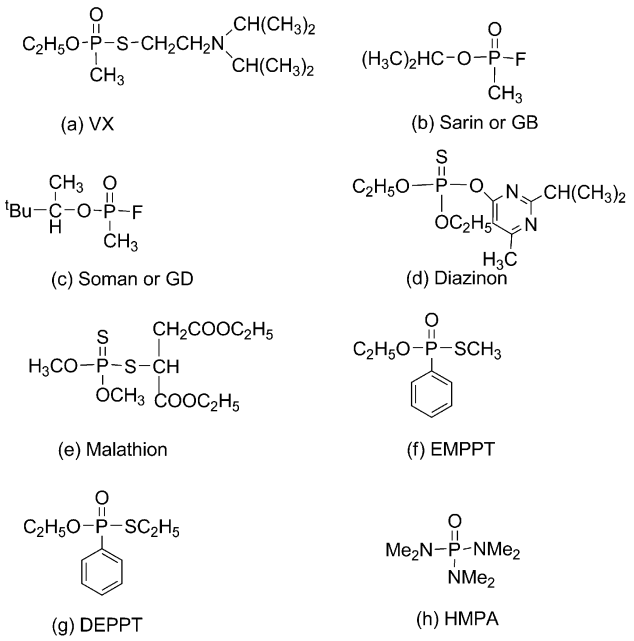

Fig. 2 Structures of the compounds studied.

butyl methylphosphonofluoridate, GD). The nerve agent simulants used were EMPPT (*O*-ethyl-*S*-methyl phenylphosphonothioate), DEPPT (*O*,*S*-diethyl phenylphosphonothioate) and HMPA (hexamethylphosphoramide). The pesticides were Diazinon and Malathion (Fig. 2).

VX, GB, and GD were obtained from Aberdeen Proving Ground (APG), MD. Reactions with chemical warfare agents were conducted on site at Edgewood Chemical and Biological Center at APG by trained personnel using applicable safety precautions. Studies on nerve gas agents must be conducted in government approved laboratories.

Proton NMR spectra were collected on samples prepared directly in NMR tubes (507-PP Wilmad Glass, Inc.) using a Bruker AVANCE 300 MHz NMR spectrometer fitted with a 5 mm broadband probe. Simulants were combined in equimolar quantities with salben(^{t}Bu)[BBr_2]$_2$ or salen(^{t}Bu)AlBr in 5 mm NMR tubes at ambient temperature in $CDCl_3$ and allowed to stand for at least 30 min as described in the literature.[17–20] Similar experiments conducted on VX, GD, and GB in $CDCl_3$ were done in 4 mm sleeves which were flame-sealed and placed in 5 mm NMR tubes which were also flame sealed prior to placing in the probe.

The reaction was monitored by the disappearance of the alkoxy peak of the phosphate and appearance of the alkyl peak of the alkyl bromide in the ^{1}H NMR spectrum and the percent conversion was calculated from the integration values. For example, with VX the α-ethoxy proton peak appears as a multiplet centered near δ 4.15 ppm prior to reaction with compound **1**. After 0.7 h following treatment with compound **1**, this peak is observed along with the α-methylene proton peak of ethyl bromide at δ 3.45 ppm (See Fig. 3).

Binuclear boron compound **1** was very effective in cleaving the phosphate ester bond of the simulants EMPPT (100% conversion in 1.5 h) and DEPPT (70.8% in 1 h) although it did not cleave HMPA. HMPA was investigated to see if compounds **1** or **2** showed any activity toward cleaving P–N–C, which neither compound did. However, for the three nerve agents, **1** was effective in cleaving only VX whereas GB and GD remained practically uncleaved. Headspace GC/MS further supported these observations by showing no isopropyl bromide in the GB reaction mixture with **1**, but it was detected in the GB reaction mixture with **2**. Ethyl bromide was detected in the VX mixtures with both **1** and **2**. GD was not tested. The reduced reactivity with Sarin and Soman could be explained by the presence of a highly electronegative fluorine atom attached to the phosphorus in either GB or GD. The fluorine reduces the nucleophilicity of the phosphoryl oxygen, thus inhibiting the formation of a phosphate coordinated cation. Cation formation was found to be required as the first step in phosphate cleaving by boron[19] and aluminium[20] Salen compounds. Neither of the pesticides Diazinon and Malathion were cleaved effectively with **1**. Both of the pesticides have P═S instead of P═O bonds. The weaker coordination with boron to sulfur compared to oxygen might be responsible for the lack of cleavage by boron compound **1**. The salen aluminium compound **2** showed dealkylation for all of the reagents but malathion. It showed significant dealkylation for VX and Soman. It is also interesting to note that **1** showed the highest activity for VX but could not cleave the isopropoxy group in GB or the 3,3-dimethylbutyl group in GD, whereas **2** showed moderate cleaving activity (24.5% in 1.2 h for Sarin and 62.6% in 6.2 h for Soman) in spite of the unfavorable electronic factor of the fluorine attached to the phosphorus. Although Diazinon was not effectively cleaved by the boron compound (**1**) (only 10.3%) it was moderately cleaved (46.7% in 1 h) with the aluminium compound **2**. This is a reflection of the better coordination of the sulfur in the P═S group with aluminium than with boron. That the salen aluminium compound was not effective in cleaving the model compounds DEPPT and EMPPT could not be explained based on the present experimental data.

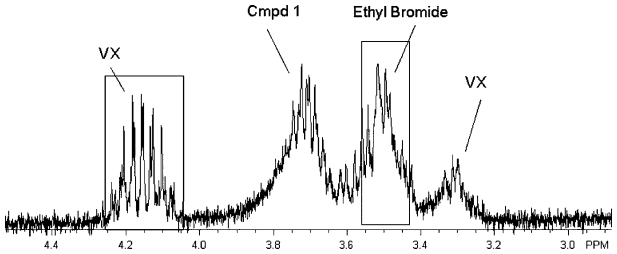

Fig. 3 ^{1}H-Spectrum of VX 0.7 h after treatment with compound **1**. Integration area assessed shown in blocks.

Tracking the reactions using ^{31}P NMR spectroscopy had limited value in that some of the reaction products may be precipitating from solution. This was noted especially for the VX mixtures which showed proton resonances corresponding to ethyl bromide, the presence of which was supported by headspace GC/MS, but showed no ^{31}P resonance corresponding to the well-known dealkylated version of VX also known as *S*-[2-(diisopropylamino)ethyl] methylphosphonothioic acid or EA-2192. Sarin, on the other hand, did show a fluorinated species of unknown identity in the reaction mixture with **2**

Table 1 Percent dealkylation observed with boron and aluminium bromide chelates. (Standard deviations from multiple integration determinations are given in parentheses)[a]

		Salben(^{t}Bu)[BBr_2]$_2$		Salen(^{t}Bu)AlBr	
	Alkyl group	%	Time/h	%	Time/h
VX	Ethyl	74.7(7)	0.7	57.1(1)	3.9
GB	*i*-Propyl	0	1.0	24.5(2)	1.2
GD	Pinacolyl	0	6.5	62.6(2)	6.2
Diazinon	Ethyl	10.3(6)	1.7	46.7(3)	1.0
Malathion	Methyl	0	0.5	0	2.0
EMPPT	Ethyl	100	1.5	10.5(1)	0.7
DEPPT	Ethyl	70.8(4)	1.0	10.1(7)	1.2
HMPA	Methyl	0	1.3	0	1.2

[a] VX = *O*-ethyl-*S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate; GB or Sarin = *O*-isopropyl methylphosphonofluoridate; Soman or GD = 3,3-dimethyl-2-butyl methylphosphonofluoridate; DEPPT = *O*,*S*-diethyl phenylphosphonothioate; EMPPT = *O*-ethyl-*S*-methyl phenylphosphonothioate; HMPA = hexamethylphosphoramide.

which may have been a complexed species of either Sarin itself or of some other derivative.

In conclusion, binuclear boron Salen compound salben (^{t}Bu)[BBr_2]$_2$ and mononuclear aluminium Salen compound salen(^{t}Bu)AlBr have been used for the dealkylation reactions of nerve gas agents and pesticides and their simulants under very mild conditions. The salen boron compound was very effective in cleaving the VX simulants EMPPT and DEPPT and nerve agent VX. The salen aluminium compound was effective in cleaving the nerve agents VX and GD and the pesticide Diazinon. Neither of the two salen compounds could cleave the P–N–C bond in HMPA. This study is the first application of any Schiff base chelate compound to the cleaving of nerve gas agents and pesticides (Table 1) Note that all of these reactions were conducted in equimolar quantities. It would be expected that much greater P–O–C bond cleavage would take place in shorter periods of time using and excess of the salen chelate. These studies are currently being conducted.

Acknowledgements

This work was supported by the Kentucky Science and Engineering Foundation (KSEF grant 148-502-04-100). Partial support from the University of Kentucky Tracy Farmer Center for the Environment is acknowledged.

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