Decontamination of Chemical Warfare Agents

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I. Introduction

Decontamination, aimed at eliminating the hazard of chemical warfare agents, is required on the battlefield as well as in laboratories, pilot plants, and chemical agent production, storage, and destruction sites. The majority of research is focused on battlefield conditions where speed and ease of application of the decontaminant are essential. Battlefield decontamination is the rapid removal of chemical agents from military vehicles, equipment, personnel, and facilities by both chemical and physical methods. Consequently, a solid surface on which chemical agents are deposited is the primary target for decontamination. The nature of the surface and the surface–agent interactions are major concerns in the design of a decontamination system.[1] Some surfaces can be easily penetrated by agents and the embedded agents are more difficult to remove than those residing on the surface.[2] Variables affecting agent diffusion such as contamination time (residence time of the agent on the surface), temperature, and contamination density (the surface density of the agent in mass per unit surface area) are also important parameters for the design of the decontamination process. Furthermore, the decontaminants must not be corrosive so that the surfaces are not damaged after decontamination. It is clear that both chemistry and engineering are required in the design of a decontamination system.

In this review, the chemical reactions of four major chemical warfare agents (1–4, Scheme I) with both the existing field decontaminants and the decontamination systems currently under investigation are described. These chemical agents are the focus of this review because of the toxicities and persistencies of these agents[3] and because of the large stockpile quantities of 1–3. HD (1) is a blistering agent that attacks the mucous membranes and is lethal at high doses.[4] The "nerve" agents VX (2), GB (3), and GD (4) can stop respiratory and nervous functions and can kill in minutes. VX as well as GB consists of two stereoisomers, whereas GD has four stereoisomers, although not all the stereoisomers are responsible for the observed toxicities.[5] The reaction chemistry of these agents is shared by a range of organic compounds such as bivalent sulfides, alkyl chlorides, organophosphorus esters, and pesticides. Since most of these compounds also react with the decontaminants, there is a broad interest in decontamination chemistry from the chemical community. For example, oxidation of sulfur has been used to detoxify HD; nucleophilic substitution at the pentavalent phosphorus has been used to detoxify the nerve agents 2–4; and enzymes have been used to catalyze the hydrolysis of the G agents (2 and 3).

Since the kinetics and mechanisms of the above organic and enzymatic reactions are strongly affected by the solvent property, the solvent system of a decontaminant (i.e. decontamination medium) is an important controlling variable for the decontamination reaction. An optimum medium is one that can both dissolve the agents and promote the desired reaction. Furthermore, the medium is sometimes required to dissolve the "thickened" agent. Chemical agents such as HD and GD are often "thickened" by mixing with 5–10% of a polymer (thickener).[6] The thickened agents are more viscous and adhere better to surfaces than the "neat" agents, making themselves more difficult to remove. It was observed that upon contact with water, a polymer film can form at the interface of the thickened agent and water. This interfacial phenomenon prevents the thickened agent from dissolving into most aqueous solutions. The possible presence of a thickener in the agent adds a significant constraint to the design of the decontamination medium.

Reactive decontaminants are usually more effective than the nonreactive ones because agent removal is more complete at increased speed. However, depending on the resources available on the battlefield, decontamination can also be accomplished by physical methods such as mechanical forces, dissolution, evaporation, or absorption in the absence of any chemical conversions. For example, a surface can be decontaminated by

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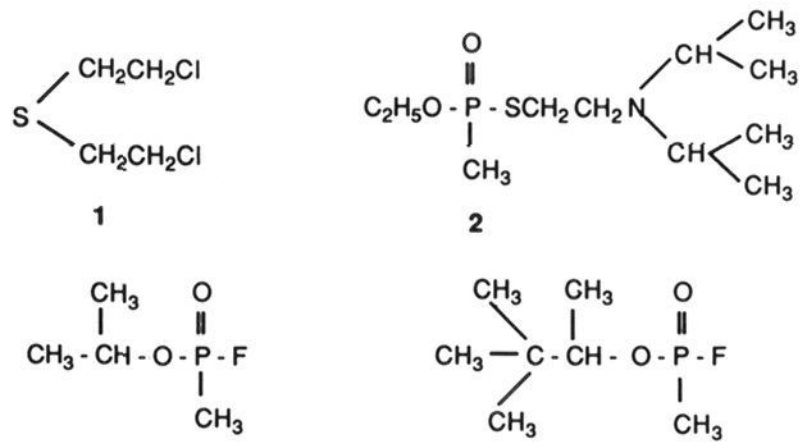
James A. Baker was born in rural Illinois and obtained his B.S. degree in Chemistry from the University of Missouri at Rolla in 1964. He then went to the University of Wisconsin (Madison) to work with Prof. H. Muxfeldt on natural product synthesis. Muxfeldt moved his group to Cornell University in 1967 and Jim finished his Ph.D. thesis on the total synthesis of 1-deoxylycorine in 1969. After a brief tour in the Army he joined the staff of Edgewood Arsenal. For the last four years he has been the Chief of the Decontamination Systems Division at the U.S. Army CRDEC. On October 1, 1992, he became the Chief Scientist of Research and Technology and is responsible for the basic research programs in chemical and biological defense at the Center.

J. Richard Ward received his undergraduate training in Chemistry at the University of Delaware graduating with a B.S. in 1964. He did his graduate studies under Professor Albert Heim at Penn State University and at the State University of New York at Stony Brook obtaining his Ph.D. in 1969. He fulfilled an ROTC commitment through service in the Army Chemical Corps in 1969–1970. He accepted a position as a research chemist with the U.S. Army Ballistic Research Laboratory (BRL) at Aberdeen Proving Ground, MD, in 1971. After ten years at BRL, he moved to the Chemical Research, Development and Engineering Center (CRDEC) where he performed research on the decontamination of chemical agents. He is presently Chief of the Chemical Division in the Research Directorate of CRDEC.

Scheme I. Structures of HD, VX, GB, and GD[a]



[a] (1) 2,2′-Dichlorodiethyl sulfide (H, HD, mustard, mustard gas, S mustard, or sulfur mustard). (2) *O*-Ethyl *S*-2-(diisopropylamino)ethyl methylphosphonothiolate (VX). (3) 2-Propyl methylphosphonofluoridate (GB or Sarin). (4) 3,3-Dimethyl-2-butyl methylphosphonofluoridate (GD or Soman).

scrubbing, spraying with a soap solution, spraying with a steam jet, or covering with carbonaceous materials. Although only the reactions of agents with decontaminants are emphasized in this paper, one should be aware that battlefield decontamination can also be achieved by nonreactive systems.

II. Development of Decontamination Systems

A. Early Decontaminants

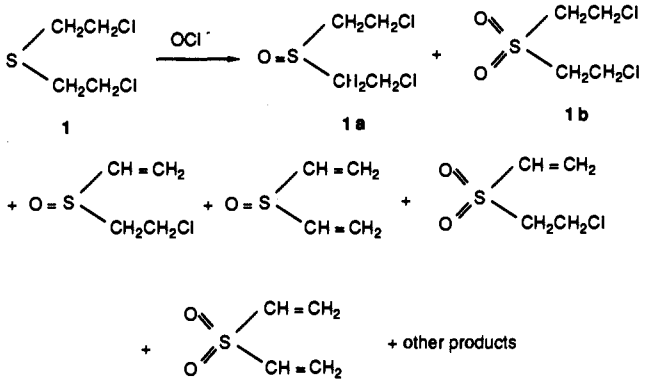
The requirement for chemical agent decontamination dates back to World War I when Germany unleashed HD on Allied troops at Ypres, France in 1915.[7] Prior to that time, the poisonous chemicals used on the battlefield, such as chlorine, were nonpersistent gases and required no decontamination. The first decontaminants used were bleaching powders (see Table I) and, to a lesser extent, potassium permanganate. The reactions of chemical agents with excess bleach are so vigorous[8] that both neat and thickened agents can be converted to less or nontoxic products at the liquid–liquid (bleach solution) or liquid–solid (bleach powder) interface in a few minutes. Solubilization of the agents in the same medium as the bleach is not required. As shown in Scheme II, HD is converted into a series of oxidation and elimination products. It is believed that the sulfoxide (**1a**) is formed first, followed by sulfone (**1b**) formation. Subsequently, both oxidation products undergo elimination reactions in the strongly basic solution to produce the corresponding monovinyl and divinyl sulfoxides and sulfones, although small amounts of additional unidentified products are also present in the final solution.[9]

By World War II, superchlorinated bleaches, as shown in Table I, were the most common general purpose decontaminants. However, there are some disadvantages to using bleach as a decontaminant: (a) the active chlorine content of the bleach gradually decreases with

Table I. Decontaminants Composed of Hypochlorites

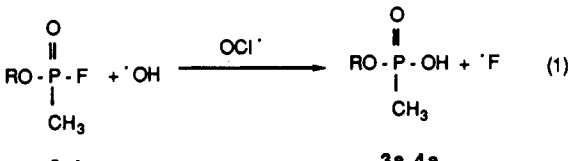
decontaminant	composition	applications
bleach	2–6 wt % NaOCl in water	skin and equipment
HTH (high test hypochlorite)	$Ca(OCl)Cl + Ca(OCl)_2$ as a solid powder or a 7% queous slurry	equipment and terrain
STB (super tropical bleach)	$Ca(OCl)_2 + CaO$ as a solid powder or as 7, 13, 40, and 70 wt % aqueous slurries	equipment and terrain
Dutch powder	$Ca(OCl)_2 + MgO$	skin and equipment
ASH (activated solution of hypochlorite)	0.5% $Ca(OCl)_2$ + 0.5% sodium dihydrogen phosphate buffer + 0.05% detergent in water	skin and equipment
SLASH (self-limiting activated solution of hypochlorite)	0.5% $Ca(OCl)_2$ + 1.0% sodium citrate + 0.2% citrate acid + 0.05% detergent in water	skin and equipment

Scheme II. Reaction Products from HD and Hypochlorite Anion



storage time so that a fresh solution must be prepared prior to each use; (b) a large amount of bleach is required for the oxidation of the agents; and, most importantly, (c) bleach is corrosive to many surfaces. As a result, buffered bleach solutions, as shown in Table I, and the more stable, less alkaline N-chloro compounds (i.e., chloramines or Fichlor, to be discussed later) have been used to overcome some of these difficulties.

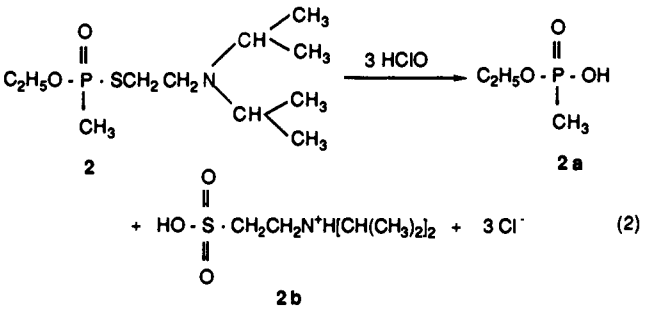
Following World War II, the Allied countries discovered German research efforts on G agents which inhibit acetylcholinesterase (AchE)[3] and are more lethal than HD. These G agents were found to be rapidly detoxified in solutions of alkali salts (e.g., Na_2CO_3, NaOH, or KOH) by conversion to the corresponding phosphonic acids as shown in eq 1.[10] Since acid is



(1)

produced, excess hydroxide ion is required for the reaction to go to completion rapidly. Furthermore, these G agents could also be rapidly detoxified in bleach solutions. As reported by Epstein et al.,[11] the hypochlorite anion behaved as a catalyst for the reaction shown in eq 1.

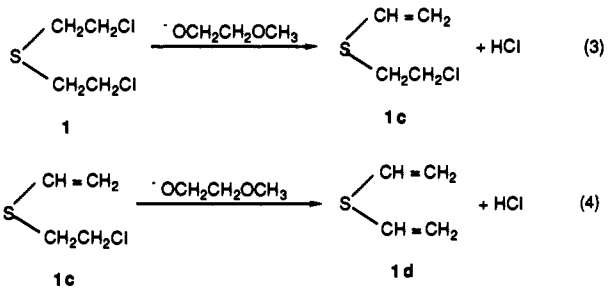
Bleach can also be used for the decontamination of VX particularly under low pH. VX readily dissolves in acidic solutions via protonation of the nitrogen while the sulfur is oxidized by HClO rapidly. As shown in eq 2, only 3 mol of active chlorine are consumed for each mole of VX. At high pH, on the other hand, the solubility of VX is significantly reduced. The deprotonated nitrogen is oxidized accompanied by the evolution of chlorine or oxygen gas and the formation of sulfate and carbonate salts. More than 10 mol of active chlorine are required to oxidize 1 mol of VX under these basic conditions. Despite the long history of alkaline bleach solutions as general purpose decontaminants for the chemical warfare agents, the precise stoichiometry at high pH has not been determined for VX.[12]



(2)

B. Decontamination Solution 2 (DS2)

After World War II, the search for a new decontaminant began as a result of the concern over the ineffectiveness of bleach solutions in cold weather operations. Development of the new decontaminant was initiated in 1951, and the result, DS2, was adopted in 1960.[13] DS2 is a general purpose, ready to use, reactive decontaminant with long-term storage stability and a large operating temperature range (−15 to 125 °F or −26 to 52 °C). This polar, nonaqueous liquid is composed, by weight, of 70% diethylenetriamine (**5**, $H_2NCH_2CH_2NHCH_2CH_2NH_2$), 28% ethylene glycol monomethyl ether (**6**, $CH_3OCH_2CH_2OH$), and 2% sodium hydroxide. The reactive component in DS2 was found to be the conjugate base of **6**, $CH_3OCH_2CH_2O^-$ (**6a**). At ambient temperatures, **6a** reacts instantaneously with all four agents. The reactions with HD are shown in eqs 3 and 4. Since both reactions are

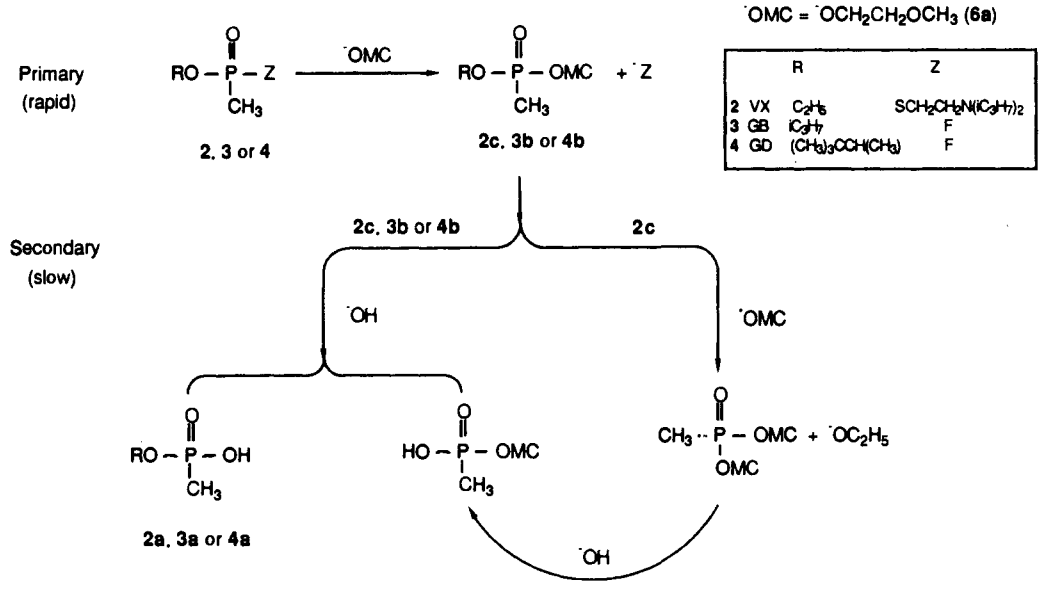


(3)

(4)

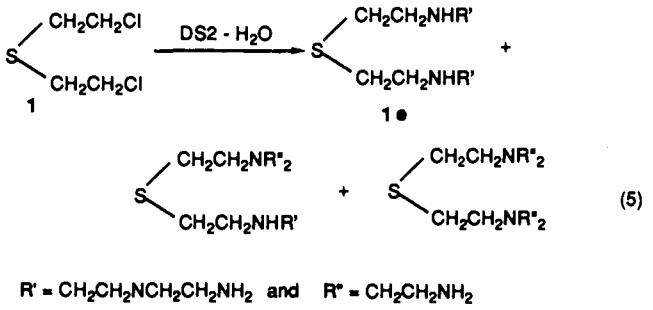
complete within 1 min at room temperature, **1d** from double elimination was observed as the only product,

Scheme III. Reactions of VX, GB, and GD with DS2



while 1c was predicted as an intermediate.[14] The nerve agents 2–4 also react with 6a rapidly to form the diesters 2c, 3b, and 4b as the primary products in Scheme III. With time, these diesters further decompose in DS2 via slower secondary reactions to form 2a, 3a, 4a, and other final products.[14] These reactions are less important since the agents have already been detoxified by the primary reaction.

While DS2 is a highly effective decontaminant and is noncorrosive to most metal surfaces, it can damage paints as well as plastics, rubber, and leather materials. To minimize these problems, the decontamination contact time of DS2 with most painted surfaces is limited to 30 min, followed by a water rinse. DS2 is also corrosive to skin, and 6 has demonstrated teratogenicity in rats. Personnel handling DS2 are required to wear respirators with eye shields and chemically protective gloves in order to avoid skin contact. After exposure to air or to relatively large amounts of water, DS2 rapidly degrades. The carbon dioxide in air is quickly absorbed by 5 to form colloidal ammonium carbonates which cause the solution to become viscous. When sufficient amounts of water are added to DS2, the reactant 6a is deactivated to 6. HD is most sensitive to the depletion of 6a in DS2. Instead of reacting with 6a via elimination, HD reacts slowly with 5 by an S_n1 mechanism to form predominantly 1e and small amounts of related substitution products shown in eq 5.[14]

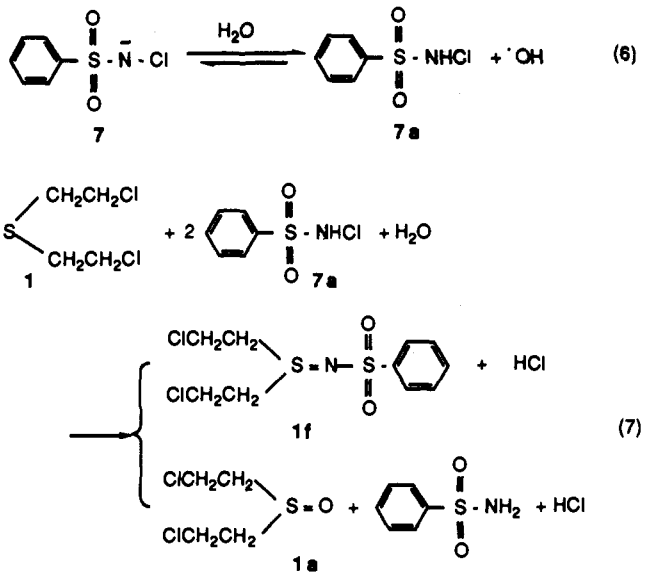


R' = $CH_2CH_2NCH_2CH_2NH_2$ and R" = $CH_2CH_2NH_2$

C. Decontaminants for Skin and Personal Equipment

The earliest decontaminants used on skin utilized bleaches, usually in dry form, in which the hydrochlorite salt was diluted with an inert solid such as silica. In 1973, a personal decontamination kit was recovered from Soviet vehicles used by Egypt in the Yom Kippur War.[15] This kit was reputed to be very effective against thickened GD. The Army mimicked the decontamination reaction in the Soviet kit and produced the M258 system in 1974 as well as the M258A1 and M280 systems in the 1980s (Table II). These kits consist of two sealed packets. Packet I contains a towelette prewetted with a decontamination solution of 72% ethanol, 10% phenol, 5% NaOH, 0.2% ammonia, and about 12% water by weight. Packet II contains a towelette impregnated with chloramine-B ($PhS(O)_2NClNa$, 7, see eq 6) and a sealed glass ampule filled with a solution of 5% $ZnCl_2$, 45% ethanol, and 50% water by weight. The ampule in packet II is broken and the towelette wetted with the solution immediately prior to use. The two wetted towelettes are used consecutively to wipe skin and personal items such as contaminated masks, hoods, gloves, overboots, and weapons.

Towellete I is effective against the G agents via rapid nucleophilic substitutions at the phosphorus. The fluoride ion in 3 or 4 is displaced by the phenoxide, ethoxide, and hydroxide anions to form, respectively, the corresponding diesters and the methylphosphonic acid 3a or 4a as shown in eq 1.[16a] The same reactions with VX are very slow. Towellete II is designed to decontaminate both HD and VX by rapid oxidation with 7. The oxidation proceeds by a different mechanism than that observed with bleach. As shown in eq 6, 7 dissolves in water to produce 7a and ^-OH; the pK_a of 7 is 9.5.[17] However, the presence of the $ZnCl_2$ maintains the pH of solution II between 5 and 6. The sulfur in HD attacks the chlorine in 7a to form a transient chlorosulfonium ion which rapidly reacts with the anion $PhS(O)_2N^-H$ to form the sulfimide (1f, eq 7), and with H_2O to form mustard sulfoxide (1a). The observed overall reaction is shown in eq 7.



VX, which contains a tertiary amino group (pK_a = 9), reacts with the chloramine-B only when the solution is sufficiently acidic so that both reactants are protonated. It was found that VX did not react with the chloramine-B in towellete II because the pH of the solution appeared to be increased by the presence of VX.[16a] In practice, VX is believed to be physically removed from the skin or equipment by the wiping action and by solubilization in the solution. A recent study[16b] showed that in an unbuffered aqueous solution of 0.2 M 7, about 50% of the 0.01 M VX hydrolyzed within a few days. At this point, sufficient acidic products are accumulated to protonate 7 which then reacted rapidly with the remaining VX. The study further showed that 0.01 M VX reacted with 0.1 M 7 in the presence of 0.25 M H_2SO_4 to give a pseudo-first-order rate behavior (Figure 1). In addition to the phosphonic and sulfonic acids (**2a** and **2b**, respectively), a sulfimide **2d** (see Scheme IV) is also produced in the final reaction mixture.[16b] This indicates that, similar to the reaction with HD, the first step in the VX

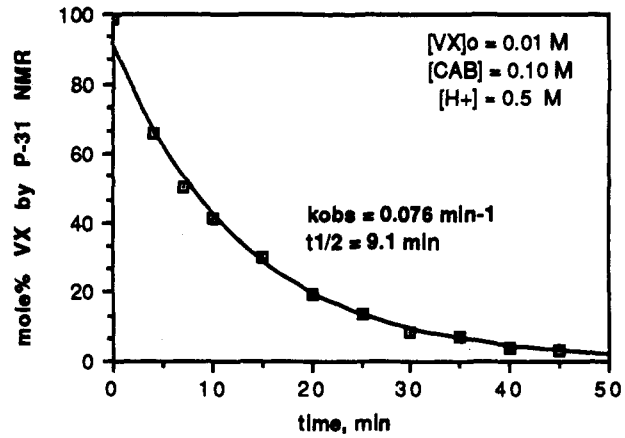


Figure 1. Reaction profile of VX and chloramine-B in acidic solution at 18 °C.

oxidation is also the formation of a chlorosulfonium ion intermediate. This intermediate rapidly reacts with both the anionic sulfonamide and H_2O to form the observed products.

On the other hand, an aqueous solution of a commercial *N*-chloro oxidant, Fichlor (sodium *N*,*N*-dichloroisocyanurate) detoxifies VX effectively by simple oxidation according to eq 8. Similar to bleach at low pH, HClO is believed to be the reactive species. Since the pH of the Fichlor solution is about 6, detoxification of G agents by this method is too slow to be effective.

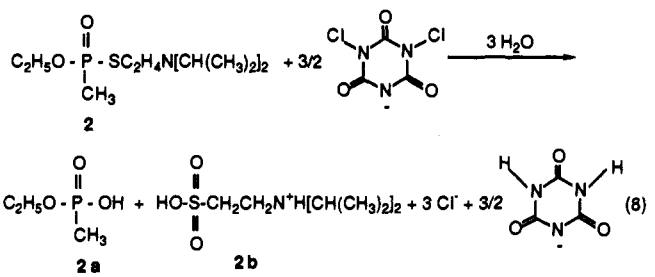


Table II contains a summary list of the decontamination systems and equipment currently available in

Scheme IV. The Reaction of VX and Chloramine-B in Acidic Solution

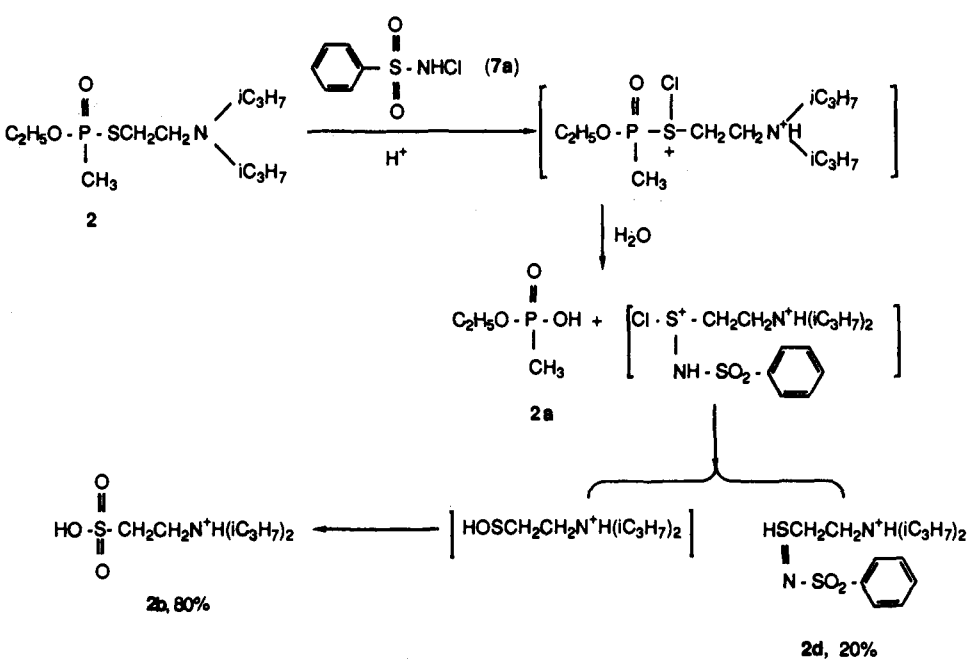


Table II. Field Decontamination Equipment and Systems

item name	description	decontaminants	applications
ABC-M11, decontaminating apparatus, portable	a fire extinguisher-like device to spray DS2; Comes with mounting bracket for attaching to vehicles	1.5 qt (1.3 L) DS2	vehicle and equipment
ABC-M12A1, decontamination apparatus, power-driven, skid-mounted	includes pump, tank, personnel shower units, and M2 water heater	water, foam, deicing liquid, DS2, or STB	washing, deicing, and showering
M258A1, decon kit, personal	consists of foil-packaged pairs of towelettes in a plastic carrying case	I. water, phenol, NaOH, ethanol, and ammonia II. water, ethanol, chloramine-B, and $ZnCl_2$	skin and individual equipment
M280, decon kit, individual equipment	consists of 20 foil-packaged pairs of towelettes in a plastic carrying case	I. water, phenol, NaOH, ethanol, and amminia II. water, ethanol, chloramine-B, and $ZnCl_2$	individual equipment
M291, skin decon kit	consists of 6 foil-packaged nonwoven fiber pads filled with XE-555 resins	2.8 g of XE-555 resins of a total water content of 25 wt %	skin
M13, decon apparatus, portable	self-contained device with a disposable 14-liter DS2 container; can be mounted to the standard fuel can which mounts on vehicles and equipment	DS2	vehicle and equipment
M17, transportable, lightweight, decon system	draws water from any natural source within 30-ft distance and less than 9-ft below pump level; delivers water at pressures up to 689 kPa and temperatures up to 120 °C; includes hoses, cleaning jets, personnel showers, and collapsible rubberized fabric tank	water	equipment, vehicle, and personnel

the U.S. Army inventory. The health hazard posed by the standard decontaminant, DS2, along with the extensive use of nonmetal materials (e.g. laminates and composites) for military equipment has intensified the need for a new liquid decontaminant. The discussion that follows highlights some of the recent research efforts aimed at identifying better decontamination systems.

III. Fundamental Reactions of Agents

In research laboratories, agent–decontaminant reactions are frequently investigated by monitoring the disappearance of agent in the decontaminant. The laboratory techniques are usually titrametric methods, GC, or GLC analyses of the agent in quenched, diluted, and solvent-extracted samples. Novel reaction paths and unstable reaction intermediates are difficult to detect by such methods. The recent application of high-field, multinuclear FTNMR, GC/MS, and direct exposure probe mass spectrometry (DEP/MS) techniques has shed new light on the reaction chemistry of agents. As will be presented in the following sections, parallel and competing reaction pathways as well as the formation of complicated reaction intermediates have been found in many of the fundamental reactions of the agents. This improved understanding of agent chemistry has made the evaluation and prediction of new decontamination systems much more accurate.

A. Chemical Agent Simulants

In order to gain a more complete understanding of agent chemistry, it is often necessary to study the reactions of a series of agent analogs under the same conditions. For example, the monofunctional derivatives of mustard, $RSCH_2CH_2Cl$ (8, R = methyl, ethyl, or phenyl) and $RSCH_2CH_2X$ (X = tosylate, brosylate, Br^-, I^-, or other leaving group), react via the same mechanisms as those of HD, but their reaction products and kinetic rate expressions are much simpler. The use of simulants makes it easier to isolate the variables that affect the agent chemistry. As discussed in the following sections, a VX analog, $(C_2H_5O)(CH_3)P(O)(SC_2H_5)$ (9, see eq 11), has also been studied to isolate the effect of the diisopropylamino group on the reaction chemistry of VX. Similarly, the reactions of a series of organophosphorus esters similar to the G agents [e.g., DMMP (dimethyl methylphosphonate), DIMP (diisopropyl methylphosphonate), DFP (diisopropyl phosphorofluoridate), and NPDP or PNPDPP (*p*-nitrophenyl diphenylphosphate)] have also been extensively investigated as model substrates. Over the past years, reaction studies of these model compounds at university and industrial laboratories have contributed significantly to the development of new decontamination systems.

Each of these simulants, however, can only mimic certain aspects of the reactivity of the specific agent. One must always be aware of the differences, both qualitatively and quantitatively, between the agents and their simulants. One must also be careful not to assume the results from the simulants automatically apply to the agents. In fact, the subtle differences between the simulants and the agent often lead to new discoveries of the chemical nature of the agent. Therefore, in selecting an agent simulant, it is important to determine which property of the agent is to be addressed. For each property, there are many simulant choices, but it is virtually impossible to simulate all the properties of an agent with a single compound.

B. Hydrolysis

1. GB and GD

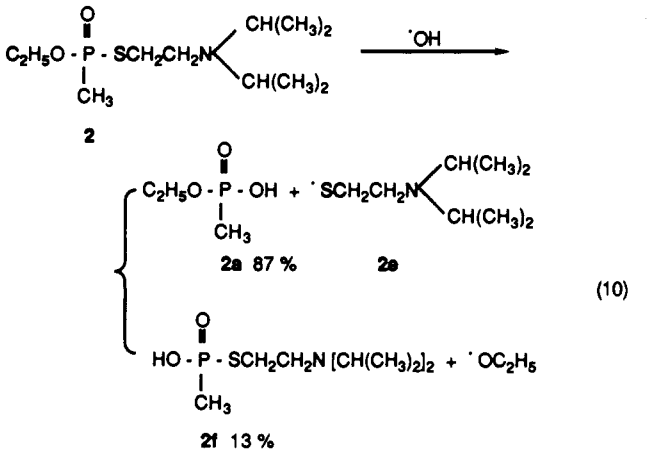
Since all four of the agents under consideration react with water, it would be ideal if hydrolysis could be used as the principal decontamination reaction. However, in order for this to be possible, significant amounts of the agent have to be soluble in water. Both GB and GD dissolve in water, and their hydrolyses under acidic, neutral, and basic conditions have been reported.[10] In dilute solutions, a general equation for the observed hydrolysis rate constant, k_{obs}, can be expressed as

$$k_{obs} = k_w + k_a[H^+] + k_b[^-OH] \quad (9)$$

where k_a and k_b are the acid and base hydrolysis rate constants, respectively, and k_a is much smaller than k_b.[10] The rate constant of neutral hydrolysis, k_w, is small compared with the rates under either acidic or basic conditions. At pH values greater than 10, as previously discussed, both GB and GD are hydrolyzed within a few minutes to their corresponding phosphonic acids (see eq 1). Since acids are produced, excess base must be present to maintain the same hydrolysis rate. It is important to note that field decontamination always involves reactions in concentrated solutions. Greater amounts of agent (10^{-2}–10^{-1} M) than those typically used in the laboratory (10^{-5}–10^{-3} M) for kinetic studies are present in the mixture.[19] The kinetics of decontamination reactions usually deviate from first-order behavior since only a small excess of the reactive component is used in the decontaminant.

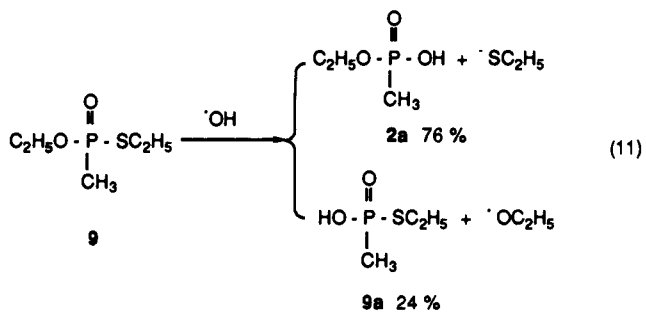
2. VX

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. The hydrolysis of 0.01 M VX takes place slowly in parallel paths even at pH 13.[20] As shown in eq 10, one of the reaction paths



(10)

leads to the formation of the stable but extremely toxic compound, **2f**. Therefore, unlike the G agents, VX cannot be detoxified by base-catalyzed hydrolysis. Similarly, eq 11 shows that a 0.01 M **9** hydrolyzes in the same manner in 0.1 M NaOH. The product ratio from 0.01 M **9** remains constant at 74/26 (P–S/P–O bond cleavages) over the range 0.1–1.0 M NaOH, and when the polarity of the solvent changes from pure water to up to 50 vol % *tert*-butyl alcohol or acetonitrile in water. Contrary to Epstein's prediction,[20a] the product ratio is not determined by the pK_a ratio of the two leaving groups, $^-SC_2H_5$ ($pK_a \sim 12$) and $^-OC_2H_5$ ($pK_a \sim 16$).



(11)

3. HD

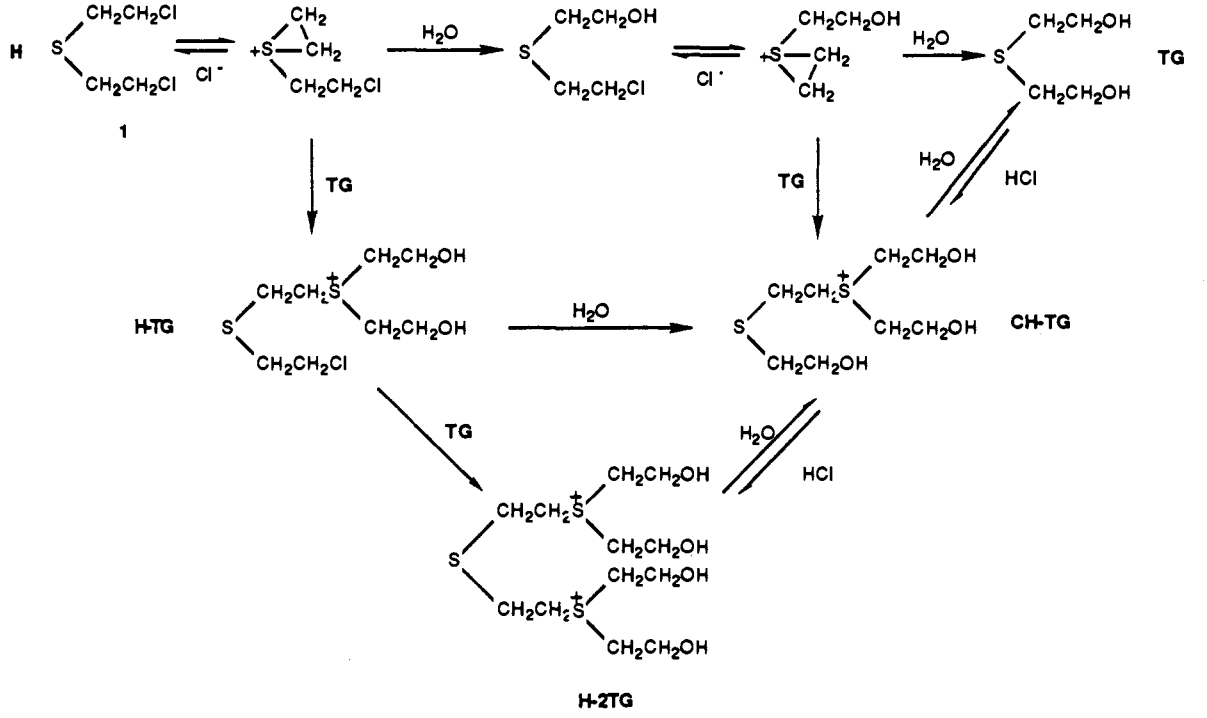
HD is insoluble in water, but can react with water at the interface to form a complicated set of ionic products (Scheme V) which then diffuse rapidly to the bulk water phase. The rate of HD dissolution is so slow that these ionic products are produced at the interface even before any HD is dissolved. This makes it virtually impossible to determine the HD solubility accurately. Furthermore, although HD has been reported to hydrolyze with a half-life of 5 min at 25 °C via an S_n1 mechanism,[18] HD cannot be detoxified by hydrolysis. The observed rate of HD hydrolysis is controlled by the rate of mass transfer and is, in fact, very slow. When a polar organic solvent is mixed with water to solubilize HD, the reduced polarity of the medium greatly reduces the S_n1 hydrolysis rate. Besides, the inhibition of HD hydrolysis by the chloride ion is significant,[18] and the rate of this ion pair return step also increases markedly as the solution becomes less polar.[21]

As shown in Scheme V, thiodiglycol (TG) is not the only product from HD hydrolysis. The sulfonium ion aggregates, H-TG, CH-TG, and H-2TG, are stable products in water at ambient temperatures, and H-TG is believed to be quite toxic.[22,23] The yields of these polymeric products increase as the initial concentration of HD increases.[21] Furthermore, TG and HCl, have been shown to react reversibly to form the same polymeric sulfonium ion intermediates.[21] The rate of this reverse reaction increases as the concentrations of both TG and HCl increase. Hence, despite the apparently rapid and irreversible hydrolysis of HD to TG in an infinitely dilute solution,[18] the hydrolysis of larger amounts of HD (~0.1 M) is a reversible process with the sulfonium ion aggregates as the predominant equilibrium species. These aggregates may, in part, account for the observed persistence of HD in the natural environment.

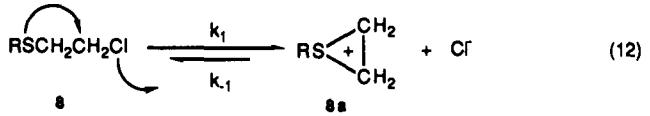
C. Nucleophile-Assisted Substitution of HD

A systematic investigation into the mechanisms of nucleophilic substitution of HD analogs was recently completed by a research group at the University of Alabama in Huntsville.[24] Using deuterated HD analogs such as $CH_3SCH_2CD_2OTs$ and $C_6H_5SCH_2CD_2Cl$, these researchers detected complete deuterium scrambling in the presence of a series of nucleophiles for almost all types of organic and aqueous solvent mixtures. Therefore, it can be concluded that the nucleophilic substitution of HD or its analogs proceeds, as predicted,

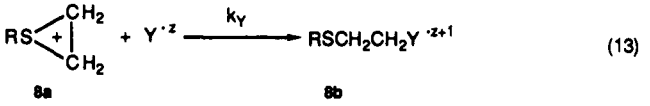
Scheme V. Reversible Formations of the Sulfonium Ion Aggregates in the Hydrolysis of Mustard (H)



exclusively via an S_n1 mechanism. The sulfur in these molecules is located at the best position to participate internally in the cleavage of the C–Cl bond by forming a transient cyclic ethylenesulfonium ion intermediate (**8a** in eq 12). Any external nucleophile Y (including water or another molecule of 8, eq 13) cannot compete with the internal sulfur. Only one exception is reported: in pure dimethyl sulfoxide in the presence of thiophenolate anion, there was no scrambling of the isotopes and the substitution was, therefore, S_n2.[24c]



(12)



(13)

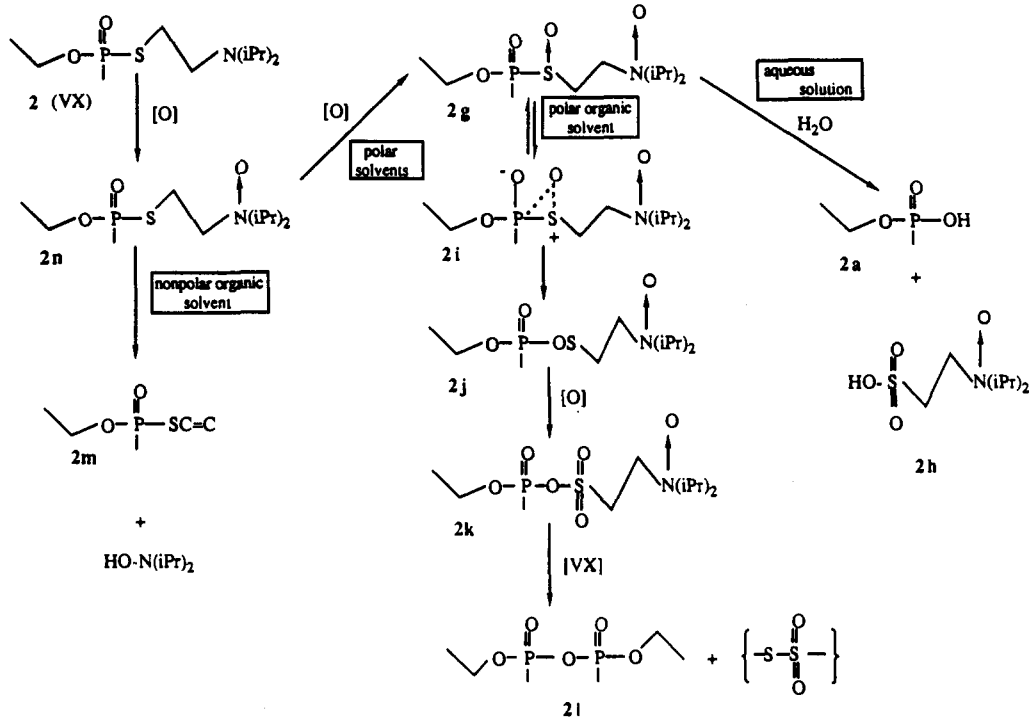
It is important to note that the observed rate of an S_n1 substitution reaction can increase in the presence of Y. This is not because of a mechanistic change but because of the competition between Y and the chloride ion as reflected in the relative magnitudes of (k_{-1}[Cl^-]) and (k_Y[Y]) (eqs 12 and 13).[25] Since the magnitude of k_Y[Y] increases with both the strength of the nucleophile and the concentration of Y, the observed rate enhancement by a nucleophile can be significant; and this enhancement may even be proportional to the concentration of Y. It is important that this rate behavior is not interpreted as an evidence for the S_n2 mechanism. Furthermore, such nucleophile-assisted substitution also reduces the formation of the stable sulfonium ion aggregates which may decompose to regenerate HD. Many such systems have been considered or recommended for the large-scale destruction of mustard. The nucleophiles proposed include amines and anions such as hydroxide, phenolate, and thiosulfate. Note that to achieve decontamination the final product (**8b**) must be nontoxic. In the presence of these nucleophiles, the reaction mechanism remains S_n1 and the rate-determining step (k_1 in eq 12) is controlled only by the solvent polarity.[21] The role of the nucleophile is 2-fold: to increase the observed rate by eliminating the return step and to eliminate the formation of the complicated products shown in Scheme V.

D. The Oxidation of HD and VX

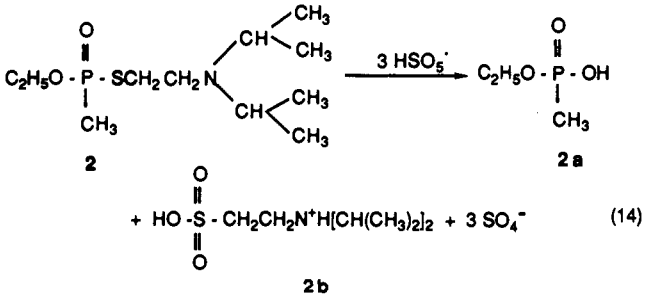
In aqueous solution, both HD and VX can be oxidatively detoxified. For a given oxidant, the sulfur in HD is oxidized at a much faster rate than the sulfur in VX. Once the sulfur in VX is oxidized, hydrolysis of the P–S bond occurs immediately to form **2a** and a sulfonic acid. Consequently, the *S*-oxide of VX (**2g** in Scheme VI) has never been identified in aqueous solution.[26] In acidic solution, the nitrogen in VX is protonated and not oxidized, whereas in basic and neutral solutions, the tertiary amine moiety is oxidized to the stable *N*-oxide more rapidly than the sulfur is oxidized. In those situations where only the nitrogen is oxidized for lack of either sufficient oxidant or a sufficiently strong oxidant to attack the sulfur, VX is not detoxified because the *N*-oxide product is still toxic.

The observed oxidation rates of both HD and VX by anionic oxidants decrease as the polarity of the solvent decreases. This is believed to be attributed to the S^+–O^- and N^+–O^- ion-pair complexes in the transition states.[26,27] In an anhydrous organic solvent, both the sulfur in HD and the nitrogen in VX can still be oxidized by strong oxidants at reasonable rates, although the rate of the sulfur oxidation in VX becomes extremely slow.[26] When the sulfur in the *N*-oxide is oxidized in an organic solvent, both the sulfonate **2k** and the toxic pyrophosphonate (anhydride **21** in Scheme VI) are identified as the final products.[26] Based on a series of publications by Casida and co-workers,[28] Scheme VI

Scheme VI. Multiple Paths in the Oxidation of VX in Neutral Solutions



was proposed for the oxidation mechanism of VX in polar organic solvents. It is proposed that **2g** is formed first and slowly rearranges via the cyclic transition state **2i** to the sulfenate **2j**,[28] which is immediately oxidized to the sulfonate **2k**. In the absence of excess oxidant, **2k** reacts with another VX molecule to form **2l**. This reaction of the sulfonate with excess substrate in the absence of water to form the anhydride was carefully examined with a thioate pesticide.[29] In this study, the formation of an ion-pair intermediate which subsequently decomposed to the observed anhydride product was proposed as the most probable mechanism. In addition, a competing and parallel reaction to sulfur oxidation exists; the *N*-oxide (**2n**) can decompose to **2m** and the hydroxylamine via the Cope reaction at a rate dependent on the polarity of the organic solvent.[26] Compound **2m** may still be toxic and contains a sulfur atom more resistant to oxidation than that in VX. Therefore, VX cannot be rendered nontoxic by oxidation in the absence of water.



(14)

As a result of these studies, a number of oxidants containing peroxygen such as *m*-CPBA (*m*-chloroperoxybenzoic acid) and MMPP (magnesium monoperoxyphthalate) were found to be effective for both HD and VX. An aqueous solution of a commercial oxidant, Oxone (active component: $KHSO_5$),[26,30] was recommended for VX detoxification and for destruction of VX in laboratories at large scales (up to 51 g).[31] The aqueous solution of Oxone also acts as an acidic buffer (pH = 1.9) and can dissolve large amounts of VX followed by fast oxidation at the sulfur. Since the nitrogen is protonated, only 3 equiv of the oxidant are required for each equivalent of VX (eq 14).[26] This method is superior to the previous laboratory decontamination method which used excess bleach in an ethanol–water mixture at high pH.[12]

Since aqueous Oxone is a simple and effective decontaminant for VX, it was also investigated for the decontamination of HD and G agents. In a solution of 0.05 M mustard, 0.1 M Oxone, and 15 vol % *N*-methyl-2-pyrrolidinone (necessary to dissolve the mustard), HD is oxidized immediately to the sulfoxide which then converts completely to the sulfone in less than 1 h. Using fast kinetic techniques and UV absorption, an HD analog, $PhSCH_2CH_2Cl$, was found to oxidize with a half-life of 7 s at 25 °C in 0.002 M Oxone and 20 vol % CH_3CN.[27] As for GB and GD, neither oxidation nor displacement of the OR groups is observed in these Oxone solutions. Simple hydrolysis of the P–F bond to form the corresponding phosphonic acids **3a** and **4a** as shown in eq 1 is the exclusive hydrolysis pathway. The acid-catalyzed hydrolysis rate profiles for GB and GD at 18 °C are shown in Figure 2. These pseudo-first-order rates for 0.03 M GB and 0.02 M GD in the pH 2 buffer of 0.1 M Oxone are relatively slow. Therefore, Oxone is a superb decontaminant for both VX and HD but cannot rapidly detoxify the G agents.

IV. Decontamination Media

As discussed earlier, rapid dissolution of agents in the decontamination medium is essential to achieve effective decontamination (i.e., rapid removal of agent from surfaces). The decontamination media can be divided into liquid and solid systems. Liquid media can be further divided into nonaqueous (organic) and

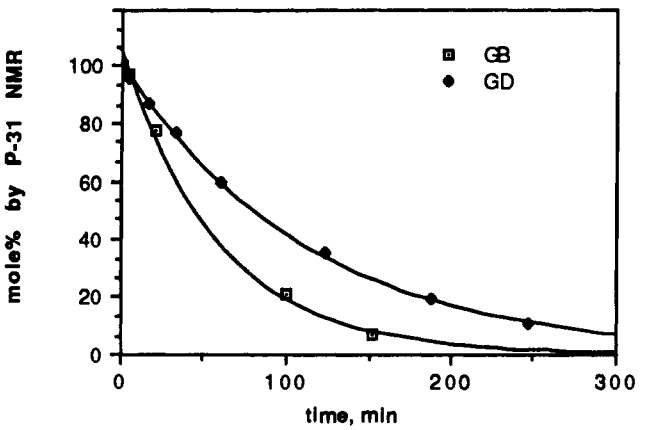


Figure 2. Hydrolysis of GB and GD in Oxone solutions at 18 °C.

aqueous media. Nonaqueous media such as DS2 offer good solubility for all agents but large amounts of organic waste are generated by the decontamination process. Aqueous media have the advantage of using water from natural resources. Soap solutions solubilize neat agents, but fail to dissolve the thickened agents; so an organic solvent is often added to the aqueous solution to improve dissolution. However, many of the oxidation and substitution reactions become slower as the solvent polarity decreases. The design of a decontamination medium is usually a compromise between solubility and optimum reactivity. Solid decontamination media have only been recently investigated. One property of these materials is the ability to absorb large amounts of liquid agents. Reactants incorporated in the solid support are usually less reactive than in a liquid solution. A few examples of these liquid and solid decontamination media are discussed below.

A. Heterogeneous Liquid Media

Since chemical agents are organic compounds of low polarity and most reactants (e.g., hydroxide ion, hypochlorite ion, and the anionic oxidants) are polar compounds, both micelles and emulsions have been investigated as potential liquid decontamination media. Of these systems, the best studied are the German emulsion (code name: C8)[32] and a microemulsion system MCBD (multi-purpose chemical, biological decontaminant).[33] In addition, a phase-transfer system was examined by Ramsden and his collaborators at the University of Florida.[34] In all of these systems, tetrachloroethylene was used as the organic phase and active chlorine was the reactant. Reactions take place at the surfaces of the droplets in both the C8 emulsion and the microemulsion (MCBD) systems. In the phase-transfer system, oxidation of sulfide takes place in tetrachloroethylene via transfer of the hypochlorite ion by the phase-transfer catalyst $[(nBu)_4N^+Cl^-]$.

The German emulsion (C8) is composed, by weight, of 15% tetrachloroethylene (the continuous phase), 76% water, 1% anionic surfactant, and 8% $Ca(OCl)_2$. Because of the organic continuous phase, it is noncorrosive and as good a solvent as pure tetrachloroethylene for the thickened agents. In addition, C8 can penetrate into paint to dissolve and react with imbedded agent without damaging the paint. When the emulsion is sprayed, a thin, coherent film is formed on the surface to allow sufficient residence time for reaction with the agents.

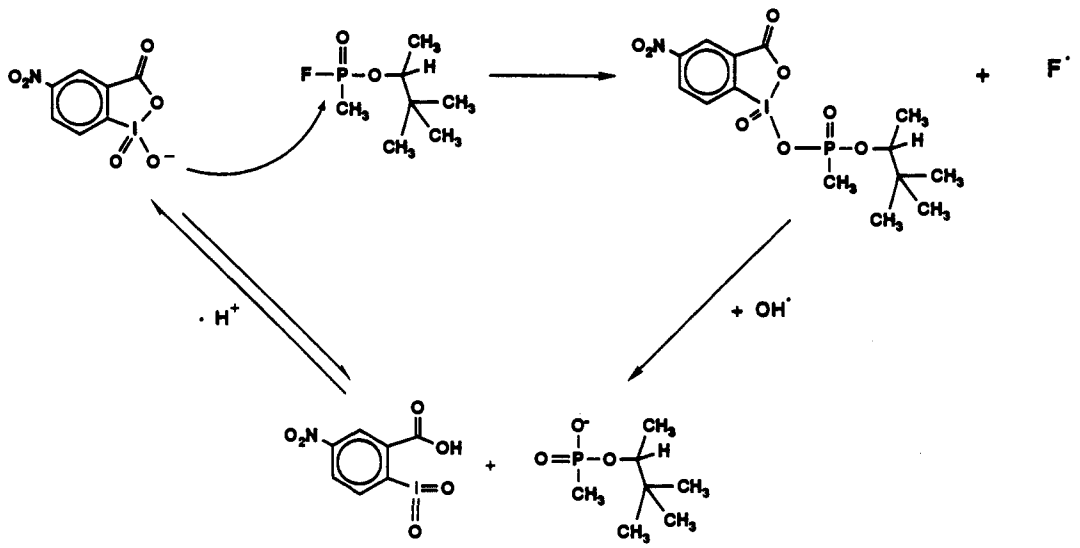
The microemulsion medium of the MCBD system is made, by weight, of 60% water (the continuous phase), 7% tetrachloroethylene, 28% CTAC (*n*-cetyl trimethylammonium chloride), and a small amount of a cosurfactant $[(nBu)_4NOH]$. To this microemulsion, 4% Fichlor, 0.1% sodium 2-nitro-4-iodoxybenzoate (IBX, see Scheme VII), and sodium borate are added for reactions with the agents. The MCBD system was designed to be superior to the C8 system because it is a more stable emulsion at a lower pH of 10, contains less tetrachloroethylene, and is partially catalytic. The catalysis by IBX, a derivative of *o*-iodosobenzoic acid (IBA), is proposed in Scheme VII, in which IBX is shown as a nucleophilic catalyst for the hydrolysis of GD.[35,36] Since the hydrolysis products are acidic, the borate buffer is essential to keep the IBX active. The IBX-catalyzed hydrolysis is significantly enhanced in cationic micelles in which both the IBX and the organic substrate are concentrated on the micellar surfaces. As a result, large rate enhancements have been observed for the more hydrophobic simulants such as PNPDPP but the hydrolyses of GB and GD, which are more polar, are only slightly accelerated.[36]

IBX was found to have little effect on the hydrolysis of VX. As shown in Figure 3, the hydrolysis of VX is catalyzed by IBX only in the initial stage of the reaction. After the first few minutes, deactivation of the catalyst is apparent in the rate profile. Perhaps the IBX, which is also an oxidant, is reduced by the thiol hydrolysis product (**2e**, eq 10) and cannot catalyze the reaction further. HD, as discussed above, is hydrolyzed via an S_n1 mechanism and, thus, cannot be catalyzed by IBX. Fichlor is added to the MCBD system to oxidize both HD and VX. Recently, Menger used a small amount of commercial bleach (5–6% NaOCl) to oxidize 2-chloroethyl ethyl sulfide in microemulsions (aqueous continuous phase) containing *tert*-butyl alcohol as the cosurfactant.[38] The oxidation was complete in 15 s and 2-chloroethyl ethyl sulfoxide was the only product. It was proposed that the hypochlorite ion was converted to *tert*-butyl hypochlorite at the droplet surfaces and reacted effectively with the HD simulant in the oil phase.

B. Polymer Powders and Supported Reagents

A solid sorbent system, the M291 kit, has recently been adopted for use as the primary skin decontaminant (see Table II). A sorbent decontaminant is a nontoxic, free-flowing, solid material which absorbs liquid agent tightly in its micropores. It is used by the soldier to wipe bulk liquid agent from his skin, clothing, and personal equipment. The major advantages of using a solid sorbent material for personal decontamination are its high capacity to absorb liquid chemical agents and the reduced weight of decontaminant that the soldier must carry compared to a liquid decontaminant of similar effectiveness. This new kit is composed of nonwoven fiber pads which are filled with a resin mixture (trade name: XE-555) developed by Rohm & Haas Company. The resins are made of a styrene/divinyl benzene copolymer and are composed of a high surface area carbonized macroreticular styrene/divi-

Scheme VII. Mechanism of IBX-Catalyzed Hydrolysis of GD



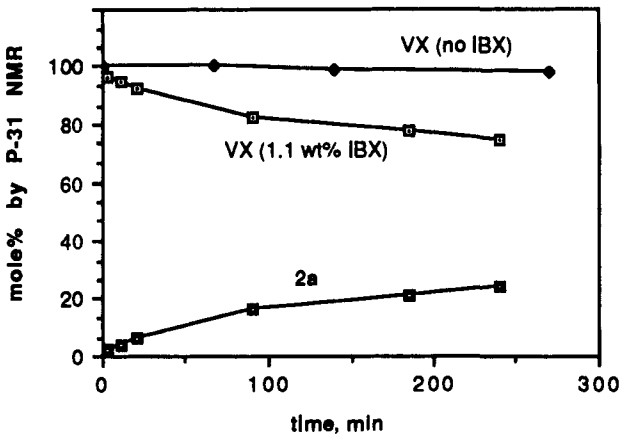


Figure 3. Hydrolysis of 0.1 M VX in a microemulsion at pH 10 and 18 °C.

nylbenzene resin (the sorptive resin), a strong acid (sulfonic acid groups) cation-exchange resin, and a strong base (tetralkylammonium hydroxide groups) anion-exchange resin. The sorptive resin can rapidly absorb liquid agents, and the reactive resins are intended to promote hydrolysis of the physisorbed agents. This resin blend was found to be less corrosive to the skin than the M258A1 system described earlier.

A recent NMR investigation of the XE-555 resin in the kit has provided the first direct evidence for agent–resin interactions.[39] The study showed that neither VX nor $^{13}CH_3SCH_2CH_2Cl$ (HD simulant) hydrolyzed on the resin surface during the first 10 days of observation. GD slowly hydrolyzed with a half-life of about 30 h. It appears that the observed rapid agent removal in field practice is achieved physically by wiping with the pad and presumably by a simultaneous physisorption of the agent on the sorptive resin component. For reasons discussed previously, it is not surprising that no hydrolysis was measured for either HD or VX. On the other hand, GD was expected to hydrolyze quickly on the basic sites of the reactive resin component. It is therefore postulated that most of the GD is absorbed on the sorptive resin sites and does not rapidly migrate to the basic sites of the reactive resin. These results demonstrate that reactions on solids are controlled by a different set of variables than those in liquid solutions. For solid decontamination materials, the sorption and physical removal processes are perhaps far more effective than any chemical reactions.

V. Applications of Catalysis to Decontamination

A. Metal Ion Catalyzed Hydrolysis

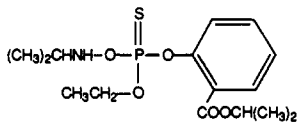
The ability of copper(II) to catalyze the hydrolysis of the G agent simulant, DFP, was first demonstrated by Warner-Jauregg and co-workers in 1955.[40] Later, Martell et al. extended the study to GB and screened the activity of a number of other metal ions.[10b,41] The authors concluded that copper(II), in particular, was a potent catalyst for the hydrolysis of GB. The rate law for the catalysis is shown to be first-order in hydroxide ion, metal ion, and GB. The observed first-order rate coefficient for metal ion catalyzed hydrolysis is shown in eq 15 where k_{hyd} is the spontaneous (noncatalytic) hydrolysis rate and is very small compared with k_2.

$$k_{obs} = k_{hyd} + k_2[^-OH][Cu^{+2}] \qquad (15)$$

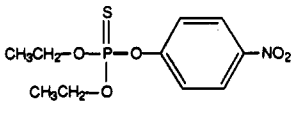
Two mechanisms for the activation step are possible. The catalytic species could be the hydroxometal complex $CuOH^+$, or Cu(II) could act as a Lewis acid by complexing with the substrate at the phosphoryl oxygen followed by attack of the hydroxide ion on the GB–Cu complex.[42] These findings generated a great deal of interest in subsequent studies attempting to verify the mechanism.[43,44]

The copper(II)-catalyzed hydrolysis of GD in a pH 7 buffer was not investigated until the 1980s.[45] As in the case of GB, the rate of GD hydrolysis is accelerated by 1 order of magnitude in the presence of 0.001 M $CuSO_4$ at 25 °C. When $CuSO_4$ is increased to 0.01 M, the reaction becomes too fast to be followed under the same conditions. Only limited Cu(II)-catalyzed hydrolysis was examined with VX. It is speculated that the diisopropylamino group of VX may be a competing site for complexing with copper; thus, the reaction may be inhibited. Because of the S_n1 nature of HD reactions via neighboring group participation, the hydrolysis of HD is expected to be inhibited if Cu(II) complexes with the sulfur. Other metal ions, such as Ag^+ and Hg^{2+}

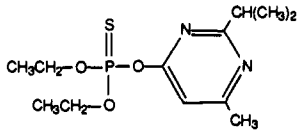
Scheme VIII. Structures of Pesticides



Isophenfos



Parathion



Diazinon

appeared to accelerate HD hydrolysis by complexing with the chloride ion. However, these ions cannot be applied to decontamination because Ag^+ is expensive and Hg^{2+} is toxic.

B. Enzymatic Decontamination and Biodegradation

1. Enzymatic Hydrolysis of Nerve Agents

In 1946, Mazur reported the first work concerned with enzymes capable of catalytically hydrolyzing organophosphorus esters.[46,47] During the 1950s and 60s, a number of groups investigated the hydrolysis of GB, DFP, and paraoxon (Scheme VIII), by enzymes from a variety of organisms (primarily mammalian tissues and bacteria).[48] A result of the increased interest in these enzymes was the proliferation of names for them. The literature is filled with references to enzymes such as DFPase, fluorophosphatase, phosphorylphosphatase, paraoxonase, phosphofluorase, phosphotriesterase, sarinase, somanase, and tabunase. In 1987, the name organophosphorus acid (OPA) anhydrase was selected as a generic name for all enzymes that are capable of catalytically hydrolyzing organophosphorus compounds of interest.

Hoskin began his research into the purification and characterization of the OPA anhydrase from squid in 1966.[49-52] The significance of the squid enzyme lies in the fact that it has major differences from all the other OPA anhydrases. The differences were great enough that in 1984 Hoskin proposed that the enzymes could be grouped into two categories, the squid-type (for which there was one example) and all others, which were referred to as Mazur-type.[53] A summary of the properties of these enzyme types is shown in Table III.[53] Because of the types of enzymes (particularly bacterial) that have been isolated and characterized within the past 10 years, these categories are no longer as simple as originally believed.

The interest in microbial enzymes for the degradation of organophosphorus compounds received a boost in the early 1970s with the isolation of bacteria capable of growing on pesticides such as diazinon, isophenfos, and parathion (Scheme VIII).[54-56] By far, the most studied bacterial enzyme is parathion hydrolase. An essentially identical enzyme has been found in *Pseudomonas diminuta* and a *Flavobacterium* species (ATCC 27551).[57] The gene for the enzyme has been cloned and sequenced and the reaction mechanism determined.[58] Parathion hydrolase has a broad substrate range with the organophosphorus pesticides,[59] but much lower activity on the chemical agents.[60]

Table III. Properties of Organophosphorus Acid Anhydrases

squid-type	Mazur-type
narrow distribution, squid nerve, saliva, hepatopancreas	Ubiquitous
molecular weight, 30–38 000	variable, 45–90 000
GD/DFP ≈ 0.25	GD/DFP, 5–50 and higher
hydrolyzes all isomers of soman; some stereoselectivity in rates	stereoselectivity variable: often quite stereospecific
Mn^{2+} indifferent or slightly inhibited	Mn^{2+} stimulated 2–20-fold and as high as 80-fold
Ca^{2+} requiring, not Ca^{2+} stimulated	May be Mg^{2+} requiring and stimulated
$(NH_4)_2SO_4$ indifferent	$(NH_4)_2SO_4$ labile
Mipafox ($[CH_3)_2N]_2P(O)F$) indifferent	Mipafox inhibited

Table IV. Comparison of Several OPA Anhydrases

	specific activity (μmol min^{-1} mg^{-1})		
enzyme	DFP	GD	paraoxon
parathion hydrolase	60	5	3200
squid hepatopancreas	300	60	
Alteromonas sp. JD6.5	300	600	12

Only two other OPA anhydrases have been purified to homogeneity and characterized. These are the squid hepatopancreas enzyme and an enzyme from a halophilic bacterial isolate tentatively identified as a strain of *Alteromonas*.[61] It is important to note that these enzymes are active for all of the optical isomers of the G agents. A comparison of these three enzymes with regard to their specific activity for DFP, GD, and paraoxon is shown in Table IV.[62] Although the halophile enzyme has by far the greatest activity, other properties such as pH, temperature optima, stability, and potential inhibitors could play an important role in the selection of enzymes for decontamination formulations. In addition, enzymes from other sources continue to be examined and may offer even greater activity and substrate range.

2. Cloning of OPA Anhydrase Genes

For enzymes to achieve a substantial impact on the development of a new generation of decontamination systems, they will need to be producible in large quantities. With the advent of genetic engineering, the prospect of bacteria and other easily cultured organisms being used as microfactories for the production of rare or important proteins has become a reality.

The OPA anhydrase from *Pseudomonas diminuta* MG and *Flavobacterium* sp. is coded for by a plasmid-borne gene (opd) of 1079 base pairs in length which is identical in both organisms even though their plasmids are totally different.[57] Recent work has focused on the overexpression of the opd gene product in better host systems. The results show that the production of mature enzyme could be achieved in *Escherichia coli*,[62b] *Drosophila melanogaster*,[63] *Streptomyces lividans*,[64] and Fall Armyworm.[65] The lack of significant activity of parathion hydrolase on GD would indicate that this enzyme is not as well suited for decontamination of the nerve agents as are some other enzymes. However, it continues to serve as an excellent model enzyme system.

Table V. Summary of ^{13}C NMR Profile of Hydrolyzed and Biodegraded Mustard

strain	% original carbon remaining	compounds detected
SH18	16	thiodiglycol sulfoxide
SH42	2–3	thiodiglycol, thiodiglycol sulfoxide, small amounts of ethers or thioethers

The OPA anhydrase from *Alteromonas* sp. JD6.5 currently demonstrates the highest activity against GD. The enzyme is a single polypeptide with a molecular weight of 60 000 Da.[61] Recently, the gene that codes for this enzyme has been cloned into *E. coli* with the Lambda ZAP expression vector.[66] Using polyclonal and monoclonal antibodies and an oligonucleotide probe derived from the partial N-terminal sequence of the JD6.5 enzyme, positive clones have been identified and purified. The OPA anhydrase gene has been found to reside within a 4 kilobase KpnI DNA fragment. Western blot analysis has indicated that the OPA anhydrase is expressed in *E. coli* and that the expressed product is enzymatically active. Efforts are now underway to sequence the cloned gene.

The third enzyme for which cloning studies are underway is the squid OPA anhydrase. While there are some variations between species of squid, the enzymes are very similar in molecular weight (30–38 000 Da). Recently, Kopec-Smyth et al.[67] constructed a cDNA library derived from squid hepatopancreas tissue in *E. coli* using the expression vector pcDNAII. One positive clone was detected through the use of polyclonal and monoclonal antibodies and two oligonucleotide probes derived from the partial N-terminal sequence of the enzyme. Preliminary data suggest that the clone contains approximately 75% of the total gene coding sequence. In addition, Lunzer et al.[68] examined an enzyme from squid optic ganglion and found that the N-terminal amino acid was blocked. These investigators also have prepared a cDNA library in the Lambda ZAP system. In order to gain further understanding of the enzyme structure, both groups are now preparing to sequence the cloned genes.

3. Biodegradation of HD

In an attempt to achieve the biodegradation of HD, soil samples were collected from areas purported to have previously been contaminated by HD. Enrichment cultures were set up with bacteria from these samples using thiodiglycol as the sole carbon source in a mineral salts medium. Two bacterial strains were isolated which utilize thiodiglycol as their sole source of carbon for growth.[69] As shown in Table V, these strains were designated SH18 and SH42 and were identified as *Pseudomonas pickettii* (37.5% fatty acid identity) and *Alcaligenes xylosoxidans* ssp. *xylosoxidans* (74.1% fatty acid identity), respectively.

Initial attempts to grow these organisms on HD proved to be unsuccessful since the organisms were killed by HD in culture. However, subsequent efforts in which the HD was shaken in mineral salts medium overnight prior to inoculation proved successful. Under these conditions, both strains of bacteria were able to utilize the hydrolyzed HD as their sole source of carbon for growth. Bacteria were grown from a single colony inoculum in mineral medium with hydrolyzed HD provided as the sole carbon source. Growth was allowed to proceed into the stationary phase for a total of 260 h. Doubling time for the cultures was approximately 10 h for strain SH18 and 40 h for strain SH42 (see Table V). ^{13}C FTNMR analysis was performed before inoculation and after growth. The cell mass was not removed during the analysis. As shown in Table V, the NMR results showed that the bacteria had degraded as much as 97% of the carbon-containing compounds in the medium. Mineralization was demonstrated by the evolution of $^{14}CO_2$ from the culture. Two different microtoxicological tests detected no toxicity in the resulting medium. Currently, efforts are underway to determine the feasibility of HD biodegradation in a pilot scale system and to conduct more extensive toxicological tests on the resulting products.

C. Catalytic Oxidation

One approach to catalytic decontamination is to activate the oxygen in air for the oxidation of both HD and VX. Although such catalysts in the form of organometallic complexes do exist,[70] the concentration of oxygen in air at ambient conditions is too low for the large amount of substrate encountered in decontamination. A number of studies using hydrogen peroxide (H_2O_2) as the model oxidant and metal ions as the catalysts have also been conducted. The oxidation of HD by H_2O_2 is slow in the absence of a catalyst. At 21 °C in an equal-volume binary solvent mixture of water and *N*-cyclohexyl-2-pyrrolidinone, the observed reaction half-life of HD with 1% H_2O_2 is 6 h, and the HD sulfoxide is the only product. This reaction could be catalyzed using a $V(O)(acac)_2$ complex (acac = $CH_3C(O)CH_2C(O)CH_3$) prepared by Drago and co-workers.[71] In CH_3CN, at 0.1 M $CH_3SCH_2CH_2Cl$, 0.01 M $V(O)(acac)_2$, and 1 M H_2O_2, all of the sulfide substrate was converted to the sulfoxide in less than 2 min at 20 °C. However, this system is not effective for the VX analog **9** (eq 11). A series of catalysts containing iron were also studied in order to examine if Fenton type chemistry[72] could be used to oxidize both VX and HD via the formation of the hydroxyl radical (•OH) as the reactive species. None of the iron catalysts tested to date are effective for either HD or VX. One reason for the lack of oxidation was the decomposition of the peroxide by the iron catalysts forming molecular oxygen, which then escaped from the reaction mixture, and deactivated the catalyst. Work in this area is continuing, since metal ions and complexes are known to be excellent oxidation catalysts. Additionally, stable oxidants need to be identified and tested against agents under decontamination conditions.

The application of a photocatalyst in the air oxidation of HD and VX has also been investigated.[73] Both VX and HD can be oxidized on irradiated TiO_2 surfaces in acetonitrile. A series of oxides and disulfides are produced from the photooxidation of mustard. However, the observed quantum yields of these reactions were low, in the 0.1–0.3% range.[74] In the absence of water, VX is primarily converted to the toxic pyrophosphate products (e.g. **21** in Scheme VI).[73b] When water is added to the solvent, nontoxic phosphonic and sulfonic acids are produced, although the solubility of air decreased in the aqueous solutions.

VI. Future Directions

Looking forward to the next century, the highest research priority in reactive decontamination is to identify both liquid and solid decontaminants which do not have adverse effects on the environment. The biodegradable *N*-alkyl-2-pyrrolidinones are being considered as the major organic components for new liquid decontaminants since these pyrrolidinones can penetrate into the thickeners.[75] Decontamination efficacy tests indicated that 4 wt % $Ca(OCl)_2$ in an equal volume mixture of *N*-cyclohexyl-2-pyrrolidinone and water can effectively detoxify the four agents.[76] In addition, preliminary data also indicate that the four agents can be detoxified by a strong base (alkoxide) in *N*-ethyl-2-pyrrolidinone in the same manner as DS2.

To develop noncorrosive decontamination systems, the search for catalysts (including enzymes) will continue. Of particular interest are those catalysts that are pH independent and those that can catalyze the oxidation of the OR groups in the G agents as well. Compared to liquid decontaminants, very little is known concerning the interaction of agents with solid decontaminants. In order to develop better solid decontamination materials, NMR imaging and magic-angle spinning (MAS) techniques will be applied to investigate the adsorption, site-exchange, and reaction characteristics of agents on solid matrices. Recently, advances in computational chemistry and access to supercomputers have opened the possibilities of predicting, modeling, and screening both liquid and solid decontamination systems containing enzymes and other types of catalysts. Finally, many of the decontamination research findings may be applied to the safe destruction of chemical weapons.[77] The Army currently incinerates the chemical agents but is also considering alternatives such as detoxification (neutralization) technologies.[78] These neutralization methods are being evaluated by a committee organized by the National Academy of Science, and their recommendations may influence future directions in the development of new decontamination systems.

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(1) A range of surfaces are substrates for decontamination. These surfaces include the painted metal of large equipment such as the exteriors of tanks, ships, and aircraft; smaller personal equipment such as helmets, weapons, portable electronic devices, and protective clothing; and human skin.

(2) Most military equipment is painted with low-gloss paint. Agent penetration into paints has been observed. In the United States, a chemical agent resistant paint was developed and used to prevent penetration. In other NATO countries, sorptive paints are still used. For details, see: (a) Thompson, J. H.; Schwartz, M. Evaluation of the Resistance of Standard Air Force Paint to Liquid Toxic Agent Sorption, ARCSL-TM-79016, 1979. (b) Thompson, J. H.; Day, S. E.; Schwartz, M.; Keck, C. H. *Development of a Chemical Agent Resistant Coating*; ARCSL-TM-80017, 1980.

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(5) For a review of the isolations and toxicities of the stereoisomers, see: Benschop, H. P.; de Jong, L. P. A. *Acc. Chem. Res.* **1988**, *21*, 368–374.

(6) The purpose of the thickener is to control the rheology of the agents as they are explosively disseminated from a munition. A typical thickener is Acryloid K125, a copolymer composed of methyl, ethyl, and butyl methacrylates produced by Rohm & Haas. Co. In addition, a polychlorinated isoprene has also been used as a thickener.

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(8) Fire has been observed when a significant quantity of HD comes in contact with HTH or STB powder.

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