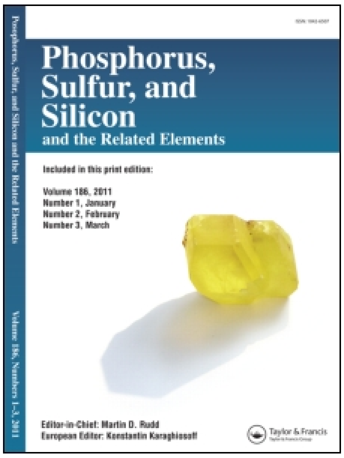

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THE CHARACTERIZATION OF SULFONIUM CHLORIDES BY GAS CHROMATOGRAPHY/MASS SPECTROMETRY AND THE DEGRADATION OF 2-CHLOROETHYL SULFIDE DERIVATIVES

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THE CHARACTERIZATION OF SULFONIUM CHLORIDES BY GAS CHROMATOGRAPHY/MASS SPECTROMETRY AND THE DEGRADATION OF 2-CHLOROETHYL SULFIDE DERIVATIVES

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Three aqueous samples containing sulfonium chloride salts of both mustard gas (2,2′-dichlorodiethyl sulfide) and its simulant 2-chloroethyl ethyl sulfide have been characterized by gas chromatography/mass spectrometry (GC/MS). These salts decompose thermally to the corresponding 2-chloroethyl and 2-hydroxyethyl sulfides, therefore GC/MS analysis is not indicative of the true composition of these solutions. Small amounts of dithioethers characteristic of the decomposition of the dimeric salts were also detected. Electron Impact (EI) ionization produces a more intense molecular ion than methane chemical ionization (CI) for the dithioethers because of the ease of formation of sulfonium ions during chemical ionization.

The decomposition products of four aged samples of 2-chloroethyl sulfides ($RSCH_2CH_2Cl$ where R = methyl, ethyl, phenyl and benzyl groups) were also characterized by GC/MS, which indicated that decomposition of these compounds may proceed via dimeric sulfonium ions. Mustard gas was detected in all but one of the samples, providing evidence for secondary sulfonium cation formation in the degradation process.

Key words: Sulfonium chlorides; 2-chloroethyl sulfides; degradation; dimeric sulfonium cations; GC/MS characterization.

INTRODUCTION

Dimeric sulfonium ions derived from the chemical agent mustard, $S(CH_2CH_2Cl)_2$, were first reported in 1946.[1] The researchers isolated these sulfonium cations as picrates and concluded that some of the salts were toxic. The study was a result of an intensive research effort during World War II but was discontinued after the war. With the advent of high-field FTNMR, direct identifications of these sulfonium salts as hydrolysis products from mustard and its derivatives ($RSCH_2CH_2Cl$, R = methyl and ethyl groups) have been made recently.[2,3] The sulfonium ions are important in the reversible transformations of mustard in water. In this study, the thermal decomposition of three of these salts in aqueous solutions under gas chromatography/mass spectrometry (GC/MS) conditions are presented. The validity of using GC/MS to analyze samples containing sulfonium salts is investigated.

It has also been reported that the degradation products in aged 2-chloroethyl ethyl sulfide (CEES) samples can be rationalized if degradation proceeds through dimeric sulfonium ions.[4] We attempted to further study this mechanism by comparing the GC/MS characterization of a series of 2-chloroethyl sulfides ($RSCH_2CH_2Cl$, R = methyl, ethyl, phenyl and benzyl) which were allowed sufficient time to degrade at ambient conditions. Since these compounds are commonly used as radioprotective materials,[5] it is important to determine what additional hazards are associated with these compounds as they degrade with time.

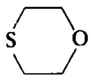
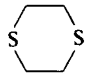
RESULTS AND DISCUSSION

1. *Sulfonium Salts in Aqueous Solutions*

The major sulfonium salts produced from the hydrolysis of mustard (H) have been identified by NMR as H–2TG and CH–TG (see Equations (1) and (3) below).[2] Two aqueous solutions, one containing predominantly H–2TG and the other CH–TG were characterized by GC/MS and the results are given in Table I. These salts decompose thermally in the injection port to primarily TG (thiodiglycol) and CH (mustard chlorohydrin). H–2TG also decomposes to significant amounts of H and dithiane. The GC/MS results are consequently not indicative of the true character of these solutions. Listed below in Equations (1) to (5) are proposed mechanisms of decomposition. The intermediate salt, H–TG, has not been identified by NMR directly. Presumably H–TG is short-lived and hydrolyzes quickly to CH–TG. As expected, higher concentrations of H were found from decomposition of H–2TG than from CH–TG. The mechanism leading to the formation of 1,4-dithiane will be discussed in the next section.

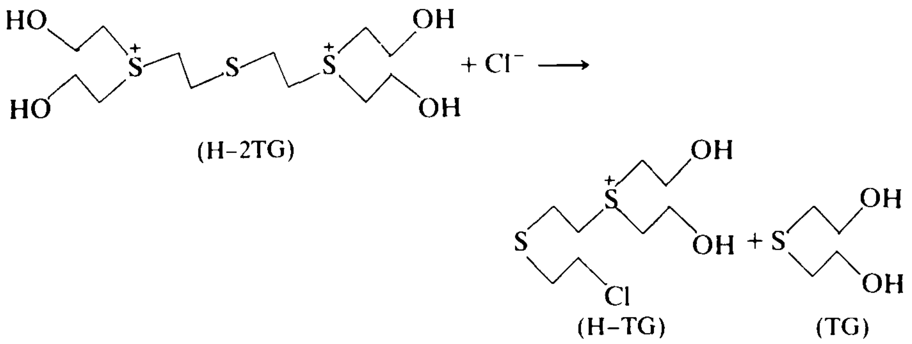
TABLE I

Decomposition of H-2TG and CH-TG in aqueous samples

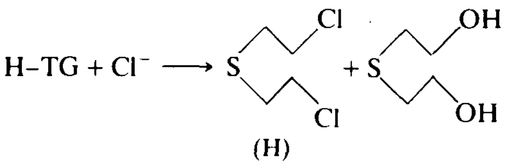
Component	GC/MS Area %	
	Sample 1[a] (H–2TG)	Sample 2[b] (CH–TG)
$HOCH_2CH_2SH$	0.05	0.7
	0.6	2.0
	11.6	0.3
$ClCH_2CH_2SCH_2CH_2Cl$ (H)	20.2	3.8
$HOCH_2CH_2SCH_2CH_2Cl$ (CH)	49.3	64.8
$HOCH_2CH_2SCH_2CH_2OH$ (TG)	15.1	25.3
Other	3.2	3.2

[a] 76 mole% H–T2G, 8 mole% CH–TG and 12 mole% TG in water and HCl by ^{13}C NMR.

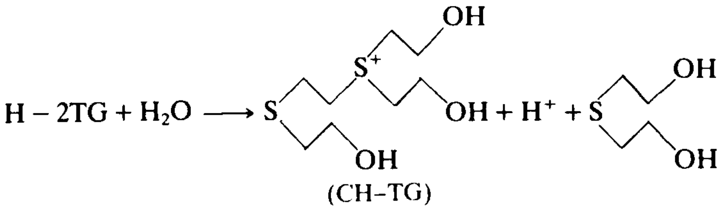
[b] 85 mole% CH–TG and 15 mole% TG in water and HCl by ^{13}C NMR.



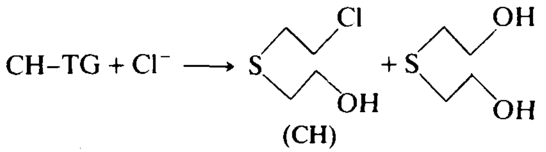
(1)



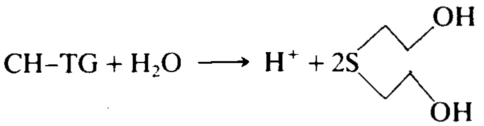
(2)



(3)



(4)



(5)

To verify the above observation, a monochloromustard derivative was studied in detail. Only one sulfonium salt was produced from the hydrolysis of 2-chloroethyl ethyl sulfide (CEES). It was identified in a previous study as EHT ($(C_2H_5)S^+(C_2H_4OH)(C_2H_4SC_2H_5)$).[2] The GC/MS characterization of the EHT sulfonium salt is shown in Table II, which indicates that this salt decomposes back to 2-chloroethyl ethyl sulfide (CEES) and 2-hydroxyethyl ethyl sulfide (HEES). Another sample of EHT (95% EHT, 5% HEES by NMR) in water and HCl was heated to 90°C at atmospheric pressure for one hour. A small organic layer appeared at the top of the reactor vessel and was analyzed by NMR. It contained primarily CEES and small amounts of $C_2H_5SCH_2CH_2SC_2H_5$ and $(C_2H_5SCH_2CH_2)_2O$. The concentration of HEES in the aqueous layer increased

TABLE II

Decomposition of EHT in an aqueous sample[a]

Component	GC/MS Area %
CH_3CH_2Cl	2.3
$ClCH_2CH_2Cl$	0.2
$C_2H_5SC_2H_5$	0.2
$C_5H_{12}S$	0.5
$CH_3SCH_2CH_2Cl$	0.1
$C_2H_5SCH_2CH_2OH$	44.9
$C_2H_5SCH_2CH_2Cl$	44.9
$iC_3H_7SCH_2CH_2Cl$	0.3
$C_2H_5SCH_2CH_2SC_2H_5$	2.4
$C_2H_5SCH_2CH_2SCH_2CH_2Cl$	trace
$C_2H_5SCH_2CH_2OCH_2CH_2SC_2H_5$	2.9
Other	1.2

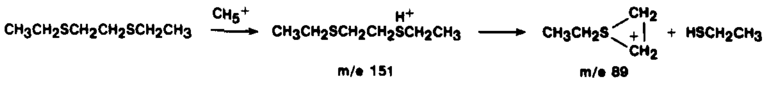
[a] Sample contained 85 mole% EHT and 15 mole% HEES by ^{13}C NMR EHT = $C_2H_5S^+(C_2H_4OH)(C_2H_4SC_2H_5)$.

while the concentration of EHT decreased. This result indicates that EHT decomposed at 90°C to primarily CEES and HEES, and is consistent with the GC/MS analyses shown in Table II. The thermal decomposition of EHT followed the same pathways as those of H-2TG and CH-TG.

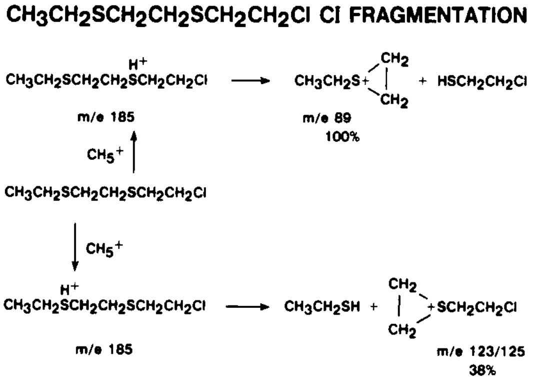
The kinetics and mechanism of the decomposition of sulfonium ions were demonstrated by Swain *et al.*[6] by monitoring the decomposition of trialkyl sulfonium chlorides at 50 to 100°C. The authors concluded that these salts decomposed via an S_N2 mechanism to form alkyl chlorides and alkyl sulfides. The decomposition of EHT exhibited the same mechanisms. Both the chloride (CEES) and the alcohol (HEES) products resulted from nucleophilic attack of Cl^- at the ethyl thioethyl ($-C_2H_4SC_2H_5$) group in EHT. The two thioether products were formed from attack of the nucleophiles on the ethyl and chloroethyl groups, respectively. The small amounts of additional decomposition products in Table II can be explained by the general decomposition scheme as well (see discussion in Section 3.)

2. *Mass Spectrometry*

Both methane chemical ionization (CI) and electron impact (EI) ionization were used to identify decomposition products in this study. The dithioethers produced are unusual in that more intense molecular ions were observed under EI than under CI conditions. The reason for this is evident in the fragmentation chemistry. During chemical ionization, protonation of the sulfur enhances the leaving group ability and promotes formation of the thermodynamically stable ethylene sulfonium ion. CI fragmentation patterns for $EtSC_2H_4SEt$ and $EtSCH_2CH_2SCH_2CH_2Cl$ are shown separately in Equation (6) and Scheme I,



(6)



SCHEME I $CH_3CH_2SCH_2CH_2SCH_2CH_2Cl$ CI fragmentation.

respectively. EI and CI spectra obtained for these two compounds are shown in Figures 1 and 2, respectively.

3. *Sulfonium Salts in Aged $RSCH_2CH_2Cl$ Derivatives*

As previously reported, the degradation of pure 2-chloroethyl sulfides ($RSCH_2CH_2Cl$) might proceed via the formation of sulfonium salts.[3,4] Direct identifications of low concentrations of these salts in a 2-chloroethyl sulfide sample with FTNMR have been difficult. However, a small amount of MHT sulfonium ion $(CH_3)S + (C_2H_4OH)(C_2H_4SCH_3)$ in aged $CH_3SCH_2CH_2Cl$ (CEMS) has been positively identified by overnight ^{13}C FTNMR scanning. It is expected that the decomposition products characteristic of MHT should be detected by GC/MS, which is more sensitive than FTNMR in detecting and separating small

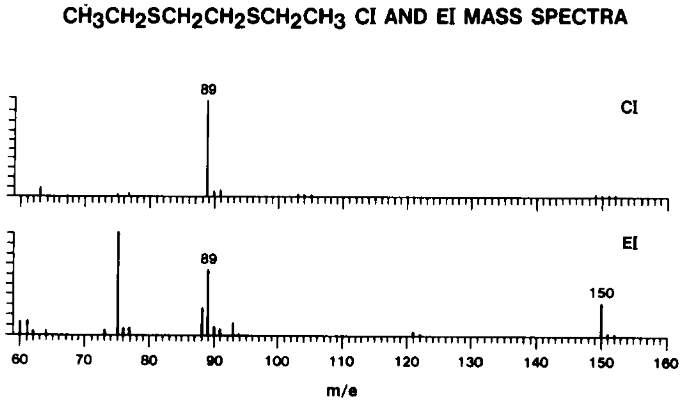


FIGURE 1 $CH_3CH_2SCH_2CH_2SCH_2CH_3$ CI and EI mass spectra.

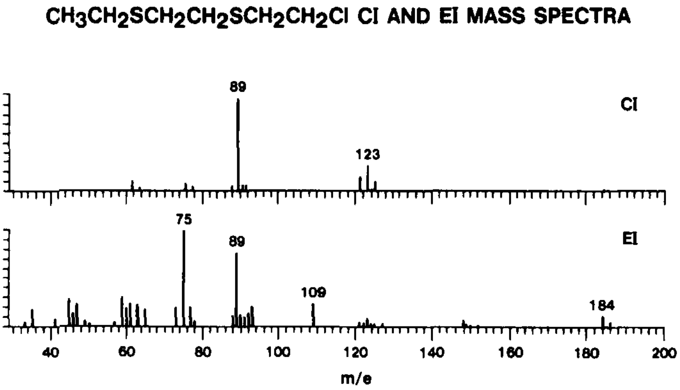


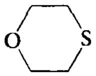
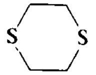
FIGURE 2 $CH_3CH_2SCH_2CH_2SCH_2CH_2Cl$ CI and EI mass spectra.

concentrations of impurities. Four aged 2-chloroethyl sulfide derivatives ($RSCH_2CH_2Cl$, where R = methyl, ethyl, phenyl and benzyl groups) were investigated. The GC/MS analyses of these samples are listed separately in Table III for compounds which might have been produced by a common degradation pattern and in Table IV for compounds which apparently are formed by other mechanisms. Also included in Table III for the purpose of comparison are published results for mustard ($R = ClC_2H_4$).

As shown in Table III, CEMS, CEES and CEPS have undergone a few percent degradation but CEBS has degraded extensively. Based on the decomposition patterns of sulfonium cations discussed in 1, the observed degradation products in Table III may also be produced from the decomposition of dimeric sulfonium ions. These products, common to all four derivatives, can be rationalized by a

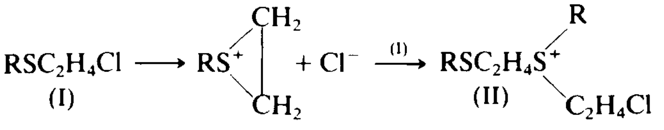
TABLE III

Common degradation products of aged $RSCH_2CH_2Cl$

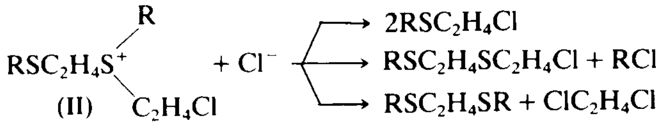
Component	Composition, Area %				
	$R = ClC_2H_4$[a] (H)	$R = CH_3$ (CEMS)	$R = C_2H_5$ (CEES)	$R = C_6H_5$ (CEPS)	$R = C_6H_5CH_2$ (CEBS)
RCl	—	0.2	—	0.4	18.2
	trace	—	—	—	trace
	0.5	0.4	1.7	—	2.3
$RSCH_2CH_2Cl$	89	93.0	94.4	95.4	44.8
RSR	—	—	0.2	0.1	13.5
RSSR	<0.5	0.6	—	0.6	—
H	(89)	0.6	0.06	—	5.6
$RSCH_2CH_2SR$	4	2.6	0.1	1.2	2.8
$RSCH_2CH_2SCH_2CH_2Cl$	—	1.1	0.1	—	7.9

[a] Data for mustard (H), $R = ClC_2H_4$ are from Reference 5.

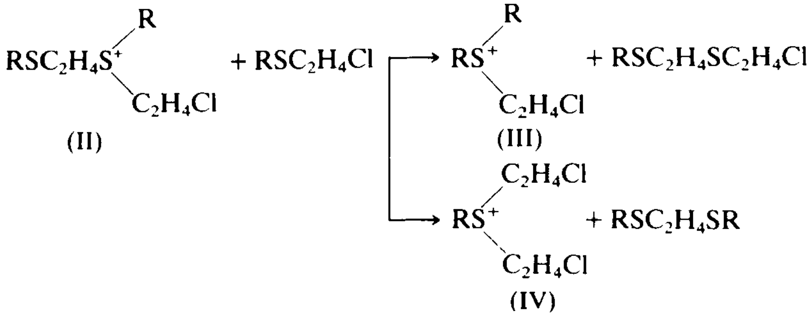
degradation mechanism in which the dimeric sulfonium cation II shown in Equation (7) gradually forms as the samples degrade with time.[8] The presence of MHT in aged CEMS could be from the hydrolysis of II in the presence of moisture.[3]


(7)

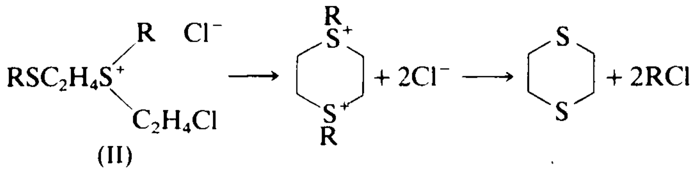
Attack of II by chloride results in three possible decomposition pathways shown in Equation (8).


(8)

It is possible that II may also be attacked by $RSCH_2CH_2Cl$ and form secondary ions III and IV shown in Equation (9).


(9)

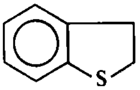
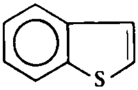
III can decompose directly to RSR, while IV can decompose to mustard and RCl. As shown in Table III, mustard, RSR, RCl and the products in Equations (8) and (9) have all been observed by GC/MS. Dithiane, which can be derived from II according to Equation (10) [3], was also detected.


(10)

Attempts to identify III and IV directly by NMR in the neat samples were unsuccessful, partly as a result of overlapping signals. The NMR analysis of CEBS, however, was consistent with the GC/MS results. Only 50 mole percent of CEBS was present in the sample. A significant amount of benzyl chloride was also measured. Recently, Lyle and his coworkers reported that CEBS decomposed to benzyl chloride and ethylene sulfide via the formation of benzylethyl-

TABLE IV

Non-common degradation products of aged $RSCH_2CH_2Cl$

$RSCH_2CH_2Cl$	Composition,	Area %
$R = CH_3$	CH_3SCH_2Cl	0.1
	C_4H_9SCl	0.5[a]
	CH_3SSSCH_3	0.6
	Others	0.3
$R = C_2H_5$	$C_2H_5SC_3H_7$	0.6[a]
	$CH_3SCH_2CH_2Cl$	0.2[a]
	$C_3H_7SCH_2CH_2Cl$	1.4[a]
	Others	1.2
$R = C_6H_5$	$ClCH = CHCl$	trace
	C_6H_5SH	trace
	$ClCH_2CH_2OCH_2CH_2Cl$	trace
	$C_6H_5SCH_3$	trace
		trace
		trace
	$C_6H_5SCH = CHCl$	1.3
	$C_6H_5SCHClCH_2Cl$	0.5
$R = C_6H_5CH_2$	$C_6H_5CH_2OH$	trace
	$ClCH_2SCH_2CH_2SCH_2CH_2Cl$	2.8
	Others	2.0

[a] Also present as impurities in the fresh sample.

enesulfonium ion.[5] We did not detect ethylene sulfide or its polymers by GC/MS or NMR. No solid material was observed, which would be anticipated if ethylene sulfide was polymerized and precipitated from the liquid CEBS sample. We suspect that benzylethylenesulfonium ion was short-lived and reacted with another CEBS molecule to form II (Equation (7)), which subsequently decomposed to benzyl chloride.

In Table IV, unique degradation products from 2-chloroethyl phenyl sulfide are observed. Cyclization of the side chain occurred, perhaps proceeding through a four-centered intermediate, to form benzothiofuran derivatives. Additional compounds from elimination/dehydrogenation reactions were also present. This suggests that the chemical reactivity of the phenyl derivatives are different from the alkyl derivatives, due perhaps to the interaction of the pi-electron clouds with the non-bonded electron pairs on the adjacent sulfur, thus making sulfur a weaker nucleophile.

EXPERIMENTAL

Materials and Sample Preparation

Mustard, $H(S(CH_2CH_2Cl)_2)$, was from our own supply. (Warning: Mustard is a potent vesicant and must be handled in a closed system or in a hood with minimum velocity of 100 ft/min.) The

2-chloroethyl sulfide derivatives ($RSCH_2CH_2Cl$) were obtained as doubly vacuum distilled special products from Fairfield Chemical Company, Blythewood, SC ($R = CH_3$ and C_2H_5) and as technical grade from Parish Chemical Company, Orem, UT ($R = C_6H_5$ and $C_6H_5CH_2$). Aged samples were stored at ambient conditions for one to two years.

Aqueous samples containing H-2TG and CH-TG were prepared by dissolving mustard in water (sample 1 in Table I), and by mixing HCl with TG (sample 2 in Table I). Similarly, aqueous samples containing EHT were prepared by dissolving CEES in water (sample in Table III) and by mixing HCl with HEES.

GC/MS Analysis.

All samples were analyzed on a Finnigan model 5100 gas chromatograph/mass spectrometer (GC/MS) using both electron impact (EI) and chemical ionization (CI) methods. The 15 m SE-54 capillary column (split ratio 50:1) was programmed from 60°C to 160°C at 10°C per minute. Injection sample size was 0.05 ul. Injector temperature was 200°C, interface temperature was 230°C and the ion source temperature was 100°C. The mass range was scanned from 60–450 amu for CI and from 30–450 for EI at one scan per second. The CI reagent gas was methane (0.6 Torr).

Spectral identification of common decomposition products were obtained by comparison to spectra in the National Bureau of Standards (NBS) 39,000 compound library (Washington, D.C.). The spectra of most of these compounds have not been compiled in commercially available libraries. These compounds were identified by comparison to spectra and GC retention times of compounds in a user library of mustard and related compounds generated in our laboratory, by comparison to spectra in the literature,[9] and on the basis of combined EI/CI fragmentation patterns. Quantitation, expressed as area percent, was obtained by integration of the area under the total ion chromatogram and does not take into account differences in detector response.

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