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CRDEC-TR-216

NUCLEOPHILE-ASSISTED HYDROLYSIS OF MUSTARD

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October 1990

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U.S. ARMY
ARMAMENT
MUNITIONS
CHEMICAL COMMAND

Aberdeen Proving Ground, Maryland 21010-5423

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*

2. REPORT DATE
1990 October

3. REPORT TYPE AND DATES COVERED
Final, 86 Oct - 88 Oct

4. TITLE AND SUBTITLE
Nucleophile-Assisted Hydrolysis of Mustard

5. FUNDING NUMBERS
PR-1C161102A71A

6. AUTHOR(S)
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Beaudry, William T., and Ward, J. Richard

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
CDR, CRDEC, ATTN: SMCCR-PPD/SMCCR-RSC, APG, MD
21010-5423

8. PERFORMING ORGANIZATION REPORT NUMBER
CRDEC-TR-216

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

The hydrolysis rate of 0.1-0.2M mustard (typical field decontamination concentrations) is inhibited by two processes: (1) the recombination of the chloride ion with the ethylenesulfonium ion to form mustard, known as the return step; and (2) the formation of stable and unreactive dimeric sulfonium chloride salts (reaction between thiodiglycol and ethylenesulfonium ions). The above inhibitions can be completely eliminated by adding a large amount of a competitive nucleophile to the reaction mixture. The hydrolysis rate can thus be increased to a first-order rate that is controlled by the solvent polarity only. In this study, the nucleophile-assisted hydrolysis rates were measured by nuclear magnetic resonance techniques in a 50 vol % acetone solution and in a microemulsion system. The competition rates of nucleophiles and chloride ion with water for reaction with the ethylenesulfonium ion are also discussed.

14. SUBJECT TERMS
Hydrolysis
Competition factor
Nucleophile
Chloride
Ethylenesulfonium ion
Sulfonium chloride
Mustard
Dimer
Inhibition
CEES
CEMS

15. NUMBER OF PAGES
30

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT
UNCLASSIFIED

18. SECURITY CLASSIFICATION OF THIS PAGE
UNCLASSIFIED

19. SECURITY CLASSIFICATION OF ABSTRACT
UNCLASSIFIED

20. LIMITATION OF ABSTRACT
UL

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18

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PREFACE

The work described in this report was authorized under Project No. 1C161102A71A, Research in CW/CB Defense. This work was started in October 1986 and completed in October 1988.

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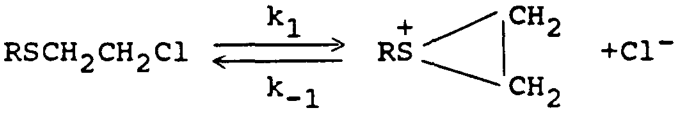
NUCLEOPHILE-ASSISTED HYDROLYSIS OF MUSTARD

1. INTRODUCTION

Previously, the first-order hydrolysis rate constants (k_1 in equation 1) for mustard and its monochloro derivatives ($RSCH_2CH_2Cl$) in acetone-water mixtures were reported.[1] A small amount of a polar, organic cosolvent had to be added to water because the dissolution rate of mustard in pure water was slower than the reaction rate. Reported first-order rate coefficients were larger than those of primary alkyl chlorides because a cyclic ethylenesulfonium ion was formed in the transition state during the rate-determining step (equation 1). In fact, the effects of acetone and ethanol on k_1 correlated with the solvent ionization power, the "Y" values, as determined from the hydrolysis of t-butyl chloride.[1,2]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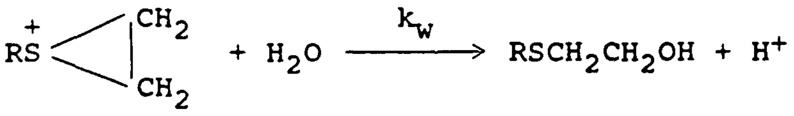
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As the initial concentration of mustard was increased, the observed hydrolysis rate, usually measured by the increase in proton concentration with time, $d[H^+]/dt$, was reduced by both the increase in cosolvent concentration necessary to solubilize the substrate and the increase in the rate of the reverse (return) reaction, $k_{-1}[Cl^-]$, as a result of greater chloride ion concentration. In addition, the reactive ethylenesulfonium ion also reacted with both $RSCH_2CH_2Cl$ and the initial 2-hydroxyethyl sulfide product ($RSCH_2CH_2OH$, equation 2) to form the stable sulfonium chlorides <u>I</u> and <u>II</u> (Figure 1). Dimer <u>I</u> is the predominant product because the sulfur atom in 2-hydroxyethyl sulfide is a stronger nucleophile than the sulfur atom in 2-chloroethyl sulfide.[3] Both <u>I</u> and <u>II</u> are relatively unreactive;[4] consequently, very little H^+ was produced, and the measured rate of hydrolysis $d[H^+]/dt$ was small.

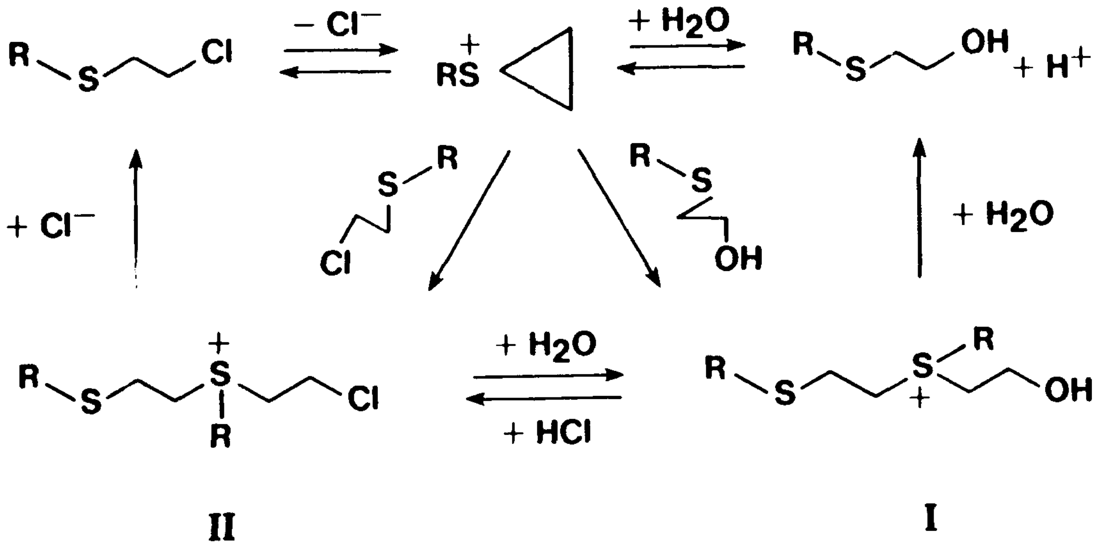


Figure 1. Reversible Hydrolysis of $RSCH_2CH_2Cl$

Therefore, it seems possible to add a large amount of a highly competitive nucleophile, X^- (a scavenger), to the solution to capture the ethylenesulfonium ion as soon as it forms. Then, the return reaction and the formation of dimers will be eliminated. A single product $RSCH_2CH_2X$ should be observed, and the observed rate of displacement, as measured by the disappearance of the substrate, $-d[RSCH_2CH_2Cl]/dt$, should be large and not retarded by the chloride ion (absence of the reverse reaction). To test this hypothesis, the hydrolysis of 0.02-0.2M $RSCH_2CH_2Cl$ was examined in both an acetone-water and a microemulsion system.[4] A strong nucleophile, thiosulfate, was used to assist the hydrolysis. The same fast first-order rate coefficient as that for pure S_N1 hydrolysis at infinite-dilute substrate is expected to be achieved.

2. BACKGROUND

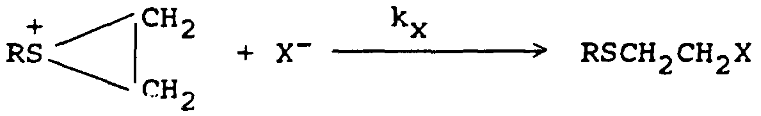
2.1 Chloride Ion Inhibition and Competition Factor.

The kinetics and mechanism of the hydrolysis of mustard $[S(CH_2CH_2Cl)_2]$ and its monochloro derivatives ($RSCH_2CH_2Cl$, $R = CH_2CH_2OH$, CH_3, C_2H_5) have been extensively investigated in a number of fundamental studies. It has been confirmed that all of the above sulfides follow the same mechanism of hydrolysis. The first step of hydrolysis is the formation of a transient cyclic ethylenesulfonium cation via the intramolecular assistance of the neighboring sulfur (equation 1); the cation then reacts quickly with water to form 2-hydroxyethyl sulfide ($RSCH_2CH_2OH$) and H^+ (equation 2). By applying a steady-state approximation to the concentration of the short-lived ethylenesulfonium cation, the observed rate ($r_{obs} = k_{obs}[RSCH_2CH_2Cl] = k_{obs}([Cl^-][H^+])$, as measured by the increase in $[H^+]$ with time, is related to the rate coefficients in equations 1 and 2 according to equation 3.

$$k_{obs} = k_1 \left(\frac{k_w}{k_{-1}[Cl^-] + k_w} \right) \qquad (3)$$

The k_{obs} in equation 3 equals k_1 only when the chloride concentration is low so that the rate of the reverse reaction

$k_{-1}[Cl^-]$ becomes negligible compared to k_w. At greater substrate concentrations, the chloride ion gradually increases such that k_{obs} becomes smaller than k_1. If a compound X that competes with water for the ethylenesulfonium ion intermediate is present, a bimolecular ionic reaction with a second-order rate coefficient $k_x(r_{obs} = k_x[X^-][RS^+CH_2CH_2])$ occurs (see equation 4).



(4)

A similar derivation of the forward reactions of equations 1, 2, and 4 results in equation 5 where the observed rate is measured by the increase in $[H^+]$ with time.

$$k_{obs} = k_1 \left(\frac{k_w}{k_w + k_x[X]} \right) \qquad (5)$$

Obviously, the presence of X^- reduces the observed hydrolysis rate as less H^+ is produced. The ratio of k_x to k_w is defined as the competition factor (F_x) of X^- with water; whereas, the competition factor of chloride is k_{-1}/k_w.[5] An accurate F_x can be determined from the slope of $1/k_{obs}$ of $RSCH_2CH_2X$ as a function of $[X^-]$ under constant ionic strength.[5] However, an approximate F_x was often measured for $[X^-]$ from $1/k_{obs}$ of $RSCH_2CH_2Cl$ as a function of $[X^-]$ at low substrate, i.e., low $[Cl^-]$, concentrations. The approximate F_x in the absence of any ionic strength control was reported in the work on mustard by Ogston, Holiday, Philpot, and Stochen.[6] Table 1 lists some of these competition factors.

The transient ethylenesulfonium ion is sufficiently stable to react selectively with nucleophiles at different rates. The F_x values in Table 1 are larger than k_w for most X. Therefore, water (even at 55M) is a poor competitor for the ethylenesulfonium ion. Nucleophiles with a bivalent sulfur were most competitive in reacting with the ethylenesulfonium ion.

Table 1. Competition Factors (F_x) for the Hydrolysis of Mustard in Pure Water*

X	F_x** = k_x/k_w, M^{-1}
dithiophosphate	130,000.0
monothiophosphate	38,000.0
phosphate	75.0
thiosulfate	27,000.0
sulfate	7.3
thiourea	150.0
ethyl mercaptan	280.0
thiodiglycol	30.0
chloride	21.0
iodide	660.0
nitrate	0.2
hydroxide	8,000.0

*Reference 6
**$k_{obs}/k_1 = 1/(1 + F_x[X])$

A competition factor of 27,000 M^{-1} was measured for thiosulfate, which was also far more powerful than both the OH^- and Cl^- anions.

2.2 Effect of Nucleophile on Rate of Displacement.

In the presence of X, the production of H^+ is smaller than the amount of sulfide consumed; therefore, the accurate rate expression for the observed rate (k'_{obs}) of the displacement reaction should be measured by the decrease in substrate concentration with time $-d[RSCH_2CH_2Cl]/dt$. In equation 6, a derivation of equations 1, 2, and 4, a different relationship from equations 3 and 5 is shown.

$$k'_{obs} = k_1 \left(\frac{k_w + k_x[X]}{k_{-1}[Cl^-] + k_w + k_x[X]} \right) \qquad (6)$$

Note that the introduction of $k_x[X]$ terms in equation 6 cannot reduce the observed rate, k'_{obs}, relative to k_1. When the amount of chloride ion is small, k'_{obs} is still equal to k_1, the rate-determining formation of the ethylenesulfonium ion. When $[Cl^-]$ is large but sufficient X with a large k_x value is also present, so that $(k_x[X])$ is significantly greater than $(k_{-1}[Cl^-])$, k'_{obs} approaches k_1 despite the large chloride ion. (Note the multiplicity of the term, e.g., its magnitude, is controlled by the magnitudes of both k_x and $[X^-]$). However, k'_{obs} can be made to approach k_1 when $(k_x[X])$ is large but cannot be made to exceed k_1 regardless of how large the $(k_x[X])$ term is. The magnitude of k_1 is determined by both the substrate (the stability of the ethylenesulfonium ion, hence the R group in $RSCH_2CH_2Cl$) and the solvent polarity. For high substrate concentrations (0.2M) encountered in practical decontamination operations, solvents of low polarity must be used to dissolve the sulfide. Therefore, the value of the limiting k_1 is much smaller than those reported for pure water and highly aqueous acetone-water solutions.[1]

The kinetic data for mustard hydrolysis in the presence of X often obeyed a second-order rate equation (e.g., $r_{obs} = k_2[X][RSCH_2CH_2Cl]$). This could be easily misinterpreted for an S_N2 mechanism. However, with careful analysis of the kinetic data, a saturation effect of X on the observed rate and a limiting first-order rate (k_1) should appear. The absence of an S_N2 mechanism for mustard hydrolysis was clearly demonstrated by Bartlett and Swain in 1949.[5] In the presence of X, although the magnitude of k_1 for the second substitution step of the intermediate, $XCH_2CH_2SCH_2CH_2Cl$, was usually different from that of mustard chlorohydrin, ($HOCH_2CH_2SCH_2CH_2Cl$), the mechanism was still S_N1. It should be emphasized that all 2-chloroethyl sulfides hydrolyze with the same S_N1 mechanism in aqueous solutions. An added nucleophile does not increase the first-order rate coefficient k_1. The observed rate may increase in the presence of a nucleophile; the reaction mechanism does not change, but the return step is eliminated by making the term ($k_{-1}[Cl^-]$) relatively insignificant. The above analysis is further tested in this study by the following kinetic experiments.

3. EXPERIMENTATION

3.1 Materials.

Vacuum-distilled mustard was used. WARNING: Mustard (H) is a potent vesicant and must be handled in a closed system or in a hood with a velocity of 150 ft/min. The mustard derivatives, $CH_3SC_2H_4Cl$ [2-chloroethyl methyl sulfide (CEMS)] and $C_2H_5SC_2H_4Cl$ [2-chloroethyl ethyl sulfide (CEES)], and their hydroxyl analogs, $CH_3SC_2H_4OH$ [2-hydroxyethyl methyl sulfide (HEMS)] and $C_2H_5SC_2H_4OH$ [2-hydroxyethyl ethyl sulfide (HEES)] were doubly vacuum-distilled products from Fairfield Chemical Company (Blythewood, SC). Acetone-d_6 (99.5% D) was used as received from Norell Chemical Company (Landisville, NJ). The ^{13}C-labelled CEMS or CE^{13}MS was prepared by Dr. Sankar Lal of Drexel University. The preparation procedure was described in a previous publication.[4]

The microemulsion was made of (by weight) 16.5% surfactant, $C_{16}H_{33}N^+(CH_3)_3\ Cl^-$ [cetyl trimethylammonium chloride (CTAC), about 0.52M]; 11.6% cosurfactant, $(nC_4H_9)_4\ N^+(OH^-)$; 7.4% organic phase, C_2Cl_4; and 1.4% emulsifier, $(n\text{-}C_8H_{17})_4\ N^+Cl^-$ (trade name Adogen 464); and water.[4] The solution was then buffered to contain both HCO_3^- and $CO_3^=$ by bubbling CO_2 gas into the solution. Initial pH was 9.8 that reduced to a pH between 8 and 9 upon standing. High-performance liquid chromatography (HPLC)-grade acetone and doubly distilled, deionized water were used for preparing all solutions.

3.2 Nuclear Magnetic Resonance (NMR) Experiments.

The NMR spectra were recorded using a Varian XL-200 Superconducting FTNMR System operating at 50 MHz for ^{13}C spectra and at 200 MHz for ^{1}H spectra. In all cases, the spectra were recorded at probe temperature (ca. 20 °C) and referenced either internally or externally to sodium 3-trimethylsilylpropionate -2,2,3,3-d4 (TSP). The accuracies of the reported chemical shift values (δ) are ±0.1 ppm for ^{13}C and ±0.05 ppm for ^{1}H. Quantitative data were obtained from the digital integration of the peak areas of interest. The ^{13}C NMR spectra were accumulated using the following parameters:

- Pulse width = 3-5 μs (31-45°)
- Sweep width = 20 kHz
- Acquisition time = 1.25-2.7 s
- Pulse delay = 2.0-3.5 s

The number of transients varied for each experiment depending on the signal-to-noise ratios required or desired; in all cases, WALTZ decoupling was used. The ^{1}H NMR spectra were accumulated using the following parameters:

- Pulse width = 3 μs (30°)
- Sweep width = 4 kHz
- Acquisition time = 3.75 s
- Pulse delay = 10.0 s

4. RESULTS AND DISCUSSION

4.1 Competition Factor of Chloride Ion.

Observed first-order rate coefficients for the disappearance of CEES and CEMS in a range of concentrations and solvents are expressed as half lives and listed in Table 2. At substrate concentrations below 0.001M, the CEES is hydrolyzed stoichiometrically to HCl and HEES.[1,4] The rate was measured by monitoring the generation of H^+ with a pH-Stat. The presence of 50 vol % acetone reduced the first-order rate coefficient, k_1, to 10% of its value in pure water. Adding the chloride ion at 0.05M retarded the rate by about 50% in pure water and as much as 90% in the acetone-water mixture. The competition factor of the chloride ion with water, k_{-1}/k_w, for the ethyl ethylenesulfonium ion intermediate (from CEES) was carefully determined by a pH-Stat technique.[7] The results shown in Figures 2-6 are excerpts from the work of Knier, Lewis, Yang, and Durst.[7]

Table 2. Reaction Half-Lives for the Disappearance of $RSCH_2CH_2Cl$ at 20 °C

Solvent	Substrate	Products	$t_{1/2}$,min
Water	4×10^{-4}M CEES	HEES and HCl	1.4^{a}
Water	3×10^{-4}M CEES and 0.05M NaCl	HEES and HCl	2.7^{a}
50 vol % acetone	4×10^{-4}M CEES	HEES and HCl	14^{a}
50 vol % acetone	3×10^{-4}M CEES and 0.05M NaCl	HEES and HCl	132^{a}
50 vol % acetone	0.17M CEES	<u>I</u>, <u>II</u>, HEES, and HCl	$42^{b,c,d}$
50 vol % acetone	0.17M CEES and 0.2M $Na_2S_2O_3$	$C_2H_5SC_2H_4S_2O_3Na$ and NaCl	13^{c}
Microemulsion	0.17M CEES	<u>I</u>,[e] HEES and HCl	$113^{b,c,d}$
Microemulsion	0.17M CEES and 0.7M $Na_2S_2O_3$	$C_2H_5SC_2H_4S_2O_3Na$ and NaCl	21^{c}
Microemulsion	0.20M $CE^{13}MS$	<u>I</u>,[e] HEMS, and HCl	$87^{b,c,d}$
Microemulsion	0.20M $CE^{13}MS$ and 0.7M $Na_2S_2O_3$	$CH_3SC_2H_4S_2O_3Na$ and NaCl	28^{c}
Microemulsion	0.020M $CE^{13}MS$ and 0.7M $Na_2S_2O_3$	$CH_3SC_2H_4S_2O_3Na$ and NaCl	28^{c}

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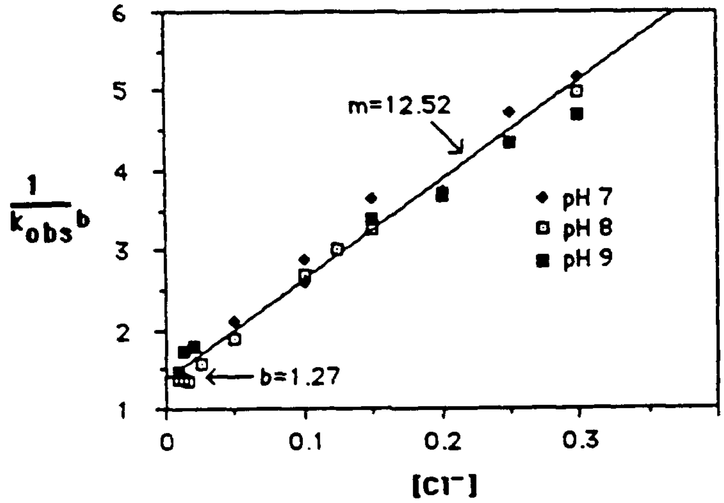
[a] Rate was followed conductometrically[1] or by pH-Stat[7]

[b] Apparent first-order rate assumed

[c] Rate data were measured by NMR

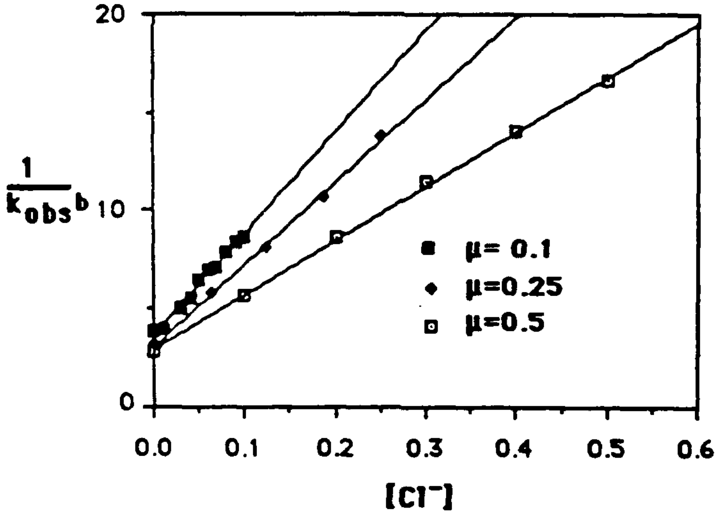
[d] Rate data were presented previously[4]

[e] The NMR signals of <u>I</u> and <u>II</u> overlapped



[a] Temperature = 25°C.
[b] Units of k_{obs} are min^{-1}

Figure 2. Inhibition of Chloride Ion on Rate vs. pH



[a] Ionic Strength maintained with $NaClO_4$. Temperature = 15.0°C
[b] Units of k_{obs} are min^{-1}

Figure 3. Inhibition of Chloride Ion at Controlled Ionic Strength

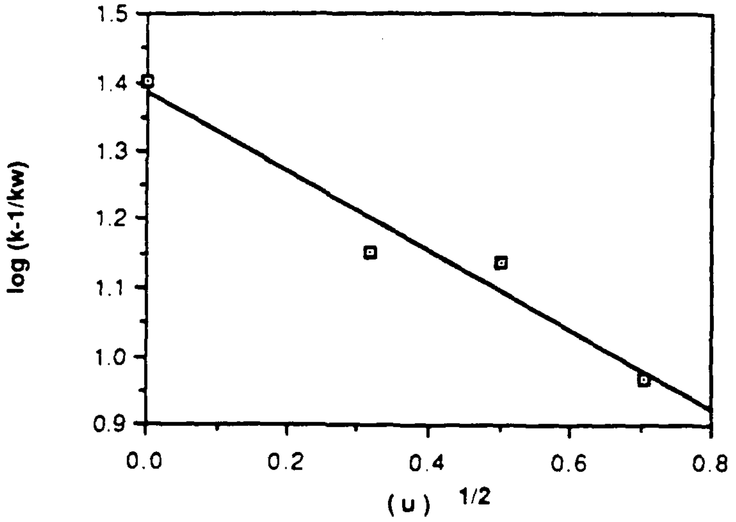
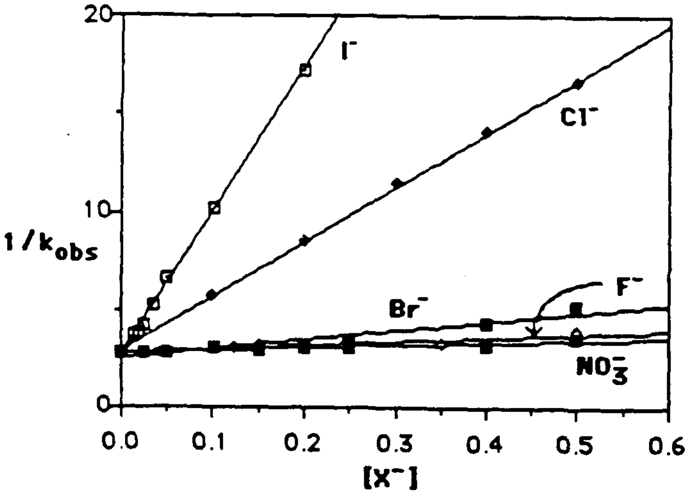


Figure 4. Bronsted Plot of k_{-1} vs. Ionic Strength



Anion	Slope
I^-	73.55
Cl^-	27.7
Br^-	4.51
F^-	1.89
NO_3^-	1.21

[a] Ionic Strength maintained at 0.5 with $NaClO_4$. Temperature 15.0°C

Figure 5. Effect of Anions on CEES Hydrolysis

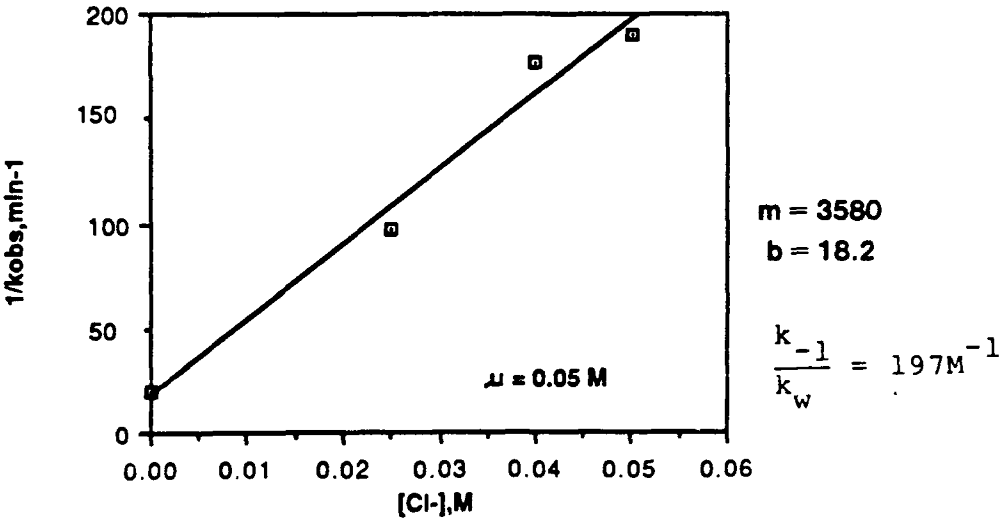


Figure 6. Chloride Inhibition Effect on CEES Hydrolysis in 50 Vol % Acetone at 20 °C

Figure 2 illustrates the first attempt in determining k_{-1}/k_w. The experiments were run at pH values 7, 8, and 9 at 25 °C with different chloride ion concentrations ranging from 0 to 0.3M. The slope, which equals $(k_{-1}/k_w)(1/k_1)$, varied slightly with pH. A careful examination of the plot also revealed that there was a downward curvature in each of the lines, indicating that k_{-1}/k_w varied with ionic strength. A second series of experiments was made at pH 8, and constant ionic strength was maintained by adding sodium perchlorate. The results are shown in Figure 3. Very good straight lines with slopes that increased with the ionic strength were obtained. The k_{-1}/k_w ratios determined from Figure 3 were significantly large; thus, chloride is a strong competitor against water. The figure also shows that the kinetic data obeyed equation 3 derived from rate theories. The variation of k_{-1} with ionic strength was also consistent with that predicted by the Bronsted Equation[5] that used the Debye-Hückle theory to predict that log (k_{-1}/k_w) would vary linearly with the square root of the ionic strength (Figure 4). The k_{-1}/k_w value for CEES increased from 14.7 to 25.1 when extrapolated to 0 ionic strength. This finding is consistent with the increase from 21 to 30 for mustard predicted in the work of Bartlett and Swain.[5] The approximate F_x for other nucleophiles (anions) was also determined for CEES, and the slopes are shown in Figure 5. Although at 0.05M ionic strength the k_{-1}/k_w was $20M^{-1}$ in pure water, in a less polar solvent system of an equal-volume mixture of acetone and water, the measured k_{-1}/k_w ratio increased sharply to 197 M^{-1} (Figure 6) at the same ionic strength (0.05M). The ethylenesulfonium ion and chloride ion recombined at a very fast rate perhaps because they were not completely separated but existed as ion pairs. Consequently, k_{obs} was greatly reduced as k_{-1} became large. An inhibition effect one order of magnitude greater was observed for the chloride ion in 50 vol % acetone-water compared with pure water. The F_x for mustard is also expected to follow the same trend.

4.2 Nucleophile-Assisted Hydrolysis.

At 0.17M substrate, not only is the inhibition effect of the chloride ion significant, but the kinetics are also complicated by the formation of I and II. As reported previously, in the homogeneous system of 0.17M CEES in a 50 vol % $(CD_3)_2CO$-water mixture,[4] three products were detected by ^1H NMR: I, II, and a small amount of HEES. Dimer II was a reaction intermediate that subsequently hydrolyzed to form I. Because CEES primarily reacted with itself, a second-order rate constant of 5.51×10^{-3} s^{-1} M^{-1} at 20 °C was determined. However, as shown in Table 2 for purposes of comparison, the reported half-life of 42 min was based on fitting the same data to a first-order rate equation with a 10% error in the resulting k_{obs}. In the presence of 0.2M sodium thiosulfate, not only was the formation of I and II (HEES and HCl) completely eliminated, but the rate inhibiting effect of the chloride ion was also overcome. Table 3 lists the rate data that followed a first-order rate equation with a half-life of 13 min. Thus, the observed half-life approached that of 14 min measured for 0.001M initial substrate concentration in the same solvent system. The agreement is remarkable, because the rate measured by pH-Stat was determined for an ideally dilute solution under better temperature control. However, it is important to point out again that the presence of X cannot affect the absolute k_1 value (see equation 6) that is controlled by the solvent polarity only.[1]

Table 3. Hydrolysis of CEES in 50 Vol % Acetone and 0.2M $Na_2S_2O_3$ at 20 °C

Time, min	Composition,* mole % by ^{13}C NMR CEES	 $C_2H_5SC_2H_4S_2O_3^-$
0	100.0	0.0
1	37.8	62.2
5	29.1	70.9
12	21.1	78.9
20	12.1	87.9
30	6.9	93.1
(18 hr)	0.0	100.0

*I, II, and HEES were detected neither during the course of the reaction nor in the final solution after 18 hr.

4.3 Hydrolysis in Microemulsion.

As reported previously in the microemulsion system,[4] complicated products were also obtained for both CEES and $CE^{13}MS$ at very slow rates, partly as a result of the high chloride ion contributed from the 0.5M CTAC surfactant (see the composition of the microemulsion in section 3). Because the microemulsion was buffered at a pH close to 10, greater yields of HEMS and HEES were observed in the microemulsion than in the acetone-water mixture. A good k_2 cannot be obtained for $CE^{13}MS$ in the microemulsion due to the higher yield of $HE^{13}MS$ in the presence of $10^{-4}M$ (OH^-) at the initial stage of the reaction. However, when 0.7M $S_2O_3^=$ is added to the microemulsion, $RSC_2H_4S_2O_3Na$ was the principle product from both CEES and CEMS. The reaction rate clearly became first order with a half-life of 28 min, as was particularly demonstrated by the same half-life at both 0.02 and 0.2M initial $CE^{13}MS$ concentration. The kinetic data are listed in Table 4.

Because the kinetics of nucleophile-assisted hydrolysis in microemulsion were the same as in acetone-water mixture, the microstructure and heterogeneity in microemulsion apparently did not affect the mechanism of the hydrolysis reaction. Therefore, the k_1 value can be used as a quantitative measure of the bulk solvent polarity (Y-value) of the microemulsion.[2] The value Y was calculated to be close to 1.00. The calculation was based on a free-energy relationship previously determined for CEES and CEMS.[1] As shown in Figure 7 from reference 2, the microemulsion is a less polar solvent than the 50 vol % acetone solution.

4.4 Reaction of Dimer I with $Na_2S_2O_3$.

The reaction of about 0.15M I ($R = C_2H_5$) produced in a final mixture of CEES and water with 0.7M of freshly added $Na_2S_2O_3$ was investigated. Because a small amount of HCl was also present in the solution as the additional hydrolysis product from CEES, a small amount of the $Na_2S_2O_3$ was decomposed to elemental sulfur by the HCl as shown by the following chemical equation:

$$S_2O_3^{=} + H^+ \longrightarrow HSO_3^- + S\downarrow \qquad (7)$$

The precipitation of sulfur is a good indication of any HCl produced in the reaction mixture. Because excess $S_2O_3^{=}$ (0.7M) was added to the final mixture, the reaction between $S_2O_3^{=}$ and I could still be monitored by ^{13}C NMR with time. A series of products were formed as I decomposed slowly by reacting with the $S_2O_3^{=}$ anion. The products are shown in Table 5 as a function of reaction time. A comparison of Table 5 with Table 3 indicated that the reaction of $S_2O_3^{=}$ with CEES was fast (S_N1), but that the reaction with I was slow (S_N2). As shown in Table 5, both HEES and the thiosulfate ester were the major products of the reaction that can be represented by the following chemical reaction:

$$C_2H_5SC_2H_4S^+(C_2H_5)(C_2H_4OH) + S_2O_3^{=} \longrightarrow$$
$$C_2H_5SC_2H_4S_2O_3^- + C_2H_5SC_2H_4OH \qquad (8)$$

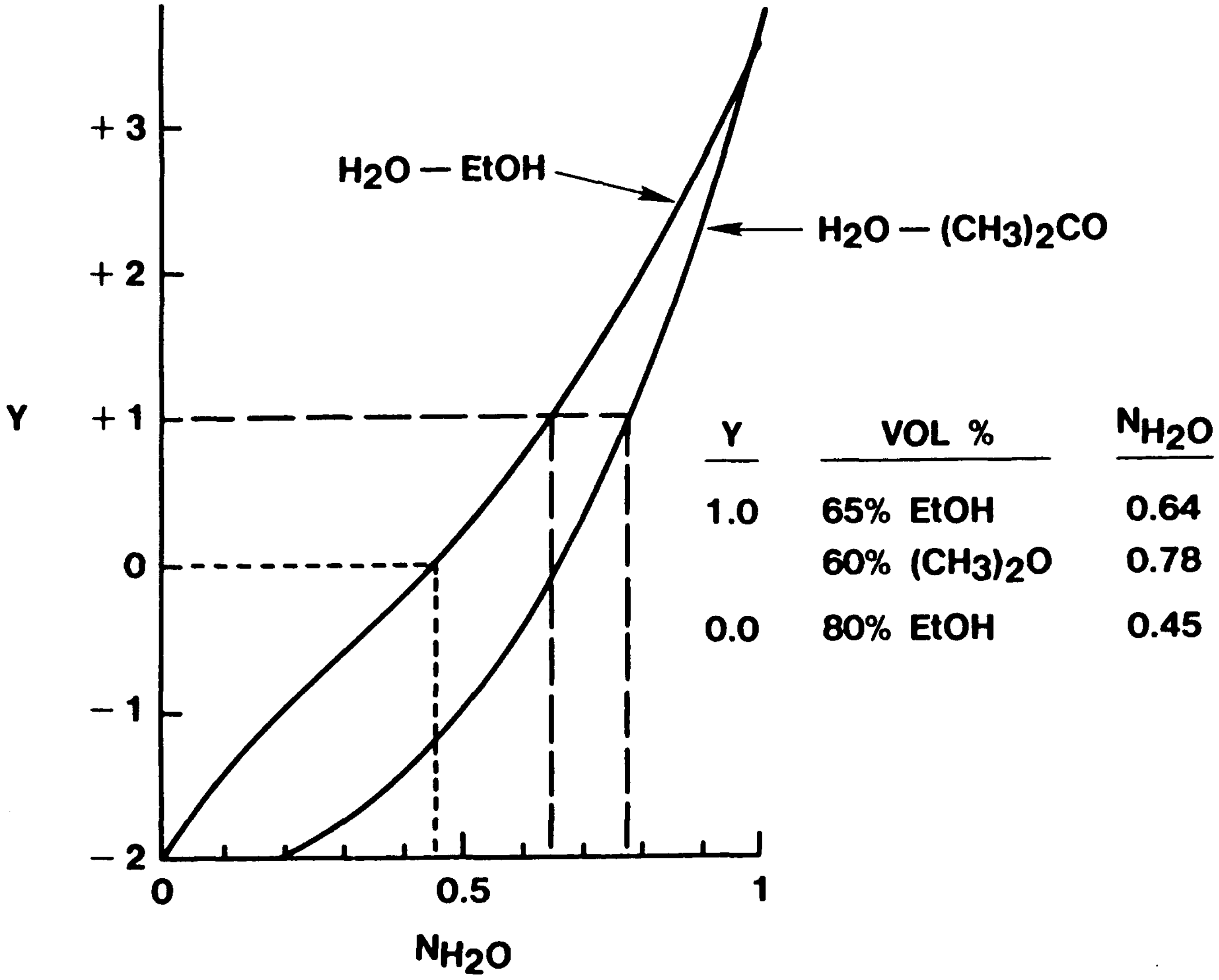
The slow production of ether and thioether was also found as I decomposed slowly or quickly at elevated temperatures.[8] The chemistry of I is very complicated and should be studied further.

Table 4. Hydrolysis of $CE^{13}MS$ in a pH 10 Microemulsion Containing 0.7M $Na_2S_2O_3$ at 21 °C

		Composition, mole % by ^{13}C NMR		
$[CEMS_o]$	Time, min	$CE^{13}MS^a$	$HE^{13}MS^a$	$^{13}CH_3SCH_2CH_2S_2O_3^{-b}$
0.2M	0	100	0	0
	1-15	81	2	17
	55-60	23	7	70
	80-88	12	7	80
	5.5-5.75 hr	0	11	89
0.02M	0	100	0	0
	30-45	38	0	62
	92-107	8	3	89
	22.5 hr	0	8	92

[a] $CE^{13}MS = {}^{13}CH_3SCH_2CH_2Cl$, $\delta = 14.9$ ppm
$HE^{13}MS = {}^{13}CH_3SCH_2CH_2OH$, $\delta = 14.8$ ppm

[b] $\delta = 14.6$ ppm



Y	VOL %	N_{H_2O}
1.0	65% EtOH	0.64
	60% $(CH_3)_2O$	0.78
0.0	80% EtOH	0.45

Figure 7. Solvent Ionization Power (Y) vs. Mole Fraction of Water (N_{H_2O})

Table 5. Reaction Between I (R = C_2H_5) and $Na_2S_2O_3$ in Water at 20 °C

Reaction Time, hr	I	HEES	Products, mole % by ^{13}C NMR			
			$R'S_2O_3^{-a}$	ether[b]	thioether[c]	Others
0	100	---	---	---	---	---
0.5	100	---	---	---	---	---
72.0	33	36	30	---	---	---
168.0	11	37	27	3	8	13
552.0	0	45	21	3	13	18

[a] $C_2H_5SC_2H_4S_2O_3^-$ (R' = $C_2H_5SC_2H_4$)

[b] $C_2H_5SC_2H_4OC_2H_4SC_2H_5$

[c] $C_2H_5SC_2H_4SC_2H_5$

4.5 Two-Phase System and Other Nucleophiles.

In a heterogeneous solution of 0.16M mustard in water containing 0.7M thiosulfate anion, the dimeric sulfonium salts of mustard, H-2TG and CH-TG[4] could not be detected in the water phase. The only reaction product in the final homogeneous solution was $(NaS_2O_3C_2H_4)_2S$ shown in Figure 8, where both chlorines in mustard were replaced. The spectra in Figure 8 clearly illustrated that the solution consisted of only one product from mustard, which normally hydrolyzed to produce very complicated products[4] in the absence of thiosulfate anion.

In a separate study,[9] a phenolate was also effective in competing with other nucleophiles in a reaction mixture of mustard in aqueous ethanol. The products being produced with time were $(C_6H_5OC_2H_4)_2S$ and $ClCH_2CH_2SCH_2CH_2OC_6H_5$ at rates comparable to the two-step S_N1 displacement reactions of mustard.[5,10]

A nucleic acid base, adenine ($C_5H_5N_5$), was also examined in both water and microemulsion for its competitiveness with water for the ethylenesulfonium ion. Unfortunately, the base (present at a concentration of a saturated solution) was completely inert. No reaction was observed between CEES and $C_5H_5N_5$. Only the typical hydrolysis products I, HEES, and HCl were detected. This result was contrary to that reported by a contract effort conducted at the University of Kentucky.[11]

4.6 Stability and NMR Parameters of Thiosulfate Ester Products.

Only one organic product, $RSCH_2CH_2S_2O_3^-$, was detected by NMR for CEES ($R = C_2H_5$) and CEMS ($R = CH_3$) in each of the solvent systems. The product did not react further when it was subsequently monitored for 2 months in the same solution. The NMR parameters in ppm for $CH_3CH_2SCH_2CH_2S_2O_3^-$ are ^{13}C (H_2O, external TSP/D_2O):16.8 (CH_3), 27.7 ($CH_3\underline{C}H_2S$), 32.9 ($S\underline{C}H_2CH_2S_2O_3^-$), and 37.3 ($SCH_2\underline{C}H_2S_2O_3^-$). The ^1H parameters [4.8 ppm standard deuterium hydrogen oxide (HDO)] are, in the same order, 1.35 (t, 3H, $J \sim 7.4$ Hz), 2.75 (q, 2H, $J \sim 7.4$ Hz), and 3.09 (t, 2H, $J \sim 7.4$ Hz). The ^{13}C NMR shift (microemulsion, external TSP/D_2O) for $^{13}CH_3$ of $^{13}CH_3SCH_2CH_2S_2O_3^-$ in the microemulsion is 14.6 ppm. The ^{13}C shifts (H_2O, external TSP/D_2O) for the product from mustard ($^-O_3S_2CH_2CH_2SCH_2CH_2S_2O_3^-$) are in ppm, 37.5 ($^-O_3S_2CH_2$) and 33.4 ($CH_2S$). The spectrum is illustrated in Figure 8.

5. CONCLUSIONS

Using thiosulfate as an example, it has been shown that the reactive ethylenesulfonium ion can be completely scavenged. We have also demonstrated that a competitive nucleophile enhances the observed rate of the displacement reactions of 2-chloroethyl sulfides. The thiosulfate anion not only competes effectively with the sulfide substrate and water, completely eliminating the formation of I, II, $RSCH_2CH_2OH$, and HCl, but also overcomes the rate inhibiting effect of the chloride ion. Thus, the observed rate at 0.1 to 0.2M substrate is faster and approaches that measured for 0.001M substrate. Therefore, the rate is only dependent on the polarity of the solvent required to dissolve the substrate. For any aqueous solvent system, the hydrolysis or displacement rate of mustard cannot be increased above the limiting value k_1. The addition of a competitive nucleophile can promote the observed rate to the limiting value of k_1.

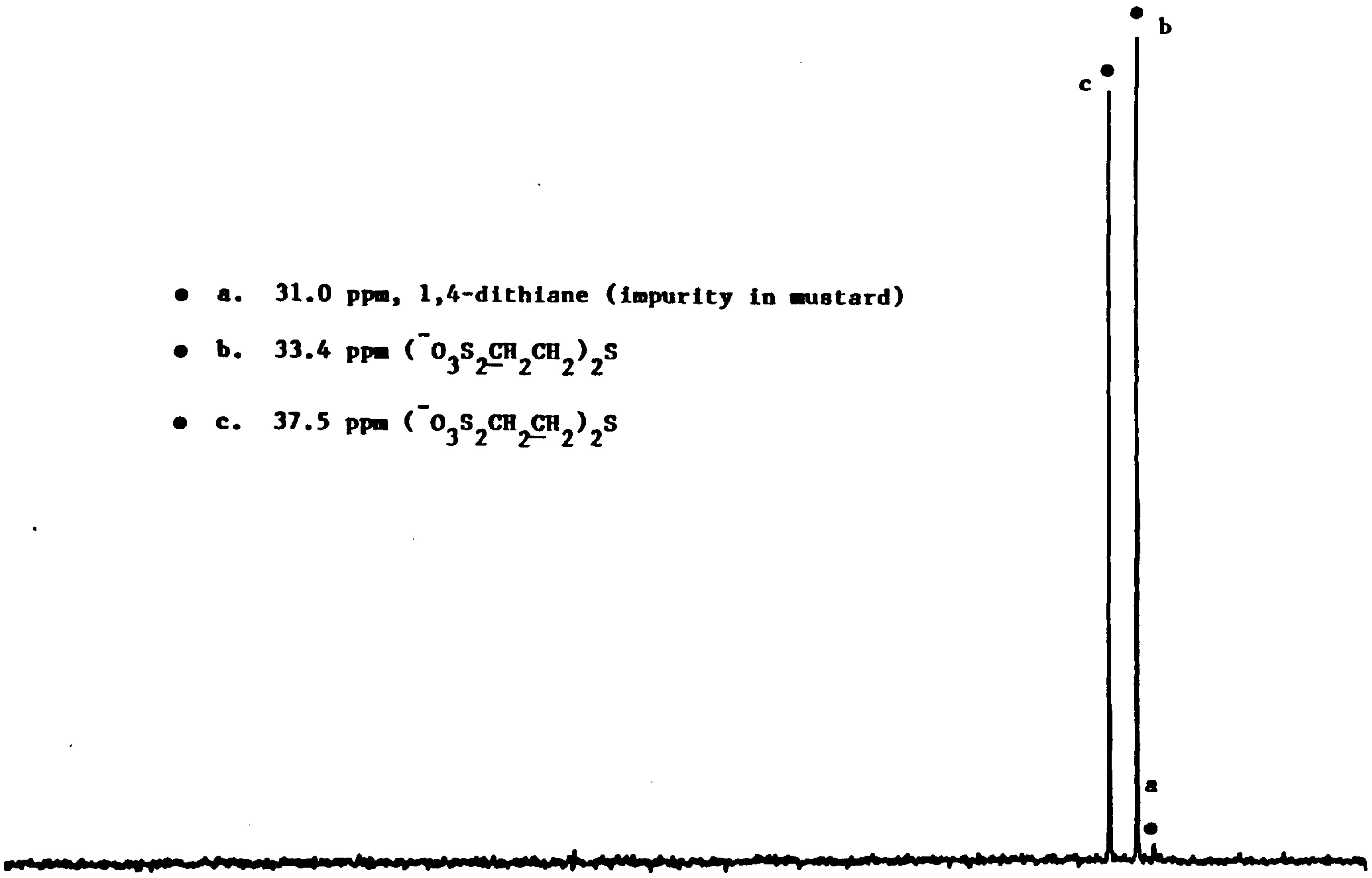


Figure 8. ^{13}C NMR Spectra of the Final Solution of 0.15M Mustard in 0.7M $Na_2S_2O_3$ Solution

6. RECOMMENDATION

Based on the above discussion, it is recommended that a large amount of a strong nucleophile, such as $Na_2S_2O_3$, be added to water for the hydrolysis of mustard. In a microemulsion, $S_2O_3^=$ can be incorporated as the counter ion of the cationic surfactant present in high concentrations. The nucleophile will speed the rate of the displacement reaction to that of the limiting first-order rate at negligible chloride ion concentration. All of the undesirable sulfonium chloride salts, which can decompose back to mustard, will also be eliminated from the reaction mixture. However, in selecting the proper nucleophile to decontaminate mustard, it is important that the product between mustard and the nucleophile be nontoxic and unreactive.

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