

Study on the Kinetics and Transformation Products of Sulfur Mustard Sulfoxide and Sulfur Mustard Sulfone in Various Reaction Media

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ABSTRACT: Considering postulates of the Chemical Weapons Convention, this article is an attempt to improve the decontamination methods of mustard gas (HD) and studying its products of decontamination. It is widely known that mustard gas sulfoxide (HDO; $\text{O}=\text{S}(\text{CH}_2\text{CH}_2\text{Cl})_2$) and sulfone (HDO₂; $\text{O}_2=\text{S}(\text{CH}_2\text{CH}_2\text{Cl})_2$) undergo further transformations to another compounds, but so far kinetics of these processes have not yet been investigated neither carefully nor thoroughly. This study is focused on determination of kinetics and mechanisms of transformation of HD oxidation products. The primary objective of this study is to assess the impact of selected factors on the kinetics of the HCl elimination reaction and to determine the conditions in which cyclization reactions of divinyl sulfoxide and sulfone proceed. The HDO and HDO₂ decay kinetics were monitored in an aqueous solution of the desired pH. The rate of HCl elimination from HDO and HDO₂ is strongly dependent on pH. For example, with pH increasing from 9 to 12 the rate of HCl elimination from HDO increased over 1200 times. In solutions of pH 9, HDO loses hydrogen chloride at approximately 100 times slower compared to HDO₂, and the difference is reduced with increasing pH. In pH 12 solutions, the rate of hydrogen chloride loss from HDO₂ is only 20 times higher than the HCl loss from HDO. Divinyl sulfoxide and sulfone undergo a further transformation in a strongly alkaline environment, leading to cyclization and formation of 1,4-thioxane sulfoxide and sulfone, respectively. Elimination of HCl from HDO and HDO₂ goes with a rapidly increasing rate with increasing pH if alkalinity of the reaction medium is relatively very high (the range of pH 9–12). Furthermore, the conversion of divinyl sulfone and

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sulfoxide to sulfoxide and sulfone thioxane, respectively, occurs at a measurable rate when the pH of the solution is in the range of 12–14. © 2017 Wiley Periodicals, Inc. *Int J Chem Kinet* 50: 75–89, 2018

INTRODUCTION

Sulfur mustard (SM or HD, this is military designation for pure sulfur mustard) is a highly toxic and persistent blistering chemical warfare agent (CWA). It is one of the oldest and most important CWAs, presenting cytotoxic alkylating properties. Hence, decontamination of that compound seems to be of considerable interest [1]. Chemical decontamination of HD immediately after contact is still the best method of protection. An effective decontamination process should cause a complete and rapid chemical decomposition of the target CWA, and reaction products should demonstrate a significantly reduced toxicity or be completely nontoxic [2]. A decontaminant is required to immediately convert HD into nontoxic products. Various methods for HD decontamination are reported in the literature [3,4]. Among them hydrolysis and oxidation are preferred. The most common and widely used process is the oxidation of HD using various oxidizing agents, which are able to achieve its rapid decontamination. With regard to the chemical decontamination of a highly toxic compound such as HD, it is necessary, for obvious reasons, to know the nature of the products formed by the decontamination reaction. As it was said earlier, methods of decontamination of HD used are very often based on oxidation. The sulfoxide formed (Fig. 1) is relatively harmless. However, oxidation can also create the sulfone, which is slightly toxic [5]. A method for rapid detoxification that promotes the production of the sulfoxide is thus required. Oxidation in a basic reaction medium can also allow the detoxification of mustard gas; elimination of HCl from the chloroethylsulfoxide or the chloroethylsulfone leads to the corresponding vinyl sulfoxide or vinyl sulfone, which are harmless compounds [6].

The reason of this article is based on two premises, namely:

Since the Convention on the “Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction” (*Chemical Weapons Convention – CWC*) [7], came into effect in 1997, there has been an increased importance of scientific research related to analysis of CWA and their transformation products [8]. Considering postulates of the CWC and a constant development of analytical methods, methods for development of increasingly sensitive and precise procedures for analysis of CWA-

containing samples and of related compounds should be sought [9]. For that reason, a careful analysis of reactions of analyzed CWAs and their degradation products is extremely significant.

Another serious problem is the chemical munitions are dumped in the Baltic Sea [10]. Chemical agents released from rusting projectiles pose a great threat to marine ecosystems. Hence, constant monitoring of dumped ammunition and of CWA degradation products is necessary.

After World War II, large amounts of chemical weapons (CW) were dumped in the Baltic Sea [11]. The dumped CWA's were sulfur mustard, phosgene, chloroacetophenone (CN), adamsite (DM), Clark I (DA), Clark II (DC), nitrogen mustard (HN3), tabun (GA), and arsine oil. CWA still present in the Baltic Sea constitute a serious threat for both the marine environment and for people. For these reasons, it is essential to know mechanisms of possible transformations of sulfur mustard. It is also important to determine the time of occurrence of individual decomposition products, because that would allow a preliminary estimation if liquid HD has leaked from the sunk ammunition, and—if yes—when. For that reason, this study is aimed at determination of the kinetics and mechanisms of transformation of HD oxidation products, namely HD sulfoxide (HDO or $\text{O}=\text{S}(\text{CH}_2\text{CH}_2\text{Cl})_2$) and sulfone (HDO_2 or $\text{O}_2=\text{S}(\text{CH}_2\text{CH}_2\text{Cl})_2$). The primary objective of this study is to analyze the effect of selected factors on the kinetics of the hydrogen chloride elimination reaction and on circumstances in which HD sulfone and sulfoxide rings are closed, and to determine the kinetic data of those reactions.

When analyzing solutions obtained as a result of detoxification of sulfur mustard with various oxidizers, it is important to know how the products formed depend on pH of the solution, where the process goes on. Therefore, there is a question: Under what conditions does HD oxidation lead to formation of divinyl sulfoxide (or sulfone), and under what conditions is 1,4-thioxane sulfoxide (or sulfone) the product?

THEORY

Oxidation of sulfur mustard follows the scheme presented in Fig. 1.

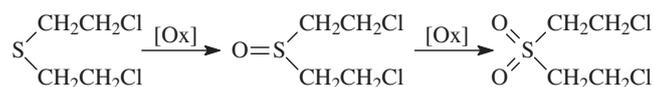


Figure 1 Sulfur mustard oxidation scheme.

Products obtained from HD oxidation (HD sulfoxide and sulfone) may undergo further transformations. Literature data presented in Tables I and II indicate that there are many, often contradictory, opinions on the course of those transformations. Products resulting from HD oxidation may, for example, lose hydrogen chloride according to the scheme presented in Fig. 2 [12].

These reactions result in the formation of divinyl sulfone and sulfoxide, respectively, and of some intermediate products. The loss of hydrogen chloride from HD oxidation products may occur under the influence of various factors. Reaction conditions and resulting products are presented in Tables I and II.

Elimination of hydrogen chloride from molecules of HD sulfone leads to various end products, depending on conditions of the process. In some cases, even in the medium characterized by a moderately alkaline pH, thioxane sulfone is formed. For example, in pH 8 solutions at 38°C, 96% of HD sulfone disappears within 2 h (determined on the basis of formed chloride negative ions) and after 3 h the disappearance reaches 99%. When HD sulfone is present in a solution of pH 7.35 at 38°C, its disappearance after 2 and 3 h is 58% and 75%, respectively [13].

Elimination of hydrogen chloride from HD sulfoxide is much less rapid: In pH 8 solutions at 38°C, only

Table I Literature Data on Transformation of HD Sulfoxide Depending on the Reaction Medium

| Parameters of the Reaction Medium | | | | | | | |
|--|----------|---------------------|---------------|--|--|---|-----------|
| Reaction Medium | pH | Temperature (°C) | Reaction Time | Product Yield | Intermediate or Side Product | Main Product | Reference |
| NaOH _(aq) hot solution | 8 | 38 | 2 h 5 h | <2% 12% | – | 2,2-Dichlorodiethyl sulfoxide | [13] |
| H ₂ O | – | 20 100 | 10 days | 0.0% – | – | No reaction The inability to measurement | [17] |
| 12g NaOH in 120 mL H ₂ O | Alkaline | Boiling temperature | 2 h | 38% | – | 1,4-Thioxane sulfoxide | [14] |
| 30 g NaOH in 300 mL Ethanol–H ₂ O (50%–50%) | Alkaline | Boiling temperature | 12 h | 22.5% | Thiodiglycol sulfoxide, 1,4-thioxane sulfoxide | Diethoxydiethyl sulfoxide | [14] |
| 10 g NaOH in 250 mL ethanol (95%) | Alkaline | Boiling temperature | 16 h | 63% | – | Diethoxydiethyl sulfoxide | [14] |
| 2% HDO 3% NaHCO ₃ in distilled water | Alkaline | – | 5 min | None AgCl after addition AgNO ₃ | – | Not identified | [18] |
| 2% HDO 3% NaHCO ₃ in distilled water | Alkaline | – | 2 h | Very faint cloudiness of AgCl after addition AgNO ₃ | – | Not identified | [18] |
| 2% HDO 3% NaHCO ₃ in distilled water | Alkaline | – | 24 h | The test of AgCl positive (flocculent precipitate) | – | Not identified | [18] |

Table II Literature Data on HD Sulfone (HDO₂) Transformations Depending on the Reaction Medium

| Parameters of the Reaction Medium | | | | | | | |
|---|----------|---------------------|--------------------------|---|----------------------------------|-------------------------------|-----------|
| Reaction Medium | pH | Temperature (°C) | Reaction Time | Product Yield | Intermediate or Side Product | Main Product | Reference |
| NaOH _(aq) hot solution | 8 | 38 | 2 h 3 h | 96% 99% | – | Divinyl sulfone | [13] |
| Ringer phosphate buffer | 7.35 | 38 | 2 h 5 h | 53% 75% | – | Divinyl sulfone | [13] |
| HDO ₂ + 1.05 Na ₂ CO ₃ | Alkaline | “Hot” | – | – | Small amount of thioxane sulfone | Thiodiglycol sulfone | [13] |
| 38 g HDO ₂ 23 g Na ₂ CO ₃ 75 mL H ₂ O | Alkaline | Heated under reflux | 1 h | 80% | Thioxane sulfone (2 g) | Thiodiglycol sulfone (26 g) | [13] |
| 38 g HDO ₂ 23 g Na ₂ CO ₃ in 75 mL water + next portion 23 g Na ₂ CO ₃ in 90 mL H ₂ O | Alkaline | Heated under reflux | 1 h + <i>next</i> 1 h | – | Thiodiglycol sulfone (9 g) | Thioxane sulfone (14 g) | [13] |
| 42g NaOH in 600 mL H ₂ O | Alkaline | Boiling temperature | 6 h | 70% | Thiodiglycol sulfone | 1,4-Thioxane sulfone | [14] |
| 20 g NaOH in 250 mL ethanol – H ₂ O (50%–50%) | Alkaline | Boiling temperature | 3 h | – | 1,4-thioxane sulfone | Diethoxy-diethyl sulfone | [14] |
| 6 g NaOH in 100 mL ethanol (95%) | Alkaline | Boiling temperature | 16 h | – | – | Diethoxy-diethyl sulfone | [14] |
| 1 g HDO ₂ 100 mL Boiling water | – | 100 | – | Partial precipitation of AgCl after AgNO ₃ | – | Probably thiodiglycol sulfone | [17] |
| 1% HDO ₂ 1.68% NaHCO ₃ in distilled water | 7.8 | – | 5 min | 27% | – | Vinyl sulfone | [18] |
| 1% HDO ₂ absence of NaHCO ₃ in distilled water | 5.5 | – | 14 days | 0% | – | Lack of products | [18] |

2% of HD sulfoxide disappears after 2 h and only 12% after 3 h [13].

Cashmore [14] observed that the reaction of HD sulfoxide or sulfone with sodium hydroxide in alcohol or aqueous medium leads to formation of thioxane sulfoxide or sulfone. That is surprising, because both HD and thiodiglycol do not react to yield thioxane in the same conditions. A strongly activating effect on the halogen atom of the sulfoxide or sulfone group is well known; therefore, the assumption is justified that dehydrohalogenation of HD sulfoxide or sulfone leads to formation of divinyl sulfoxide and sulfone, respectively. Resulting products may easily undergo a reac-

tion of partial addition of a water molecule, resulting in formation of vinyl 2-hydroxyethyl sulfone or sulfoxide, respectively, that may transform into thioxane sulfone or sulfoxide according to the scheme presented in Fig. 3 [15].

HD sulfone in aqueous solution of sodium carbonate is transformed mostly into thiodiglycol sulfone, and only in a minor extent into thioxane sulfone [13]. In comparison, in diluted aqueous solutions of sodium hydroxide, HD sulfone is transformed into thioxane sulfone in 80% yield [16]. In the course of heating, the aqueous solution of HD sulfone solution with an addition of Na₂CO₃, thioxane sulfone is formed,

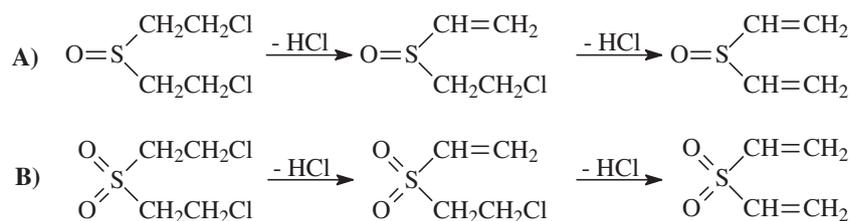


Figure 2 Hydrogen chloride loss scheme for the molecule of (A) HD sulfoxide and (B) HD sulfone.

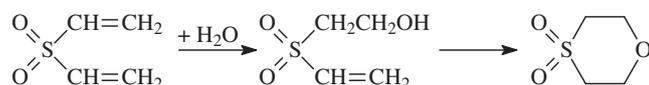


Figure 3 The schematic reaction of divinyl sulfone transformation into thioxane sulfone.

with formation of divinyl sulfone as an intermediate stage. However, it is much more probable that vinyl 2-hydroxyethyl sulfone is an intermediate product of that process, formed in consequence of partial hydration of divinyl sulfone, according to the scheme presented in Fig. 3 [15].

EXPERIMENTAL

Chemicals and Materials

Pure sodium hydroxide (NaOH), hydrochloric acid (HCl), dichloromethane, hexane, acetone, ethanol, magnesium sulfate, phosphoric acid, acetic acid, boric acid, and sodium chloride were purchased from Chempur (Piekary Śląskie, Poland). N,O-Bis(trimethylsilyl)trifluoroacetamide was purchased from Aldrich (St. Louis, MO).

Sulfur mustard sulfoxide (HDO) and sulfone (HDO₂) were obtained in the Institute of Chemistry of the Military Technical University (Warsaw, Poland), and their purity was verified using gas chromatography with mass spectrometry. The purity of synthesized compounds was 97.5% and 98.2% for HDO and HDO₂ respectively.*

Britton–Robinson buffer was used for providing a suitable pH of the reaction medium. Britton–Robinson buffers were prepared in a usual way, i.e., by mixing a solution of 0.04 mol L⁻¹ phosphoric acid, 0.04 mol L⁻¹ acetic acid, and 0.04 mol L⁻¹ boric acid with the appropriate amount of 0.2 mol L⁻¹ sodium

hydroxide solution [19]. Chemicals for the preparation of the Britton–Robinson buffers were obtained from Chempur (Piekary Śląskie, Poland).

Instruments

Analyses were performed using an HP Model 6890 gas chromatograph with an HP Model G2350A atomic emission detector (Hewlett-Packard, Wilmington, DE). Separation of analytes was completed on an HP-5 capillary column (30 m × 0.32 mm × 0.25 μm) from Agilent Technologies. The analysis was carried out using the following temperature program: The column was heated from 70 to 250°C at a rate of 10°C min⁻¹, and the final temperature was maintained for 12 min. Helium was the carrier gas, with a gas flow of 1 mL min⁻¹. Injector temperature was 270°C. The detector temperature and transfer line temperature were 270°C. HP Chemstation software was used for the GC system control and data acquisition. Identification of reaction products were taken using a gas chromatograph (Agilent Technologies 7890A) coupled with a tandem mass spectrometer Agilent Technologies 7000 GC/MS triple quadrupole (Agilent Technologies, Palo Alto, CA). The analysis was completed using a BP-5 capillary column (30 m × 0.25 mm × 0.25 μm) from SGE and was carried out using the following temperature program: The column was heated from 70 to 250°C at a rate of 10°C min⁻¹, and the final temperature was maintained for 12 min. Helium was the carrier gas, and the gas flow rate was 1 mL min⁻¹. The injector temperature was variable at around 250°C. The temperatures of the transfer line, ion source, and quadruples were 250, 230, and 150°C, respectively. During the analysis, the injector was in split mode (100:1).

* Warning: Mustard and some of its transformation products are a potent vesicants and must be handled with proper safety precautions in a closed system or in a hood with good ventilation.

HD Sulfoxide Synthesis

Sulfur mustard sulfoxide was obtained using a modified procedure [12]. In a round-bottom flask equipped with a mixer, thermometer, reflux condenser, and a funnel, 50 mL of condensed nitric acid was placed. Then 10 mL of sulfur mustard was added dropwise, maintaining a constant temperature of approximately 20°C. After the whole amount of HD was added, mixing was continued for another 60 min; next the reaction mixture was poured into a flask containing ice/water. When the ice melted, the whole solution was transferred into a separator and extracted three times with methylene chloride. The resulting solution was dried over anhydrous magnesium sulfate. The next day, the mixture was filtered and the solvent was removed using a vacuum evaporator. The sediment obtained was crystallized from water with the addition of ethanol.

HD Sulfone Synthesis

Sulfur mustard sulfone was obtained according to a modified procedure [12]. Fifty milliliters of glacial acetic acid was added to 12 g of anhydrous chromium oxide (CrO_3). The mixture was heated to 100°C, and 2 mL of sulfur mustard was added dropwise. After the whole volume of HD was added, the reaction mixture was mixed for another 2 h, maintaining a constant temperature of 100°C. Then the flask contents were poured into a container with ice/water. When the ice melted, the whole solution was transferred to a separator and extracted three times with methylene chloride. The extracts obtained were combined, and the resulting solution was dried over anhydrous magnesium sulfate. The next day, the mixture was filtered to separate the MgSO_4 sediment, and the solvent was removed using a vacuum evaporator. The resulting sediment was crystallized two times from the acetone/hexane mixture.

Reaction Methodology

Ninety-nine milliliters of buffer of desired pH and a magnetic dipole were placed in an Erlenmeyer flask with a ground glass neck. The prepared reaction set was placed in a thermostated vessel with a magnetic stirrer. The contents of the flask were mixed for 10 min to stabilize the temperature, and 1 mL of acetone with a corresponding amount of HD sulfoxide or sulfone was added; so that the initial concentration of HD sulfone or sulfoxide was 1 mM. The reactions were carried out at a temperature of 25°C. This is different from the temperature at the bottom of the Baltic Sea, which is 4–7°C. In case of sea conditions, the reactions studied in this experiment would be very slow and could even take

a year. In contrast, a temperature of 25°C allows for a quick and accurate investigation of HDO and HDO_2 transformations. The pH is in the range from 7 to 8.5 in the Baltic Sea, whereas the experiments were carried out in a wider pH range from 8 to 14, because for pH below 8 HDO and HDO_2 reactions time are very long, which may create problems during the monitoring of these reactions.

Sampling and Sample Preparation

Samples for chromatographic analysis were prepared using the liquid–liquid extraction method. The technique allows relatively rapid extraction of analyzed substances from the reaction mixture, and thus stopping the reaction. Selection of extraction solvents demonstrated that dichloromethane offered the best properties. That solvent allowed high recovery of analytes and had a low boiling point, thus making it easy to separate from the analyzed mixture during the chromatographic analysis.

Two milliliters of the reaction mixture was drawn with a pipette in defined time point. The sample was transferred to a screw-capped test tube containing 2 mL of methylene chloride and approximately 0.1 g of sodium chloride. The content was shaken vigorously for 15 s. To achieve a precise separation of phases, the test tube was centrifuged for 3 min at 2000 rpm. Then the lower phase was transferred to another test tube containing approximately 0.5 g of anhydrous magnesium sulfate. It was shaken for 5 min at the rate of 1500 shakes per minute, which allowed removal of trace amounts of water from the organic phase. The dried solution was decanted from over the sediment of MgSO_4 and analyzed with GC-AED.

RESULTS AND DISCUSSION

Kinetics of Hydrogen Chloride Elimination Reaction

With increased alkalinity of HDO and HDO_2 solutions, reduced concentrations of both compounds were observed, along with the appearance of some unidentified substances in the solution. Using GC-MS, they were identified as mono- and divinyl derivatives of HD sulfoxide and sulfone, respectively. It was determined that the hydrogen chloride elimination reaction in alkaline solutions of HD sulfoxide and/or sulfone is a typical consecutive reaction, which means that product of a first reaction is a substrate in another, proceeding according to the scheme presented in Fig. 2.

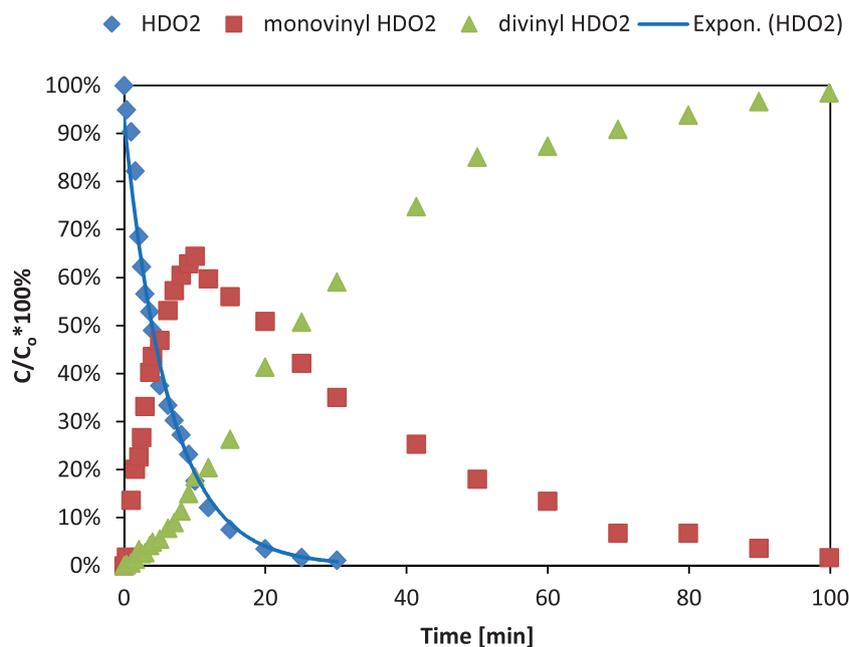


Figure 4 Kinetics of HDO₂ loss during elimination of hydrogen chloride with formation of HDO₂ monovinyl derivative (intermediate product) and divinyl sulfone (final product); reaction medium – aqueous Britton–Robinson buffer solution, pH 10. [Color figure can be viewed at wileyonlinelibrary.com]

Figure 4 presents an example graph of kinetics of hydrogen chloride elimination from molecules of HD sulfone. The consecutive character of the reaction is discernible. In the alkaline medium, the concentration of HD sulfone (HDO₂) decreases exponentially. The loss of HDO₂ is accompanied by an initial increased concentration of the monovinyl derivative (monovinyl HDO₂) reaching a maximum, followed by a gradual decrease of the concentration. Elimination of the second hydrogen chloride molecule leading to formation of a divinyl derivative (green color) may be evidenced by a gradual increase of its amount in the reaction mixture.

Examples of chromatograms obtained during the analysis of the samples containing sulfur mustard sulfone or sulfoxide and products of elimination reactions are shown in Fig. 5. The mass spectra of all compounds identified during the experiments are shown in Fig. 6. It should be mentioned that the mass spectrum of divinyl sulfone and vinyl chloroethyl sulfone are not available in any MS databases.

The Consecutive Hydrogen Chloride Loss Reaction

Elimination of hydrogen chloride from oxidized forms of sulfur mustard is a typical consecutive reaction. Its general scheme is presented in Fig. 7.

While determination of the reaction rate constant (k_1) for conversion of compound A into compound B is not problematic; the determination of the k_2 constant, corresponding to transition of compound B into compound C requires some mathematical transformations.

The rate of substrate, intermediate product, and final product concentration changes may be expressed with differential equations:

$$\frac{d[A]}{dt} = -k_1 [A] \quad (1)$$

$$\frac{d[B]}{dt} = k_1 [A] - k_2 [B] \quad (2)$$

$$\frac{d[C]}{dt} = k_2 [B] \quad (3)$$

If at the starting point $t = 0$, there is only the substrate A present in the system, then $[A] = [A_0]$ and $[B] = 0$ and $[C] = 0$. Based on the law of conservation of mass, in any moment of the reaction the sum of interim concentrations of all reagents is equal to the initial concentration of the substance A:

$$[A_0] = [A] + [B] + [C] \quad (4)$$

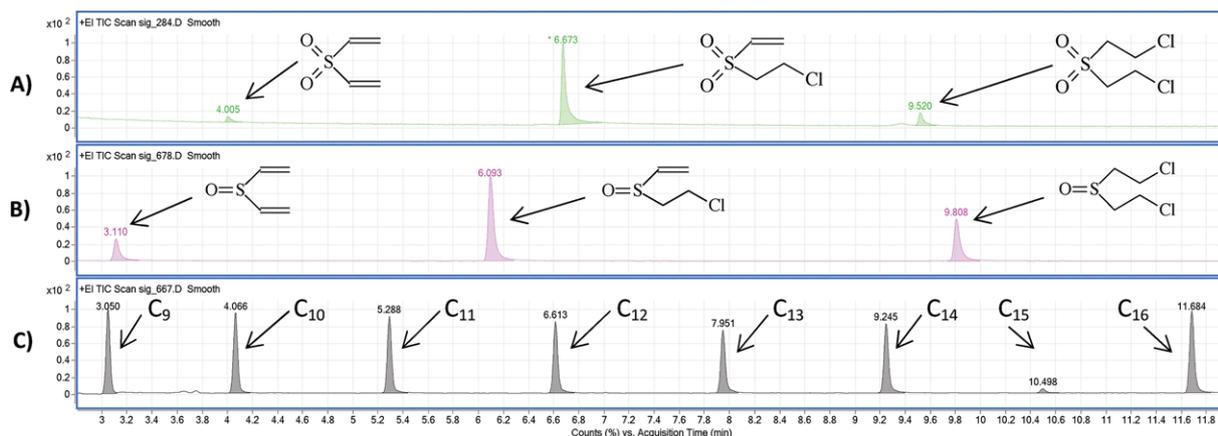


Figure 5 Parallel presentation of chromatograms obtained during the analysis of (A) alkaline HDO solution, (B) alkaline HDO₂ solution, and (C) *n*-alkanes C5–C17. [Color figure can be viewed at wileyonlinelibrary.com]

Following separation of variables and bilateral integration, there is the following equation for temporary concentration of the substance A:

$$[A] = [A_0] e^{-k_1 t} \quad (5)$$

Equation (5) may be substituted into Eq. (2)

$$\frac{d[B]}{dt} = k_1 [A_0] e^{-k_1 t} + k_2 [B] \quad (6)$$

Following integration of Eq. (6), with the assumption that $[B]_0 = 0$, the following expression is obtained, describing the change of concentration of substance B during the reaction:

$$[B] = [A_0] \left(\frac{k_1}{k_2 - k_1} \right) (e^{-k_1 t} - e^{-k_2 t}) \quad (7)$$

Then, using Eq. (4), (5), and (7), it is possible to determine the relationship that describes change of concentration of the substance C as a function of time, considering the initial concentration of the substance A and kinetic constants of individual reactions:

$$[C] = [A_0] \left(1 + \frac{k_1}{k_2 - k_1} e^{-k_2 t} - \frac{k_2}{k_2 - k_1} e^{-k_1 t} \right) \quad (8)$$

$$[C] = [A_0] \left(1 + \frac{1}{k_2 - k_1} (k_1 e^{-k_2 t} - k_2 e^{-k_1 t}) \right) \quad (9)$$

Following integration of Eq. (7) and equating the derivative to zero ($\frac{d[B]}{dt} = 0$), it is possible to determine expressions describing the maximum concentration of

the substance B and the time when it is reached:

$$[B]_{\max} = [A_0] \left(\frac{k_2}{k_1} \right)^{\left(\frac{k_2}{k_1 - k_2} \right)} \quad (10)$$

$$[B]_{\max} = [A_0] \left(\frac{k_1}{k_2} \right)^{\left(\frac{k_2}{k_2 - k_1} \right)} \quad (11)$$

$$t_{\max} = \frac{1}{k_1 - k_2} \ln \left(\frac{k_1}{k_2} \right) \quad (12)$$

Following experimental determination of values $[B]_{\max}$ and t_{\max} , values of both k_1 and k_2 may be calculated using the system of two Eq. ((11) and (12)) with two unknowns.

The correctness of these transformations may be verified by comparison of theoretical results with experimental ones. Figure 8 presents a comparison of the real course of the reaction of hydrogen chloride elimination from molecules of HD sulfoxide in the pH 12 Britton–Robinson buffer with data obtained theoretically, based on the previously mentioned mathematical transformations. The comparison indicates that theoretical curves obtained from mathematical deliberations and transformations are consistent (with a certain margin of error) with experimental data. Therefore, experimentally determined k_1 and k_2 values are correct.

The Effect of pH on the Rate of HCl Elimination Reaction

The hydrogen chloride elimination rate from both sulfur mustard sulfoxide and sulfone molecules depends

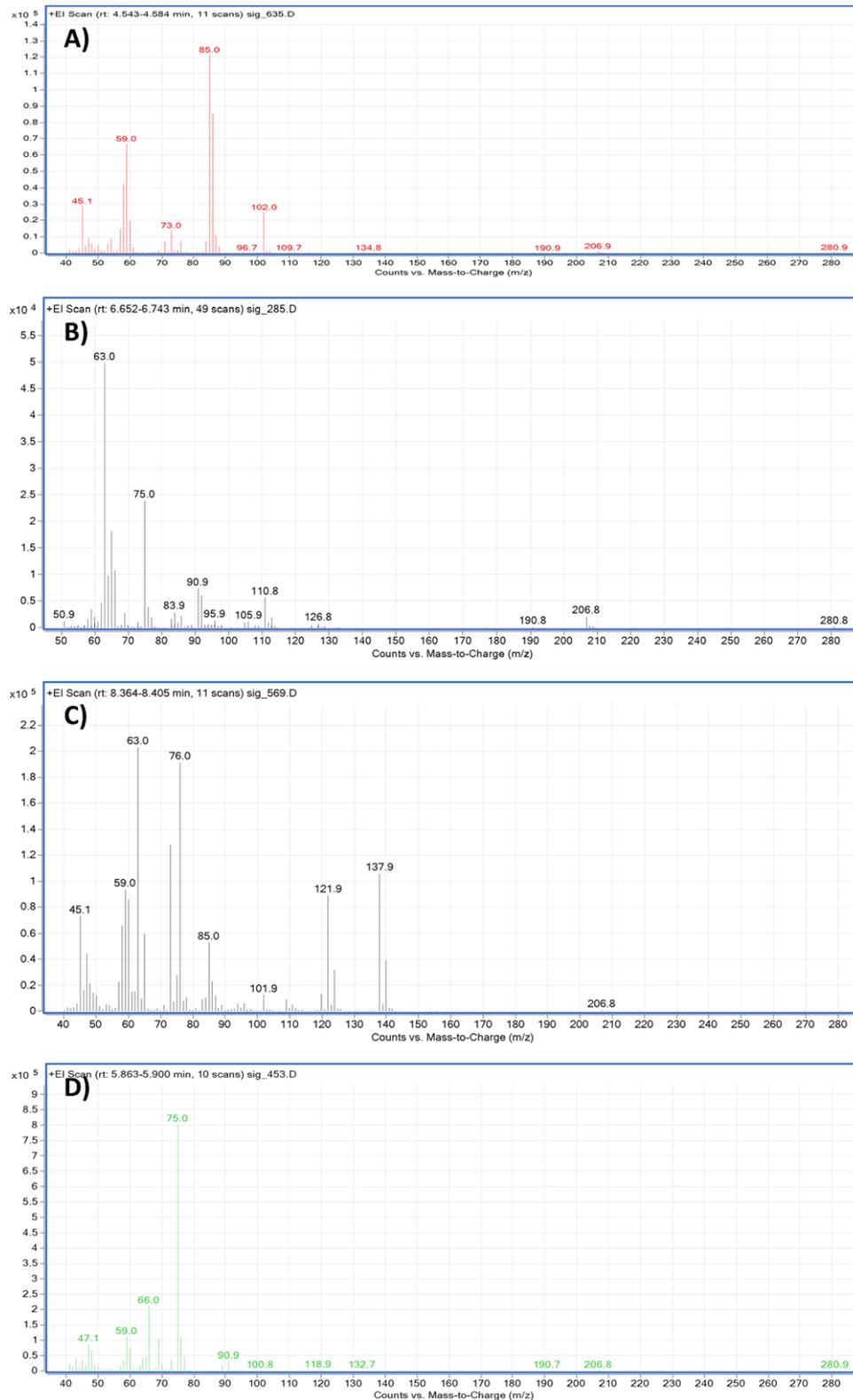


Figure 6 The resulting mass spectrum (EI ionization) of (A) divinyl sulfone, (B) vinyl-chloroethyl sulfone, (C) divinyl sulfoxide and (D) vinyl-chloroethyl sulfoxide. [Color figure can be viewed at wileyonlinelibrary.com]

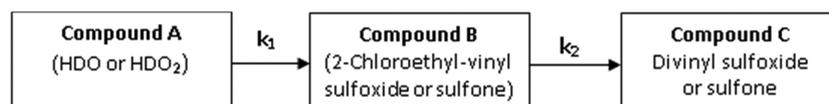


Figure 7 Flow chart of consecutive reactions.

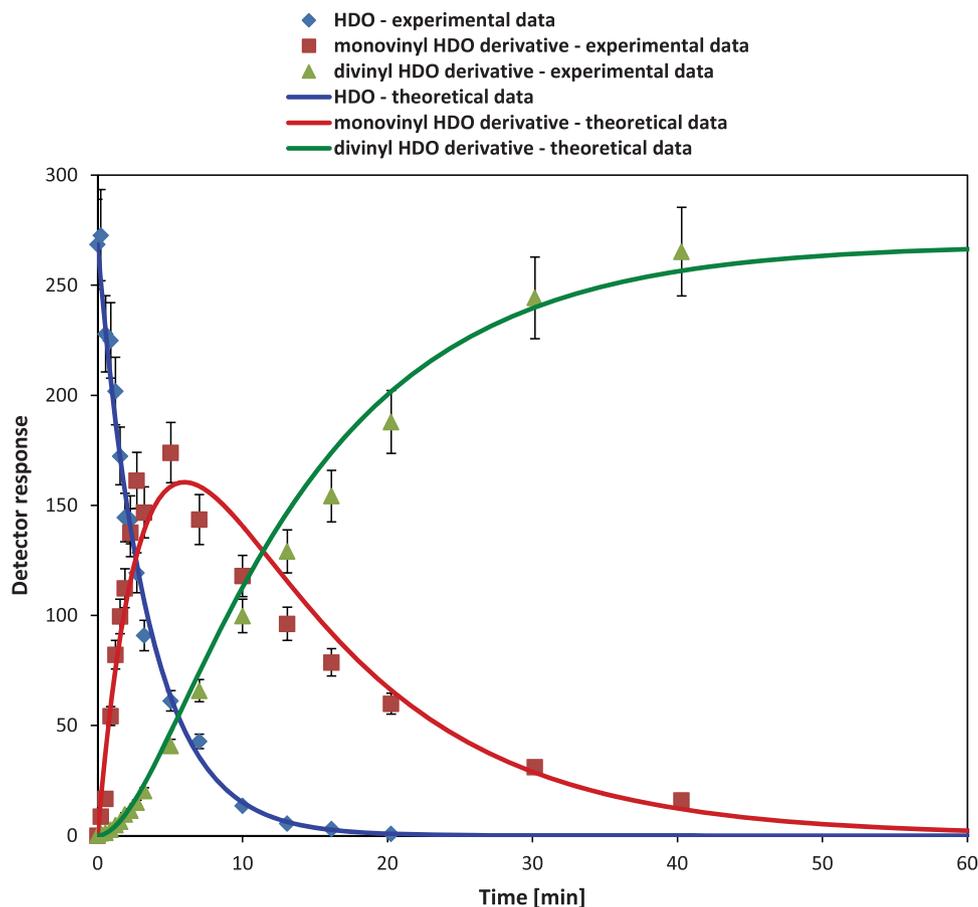


Figure 8 Experimental data and the best-fitted kinetic curves in the example of hydrogen chloride elimination from HDO molecules in aqueous pH 12 Britton–Robinson buffer solution. t_{\max} and $[B]_{\max}$ were read from the graph and then used for the determination the theoretical curves. [Color figure can be viewed at wileyonlinelibrary.com]

on the pH of the reaction medium and increases (exponentially) with increasing pH of the solution. The rate of hydrogen chloride elimination from HDO and HDO₂ molecules determined experimentally for the alkaline medium is presented in Table III.

Figure 9 presents a comparison of all determined reaction rate constants, converted to half-lives. Upon application of the logarithmic scale to half-life, a linear character of HCl elimination is clearly visible for both the first and the second branch of HDO and HDO₂. Moreover, reaction rate constants k_1 and k_2 dependence on pH are parallel to each other, both for HD sulfoxide and HD sulfone. Therefore, the mech-

anism for the release of HCl from the chloroethyl groups of all compounds in the studied pH range is not changed. The graph suggests that HD sulfone and its monovinyl derivative loses HCl much more rapidly than the sulfoxide and its monovinyl derivative in analogous reaction conditions. Therefore, it may be stated that HD sulfone is much more reactive than HD sulfoxide. The difference is more evident for lower pH values. For pH 9, the ratio of the rate constant for HCl elimination from the sulfone molecule to that for HCl elimination from the sulfoxide is approximately 83.5, but for pH 12 the ratio is 19.2.

Table III Kinetic Parameters of HCl Elimination from HDO and HDO₂ and Their Monovinyl Derivatives Depending on the pH Value at 25°C

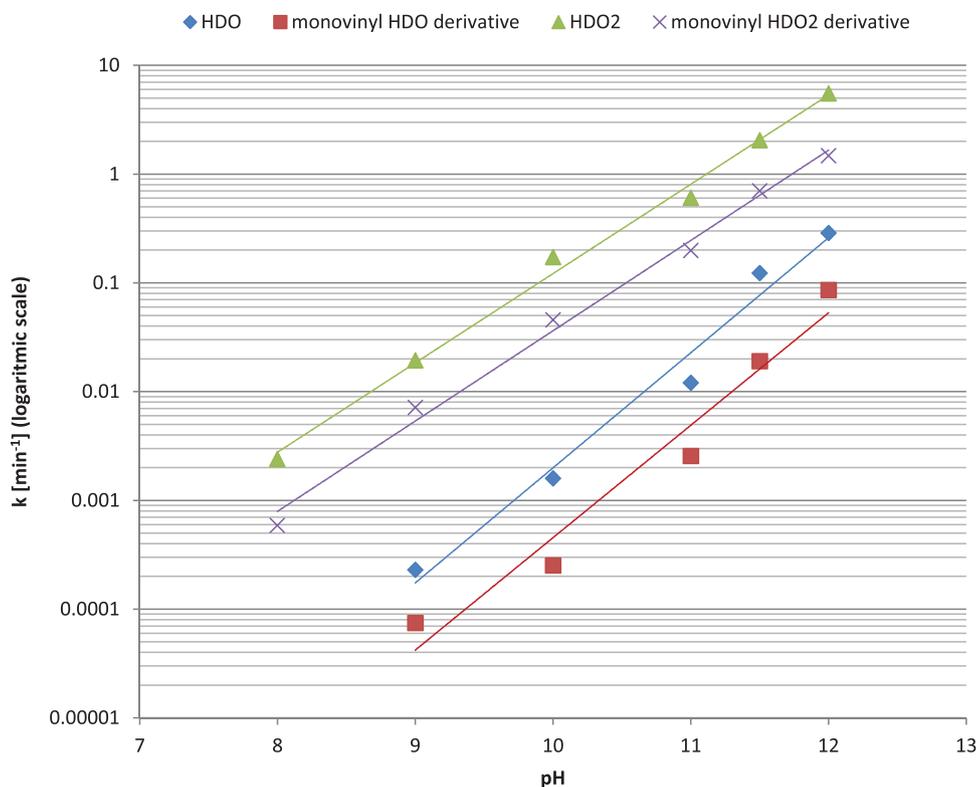
| pH | HDO | | | | | | HDO ₂ | | | | | |
|------|-------------------------------------|----------------------|-----------------------------|-------------------------------------|----------------------|-----------------------------|---|----------------------|-----------------------------|---|----------------------|-----------------------------|
| | k_1 (HDO) (min ⁻¹) | $t_{1/2 A}$ (min) | Error Calculation (%) | k_2 (HDO) (min ⁻¹) | $t_{1/2 B}$ (min) | Error Calculation (%) | k_1 (HDO ₂) (min ⁻¹) | $t_{1/2 A}$ (min) | Error Calculation (%) | k_2 (HDO ₂) (min ⁻¹) | $t_{1/2 B}$ (min) | Error Calculation (%) |
| 8 | n.d. | n.d. | n.d. | n.d. | n.d. | n.d. | 0.0024 | 289 | 6.8 | 0.0006 | 1175 | 7.8 |
| 9 | 0.0002 | 3014 | 7.6 | 0.00008 | 9279 | 8.1 | 0.0194 | 367 | 7.3 | 0.0072 | 97 | 7.3 |
| 10 | 0.0016 | 433 | 6.9 | 0.00025 | 2740 | 7.6 | 0.1727 | 4 | 7.6 | 0.0458 | 15 | 7.5 |
| 11 | 0.0121 | 57 | 7.2 | 0.00257 | 270 | 6.9 | 0.6061 | 1.1 | 8.0 | 0.1994 | 3.5 | 8.2 |
| 11.5 | 0.1229 | 6.5 | 8.1 | 0.01906 | 36 | 7.8 | 2.048 | 0.3 | 8.1 | 0.7007 | 1 | 6.9 |
| 12 | 0.2879 | 2.5 | 7.9 | 0.08595 | 8 | 8.2 | 5.531 | 0.1 | 7.2 | 1.478 | 0.5 | 7.5 |

k_1 : The reaction rate constant for the loss of the first HCl molecule.

k_2 : The reaction rate constant for the loss of the second HCl molecule.

$t_{1/2}$: HDO, HDO₂, and their corresponding vinyl derivatives half-lives.

n.d.: The rate of hydrogen chloride loss from HDO is very small, since that the determination of k_1 and k_2 is very difficult because the $t_{1/2}$ for the first reaction is more than 70 days.

**Figure 9** The effect of pH of the reaction medium on the reaction rate constant of HD sulfone and sulfoxide during the elimination of hydrogen chloride from chloroethyl groups of these compounds. [Color figure can be viewed at wileyonlinelibrary.com]

Closure of HD Sulfoxide and Sulfone Rings

Divinyl sulfoxide and sulfone, formed as a result of elimination of two molecules of hydrogen chloride from sulfur mustard sulfoxide (HDO) and sulfone (HDO₂), respectively, undergo a further transformation in strongly alkaline environment, leading

to cyclization and formation of 1,4-thioxane sulfoxide and sulfone, respectively, according to the reaction equation presented in Fig. 10. Reactions of that kind are long known and may be used for production of 1,4-thioxane sulfoxide or sulfone [13,16]. During the study of these reactions, we have found that

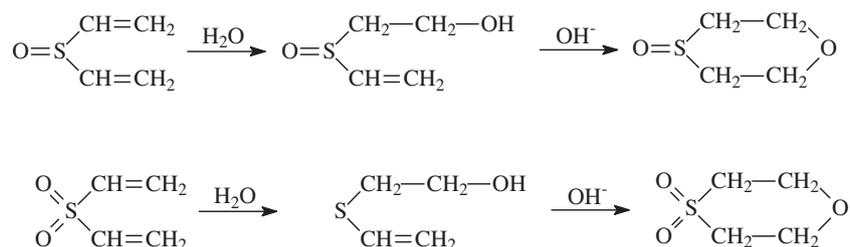


Figure 10 Schematic presentation of cyclization of divinyl derivative of HD sulfoxide and sulfone in alkaline medium.

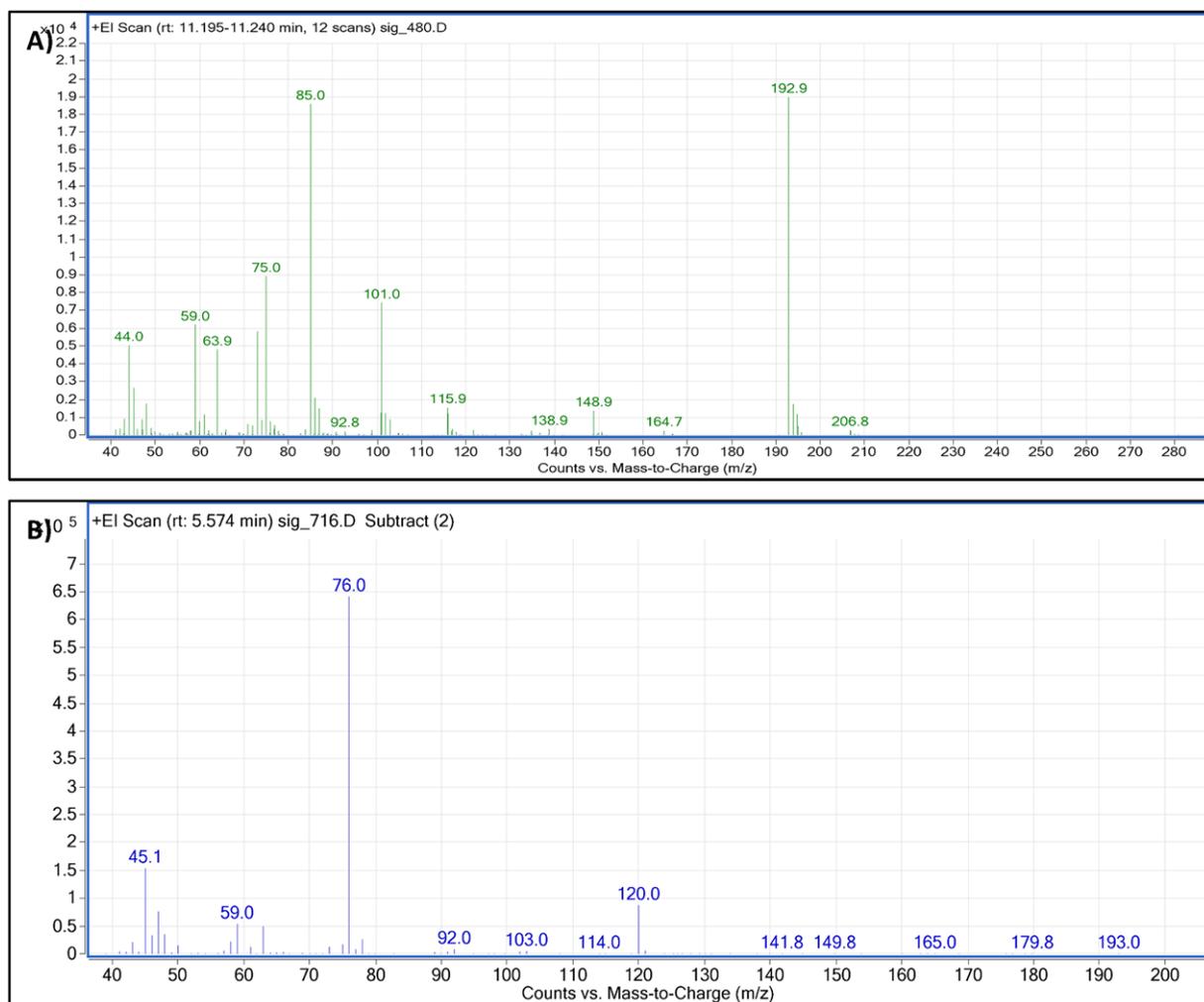


Figure 11 Mass spectrum of (A) 2-hydroxyethyl vinyl sulfone after BSTFA derivatization and (B) 2-hydroxyethyl vinyl sulfoxide. [Color figure can be viewed at wileyonlinelibrary.com]

the intermediate product is vinyl hydroxyethyl sulfoxide and sulfone, respectively. As a result of the experiments, we were able to isolate and identify the intermediate product of the divinyl sulfone and sulfoxide cyclization reactions. The intermediate prod-

uct was identified by GC-MS analysis after derivatization. Derivatization conditions were as follows: solvent –1 mL CH_2Cl_2 ; derivatization agent –10 μL N,O -Bis(trimethylsilyl)trifluoroacetamide (BSTFA); reaction temp.: 40°C ; and reaction time –30 min. Mass

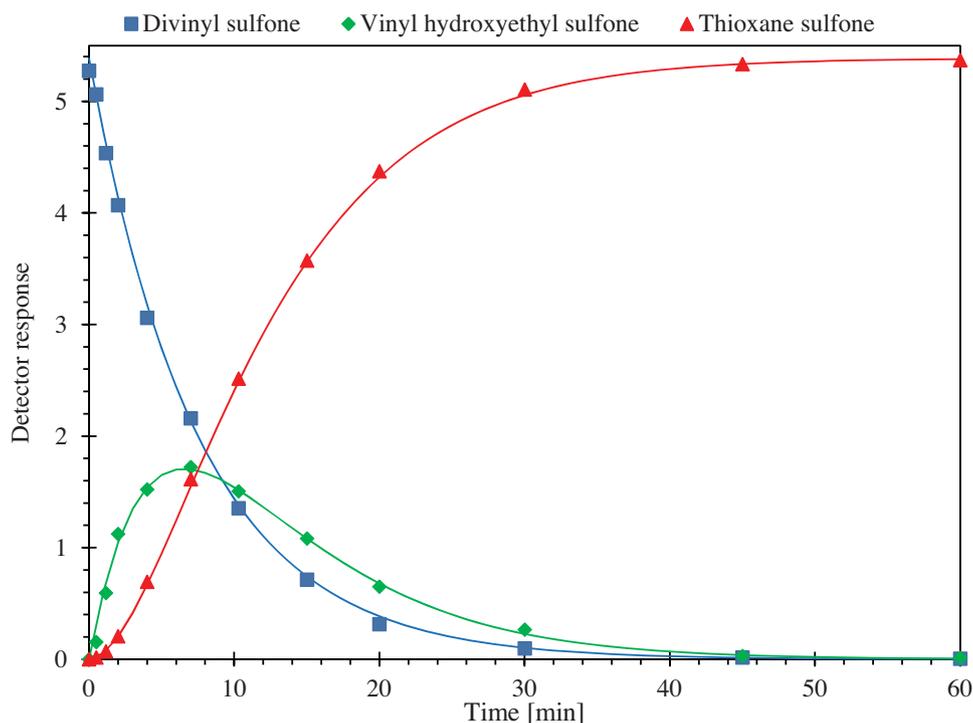


Figure 12 Kinetics of cyclization of divinyl sulfone with formation of 2-hydroxyethylvinyl sulfone (as an intermediate product) and 1,4-thioxane sulfone (a final product); pH 12.96. [Color figure can be viewed at wileyonlinelibrary.com]

spectrum of vinyl hydroxyethyl sulfoxide is shown in Fig. 11.

The rates of reaction leading to formation of 1,4-thioxane sulfoxide and sulfone were studied. Based on the results shown in Fig. 12, it can be concluded that the mechanism of the reaction is very similar to the elimination reaction of sulfur mustard sulfoxide and sulfone. The cyclization reactions of divinyl sulfoxide and sulfone also proceed in two stages as it was in the case of HDO and HDO₂. This reaction also allows the application of subsequent reactions kinetics, which is described in Section 3.1. The theoretical equation for these kinetics can properly be used in the cyclization reaction of divinyl sulfoxide and sulfone. The solid lines in Fig. 12 represent the theoretical kinetic curve, and the points are experimental data. Based on these data, it can be assumed that the applied mathematical model is correct. Because of the long-time duration of the divinyl sulfoxide transition, it was impossible to draw the same curve as for divinyl sulfone.

Figure 13 presents a relationship between the half-time necessary for transformation of divinyl sulfoxide or sulfone into thioxane sulfoxide or sulfone (respectively) and pH of the reaction medium with strongly alkaline pH values.

The half-time of transformation of divinyl sulfoxide and sulfone into thioxane sulfoxide and sulfone, respectively, presented in the logarithmic scale, indicates a linear decrease with increasing pH. The analysis of data presented in Fig. 13 demonstrates that when pH of the medium increases from about 12 to about 14, the rate of transformation of divinyl sulfoxide into thioxane sulfoxide increases by more than two orders of magnitude, whereas the increased rate of transformation of divinyl sulfone into the corresponding thioxane sulfone is only one order of magnitude higher with the same pH range.

CONCLUSIONS

In natural conditions, sulfur mustard may be oxidized to the sulfoxide and subsequently to the sulfone. Compounds formed in these reactions may, in appropriate conditions, be easily transformed into divinyl sulfoxide and sulfone, which may undergo a subsequent cyclization to thioxane sulfoxide and sulfone, respectively. Based on results of the present study, it may be stated that the summary reaction of hydrogen chloride elimination from HD sulfoxide or sulfone is limited by the second stage of the reaction; that is, by HCl loss

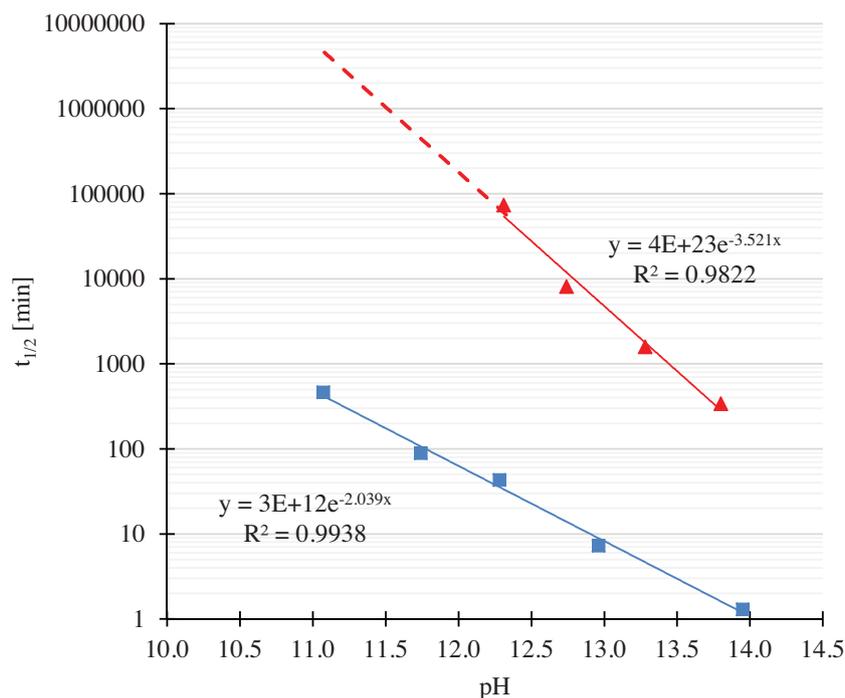


Figure 13 Cyclization reaction rates of divinyl sulfoxide and sulfone (formed from HDO and HDO₂, respectively in the dependence on reaction medium pH). The dashed line extrapolates the relationship between the half-life and the pH in range 11–12.5 for divinyl sulfoxide. [Color figure can be viewed at wileyonlinelibrary.com]

from the second chloroethyl branch. That hypothesis is confirmed by experimentally determined reaction rate constants. For example, in case of hydrogen chloride elimination from a molecule of HDO₂ in a pH 9 medium, these constants are $k_1 = 0.0194 \text{ min}^{-1}$ and $k_2 = 0.0072 \text{ min}^{-1}$ (the rate constant is reduced approximately 2.7 times), respectively, whereas in the same conditions for HDO the rate constants are $k_1 = 0.00023 \text{ min}^{-1}$ and $k_2 = 0.000075 \text{ min}^{-1}$ (the rate constant is reduced approximately three times), respectively. The rate of hydrogen chloride elimination reaction from both HDO and HDO₂ is greatly influenced by pH of the reaction medium—with increasing pH, the elimination reaction rate increases; for example, with pH increasing from 9 to 12 the HCl elimination from HDO reaction rate increases over 1200 times, and with the same increase of pH the rate of HCl elimination from HDO₂ increases only 200 times. A similar relationship may be determined for the divinyl sulfoxide and sulfone cyclization reactions. The rate of these processes also increases with increasing pH of the reaction medium. Elimination of HCl from both HDO and HDO₂ goes with reasonable speed in the pH range 9–12. In contrast, conversion of divinyl sulfone and sulfoxide to sulfoxide and sulfone thioxane, respectively, occurs at a reasonable rate when the pH of the solution is in the

range 12–14. For example, at pH 12, the total reaction time of HDO is 17 min and HDO₂ is 42 s. While at pH 9, this time is 13 days for HDO and 3.5 h for HDO₂.

However, it is doubtless that in solutions of pH 9, HD sulfoxide loses hydrogen chloride at approximately 100 times slower rate compared to HD sulfone and that the difference is reduced with increasing pH. In pH 12 solutions, the rate of hydrogen chloride loss from HD sulfone molecules is only 20 times higher than the rate of HCl loss from HD sulfoxide.

The study suggests that analysis of environmental samples, including sea water and bottom sediments demonstrating a low alkaline reaction, products of HD oxidation present in that environment will be transformed first into monovinyl and then into divinyl derivatives, and the presence of cyclic compounds will be unlikely as they are formed in a very slow process and at pHs much higher than those encountered in the marine environment. In pH 12 solutions, HD sulfoxide becomes completely transformed into divinyl sulfoxide within 1 h, and divinyl sulfoxide formed in that medium becomes transformed into thioxane sulfoxide within approximately 11,000 h, which is equal to 458 days. In the case of HD sulfone at pH 12, transformation into the divinyl derivative occurs within a few minutes, and the further transformation into thioxane

sulfone occurs within approximately 5 h. The conversion of vinyl derivatives into cyclic compounds is most affected by pH. As the pH increases, the amount of these compounds in the final products increases. However, at pH below 11, cyclic products were not observed.

This article provides evidence that as a result of the hydrogen chloride elimination reaction the β -chloroethyl sulfones are converted into vinyl derivatives much faster than β -chloroethyl sulfoxides. This finding contradicts the reported statement: "In a basic medium the reaction of elimination run faster for sulfoxides than for sulfones" [20].

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