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Oxidative Decontamination of Chemical Warfare Agents in Swellable Hypercrosslinked Polymers

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An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Sciences with Honors

Department of Chemistry

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Abstract

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The use of chemical warfare agents as a weapon of mass destruction has been well-documented for thousands of years, with chemical warfare in the modern era beginning during World War I. Sulfur mustard, commonly known as mustard gas, is of particular interest due to its high toxicity and potential for large-scale release. A catalytic system containing Br_x/NO_x species for the selective oxidation of mustard gas was developed in the Hill lab by Zhen Luo and was further advanced into the fastest known system for the selective sulfoxidation of a mustard gas analogue by Kevin Sullivan. Following the optimization of this catalytic system, a swellable hypercrosslinked polymer network, synthesized from the fluorobenzene monomer, was used to develop a solid-state system for the selective sulfoxidation of 2-chloroethyl ethyl sulfide, the mustard analogue. Delivery of this catalytic system into the pours of the polymer network was successful, and the swellability of the polymer was not significantly affected by the addition of the catalyst. It was shown that this polymer, following the integration of the catalytic system, is capable of selectively and completely oxidizing neat liquid 2-chloroethyl ethyl sulfide to the far less toxic oxidized product within 24 hours. This solid-state system is more potentially useful than previously reported oxidant systems, as they are often only functional in solution, which is impractical outside of a laboratory setting. Furthermore, this polymer's swelling capabilities provides a unique opportunity to develop a material that both entraps an undesirable target such as a chemical warfare agent (CWA), like mustard, and decontaminates this entrapped agent. If such a multifunctional system could simultaneously signal the existence of the toxic compound, this multifunctional material would be even more interesting and potentially useful. This thesis addresses the possibility of such a multifunctional system.

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I would like to thank Dr. Tracy Scott for helping me to realize my interests outside of natural sciences. It is easy to become all-consumed in one's major, neglecting the opportunity to explore other disciplines. Your sociology courses have been some of my favorite at Emory, and I have always enjoyed our conversations outside of the class room.

Finally, I would like to thank all of my friends and family for their constant love and support throughout the past four years. I feel truly blessed that there is always someone for me to turn to during times of stress, which have been plentiful during my studies. Thank you to anyone that has assisted me during this journey, I appreciate all of you deeply.

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1. Introduction

I. Chemical Warfare Agents

Chemical warfare agents (CWAs) have threatened the welfare of civilians and militants starting as far back as 600 B.C.E.[1] and continue to pose a threat in modern society. A rapid increase in the use of CWAs as weapons of mass destruction was seen during World War I, when Germany released chlorine gas as a method of attack.[2] The use of CWAs during World War I led to an estimated 1.3 million deaths.[3] The deployment of CWAs did not cease throughout the twentieth century, causing millions of civilian deaths from hydrogen cyanide gas during World War II.[3] It was not until 1993 that the use, production, and stockpiling of CWAs were formally outlawed through ratification of the Chemical Weapons Convention (CWC), the first major step towards global reduction of chemical stockpiles.[4] The CWC currently includes 193 state-parties, with only Egypt, North Korea, and South Sudan failing to sign or ratify the convention.[5] Since the ratification of the CWC, over 66,000 metric tons of chemical stockpiles, 92% of reported stockpiles, have been safely destroyed.[4] Despite this major advancement in the reduction of chemical stockpiles, CWAs still pose a major threat to the global community due to noncompliance with the CWC. The high toxicity and potential for malevolent use of CWAs has prompted research in the decontamination of these compounds.

Various classifications of CWAs have been developed in order to describe the way in which a given CWA will affect the body. These chemicals can be categorized as nerve agents, blistering agents, choking agents, blood agents, riot-control agents, psychomimetic agents, and toxins.[3] The selective oxidation of the blistering agent sulfur mustard [*bis*(2-chloroethyl)sulfide; (HD)], commonly known as mustard or mustard gas, is of particular interest due to its high toxicity[6] and potential for large-scale release. HD can be absorbed through inhalation or dermal contact, easily penetrating the skin and mucosal membranes undetected, which can lead to long-term health consequences such as cancer.[7] Once inside the body, HD is able to alkylate nucleic acids, which can lead to DNA cross-linking and apoptosis.[8]

While decontamination of HD can be achieved using strong oxidants, such as bleach, these often come with negative side effects themselves. Strong oxidants often do not selectively oxidize HD, producing sulfones in the process, a compound with similar toxicity[9], the mechanism of which can be seen in the figure below.

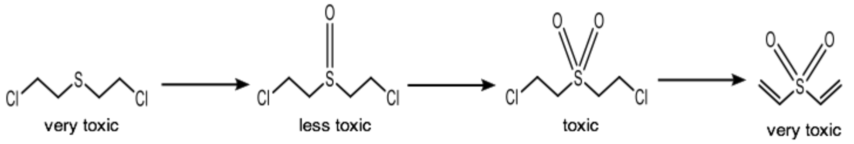

Figure 1. Potential products of non-selective oxidation of sulfur mustard.

Bleach can successfully oxidize HD without formation of toxic sulfones, yet is highly corrosive, environmentally deleterious, must be used in large quantities, and often becomes less effective over time.[10] An ideal system for the decontamination of HD would be selective, fast, and efficient under normal conditions, preventing exposure while detoxifying the environment without production of hazardous byproducts.

II. Br_x / NO_x Catalytic System for Aerobic Sulfoxidation

The catalytic system for aerobic sulfoxidation using Br_x and NO_x species was developed by Kevin Sullivan following the preliminary research on the system by Zhen Luo in the Hill lab. Tetrabutylammonium bromide (TBABr) and tetrabutylammonium nitrate ($TBANO_3$) act to catalytically oxidize CEES to CEESO by O_2 (air) in the presence of acid.[11] Dr. Sullivan has since enhanced the system drastically, developing the fastest catalytic system for the selective air-based oxidation of CEES, while also performing several mechanistic studies in an attempt to understand the complicated process by which this catalytic system facilitates selective aerobic sulfoxidation.[12]

A notable development of the system is the addition of the transition metal Cu(II), which significantly increases the rate of oxidation while also working as a very useful color indicator. With the addition of copper, there is a drastic color change from light yellow to dark green in the presence of CEES. This color change is reversed once the CEES has been fully oxidized to CEESO.

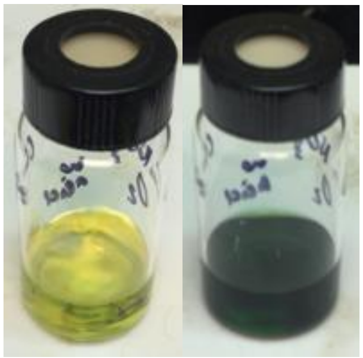

Figure 2. The addition of Cu(II) to the catalytic system acts as a useful color indicator. In the presence of CEES, the solution turns to dark green (right), and returns to a light yellow once the CEES has been completely oxidized to CEESO (left).

HD does not cause any sensation as it penetrates the skin, demonstrating the benefit of an indicator to signal the need for rapid decontamination and clean-up in the case of exposure.[13] As stated before, in addition to its use as a color indicator, the addition of Cu(II) to the catalytic system causes a significant increase in the reaction rate, which can be seen in the figure below.

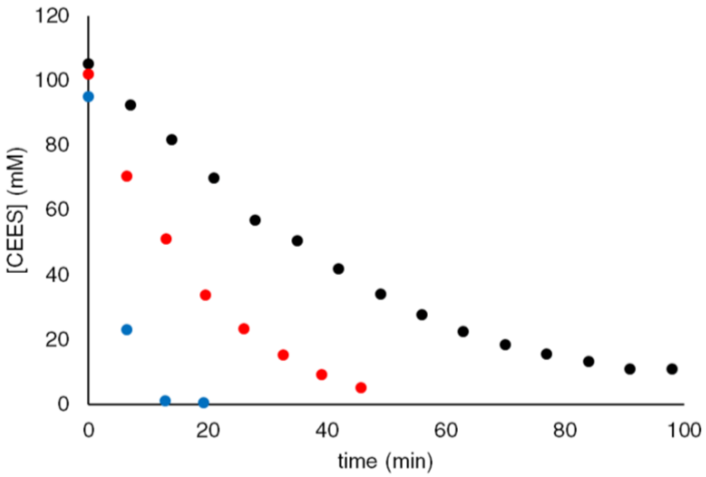

Figure 3. A comparison of reaction rates using varying amounts of Cu(II) in the system. (●) [TBA-NO$_3$] = 5 mM, [TBA-Br$_3$] = 5 mM; (🔴) [TBA-NO$_3$] = 1.67 mM, [Cu(NO$_3$)$_2$] = 1.67 mM, [TBA-Br$_3$] = 3.33 mM;. (🔵) [TBA-NO$_3$] = 1.67 mM, [Cu(NO$_3$)$_2$] = 1.67 mM, [TBA-Br$_3$] = 3.33 mM.

The use of halogens, such as Cl_2 and Br_2, have been found to successfully oxidize sulfides.[14] However, the use of these halogens alone often leads to the production of HCl and HBr. The addition of tertiary amines along with TBABr$_3$ and TBANO$_3$, can stoichiometrically decompose the possible halide byproducts.[15] The addition of tribromide into the system has shown a significant increase in reactivity relative to the addition of bromide. It is unknown whether the active oxidant in the system is Br_3^- or Br_2, as an equilibrium between the two is naturally established (eq. 1).

$$Br_2 + Br^- \rightleftharpoons Br_3^- \qquad (1)$$

The addition of nitrogen oxide (NO_x) species to the system reoxidizes bromide, allowing for the continuation of sulfoxidation without the continuous addition of additional tribromide. The nature of the relationship between these two species makes it difficult to determine the true reaction mechanism of this catalytic system. In 2011, Luo hypothesized the mechanism in Figure 4 for the aerobic sulfoxidation by the Br_x/NO_x catalytic system.

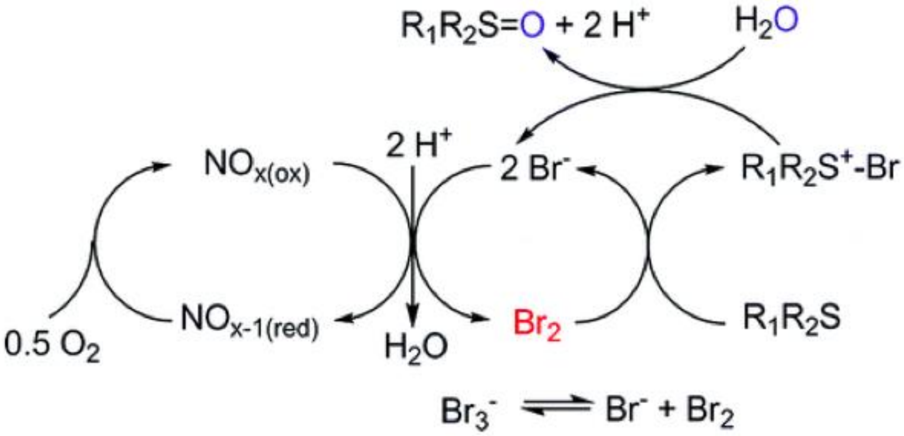

Figure 4. Proposed reaction mechanism for aerobic sulfoxidation catalyzed by bromide and nitrogen oxides. Reprinted with permission from Luo et. al., *ACS Catalysis* **2011**, 1 (10), 1364-1370. Copyright 2011 American Chemical Society.[11]

Le et. al. has proposed an additional mechanism, in which NO_3^- has a direct role in the oxidation of a bromosulfonium intermediate, producing the final oxidized product.

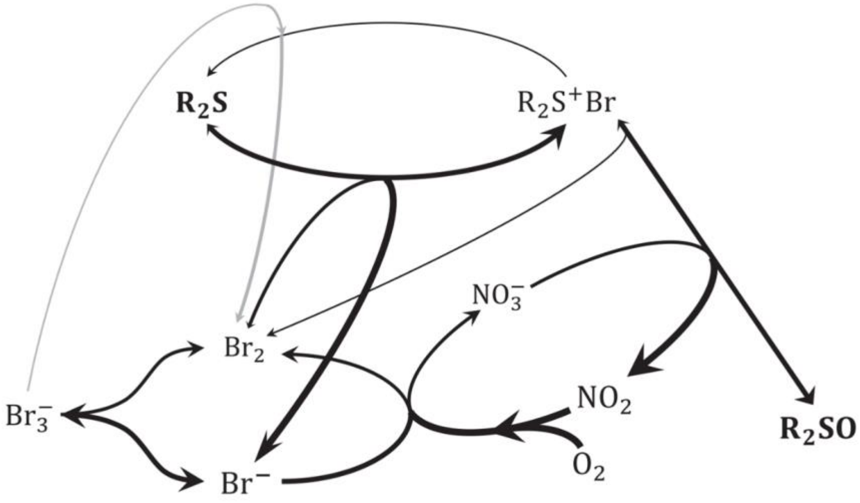

Figure 5. Proposed mechanism for aerobic sulfoxidation in Br_x/NO_x systems by Le et. al. Reprinted with permission from Le et. al., *J. Hazard. Mater.* **2019**, 365, 511-518. Copyright 2019 Elevisier.[16]

Although these systems have been studied mechanistically for years, the complexity of this oxidation reaction makes it difficult to fully understand all aspects of the actual mechanism.

Despite our inability to fully determine the reaction mechanism for this sulfoxidation, Dr. Sullivan's research has demonstrated the significant difference in reaction rates between systems containing TBABr and TBABr$_3$ (see Figure 6).

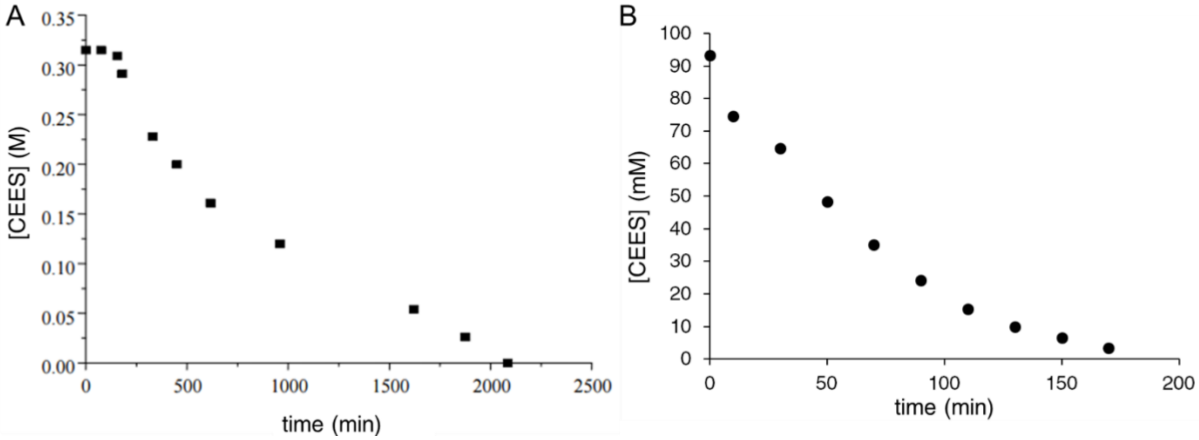

Figure 6. Comparison of Br$_x$/NO$_x$ catalytic conditions between Luo et. al. and Dr. Sullivan's work. (**A**) [CEES] = 320 mM, [TBA-NO$_3$] = 16 mM, [TBA-Br] = 16 mM, MeCN, 70 ºC, 1 atm air. (**B**) [CEES] = 100 mM, [TBA-NO$_3$] = 5 mM, [TBA-Br$_3$] = 5 mM, MeCN, 23 ºC, 1 atm air.

The Br$_3^-$ -containg reaction is more than one order of magnitude faster than the Br$^-$ -containing one for oxidation of CEES to CEESO.

To ensure selectivity of this catalytic system, the products of the sulfoxidation reactions were evaluating using ^{13}C NMR (Figure 7). The only peaks are those of the desired sulfoxide product, CEESO; no peaks of CEES reactant or the undesirable sulfone product, CEESO$_2$, are seen. Furthermore, this result is observed either with or without the presence of Cu(II).

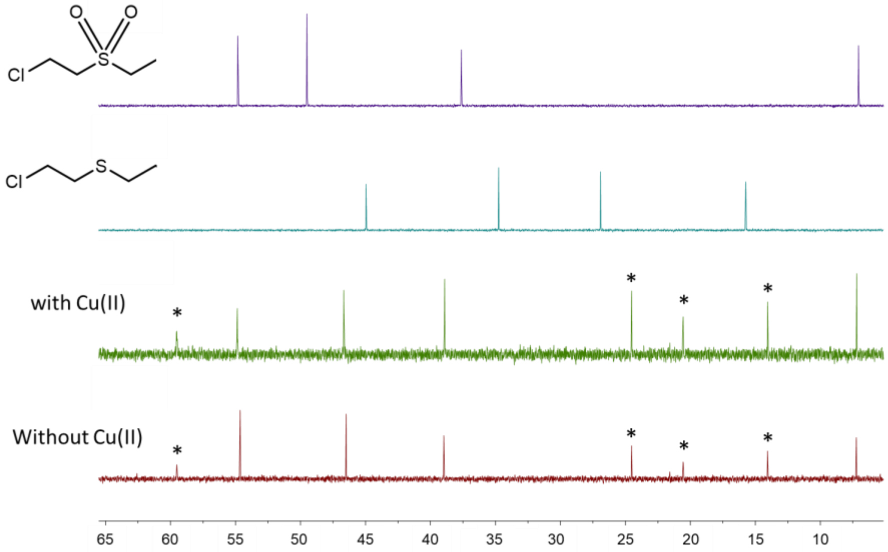

Figure 7.[12] ^{13}C NMR of products of sulfoxidation reactions. Conditions for catalytic trials prior to NMR analysis: [CEES] = 100 mM, [TBA-NO_3] = 5 mM, [TBA-Br_3] = 5 mM, [p-TsOH] = 10 mM, 2% H_2O and 10% CD_3CN in MeCN, 23 ºC, 1 atm air. Reaction run with copper: [$Cu(ClO_4)_2$] = 1.5 mM. (*) = TBA counter cations.

III. Swellable Hypercrosslinked Polymer Networks

To avoid exposure to CWAs, as well as other toxic compounds, it is critical for the removal of such compounds to be swift and efficient, minimizing the time at which these chemicals are in contact with their surroundings. The use of an absorbent or porous material to remove toxins has been documented using metal-organic frameworks (MOFs)[17-19], activated carbon[20], and, most recently, swelling networks.[21-23] The swelling of materials when exposed to CWAs provides a unique protection against the toxic compounds that other decontamination systems lack; swellable systems entrap toxic chemicals while simultaneously forming a barrier against further penetration.

In 2017, three different types of swelling materials with similar entrapment capabilities were reported. A polyoxometalate-based polymer was synthesized by Kevin Sullivan in the Hill laboratory, which swells upon immediate contact with certain liquids, including the CWA (nerve agent) analogue, dimethyl methylphosphonate (DMMP).[21] Additionally, this polymer catalyzes selective oxidation of the HD analogue, 2-chloroethyl ethyl sulfide (CEES), by hydrogen peroxide in acetonitrile (MeCN).[21] Another laboratory showed similar swelling (gelation) activity when CWAs were exposed to poly(styrene-vinyl benzyl chloride-divinylbenzene) a highly porous copolymer, referred to as a cross-linked poly high internal phase emulsion polymer (polyHIPE).[23] The third type of swellable polymer is a major component of this thesis and is described in the following section. Several different hypercrosslinked polymers (HCPs) were developed with differing monomers: chlorobenzene, fluorobenzene, toluene, anisole, or phenol.[22] These different monomers result in polymers of varying swellability, with the fluorobenzene-based HCP showing the greatest swelling and therefore potential value for CWA uptake. Unlike the first polymer, neither of the latter 2 swellable polymers catalyze decontamination.

IV. Scope of Current Work

This project aims to develop an efficient solid-state system for the selective oxidation of the HD analogue, CEES, by integrating the optimized Br_x / NO_x catalytic system for aerobic oxidations into an HCP without removing the HCP’s ability to entrap small molecules by gelation. A solid-state catalytic system for CWA decontamination is more useful than one in solution for use in real work (outside-the-laboratory) settings. This catalytic system is desirable due to the consistent availability of the oxidant, air (O_2), under mild conditions. Unlike aerobic (air-based) oxidative systems, those based on hydrogen peroxide, such as that with the polyoxometalate-based polymer, require a constant supply of hydrogen peroxide for the reaction to continue to completion. With O_2 as the oxidant, the reaction can proceed to completion without the addition of more reagent. This is also considered a “green” reaction, as formation of hazardous waste, such as sulfoxides and sulfones is avoided.[24]

The Br_x / NO_x catalytic system was first optimized to increase the speed and efficiency of the oxidation of CEES. I then used the optimized catalytic system and the polymer in combination to assess and then optimize conditions for both CEES entrapment by gelation and catalytic air-based CEES removal by sulfoxidation.

2. Methods and Materials

I. *Optimization of Br_x / NO_x Catalytic System*

Optimization of the catalytic system was conducted by varying the concentration of $TBABr_3$, $TBANO_3$, and *para*-toluene sulfonic acid (*p*-TsOH). One component was varied while the other remaining variables were held constant. In each trial, the oxidation of 20 mmol of CEES was tracked by monitoring the ratio of CEES to internal standard (40 μL of 1,3-dichlorobenzene, 1,3-DCB), using gas chromatography (GC). A Hewlett Packard HP 6890 GC system equipped with a HP-5 5% phenyl methyl siloxane column was used to collect all data. Approximately 0.15-0.20 μL of the sample was injected into the GC column using a gastight syringe. Each solution had a total volume of 5 mL, kept constant by addition of the appropriate volume of acetonitrile. While the amount of $TBABr_3$, $TBANO_3$, and *p*-TsOH varied with the given trial, the amount of internal standard, CEES, copper nitrate ($Cu(NO_3)_2$), and water (2 % of the total volume) were consistent throughout all runs.

II. *Synthesis and Characterization of Polymer*

The polymer was synthesized using the method of Wilson and co-workers. [22] Various monomers could be used, but fluorobenzene was chosen as it produced the polymer with the largest reported swellability and thus the greatest potential for successful uptake of CWAs (Figure 8). Fluorobenzene (10 mmol) was added to excess 1,2-dichloroethane and 2 equivalents of formaldehyde dimethyl acetal under a constant flow of argon on a Schlenk line. The product (Figure 9) was purified through Soxhlet extraction with methanol, then dried *in vacuo* for 18 hours at 60 ºC.

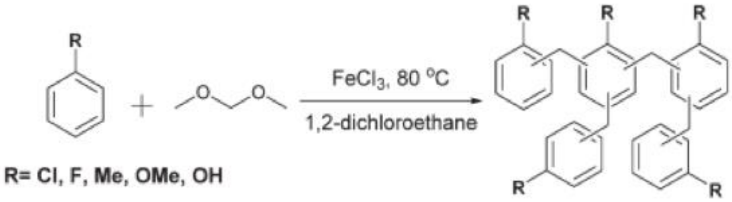

Figure 8. Conditions for synthesis of the hypercrosslinked polymer network, carried out under a constant flow of argon on the Schlenk line. Reprinted with permission from Wilson et. al., *Polym. Chem.* **2017,** *8* (12), 1914-1922. Published by The Royal Society of Chemistry.[22]

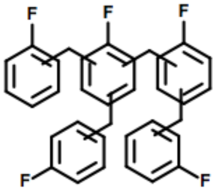

Figure 9. The polymer obtained using fluorobenzene as the monomer.

Following the synthesis, the identity of the polymer was confirmed through fourier-transform infrared (FT-IR) spectroscopy. The peaks found matched well with those reported in the literature.[22]

III. *Oxidation of CEES in Solution*

Following the optimization reactions, the polymer and corresponding concentrations of the catalytic components were tested for reactivity in MeCN. In order to insert the catalyst into the polymer network, 50 mM solutions of the catalysts in MeCN were prepared and added to approximately 10-11 mg of polymer. The concentrations of each component are summarized in

Table 1. Water (2%) and 1,3-DCB (40 μL) were also added to the solution before the addition of 60 μL of CEES to begin the reaction. The oxidation of CEES to CEESO was followed using the same protocol as outlined in section 2.1.

Table 1. The concentration of each catalytic component inside the HCP network.

Catalytic Component	Concentration (mM)
$TBABr_3$	12.5
$TBANO_3$	17.5
p-TsOH	17.75
$Cu(NO_3)_2$	1

IV. *Neat CEES Reaction in a Hypercrosslinked Polymer*

In order to place the catalytic components inside the polymer network, varying volumes of 50 mM solutions of each component in MeCN were mixed with 10-11 mg of the polymer. The volume for each catalytic component depends on the desired concentration, which is listed in the previous section. A vial with the polymer and catalytic components was left open to the atmosphere inside of the hood to allow for the MeCN to evaporate. Any additional MeCN was removed in the vacuum oven at room temperature. Once the appropriate amount of samples was prepared (one sample for each time point), 20 mmol of neat liquid CEES (60 μL) was added to each vial. The vials were sealed with a rubber septum and a balloon filled with O_2 was attached to ensure that the aerobic sulfoxidation could continue throughout the duration of the reaction.

To take a time point, the reaction was stopped by the addition of cyclohexane and 1,3-DCB. All catalytic components were found to be insoluble in cyclohexane, while CEES is soluble. Thus, treatment of the reaction mixture by cyclohexane and 1,3-DCB removes CEES from the molecular proximity of the catalytic components embedded in the polymer and stops further CEES oxidation. The extent of aerobic oxidation of CEES to CEESO was, again, monitored by tracking the ratio of CEES:1,3-DCB, as described in Section 2.1.

V. *Swellability of Hypercrosslinked Polymer-Catalyst*

The swellability of the polymer was studied both qualitatively and quantitatively. The swellability of the polymer, with and without the catalytic components, was observed visually after exposure to various solvents, such as MeCN, dimethylformamide (DMF), and dipropyl sulfide. The swellability, (eq. 2) was calculated for the polymer, again with and without the catalytic components present in the HCP network.

$$Q = \frac{(Weight_f - Weight_i)\ (mL)}{Weight_{polymer}(g)} \qquad (2)$$

Approximately 20-25 mg of sample was placed inside of a Pasteur pipet with glass wool before 5 mL of solvent was passed through as illustrated in Figure 10.

Figure 10. The apparatus to determine the swellability, Q, of the polymer in various solvents.

The glass wool ensured proper filtration of the solvent as it flowed through the polymer, and prevented any polymer from flowing out of the pipet. This apparatus was weighed before and after exposure to the solvent in order to determine the amount of solvent absorbed by the polymer. This was then divided by the original amount of polymer used to calculate the swellability (eq. 2). A video of this procedure can be seen under Supplementary Information.

3. Results

I. Optimization of Br_x / NO_x Catalytic System

In order to optimize the catalytic activity of the Br_x/ NO_x system, varying concentrations of each component were studied to determine optimal conditions. The results of these experiments helped to establish an efficient protocol for the use of the polymer as a solid-state system in the selective oxidation of CEES. The amounts of $TBABr_3$, $TBANO_3$, and *p*-TsOH were all independently varied to determine the respective amount of each component that yielded the fastest reaction rate.

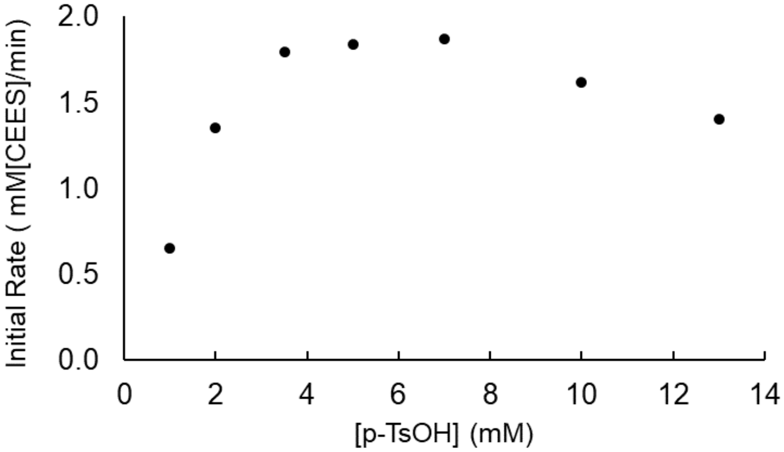

Figure 11. Initial rate of aerobic CEES oxidation catalyzed by the Br_x/NO_x system as a function of acid (*p*-TsOH) concentration. [CEES] = 100 mM, [TBA-NO_3] = 5 mM, [TBA-Br_3] = 5 mM, 2% H_2O in MeCN.

Figure 11 shows an interesting inverse parabolic dependence of the rate on the acid concentration, [*p*-TsOH]. An increase in the rate is seen up until about ~8 mM acid, then the rate slowly decreases at higher concentrations. In the proposed mechanism in Figure 4, the concentration of [H^+] has the potential to affect various pathways, so we are unable to accurately explain why the rate begins to decrease after a certain concentration. Regardless of this complexity, this experiment allows us to determine the optimal concentration of *p*-TsOH to use in future reactions.

The reaction rate as a function of [TBABr3] begins to plateau at a concentration of 2.5 mM, with the optimal rate occurring at 5 mM (Figure 12). This relationship is less complex than that seen with the acid concentration, allowing for easy determination of the optimal amount of TBABr3 for subsequent experiments. It is likely that the plateau occurs as a result of the rate of diffusion of O_2 into the solution, so adding additional [Br_3^-] will not increase the rate above *ca*. 5 mM of TBABr3.

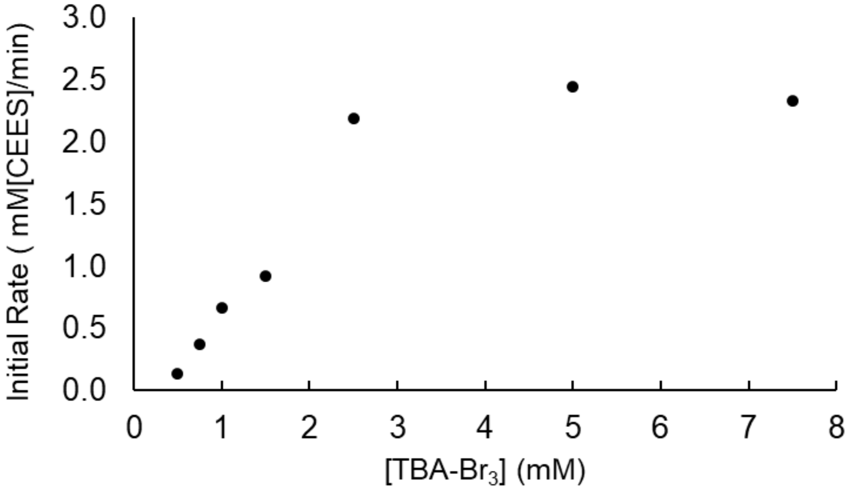

Figure 12. Initial rate of aerobic CEES oxidation catalyzed by the Br_x/NO_x system as a function of acid Br_3^- concentration. [CEES] = 100 mM, [TBA-NO_3] = 5 mM, [*p*-TsOH] = 5 mM, 2% H_2O in MeCN.

The effect of [NO_3^-] on the reaction rate is again straightforward, with a plateau starting at *ca*. 7 mM and a maximum initial rate above *ca*. 8 mM.

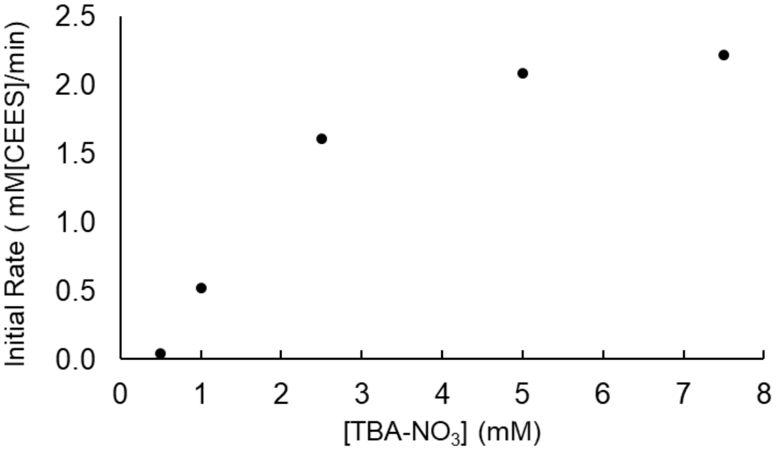

Figure 13. Initial rate of aerobic CEES oxidation catalyzed by the Br_x/NO_x system as a function of nitrate concentration. [CEES] = 100 mM, [TBA-Br_3] = 5 mM, [*p*-TsOH] = 5 mM, 2% H_2O in MeCN, 23 °C, 1 atm air.

II. Synthesis and Characterization of Polymer

The successful synthesis of the desired polymer was determined by FT-IR (the spectral peaks of the sample were very similar to the reported literature values), as well as elemental analysis by Atlantic Microlab, Inc. and Galbraith Laboratories, Inc. The FT-IR spectrum of the synthesized polymer is shown in Figure 14, with each major peak noted in Table 2.

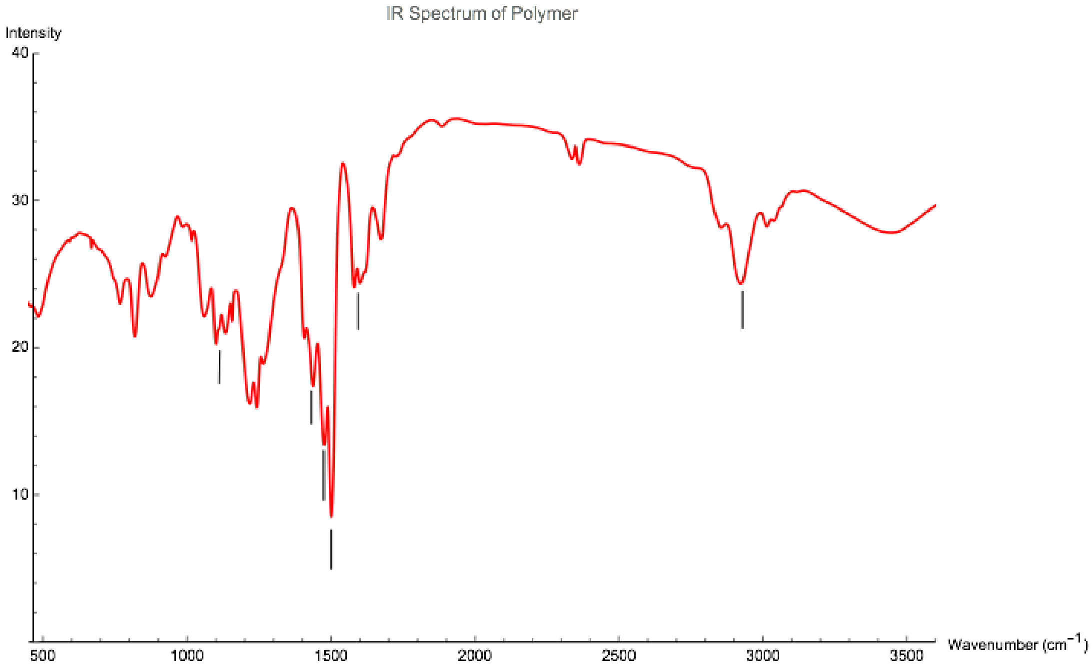

Figure 14. The FT-IR spectrum of the synthesized HCP with characteristic peaks labeled.

The FT-IR spectrum of the synthesized polymer aligns with the reported literature values, confirming the desired product. After inserting the multicomponent catalyst into the HCP network, samples were sent for elemental analysis to ensure that the components were being taken-up in the expected amounts. The results of this analysis are summarized in Table 3.

Table 2. The observed FT-IR peaks of the synthesized HCP with the corresponding reported literature values.

Observed Peaks (cm^{-1})	**Literature Peaks (cm^{-1})**
2923.17	3000
1600.04	1600
1500.84	1500
1437.43, 1476.39	1450
1100.17	1100

Table 3. Elemental analysis of the HCP with the containing the multi-component Br_x/NO_x catalyst. Data retrieved from Atlantic Microlabs, Inc. and Galbraith Laboratories, Inc.

Element	Theoretical %	Actual %
Carbon	78.67	75.70
Hydrogen	8.97	7.91
Nitrogen	3.98	3.20
Bromine	17.10	11.95
Copper	0.362	0.253

These results confirm that the actual percentage of each element lies within a close range of the expected amount.

III. Oxidation of CEES in Solution

In order to assess the concentrations of the HCP-incorporated catalyst, as well as the activity of this polymer-catalyst material, the aerobic CEES oxidation reactions were initially conducted in MeCN solution. The optimal concentrations of each catalytic component noted above were tested to ensure that the reaction proceeded as predicted. The rate of oxidation of CEES to CEESO is shown in Figure 15.

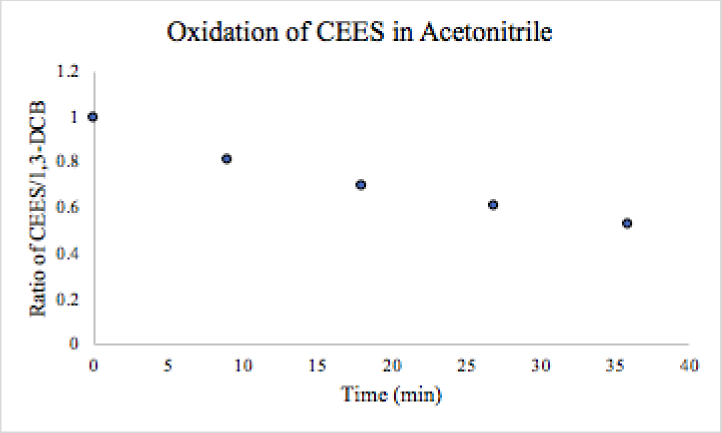

Figure 15. The aerobic oxidation of CEES in the presence of the HCP-catalyst material in a MeCN suspension. The oxidation of CEES to CEESO was monitored by tracking the ratio of CEES to the internal standard, 1,3-DCB.

Figure 15 shows that approximately 50% of the CEES is oxidized to CEESO in less than 40 minutes. This fast initial rate confirmed that the concentrations of catalysts used was sufficient and would hopefully produce similar rates in the solid-state reaction with neat liquid CEES.

IV. Neat CEES Reaction in a Hypercrosslinked Polymer

The oxidation of neat liquid CEES was initially tested using 20 mmol of CEES (Figure 16). There is a significant decrease in the amount of CEES (100% to 70%) within the first hour, but the reaction rate slows subsequently. This system failed to go to completion, only oxidizing approximately 80% of the CEES.

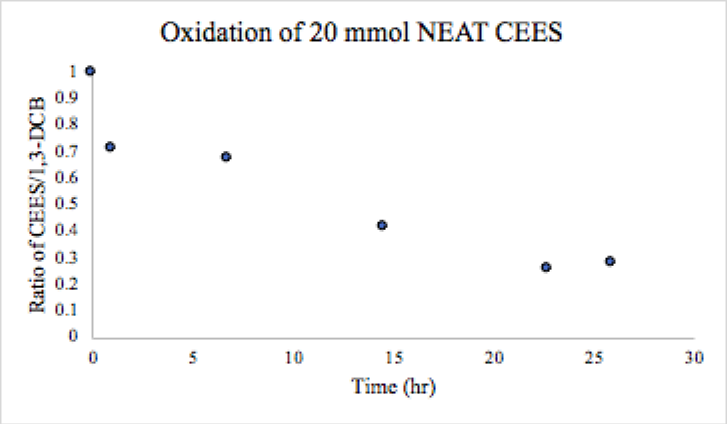

Figure 16. Aerobic oxidation of 20 mmol of neat liquid CEES using a solid-state HCP-Br_x/NO_x polymeric catalyst.

Additional reactions were run in an attempt to see this catalyzed reaction go to completion, but *ca.* 15-20% of CEES remained after 24 and 48 hours, at which point the catalysis appeared to terminate. To determine whether the reaction would ever reach completion, the reaction was replicated using only 10 mmol of neat CEES. As seen in Figure 17, this reaction did proceed to completion.

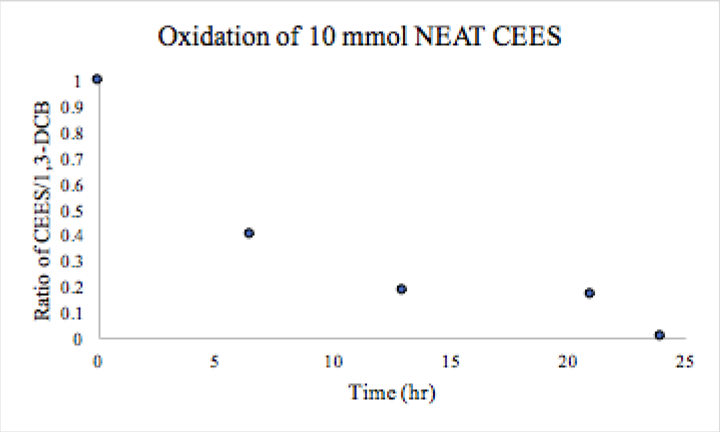

Figure 17. Aerobic oxidation of 10 mmol of neat liquid CEES using a solid-state HCP-Br_x/NO_x polymeric catalyst.

In order to determine if the polymer (HCP) alone (no Br_x/NO_x catalyst) possessed any activity, a control reaction was run where the ratio of CEES:1,3-DCB was followed. Over 90% of the initial CEES remained, indicating that the polymer alone was catalytic inactive.

After a reaction with 10 mmol of neat CEES, cyclohexane was added, the mixture swirled, and then the cyclohexane solution decanted into a separate beaker. The polymer samples were subsequently washed three times with 2 mL of cyclohexane to remove any excess CEES. Finally, a solution of cyclohexane and 1,3-DCB was used in each sample to determine if any CEES remained in the polymer following the multiple washings. It was found that no CEES remained in any of the samples, indicating that the HCP-Br_x/NO_x polymeric catalyst can be recovered and potentially reused.

V. Swellability of Hypercrosslinked Polymer-Catalyst

The swellability of the HCP-Br_x/NO_x polymeric catalyst was determined both quantitatively and qualitatively, through various swelling tests. The swellability of the HCP without the catalyst present was also measured to determine the effect of the presence of the catalyst on the polymer's ability to swell and encapsulate CWAs. The polymer was also tested with a variety of different solvents, including DMF, dipropyl sulfide, and neat liquid CEES. The following figures illustrate the polymer's swellability in these solvents.

Figure 18. Polymer swellability at 3 minutes (middle) and 24 hours (right) following exposure to DMF without catalytic components present in the HCP network.

Figure 19. Polymer swellability following exposure to dipropyl sulfide without catalytic components present in the HCP network.

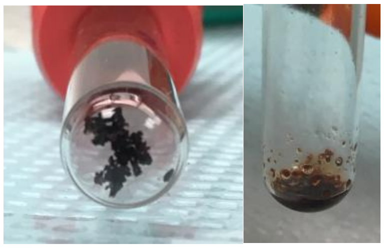

Figure 20. Polymer swellability following exposure to neat CEES with catalytic components present in the HCP network.

A quantitative determination of the swellability, Q, of the polymer with and without the catalytic components present was also conducted in both DMF and dipropyl sulfide. Table 4 documents that the polymer has slightly greater swellability (Q value) when it does not contain the catalytic components. This swellability difference appears to be outside experimental error. The HCP-Br_x/NO_x polymeric catalyst also consistently has a higher Q in DMF than in dipropyl sulfide. Due to the large volume of CEES necessary to determine the swellability of the polymer by neat CEES, we were unable to obtain quantitative swellability data for the polymeric catalyst under these conditions. However, as is seen in Figure 20, swelling does occur in the presence of CEES.

Table 4. The swellability, Q, of the HCP with and without the embedded Br_x/NO_x catalytic components in both DMF and dipropyl sulfide.

Swellability Q (mL g^{-1})		
	DMF	Dipropyl Sulfide
Polymer (HCP) only	5.98	4.20
Polymer with Catalyst (HCP-Br_x/NO_x)	3.80	3.93

4. Discussion

The development of the Br_x/NO_x catalytic system represents a significant advancement in the decontamination of CWAs as this system is currently the fastest selective oxidative system for CEES, to our knowledge. Optimizing the concentrations of each catalytic component has increased the reaction rate further. Despite these advancements, the dependence of the system occurring in solution decreases its practicality. The ability of the polymer to selectively oxidize neat CEES to the desired sulfoxide, CEESO, and to do so to reaction completion indicates a real potential for using this polymer as a solid-state remediation or decontamination catalyst requiring only air to function.

In addition, the swelling of the HCP-Br_x/NO_x polymeric catalyst provides an important capability that other catalytic systems lack. The entrapment of CWAs ensures that further exposure of the CWA will be minimized while the decontamination process proceeds. The swelling also serves as a signal, indicating that a toxic compound is present. In the case of CWAs that lack any distinguishable odor, such as the extremely lethal nerve agent VX,[25] the rapid swelling of the polymer could signal that there is an immediate danger that may otherwise go unnoticed, with deadly consequences. Also, as the polymer begins to swell it forms a barrier, preventing penetration of the CWA-swollen gel by addition CWA. This could prove to be potentially useful if the HCP-Br_x/NO_x polymeric catalyst is placed on the outer surface of a garment, such as a hazmat suit, or a vehicle, etc. to entrap and also decontaminate a toxic compound such as the CWA mustard.

While this catalytic solid-state system is promising in its applicability in the selective oxidation of CWAs and other toxic compounds, some remaining technical challenges should be noted. As reported in section 3.4, when 20 mmol of CEES is used in the reaction, the system fails to proceed to completion. It is suspected that some amount of the CEES vaporizes, potentially condensing on the side of the vial during the experiment. The vial is sealed off, so the vaporized CEES would be unable to leave the system. When the cyclohexane and 1,3-DCB is added to the vial, it would wash the vaporized CEES off of the walls of the vial. This could account for the 15-20% of CEES that fails to be oxidized. If not all the CEES becomes entrapped in the polymer due to a limiting quantity of polymer available, or because the bottom of the vial where the polymer resides is limited, the excess CEES could vaporize and begin to coat the walls. When only 10 mmol of CEES is used, all of this substrate is consumed suggesting that more HCP-Br_x/NO_x polymeric catalyst may be needed in such cases.

The decision of which monomer to use in the synthesis of the polymer was determined by the swellability of each different HCP when exposed to different solvents. The fluorobenzene-based HCP exhibited the greatest swelling, making it the best contender for potential success.

With incorporation of the Br_x/NO_x aerobic oxidation catalyst into the pores of the HCP, there was concern that the swellability of HCP-Br_x/NO_x polymeric catalyst on exposure to mustard or other CWA (or their simulants) would be substantially inhibited. The swellability of the HCP-Br_x/NO_x material dictates the ability for CWA entrapment, barrier formation, and detection, thus the ability of the polymer to swell when it contains the catalyst is a key feature. Thus the data in Table 4 (no drastic change in swellability, Q, of the HCP in DMF or dipropyl sulfide after catalyst incorporation) are encouraging. However, the Q values for the polymer-catalyst are, nonethesless, lower than those reported in the original paper.[22] This difference is likely due to the difference in methodology for determining swellability. Wilson et. al. allowed the polymer to sit in the stimulant for 24 hours prior to filtering off the remaining solvent.[22] With the pipet, much of the solvent drained through almost immediately and had to be continuously run back through the polymer, likely affecting the overall amount absorbed. That group was also able to assess their various HCPs for swellability with live CWAs, including HD, GB, and VX. Our laboratory, like other academic ones, is not equipped to conduct experiments with live agents. However, I will send samples to a collaborator with the necessary resources to do such assessments in the near future.

Following the reaction with 10 mmol of CEES, the samples of polymer and catalysts were washed with cyclohexane multiple times in hopes of removing any remaining CEES from the pores of the polymer. GC analysis showed that all remaining CEES is successfully removed from the polymer after three washings. In order to remove any remaining cyclohexane the samples were left open in the hood overnight, allowing for evaporation to occur. The polymer also returned to the contracted solid form. The ability to recover the polymer samples following a reaction with CEES indicates that such HCP-Br_x/NO_x materials may be re-cycled and reused.

Due to the nature of the aerobic oxidations catalyst used in this thesis, all Br_3^- and NO_3^- should theoretically be retained in the HCP at the end of the reaction. Additionally, these catalysts are completely insoluble in cyclohexane, so the concentrations should remain the same throughout the washing process. The only component of this system that would need to be replenished following one complete oxidation of CEES reaction would be O_2. Outside of a laboratory setting, O_2 would likely be readily available for use, allowing the reaction to proceed following the recovery of the polymer. Although this has not been assessed, it is likely that the polymer will be capable of reuse for multiple cycles of sulfoxidation, recovery and reuse.

5. Conclusions

Despite the ratification of the Chemical Weapons Convention in 1993, which formally outlawed the use, production, and stockpiling of CWAs, these toxic chemicals still pose a major threat to the global community due to noncompliance with the CWC. Research on decontaminating HD remains a priority due its high toxicity, potential for large-scale release, and the relative ease at which it can be synthesized. It has been shown that HD can be easily decontaminated using strong oxidants, but these oxidants are often corrosive or toxic themselves and not selective for production of the desirable decontaminated sulfoxide product.

The catalytic Br_x/NO_x system developed by Dr. Kevin Sullivan is a major advancement in selective sulfoxidation showing the fastest decontamination rates for CEES to our knowledge. The reaction rate of this system has been optimized by varying the concentrations of three of the catalytic components, $TBABr_3$, $TBANO_3$, and *p*-TsOH. Although a very effective system, it had primarily been tested and used for decontamination of CEES in MeCN. A hypercrosslinked polymer, HPC, derived from the monomer fluorobenzene, was synthesized in hopes of developing a solid-state system for the Br_x/NO_x catalytic components with swellability capabilities.

The catalytic components were successfully inserted into the HCP network, and the swellability of the polymer was not drastically altered upon incorporation of the catalysts into the polymer pores. This new system was able to selectively oxidize CEES to the less toxic CEESO to completion within 24 hours. The polymer was then recovered for potential reuse in additional oxidation reactions, studies that I will continue in the future. This polymer not only contains the fastest known catalytic system for the oxidation of CEES, but the polymer's swellability also provides unique characteristics that other decontaminating systems lack. Swelling in the presence of CWAs allows the polymer to entrap the toxic chemicals, prevents further exposure by forming a barrier to protect against further CWA penetration, and can act as an indicator to signal the presence of otherwise undetectable toxic compounds. Ideally, the system presented in this manuscript will be able to serve as a solid-state defense against CWAs, providing an efficient way of entrapping, decontaminating, and protecting against exposure to mustard gas.

6. References

1. Szinicz, L., History of chemical and biological warfare agents. *Toxicology* **2005,** *214* (3), 167-81.

2. Fitzgerald, G. J., Chemical warfare and medical response during World War I. *Am J Public Health* **2008,** *98* (4), 611-25.

3. Ganesan, K.; Raza, S. K.; Vijayaraghavan, R., Chemical warfare agents. *J Pharm Bioallied Sci* **2010,** *2* (3), 166-78.

4. Walker, P. F., A Century of Chemical Warfare: Building a World Free of Chemical Weapons. In *One Hundrer Years of Chemical Warfare: Research, Deployment, Consequences* Friedrich, B. H., D.; Renn, J.; Schmaltz, F.; Wolf, M., Ed. Springer International Publishing Cham, 2017; pp 379-401.

5. Kimball, D. G. The Chemical Weapons Convention (CWC) at a Glance. https://www.armscontrol.org/factsheets/cwcglance.

6. Singh

6. Ghabili, K. A., P. S.; Ghanei, M.; Ansarin, K.; Shoja, M. M., *J. Appl. Toxicol.* **2010,** *30*, 627-643.

7. Humans, I. W. G. o. t. E. o. C. R. t., Chemical agents and related occupations. *IARC Monogr Eval Carcinog Risks Hum* **2012,** *100* (Pt F), 9-562.

8. Alexander, P.; Fox, M.; Stacey, K. A.; Smith, L. F., The Reactivity of Radiomimetic Compounds .1. Cross-Linking of Proteins. *Biochem J* **1952,** *52* (2), 177-184.

9. Stahmann, M. A. G., C.; Stein, W. H.; Fruton, J. S., Chemical Reactions of Mustard Gas and Related Compounds. VII. The Chemistry of Bis(B-Chloroethyl)-Sulfone, Divinyl Sulfone and Divinyl Sulfoxide. *The Journal of Organic Chemistry* **1946,** *11* (6), 719-735.

10. Yang, Y. C.; Baker, J. A.; Ward, J. R., Decontamination of Chemical Warfare Agents. *Chem Rev* **1992,** *92* (8), 1729-1743.

11. Luo, Z.; Geletii, Y. V.; Hillesheim, D. A.; Wang, Y.; Hill, C. L., Mechanistic Studies of O2-Based Sulfoxidations Catalyzed by NOx/Br Systems. *ACS Catalysis* **2011,** *1* (10), 1364-1370.

12. Sullivan, K. P. Oxidative Studies in Decontamination and Water Oxidation Catalysis. Emory University, 2019.

13. In *Strategies to Protect the Health of Deployed U.S. Forces: Force Protection and Decontamination*, Wartell, M. A.; Kleinman, M. T.; Huey, B. M.; Duffy, L. M., Eds. Washington (DC), 1999.

14. Kowalski, P. M., K.; Ossowska, K.; Kolarska, Z. , Oxidation of sulfides to sulfoxides. Part 1: Oxidation using halogen derivative *Tetrahedron* **2005,** *61* (8), 1933-1953.

15. Bohra, A. S., K. P.; Banerji, K. K., Kinetics and Mechanism of the Oxidation of Organic Sulfides by Bis(2,2'-bipyridyl)copper(II) Permanganate. *J. Org. Chem.* **1997,** *62*, 3562-3567.

16. Le, N. H.; Han, Y.; Ryu, S. G.; Cho, J. Mechanistic reaction model for oxidation of sulfur mustard stimulant by a catalytic system of nitrate and tribromide. *J. Hazardous Materials*. **2019**, *365*, 511-518.

17. DeCoste, J. B.; Peterson, G. W., Metal-organic frameworks for air purification of toxic chemicals. *Chem Rev* **2014,** *114* (11), 5695-727.

18. Peterson, G. W.; Moon, S. Y.; Wagner, G. W.; Hall, M. G.; DeCoste, J. B.; Hupp, J. T.; Farha, O. K., Tailoring the Pore Size and Functionality of UiO-Type Metal-Organic Frameworks for Optimal Nerve Agent Destruction. *Inorg Chem* **2015,** *54* (20), 9684-6.

19. Asha, P.; Sinha, M.; Mandal, S., Effective removal of chemical warfare agent simulants using water stable metal–organic frameworks: mechanistic study and structure–property correlation. *RSC Advances* **2017,** *7* (11), 6691-6696.

20. Westreich, P. F., H.; Flynn, S.; Foster, S.; Dahn, J. R., Exclusion of Salt Solutions from Activated Carbon Pores and the Relationship to Contact Angle of Graphite. *J. Phs. Chem. C* **2007,** *111*, 3680-3684.

21. Sullivan, K. P.; Neiwert, W. A.; Zeng, H.; Mehta, A. K.; Yin, Q.; Hillesheim, D. A.; Vivek, S.; Yin, P.; Collins-Wildman, D. L.; Weeks, E. R.; Liu, T.; Hill, C. L., Polyoxometalate-based gelating networks for entrapment and catalytic decontamination. *Chem Commun (Camb)* **2017,** *53* (83), 11480-11483.

22. Wilson, C.; Main, M. J.; Cooper, N. J.; Briggs, M. E.; Cooper, A. I.; Adams, D. J., Swellable functional hypercrosslinked polymer networks for the uptake of chemical warfare agents. *Polymer Chemistry* **2017,** *8* (12), 1914-1922.

23. Wright, A. J.; Main, M. J.; Cooper, N. J.; Blight, B. A.; Holder, S. J., Poly High Internal Phase Emulsion for the Immobilization of Chemical Warfare Agents. *ACS Appl Mater Interfaces* **2017,** *9* (37), 31335-31339.

24. Mata, E. G., Recent Advances in the Synthesis of Sulfoxides from Sulfides. *Phosphorus, Sulfur, and Silicon and the Related Elements* **1996,** *117* (1), 231-286.

25. Facts about VX. https://emergency.cdc.gov/agent/vx/basics/facts.asp.