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## Oxidative Detoxification of Sulfur-Containing Chemical Warfare Agents by Electrophilic Iodine

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## Abstract

Mild oxidation of sulfur-containing chemical warfare agents (CWAs) was performed in organic medium by electrophilic iodine reagents. Kinetic experiments on sulfur mustard (HD, 1) showed rapid ( $t_{1/2} < 3 \text{ min}$ ) and selective oxidation to the non-vesicant sulfoxide product (HD-SO, 5) in acetonitrile or propylene carbonate solutions (9% water added) containing excess of NIS (N-iodosuccinimide). Molecular iodine solutions in these solvents led to similar results as with NIS, however at much slower rates ( $t_{1/2}$ ~90 min). Higher donor number (DN) solvents, such as THF, DMF or DMSO, showed slower rates with both iodine and NIS. The oxidation of the nerve agent VX (O-ethyl-S-2-(N,Ndiisopropylaminoethyl)methylphosphonothioate, 2) selectively to the non-toxic EMPA (ethyl methylphosphonic acid, 7) product exhibited fast rates ( $t_{1/2}=6$  min) using NIS in DMSO solution. In all other solvents tested with 2, rates were slower ( $t_{1/2}$ ~30-70 min). Oxidation experiments under the same conditions with chloroethyl-ethylsulfide (CEES, HD simulant, 3) and O,S-diethyl methylphosphonothioate (DEMPT, VX simulant, 4) led to much faster reaction rates. These transformations are believed to proceed through electrophilic iodine attack on the sulfur moiety, and display solvent dependency based on the agents' structural and chemical properties.

## Introduction

Development of new, mild and universal decontamination/detoxification solutions against chemical warfare agents (CWAs) is a continuous effort, especially under the circumstances of using these malicious means in recent years.<sup>1,2</sup> Among all known CWAs, the vesicant sulfur mustard (bis-(2-chloroethyl)sulfide, HD, **1**) and the toxic nerve agent VX (*O*-ethyl-*S*-2-(*N*,*N*-diisopropylaminoethyl)methylphosphonothioate, **2**) are considered as the most persistent (Figure 1).<sup>3</sup> Due to their high stability and low volatility, **1** and **2** can persist for months, posing physiological and ecological threat.<sup>4-7</sup> In an attempt to deal with these hazardous CWAs, numerous detoxification approaches have been examined over the last decades, including simple reactions such as hydrolysis, elimination, substitution and oxidation.<sup>8,9</sup> It is worth mentioning that a considerable part of these studies have been conducted on CWAs simulants, such as CEES (chloroethyl-ethylsulfide, **3**) and DEMPT (*O*,*S*-diethyl methylphosphonothioate, **4**) (simulants of **1** and **2**, respectively).<sup>8</sup>



Figure 1. Sulfur containing CWAs and their simulants.

Usual CWAs degradation procedures require harsh reagents (such as strong bases/acids/oxidants) in order to reach full degradation,<sup>8</sup> however, with high ecological and environmental cost. In order to avoid these conditions, development of benign procedures is preferred. However, under mild conditions, toxic byproducts could also be formed. For example, in the over oxidation of **1**, the formation of the vesicant HD-SO<sub>2</sub> (bis-(2-chloroethyl)sulfone, **6**) could be observed in addition to the non-vesicant HD-SO ((bis-(2-

chloroethyl)sulfoxide, **5**).<sup>9</sup> As well, in the hydrolysis of **2**, the toxic desethyl-VX (*S*-2-(*N*,*N*-diisopropylaminoethyl)methylphosphonothioic acid, **8**) could be formed in addition to the non-toxic EMPA (ethyl methylphosphonic acid, **7**) (Scheme 1).<sup>10</sup> Therefore, the development of a selective and mild method for the degradation of **1** and **2** to their corresponding non-vesicant and non-toxic products still remains a challenge.

Scheme 1. Non-Selective degradation of 1 and 2 to their products.



Oxidation is one of the important approaches for CWAs detoxification,<sup>8</sup> of which hypochlorite derivatives and peroxide solutions are the most popular. Examples of such formulas are bleach (sodium hypochlorite),<sup>9</sup> STB (calcium hypochlorite),<sup>9</sup> Fichlor (sodium *N*,*N*-dichloroisocyanurate),<sup>9</sup> L-Gel<sup>11</sup> and Decon Green (based on peroxides).<sup>12</sup> However, these oxidants are characterized by several drawbacks. In addition to their non-selective mode of action and tendency to over-oxidize, they are usually used as high polarity waterbase solutions, which restrict their interaction with hydrophobic agents such as **1** and **2**, especially in large quantities. Moreover, in some cases, the slow rates of oxidation reactions require the use of special conditions such as high pH and elevated temperatures. Recently, in addition to the aforementioned, inorganic macromolecules as some modified MOFs (metal organic frameworks)<sup>13</sup> and POMs (polyoxometalates)<sup>14</sup> have been introduced to the field of CWAs oxidation. To the best of our knowledge there is only one example in which actual CWA has been proven to react through an oxidation mechanism with MOFs.<sup>13b</sup> With regard to POMs, all the oxidation processes were reported solely on

simulants of **1**.<sup>14</sup> Most recently, an efficient photocatalytic oxidation of **1** by an organic photosensitizer incorporated in polymer coating and fabrics was reported.<sup>15</sup>

Following our ongoing studies to find benign and universal formulations for CWAs decontamination,<sup>16-19</sup> we examined the possibility of using electrophilic iodine reagents as mild oxidants for sulfur containing CWAs. In the arsenal of CWAs degradation formulas only few examples of iodine-containing reagents can be found. IBX (*O*-iodoxy benzoic acid) and its derivatives are the most known, but they exert their reactivity by acting as  $\alpha$ -nucleophiles.<sup>20</sup> Moreover, there are several reports using povidon-iodine and solution of iodine/tetraglycol/ethanol as topical ointments against skin lesions induced by 1.<sup>21-23</sup> The effect of these formulations was limited and their mode of action is not clear.

Iodine and iodination reagents are known for their high solubility in organic solvents and their ability to oxidize sulfides. Nonetheless, there are only few literature examples where molecular iodine is used for sulfide oxidation, all of which are catalyzed by certain nucleophiles.<sup>24,25</sup> As reported, such reactions include sulfide nucleophilic attack on iodine to form a postulated iodosulfonium cation, which subsequently reacts to yield a sulfoxide.<sup>26</sup> Another well-known iodination/oxidation reagent is NIS (*N*-iodosuccinimide), which is widely used for the activation of thioglycosides in carbohydrate chemistry.<sup>27</sup>

Inspired by this chemistry, we sought to use iodonium ion generated either by molecular iodine or NIS, as a mild oxidant for the decontamination of divalent sulfur containing CWAs, i.e. 1 and 2. Herein, we disclose our results on the selective and efficient degradation of these agents by iodonium species relative to their common simulants (3 and 4).

#### **Results and Discussion**

Screening of iodine-containing oxidants. Several iodine-based oxidants were initially screened for potential degradation of sulfur containing CWAs. This screening for the oxidation of **3** included KIO<sub>4</sub>, KIO<sub>3</sub>, KI<sub>3</sub> and I<sub>2</sub> in organic solutions (such as acetonitrile (ACN) and propylene carbonate (PC)) containing water as a reagent (10:1 v/v

respectively). In a typical experiment, **3** was reacted with excess of oxidant (5-11 equiv.) at room temperature and monitored by  ${}^{13}C{}^{1}H$  NMR. From all the aforementioned oxidants, only I<sub>2</sub> exhibited reactivity towards the oxidation of **3**, and therefore was selected for further investigation.

Reactions of 1 and 3 with Iodine (I<sub>2</sub>). Decontamination methodologies usually require excess of decontaminant for an efficient process. First attempts have shown maximum solubility of 11 equivalents of iodine under the experimental conditions in most tested organic solvents (2  $\mu$ L of 3 in 1 mL solvent at room temperature). Aprotic organic solvents containing water (10:1 v/v, respectively) were screened for optimal reaction rates. The results are summarized in Table 1. Sulfide 3 was oxidized by I<sub>2</sub> in a selective and fast manner to the corresponding sulfoxide 9 (Scheme 2) in ACN, PC and acetone (AC) solutions (entries 1-3). No further oxidation to sulfone was observed even after 18 hours from reaction completion (Figure S1 in the supporting Information). DMF showed fast reaction, however, with lower selectivity forming different by-products. Oxidation in THF or DMSO was selective, but with longer reaction times (entries 4, 6). The high selectivity of this reaction (in spite of the high excess of oxidant used) coupled with the fast reaction rates, encouraged us to further investigate this transformation.

Entry	Solvent <sup>a</sup>	$t_{1/2}$ of <b>3</b> oxidation (min)	$t_{1/2}^c$ of <b>1</b> oxidation (min)	
1	ACN	<3	92	
2	PC	<3	88	
3	AC	<3	$\mathbf{N}\mathbf{A}^{d}$	
4	THF	7	1080	
5	DMF	$\mathrm{NA}^b$	$\mathbf{N}\mathbf{A}^{d}$	
6	DMSO	30	960 <sup>b</sup>	

Table 1. Kinetic rates for the oxidation of 1 and 3 by molecular iodine in different solvents

<sup>*a*</sup> Solvent/water 10:1 (v/v). <sup>*b*</sup> Mixture of products. <sup>*c*</sup> Due to iodine decomposition during the reaction course and deviation from first order kinetics, an average half-life times were calculated. <sup>*d*</sup> Reaction stopped at 40% conversion after 400 min.





Figure 2. <sup>13</sup>C{<sup>1</sup>H} NMR spectra showing the oxidation of 1 by iodine in ACN/H<sub>2</sub>O (10:1) to the sulfoxide products (5 and 10) at: (A) 27 min; (B) 93 min; (C) 188 min; (D) 448 min; (E) 1048 min.

In a similar manner, **1** was treated with molecular iodine under the same conditions as **3** to form sulfoxide **5**. Oxidation rates were much slower, presumably due to the additional electron withdrawing chlorine atom.<sup>28</sup> In ACN and PC the average half-life times were ~90 minutes (Table 1, entries 1-2 and Figures S2-S4 in the Supporting Information). During

the reaction, **5** further reacts with water to afford the hydrolyzed sulfoxide **10** (Scheme 2 and Figure 2). In other solvents, the reaction rates were much slower (entries 3-6), and in some cases the reaction stopped without reaching full conversion (entries 3, 5). Moreover, a deviation from first order reaction kinetics was observed, seemingly due to the decrease in iodine concentration, which is consumed by competitive reactions. It is known from previous reports, iodine decays slowly in organic solvents to the non-active triiodide anion and other species, and water accelerates this decay.<sup>29</sup> Indeed, iodine solutions that were prepared 24 hours prior to reaction were not reactive. Therefore, in order to improve the rates and the efficiency of the reaction, the more stable iodonium source NIS was used.

**Reactions of 1 and 3 with NIS.** The reagent NIS turned out to be highly efficient. Under the same reaction conditions described above for iodine, **3** was oxidized selectively to the corresponding sulfoxide **9** in all solvents tested in less than 15 minutes ( $t_{1/2} < 3$  min). Furthermore, the oxidation of **1** by NIS to the non-vesicant sulfoxide **5** was significantly faster in comparison to iodine. Reactions in ACN, PC and AC reached full conversion within 10-15 min ( $t_{1/2} < 3$  min). Reactions in THF, DMF and DMSO also reached full conversion in shorter half-life times relatively to the slow rates and partial conversions with iodine (Table 2 and Figure S5 in the Supporting Information). It is worth mentioning that in contrast to iodine solutions, NIS solutions were found to be stable for prolonged periods of time (over a month) without significant decomposition.

The results with NIS showed a clear dependence between the solvent and the reaction rate. While there was no obvious indication for correlation with solvent polarity, a correlation was observed between the reaction rates and the solvent basicity (donor number, DN). Namely, the lower the solvent's DN, the higher the kinetic rate constant of the oxidation reaction. For example, while the reaction was very fast in ACN (DN=14.1, entry 1), it was relatively slow in DMSO (DN=29.8, entry 6).

The reactivity of NIS towards **1** was compared to its common bromine derivative NBS (*N*-bromosuccinimide). The same trend as with NIS was observed in the reaction of **1** with NBS in ACN vs. DMSO. In ACN the reaction was fast (entry 8) yet not selective, affording

a mixture of sulfoxide **5** and the bromination product **12** (Figure 3). In DMSO the conversion was much slower (entry 9), but selective in respect to the sulfoxide product.

### Table 2: Kinetic rates for the oxidation of 1 and 3 by NIS or NBS in different solvents.

_	Entry	Solvent <sup>a</sup>	Oxidant	Donor number	t <sub>1/2</sub> of <b>3</b> oxidation (min)	t <sub>1/2</sub> of <b>1</b> oxidation (min)	
	1	ACN	NIS	14.1	<3	<3	
	2	PC	NIS	15.1	<3	<3	
	3	AC	NIS	17.0	<3	<3	
	4	THF	NIS	20.0	<3	4	
	5	DMF	NIS	26.6	<3	53	
	6	DMSO	NIS	29.8	<3	62	
	7	DMSO <sup>b</sup>	NIS		-	148	
	8	ACN	NBS	14.1	-	<3c	
_	9	DMSO	NBS	29.8	-	35	
<sup>a</sup> Solver	<sup><i>a</i></sup> Solvent/H <sub>2</sub> O 10:1. <sup><i>b</i></sup> Solvent/D <sub>2</sub> O 10:1. <sup><i>c</i></sup> Mixture of <b>5</b> and <b>12</b> was obtained.						



Figure 3. <sup>13</sup>C{<sup>1</sup>H} NMR spectra presenting the oxidation reaction of 1. (A) starting material (1); (B) oxidation by NIS in ACN/H<sub>2</sub>O (10:1) to the sulfoxide product (5); (C) oxidation by NBS in ACN/H<sub>2</sub>O (10:1) to a mixture of 5 and 12.

**Mechanism of HD (1) oxidation: solvent role.** In order to understand the mechanism of the oxidation of sulfides with NIS and the role of the solvent, we looked for a sulfide that undergo rather slow oxidation process. Ethylphenylsulfide **13** undergoes slow enough oxidation in PC to enable reaction monitoring on <sup>13</sup>C NMR timescale. In less than two minutes after reacting **13** with 4 equivalents of NIS in PC (no water added), changes in the  $^{13}C{^{1}H}$  NMR chemical shifts spectrum were observed, especially for the carbons adjacent to the sulfur atom (Figures S6-S7 in the Supporting Information). These changes are attributed to the formation of an intermediate believed to be a sulfonium complex. Next, water was added to complete the reaction. At this point, formation of the sulfoxide **14** via substitution of the iodide by water was observed. The latter transformation was significantly slower than the first step, taking 12 min to complete after the addition of water (Figure S6C-E in the Supporting Information). This difference implies that the second step, substitution by water, is the slower step. Additional support was obtained from kinetic

isotope effect (KIE) experiments. **1** was reacted with NIS in DMSO/D<sub>2</sub>O in comparison to DMSO/H<sub>2</sub>O under the same conditions above. A slowdown in the reaction rate was observed with  $k_H/k_D = 2.4$  (Table 2, entries 6-7) in accordance with reported hydrolysis values of secondary solvent isotope effect.<sup>30</sup> Based on these results, we propose a mechanism for the oxidation of **1** by NIS/H<sub>2</sub>O, which explains the kinetic rate dependence on solvent (scheme 3).

In this mechanism the postulated sulfonium cation is stabilized by the solvent. The higher the solvent's Lewis basicity (higher DN) the stronger the interactions with the sulfonium cation intermediate, thus reducing the reaction rate. DMSO (with the highest DN of all the tested solvents) displays the lowest rate of sulfide to sulfoxides transformation with both NIS and NBS (Scheme 3 and Table 2, entries 6 and 9).

Scheme 3. Proposed mechanism of the oxidation of 1 by NIS in solvent/H<sub>2</sub>O.



Mechanism of HD (1) oxidation: oxidant role (NIS vs. NBS). We have noticed that immediately after addition of NIS, the color of the reaction solution turns brown. This may imply on the formation of molecular iodine during the reaction. The same visual result was obtained when KI was added to NIS solution. In addition, in reactions conducted with different ratios of NIS to sulfide, at least two equivalents were found to be the minimum needed to reach full conversion to sulfoxide. On the other hand, reaction with NBS was colorless, and one equivalent was needed to reach a full conversion. When more than one equivalent was used, the reaction did not yield the sulfoxide selectively. Based on these observations, we propose that the reaction with NIS forms HI, which immediately reacts with another equivalent of NIS to produce iodine (Scheme 3). Hence, the reaction solution stays close to neutral (pH  $\sim$  6). In contrast, the reaction with NBS produces HBr, which lowers the pH of the solution (pH  $\sim$  1) without consuming NBS (Figure S8 in the

to completion, probably due to the decomposition of iodine (Table 3, entries 3-6).

Supporting Information). The low pH accelerates the release of bromonium cation, hence, increasing the reaction rate of sulfide oxidation. When an excess of NBS is used, the released bromide anion continues to react with the sulfonium cation to produce a bromination by-product presumably via Pummerer type reaction in addition to the sulfoxide product.<sup>31,32</sup> **Reactions of 2 and 4 with Iodine (I<sub>2</sub>) and NIS.** In light of the oxidation results with **1**, we were intrigued to examine whether electrophilic iodine will be efficient oxidant for the degradation of the thiophosphonates **2** and **4** in organic solutions. The reaction of **4** with I<sub>2</sub> (11 equivalents, solvent/water 10:1) monitored by <sup>31</sup>P NMR showed selectivity towards P-S bond cleavage, yielding only the hydrolysis product **7**. The reactions did not proceed

_	Entry	Solvent <sup>a</sup>	Oxidant	$t_{1/2}$ of <b>4</b> oxidation (min)	$t_{1/2}$ of <b>2</b> oxidation (min)	t <sub>0.9</sub> of <b>2</b> oxidation (min)
	1	ACN	$I_2$	<3	93	3980
	2	PC	$I_2$	<3	27	280 <sup>f</sup>
	3	AC	$I_2$	$<\!\!6^{b}$	320 <sup>d</sup>	
	4	THF	$I_2$	<4 <sup>c</sup>	43	2920 <sup>f</sup>
	5	DMF	$I_2$	<10 <sup>c</sup>	NR	
	6	DMSO	$I_2$	<3°	16 <sup>c</sup>	
	7	ACN	NIS	<3	69	
	8	РС	NIS	<3	30 <sup>e</sup>	
	9	AC	NIS	<3	44	
	10	THF	NIS	<3	60	
	11	DMF	NIS	<3	45 <sup>d</sup>	
	12	DMSO	NIS	<3	6	

#### Table 3. Kinetic rates for the oxidation of 2 and 4 by I<sub>2</sub> or NIS in different solvents.

<sup>*a*</sup> Solvent/H<sub>2</sub>O 10:1. <sup>*b*</sup> Stopped at 80% conversion. <sup>*c*</sup> Stopped at 95-97% conversion. <sup>*d*</sup> Stopped at ~50% conversion. <sup>*e*</sup> Averaged result (deviation from first order reaction kinetic). <sup>*f*</sup> Stopped at ~90% Conversion.

Next, we evaluated the reactivity of **2** with iodine. In the same manner, **2** was reacted with iodine to give solely the product **7**, without forming the toxic product **8** (cleavage of P-O bond). In comparison to **4**, the rates were slower (time scale of hours) with the exception of DMSO, which was considerably faster (entry 6). In neither cases full conversion was obtained (entries 1-6), and in some solvents deviation from first order reaction kinetics was observed (in these cases  $t_{1/2}$  and  $t_{0.9}$  were measured, entries 1,2,4).

As with sulfides, NIS showed better performance than iodine towards the degradation of the thiophosphonates (entries 7-12). 4 underwent very fast decomposition ( $t_{1/2}$ < 3 min) in all tested solvents giving selectively product 7. The  $t_{1/2}$  reaction of 2 with NIS in ACN, PC,

AC and THF ranged between 30-70 minutes (Figure S9 in the Supporting Information). Contrary to iodine, the reactions with NIS reached full conversion (except in DMF). Moreover, in some solvents, acceleration during the reactions course was observed, probably due to the decrease in pH induced by the formation of **7** (Figure S10 in the Supporting Information). In contrast to the sulfide trend, no correlation between solvents' DN and the kinetic rates was observed. However, as with iodine, the reaction with NIS in DMSO was exceptionally faster under the same conditions ( $t_{1/2} = 6$  min, entry 12, Figure S11 in the Supporting Information). For comparison reasons, NBS was reacted with **2** under the same conditions as with NIS. The reaction was selective as well and afforded only product **7**. NBS shows faster reaction rates in all solvents tested ( $t_{1/2} < 5$  min). This can be explained by the low pH induced by HBr liberation in the oxidation process as previously described.

**Insights into the oxidation mechanism of thiophosphonates 2 and 4.** Two important observations resulted from the above-mentioned experiments: (1) The oxidative degradation rate of **4** was much faster than that of **2** (Table 3, entries 7-12). (2) The oxidative degradation rate of **2** itself was faster in DMSO relatively to the other solvents (note that the oxidation of sulfide **1** in DMSO was the slowest).

Regarding the first point, previous studies have established that thiophosphonates (such as 4, the 'head' part of 2) undergo oxidation to the corresponding sulfonium ion intermediate, which in turn serves as a good leaving group for a sequential fast hydrolysis reaction (Scheme 4, reaction A).<sup>33,34</sup> Yang et al. have shown that in the presence of an amine group, such as in the case of 2, the amine is the first to be oxidized under neutral and basic conditions. When an excess of oxidant was used, it was suggested that the *N*-oxide intermediate can be further oxidized on the sulfur moiety at a slower rate.<sup>34</sup> Moreover, tests we have conducted separately on diisopropylethylamine **15** (the amine 'tail' of **2**) under the same conditions (NIS, ACN/H<sub>2</sub>O) showed a very fast decomposition to acetaldehyde and diisopropylamine (Scheme 4, reaction B). A similar reaction was previously described for tertiary amines and NBS.<sup>35</sup> Since reactions (A) and (B) are both faster than reaction (C) (Scheme 4), we can assume that the formation of electron deficient species from **2**, such as *N*-iodoammonium, *N*-oxide or aldehyde, will reduce the reactivity of the sulfur moiety

towards oxidation. This may explain the relatively slow rate of the decomposition of 2 by  $I_2$  or NIS in comparison to 4.





Comperative Reaction Rates: (A) > (C), (B) > (C)

Regarding the second point, it was shown that the oxidation step in oxidative degradation of thiophosphonates is the rate-limiting step.<sup>36</sup> Consequently, the hydrolysis step is the fast step. The rate increase observed with I<sub>2</sub> and NIS when DMSO is used can be rationalized by DMSO ability to stabilize the charged transition-state of this rate-limiting step. On the other hand, in the case of sulfide 1 oxidation, the rate-limiting step is the hydrolysis. Thus, stabilization of the positively charged sulfonium intermediate by DMSO (high DN) will slow the reaction rate. The different stages DMSO is involved in the oxidation reaction of both sulfides and thiophosphonates, explains the opposite trend observed in reactions kinetics. Namely, when DMSO is used as solvent, sulfide degradation is slower while thiophosphonate degradation is faster.

## Conclusions

According to the experimental results presented here, mild organic solutions (9% water v/v) of NIS in ACN or PC were able to decontaminate **1** in a selective and very fast manner to the non-vesicant sulfoxide **5**. For the decontamination of **2**, DMSO and PC solutions showed the best results affording exclusively the non-toxic product **7**. Although NBS showed faster decontamination rates of **2**, its non-selective mode of action toward **1** oxidation (when using excess of NBS) and the corrosivity of its solutions make it less favorable than NIS as a universal decontamination agent. Hence, the use of NIS with the green solvent PC<sup>37</sup> makes it a powerful and attractive system for universal decontamination process. In addition, our results showed that decomposition by oxidation of **3** (simulant of **1**) and **4** (simulant of **2**) were much faster relative to **1** and **2**. These results should be taken under consideration when establishing decontamination procedures only on simulants.

## **Experimental Section**

Caution! These experiments should only be performed by trained personal using applicable safety procedures.

**Chemicals**. VX (2), HD\* (<sup>13</sup>C labeled of 1) and DEMPT (4) were obtained locally at IIBR (>99% purity). (2-chloroethyl)ethyl sulfide (CEES, 3), ethylphenylsulfide (13), N-iodosuccinimide (NIS), N-bromosuccinimide (NBS) and all solvents (HPLC grade) were purchased from commercial suppliers and used without further purification. Deionized water was obtained from a laboratory water purification system.

**NMR spectroscopy.** <sup>13</sup>C{<sup>1</sup>H} and <sup>31</sup>P{<sup>1</sup>H} spectra were obtained at 125 and 202 MHz, respectively, at room temperature on a 11.7 T (500 MHz) Bruker spectrometer (Avance III HD). Chemical shifts were calibrated to TMS (for <sup>13</sup>C) and Trimethylphosphate (for <sup>31</sup>P) as 0 ppm. The spectra were recorded using the standard parameters of the TopSpin NMR software (version 3.5). Each data point was obtained from 32-64 scans, at a spectral width of 200 ppm and 2s relaxation time. For comparison purposes, spectra of the kinetic experiments were recorded under identical conditions. Integration was carried out automatically using the Dynamic Center of Topspin software.

**Degradation kinetics**. Oxidant (Iodine, NIS or NBS, 11 equivalents, unless otherwise mentioned) was added to a solution of solvent/water 10:1 v/v (1 mL) and stirred for two minutes until all dissolved. The tested compound (CWA or simulant,  $2\mu$ L, 1 equiv.) was carefully added and the solution was transferred as is into a NMR tube for kinetic analysis. Kinetic NMR acquisition sampling started as soon as possible (without lock or shimming) until completion or no further change in reaction conversion was observed. Postacquisition analysis was performed by Dynamic Center software using build-in first order fitting functions to determine half-life times.

**Oxidation of Ethylphenelsulfide (13).** Sulfide **13** (5  $\mu$ L, 0.037 mmol) and NIS (33 mg, 4 equiv.) were added to 1 ml propylene carbonate (PC) (without added water) and the reaction was monitored by <sup>13</sup>C NMR. After identification of the sulfonium cation, 100  $\mu$ L of water were added and the reaction was furthered monitored by <sup>13</sup>C NMR until full conversion to the corresponding sulfoxide.

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#### Notes

The authors declare no competing financial interest.

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### **Associated Content**

## **Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website.

Oxidation kinetic profiles of HD (1) and VX (2); NMR spectra of oxidation reactions; proposed mechanism for the oxidation of HD (1).

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