

Reductive Destruction of Chemical Warfare Agent Simulants in Water

James J. Kiddle*,† and Stephen P. Mezyk*,‡

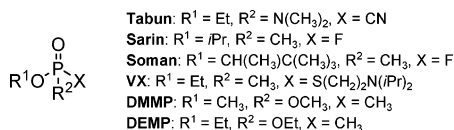
Department of Chemistry, Western Michigan University, 3425 Wood Hall, Kalamazoo, Michigan 49008, and
Department of Chemistry and Biochemistry, California State University Long Beach, 1250 Bellflower Blvd.,
Long Beach, California 90840

Received: May 17, 2004; In Final Form: May 26, 2004

The efficient detection, decontamination, and destruction of chemical warfare (CW) agents remain an active area of scientific research. Rate constants for the reaction of substituted diethyl phosphates and phosphonates with the hydroxyl radical and hydrated electron have been measured in water to elucidate the primary destruction pathway for the CW agents Tabun (GA), Sarin (GB), Soman (GD), and VX with these two species. The measured kinetics for simulants with leaving groups that more closely mimic these actual CW agents predict that reductive destruction will be the most efficient mechanism, and that nontoxic simulants such as alkyl phosphonates undergo different redox chemistry.

Recent world events have focused the scientific community's attention on chemical warfare (CW) agents. In particular, chemists have focused their attention on improving the ability to detect,^{1–4} decontaminate,^{5–7} and destroy^{8–14} CW agents. CW agents, which are organophosphorus compounds, exert their toxic effects through the inhibition of acetylcholinesterase. Because of their extreme toxicity, and restricted use through the 1992 Chemical Weapons Convention Treaty,¹⁵ actual CW agents (Chart 1) such as Tabun (GA), Sarin (GB), Soman (GD), and VX are not regularly used in studies at academic laboratories. Instead, simulants that mimic the structural and electronic properties of actual CW agents are often utilized. Simulant chemicals also have a range of toxicities, from the hazardous paraoxon (LD₅₀ Rat: i.p. 0.54 mg/kg)¹⁶ to the less toxic diisopropylfluorophosphate (DFP, LD₅₀ Rat: i.p. 1.3 mg/kg)¹⁷ to the relatively nontoxic diethyl methylphosphonate (DEMP, LD₅₀ Mouse: i.p. 2240 mg/kg).¹⁸

CHART 1: Structure of CW Agents and Phosphonate Simulants



Previous work has demonstrated¹⁴ that oxidizing hydroxyl radicals degrade DEMP (Chart 1) and the analogous dimethyl methyl phosphonate (DMMP) in aqueous solution, but reducing hydrated electrons and superoxide anion radicals were unreactive. In this letter, we describe the reaction of five CW agent simulants (Table 1) with both the hydroxyl radical and hydrated electron, clearly showing that hydrated electrons react appreciably with simulants that are more accurate analogues of CW agents.

Compounds **1**, **3**, **4**, and DEMP are commercially available; the synthesis of simulants **2** and **5** can be accomplished from

TABLE 1: Rate Constants for the Reaction of Chemical Warfare (CW) Agent Simulants

simulant	X	pK _a ^a	k(e ⁻) (M ⁻¹ s ⁻¹)	k(HO•) (M ⁻¹ s ⁻¹)
1	H	35	(2.21 ± 0.02) × 10 ⁸	(7.87 ± 0.08) × 10 ⁸
2	F	3.2	(1.83 ± 0.05) × 10 ⁹	(4.73 ± 0.11) × 10 ⁸
3	Cl	−7	(3.93 ± 0.04) × 10 ¹⁰	(1.37 ± 0.03) × 10 ¹⁰
4	CN	9.2	(3.52 ± 0.15) × 10 ⁹	(9.04 ± 0.20) × 10 ⁷
5	CF ₃	27 ^b	(5.3 ± 1.2) × 10 ⁸	(7.66 ± 0.18) × 10 ⁸
DEMP ^c	CH ₃	48	(3.36 ± 0.74) × 10 ⁷	(6.20 ± 0.09) × 10 ⁸

^a Values taken from March, J.; Smith, M. B. *Advanced Organic Chemistry*; Wiley, New York, 2001; pp 329–331. pK_a values represent the ionization of H–X in water. ^b Value taken from Symons, E. A.; Clermont, M. J. *J. Am. Chem. Soc.* **1981**, *103*, 3127. ^c Data taken from unpublished work by S. P. Mezyk.

diethylchlorophosphate (**3**). Synthesis of the diethyl fluorophosphate (**2**) can be safely accomplished in quantitative yield by a solid-phase approach that was developed in our laboratory.¹⁹ Subsequent reaction of **2** with 2 equiv of TMSF₃ and a catalytic amount of CsF produces the diethyl trifluoromethylphosphonate analogue (**5**) in excellent yield (85%).²⁰

Initially, it was thought that hydrolysis might interfere in the accurate determination of the rate constants for these simulants. However, the literature clearly indicated that both simulants and CW agents where X = F, Cl, or CN show only rapid hydrolysis at either high or low pH, whereas, at neutral pH, aqueous hydrolysis occurs slowly.^{21,22}

Reaction rate constants for the CW agent simulants with the hydrated electron and hydroxyl radical are presented in Table 1. Reducing hydrated electron reaction rate constants were directly measured in neutral pH solutions from the rate of change of its near-IR absorbance.²³ Rate constants for oxidizing hydroxyl radical reactions were determined by competition kinetics, using thiocyanide as a standard.²⁴ It is evident that simulants that more precisely resemble CW agents in their structure have reduction rate constants that are 20–40 times faster than those for their oxidation.

The Brönsted plots for the series of CW simulants are presented in Figure 1. Analysis of the plot for reaction of the

* Author to whom correspondence should be addressed. E-mail address: james.kiddle@wmich.edu.

† Western Michigan University.

‡ CSU—Long Beach.

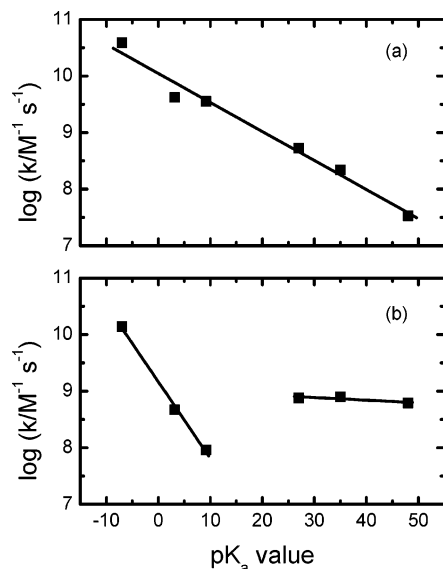
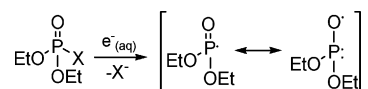


Figure 1. Brønsted plots for the reaction of CW agent simulants with (a) hydrated electron and (b) hydroxyl radical in aqueous solution at neutral pH.

hydrated electron (Figure 1a) reveals excellent linearity for the six simulants ($\beta = 0.980$) over the entire range of pK_a values of the leaving groups. The linear plot suggests a single mechanism for reaction of the hydrated electron with the simulant compounds.²⁵ This mechanism is consistent with electron capture at the P atom and loss of the leaving group (Scheme 1). In addition, transient spectral data obtained for **3** showed that the loss of absorption for the hydrated electron (700 nm) directly correlated with the growth of a new transient at 340 nm. The transient is attributed to the phosphinoyl radical, which is formed by the loss of the chloride; however, it is not clear which of the two canonical structures is responsible for the absorption (Scheme 1).²⁶

SCHEME 1: Reaction of Simulants with Hydrated Electron



The measured rate constants are faster for compounds **2–4**, which have good leaving groups, where it is reasonable that the reduced X^- is released into solution. However, compounds that have a poor leaving group (**1**, **5**, and DEMP) undergo much slower reaction and may be eliminating radical fragments (X^\cdot , $\text{C}_2\text{H}_5^\cdot$), by analogy with the loss of H atoms from the reaction of hydrated electrons with phosphate (H_2PO_4^- , $k = 1.5 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$),²⁷ which is suggestive of a slightly different reaction mechanism, despite the excellent linear correlation of the plot (see Figure 1).

Interestingly, analysis of the Brønsted plot for the reaction of simulants with the hydroxyl radical (Figure 1b) shows a distinct break in the leaving group dependence, clearly indicating a change in mechanism between the simulants with good and poor leaving groups. This is not a surprise, because the net atomic charge on phosphorus will be greater in those compounds with deactivating groups and favor initial attack of the hydroxyl radical on the P atom. Alternatively, simulants **1**, **5**, and DEMP are likely to undergo hydrogen atom abstraction from the methylene carbon to produce a carbon-centered radical,¹⁴ instead of a substitution reaction.

TABLE 2: Estimated Rate Constants for the Reaction of CW Agent in Water

nerve agent ^a	leaving group	$\sim pK_a^b$	$k(\text{e}^-)$ ($\text{M}^{-1} \text{ s}^{-1}$)	$k(\text{HO}^\cdot)$ ($\text{M}^{-1} \text{ s}^{-1}$)
Tabun, GA	CN	9.2	3.7×10^9	8.7×10^7
Sarin, GB	F	3.2	7.5×10^9	4.9×10^8
Soman, GD	F	3.2	7.5×10^9	4.9×10^8
VX	$\text{S}(\text{CH}_2)_2\text{N}(\text{iPr})_2$	10.6 ^c	3.5×10^9	8.1×10^7

^a Complete structures are shown in Chart 1. ^b Values taken from March, J.; Smith, M. B. *Advanced Organic Chemistry*; Wiley: New York, 2001; pp 329–331. pK_a values represent the ionization of H-X in water. ^c Value for $\text{CH}_3\text{CH}_2\text{SH}$ taken from Silva, C. O.; da Silva, E. C.; Nascimento, M. A. C. *J. Phys. Chem. A* **2000**, *104*, 2402.

Based on the data in the Brønsted plots, we can readily extrapolate hydrated electron and hydroxyl radical rate constants for actual CW agents in water, based on the pK_a values for the leaving groups in the actual CW agents (Table 2).

The predicted rate constants for the CW agents also demonstrate that reductive destruction would be more efficient than oxidation. This finding suggests that treatments that can generate both oxidizing and reducing species in water (for example, advanced oxidation processes (AOPs) such as heterogeneous catalysis by TiO_2 , sonolysis, and electron beam irradiation²⁸) would be efficient approaches to the destruction of these types of agents. The latter process would be particularly efficient, because its high rate of delivered dose quickly removes all interfering dissolved oxygen.

In summary, the reaction of chemical warfare (CW) simulants containing leaving groups that mimic those in actual agents are better representatives for the development of methods for the detection, decontamination, and destruction of CW agents. The kinetic evidence suggests that reductive destruction of CW agents in water will be efficient, and that alkyl phosphonates such as diethyl methylphosphonate (DEMP), although easy to handle, may undergo different oxidation and reduction chemistry. Therefore, caution should be exercised when suggesting that these latter, nontoxic compounds are automatically reasonable models for CW agents.

Acknowledgment. We would like to thank the Radiation Laboratory at the University of Notre Dame for the use of their accelerator facilities.

References and Notes

- Zhang, S.-W.; Swager, T. M. *J. Am. Chem. Soc.* **2003**, *125*, 3420.
- Yang, Y.; Ji, H.-F.; Thundat, T. *J. Am. Chem. Soc.* **2003**, *125*, 1124.
- Han, M. S.; Kim, D. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3809.
- Sohn, H.; Létant, S.; Sailor, M. J.; Trogler, W. C. *J. Am. Chem. Soc.* **2000**, *122*, 5399.
- Wagner, G. W.; Yang, Y.-C. *Ind. Eng. Chem. Res.* **2002**, *41*, 1925.
- Yang, Y.-C. *Acc. Chem. Res.* **1999**, *109*, 9.
- Yang, Y.-C.; Baker, J. A.; Ward, J. R. *Chem. Rev.* **1992**, *92*, 1729.
- Hill, C. M.; Li, W.-S.; Thoden, J. B.; Holden, H. M.; Raushel, F. M. *J. Am. Chem. Soc.* **2003**, *125*, 8990.
- Tsang, J. S.; Neverov, A. A.; Brown, R. S. *J. Am. Chem. Soc.* **2003**, *125*, 7602.
- Terrier, F.; Le Guével, E.; Chatrousse, A. P.; Moutiers, G.; Buncel, E. *J. Chem. Soc., Chem. Commun.* **2003**, 600.
- Keizer, T. S.; De Pue, L. J.; Parkin, S.; Atwood, D. A. *J. Am. Chem. Soc.* **2002**, *124*, 1864.
- Lion, C.; Da Conceição, L.; Hecquet, G.; Pralus, C.; Requieme, B.; Schirmann, J.-P. *New J. Chem.* **2002**, *26*, 1515.
- Wagner, G. W.; Procell, L. R.; O'Conner, R. J.; Munavalli, S.; Carnes, C. L.; Kapoor, P. N.; Klabunde, K. J. *J. Am. Chem. Soc.* **2001**, *123*, 1636.
- Aguila, A.; O'Shea, K. E.; Tobien, T.; Asmus, K.-D. *J. Phys. Chem.* **2001**, *105*, 7834.
- Conference on Disarmament. The Convention of the Development, Production, Stockpiling and Use of Chemical Weapons and on Their Destruction, CD/1170, Geneva, Switzerland, August 1992 (see http://www.dfait-maeci.gc.ca/ndi-agency/cwc_1-en.asp).

- (16) Benschop, H. P.; Van den Berg, G. R.; Van Hooidonk, V.; De Jong, L. P. A.; Kientz, C. E. *J. Med. Chem.* **1979**, 22, 1306.
- (17) Technical Information Bulletin AL-122, Sigma-Aldrich, St. Louis, MO.
- (18) Munro, N. B.; Talmage, S. S.; Griffin, G. D.; Waters, L. C.; Watson, A. P.; King, J. F.; Hauschild, V. *Environ. Health Perspect.* **1999**, 107, 933.
- (19) Sierakowski, T.; Kiddle, J. J. Unpublished results.
- (20) Tworowska, I.; Dabkowski, W.; Michalski, J. *Angew. Chem., Int. Ed.* **2001**, 40, 2898.
- (21) Black, R. M.; Harrison, J. M. In *The Chemistry of Organophosphorus Compounds, Volume 4*; Hartley, F. R., Ed.; Wiley: New York, 1996; pp 781–840.
- (22) ^{31}P NMR experiments indicated that compounds **2–4** were stable for over one week in a 1:1 solution of $\text{H}_2\text{O}/\text{D}_2\text{O}$, showing no products of hydrolysis.
- (23) Hug, G. L. In *Optical Spectra of Nonmetallic Inorganic Transient Species in Aqueous Solution*; NSRDS-NBS 69; U.S. Department of Commerce, National Bureau of Standards: Washington, DC, 1981.
- (24) Buxton, G. V.; Greenstock, C. L.; Helman, W. P.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1988**, 17, 513.
- (25) Bell, R. P. In *Correlation Analysis in Chemistry*; Chapman, N. B.; Shorter, J., Eds; Plenum Press: New York, 1978; pp 55–84.
- (26) Bentrude, W. G. In *Free Radicals, Volume II*; Kochi, J. K., Ed.; Wiley: New York, 1973; p 616.
- (27) Christensen, H.; Sehested, K.; Logager, T. *Radiat. Phys. Chem.* **1994**, 43, 527.
- (28) Melin, G.; Hogan, T., Eds. In *Treatment Technologies for the Removal of Methyl Tertiary Butyl Ether (MTBE) from Drinking Water*, 2nd ed.; Publication NWRI-99-06; National Water Research Institute: Fountain Valley, CA, 2000.