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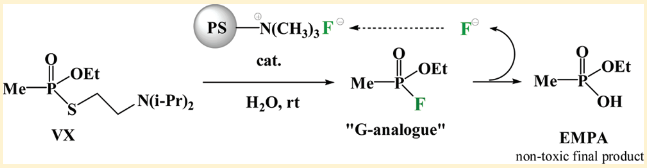
Catalytic Degradation of the Nerve Agent VX by Water-Swelled Polystyrene-Supported Ammonium Fluorides

Daniele Marciano, Michael Goldvaser, Ishay Columbus,* and Yossi Zafrani*

The Department of Organic Chemistry, Israel Institute for Biological Research, Ness-Ziona, 74100, Israel

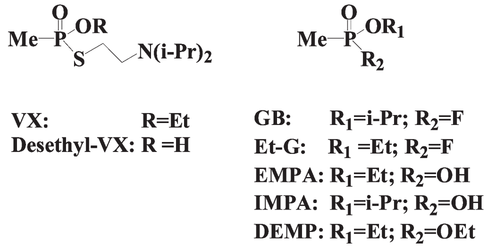
Supporting Information

ABSTRACT: The catalytic degradation of the nerve agent VX (*O*-ethyl *S*-2-(diisopropylamino)ethyl methylphosphonothioate) by water-swelled polymer-supported ammonium fluorides is described. VX (0.06−0.53 mol/mol F^-) is rapidly degraded ($t_{1/2} \sim$ 10−30 min) to form the "G-analogue" (*O*-ethyl methylphosphonofluoridate), which hydrolyzes ($t_{1/2} \sim$ 1−1.5 h) to the nontoxic EMPA (ethyl methylphosphonic acid). The toxic desethyl-VX is not formed. The catalytic effect of fluoride is maintained even when 6 equiv of VX are loaded. GB (*O*-isopropyl methylphosphonofluoridate) and desethyl-VX agents are also degraded under these conditions.



Decontamination of chemical warfare agents (CWAs) such as VX (*O*-ethyl *S*-2-(diisopropylamino)ethyl methylphosphonothioate), GB (*O*-isopropyl methylphosphonofluoridate or sarin), or HD (sulfur mustard) is important for defense and environmental reasons. One approach to destroy these extremely toxic agents is to use reactive sorbents that can absorb and chemically convert them into nontoxic products. In the past decade, various powders, for instance, nanosize particles of MgO,[1] CaO,[2] NaY and AgY zeolite,[3] Al_2O_3,[4] and TiO_2,[5−7] as well as various types of KF/Al_2O_3,[8,9] have been shown to be destructive sorbents for the degradation of these CWAs. This approach is linked to a scenario in which destructive sorption of CWA from sewage, skin, or other contaminated surfaces is needed. Polymers functionalized with α-nucleophiles like oximates[10,11] and primary amines or imines,[12−14] amidoximes,[15] and sulfonamides[16] have also been used.

Based on our studies on the reactivity of alumina-supported fluoride ions against CWAs,[8,9] we hypothesized that organic polymers functionalized with ammonium fluoride groups may also be reactive in the presence of water toward these toxic agents. A good candidate for this purpose is the commercial resin Amberlite IRA 900 F^-, a styrene−divinylbenzene copolymer substituted with benzyltrimethyl ammonium fluoride. Its uses in fluorination, desilylation, and carbon−carbon coupling reactions have been reviewed.[17] To the best of our knowledge, the only reported data in the field of phosphorus chemistry is the preparation of pentavalent phosphorus fluorides from their chloride analogues.[18] The only published work in relation to CWAs describes the decomposition of HD to divinyl sulfide in the gas phase (60 °C).[19] Herein, the catalytic degradation of VX on the resin Amberlite IRA 900 F^- will be described. The role of the solid-supported fluoride ion in the catalytic decomposition of VX as well as in the fate of GB and desethyl-VX will be also discussed.



In the present study, special attention was given to the choice of an appropriate solvent for the resin swelling, which would be suitable for a rapid degradation of the CWA. Among the solvents screened for their swelling capabilities, only acetonitrile, ethanol, and water gave satisfying results with a volume increase of ca. 2-fold. VX (0.06−0.09 equiv)[20] was loaded onto the resin after swelling with these solvents. The results are presented in Table 1. In ethanol and acetonitrile, a single ^{31}P signal of VX at δ 50−55 ppm (spectra S17−S18, Supporting Information) was observed, while in water a second signal at δ 60 ppm appeared (Figure 1). This signal has been attributed to protonation or solvation of VX by water.[1,15,21] The general trend was that swelling with water favors VX degradation ($t_{1/2}$ 0.26 h)[22] as compared to acetonitrile and ethanol. After 4 h, only nontoxic EMPA was present (run 5). This was confirmed by experiments with water−acetonitrile mixtures (runs 3 and 4). In ethanol (run 1), traces of diethyl methylphosphonate (DEMP) were also detected. Interestingly, in all experiments, the "G-analogue" of VX (*O*-ethyl methylphosphonofluoridate or Et-G) is formed as an intermediate, which eventually hydrolyses to EMPA (Figures 1 and 2). Et-G gives typical doublets at δ −61.6 ppm and δ 29.0 ppm (J_{PF} = 1045 Hz) in ^{19}F-MAS NMR and ^{31}P-MAS NMR, respectively.[23] Moreover, a reaction identical to run 3 was quenched after 2.5 h, and Et-G was isolated and identified by NMR (spectra S20 and S21, Supporting Information). The basic hydrolysis of Et-G is faster than that of VX itself, and therefore, its formation in our process accelerates the overall degradation of VX. One should note that because the relatively high boiling point of G-agents (160−200 °C),[24] there is no actual risk of "G-analogue" evaporation to

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the environment when it is formed as unstable intermediate in the aqueous medium.

It is noteworthy that although the reaction is performed in the presence of water at pH ~9, the toxic side product desethyl-VX is not formed. For comparison, in the degradation of VX in unbuffered water ($t_{1/2}$ ~ 57.3 h), a significant amount of desethyl-VX is formed (50%).[25] At pH above 10, the hydrolysis is faster ($t_{1/2}$ ~ 31 min) and at least 13% desethyl-VX is formed.[24] Hence, the present approach is advantageous from both kinetic and toxicological points of view.

Another aspect of this process is the fate of the fluoride ion after the hydrolysis of the phosphonofluoridate intermediate Et-G to EMPA. In an experiment where sequential amounts of VX were added to the same rotor loaded with water-swelled resin, we observed that even when the overall quantity of VX exceeds the theoretical amount of fluoride ions, the formation of Et-G still takes place, followed by the expected hydrolysis to EMPA (Table 2, run 7; graph S15 and spectrum S24, Supporting Information). This data supports a catalytic mechanism in which the fluoride ion returns to the ammonium moiety attached to the resin and can eventually participate in the nucleophilic attack of another VX molecule. The degradation rate of VX is barely affected by the accumulation of EMPA on the resin during the process ($t_{1/2}$ 0.10–0.22 h, Table S2, Supporting Information), and the total time for EMPA formation remains constant (t_{total} ~ 6 h). Further, a large excess of VX (10 mg, 6 equiv) was loaded on a very small amount of resin (2 mg), and the degradation of VX was completed in 6.2 days (Table 2, run 8).[26] Nine days later, the nontoxic EMPA was the sole organophosphorus (OP) compound which could be detected (Spectrum S28, Supporting Information). This experiment is strong evidence for the catalytic nature of the degradation of VX on Amberlite IRA 900 F^-. It also suggests the potential for destruction of big quantities of VX on a minimal volume of resin.

In order to estimate the role of water in this system, another experiment with sequential additions of VX (0.06–0.58 equiv) was conducted without swelling of the resin.[27] The degradation rate of VX ($t_{1/2}$ 0.13–0.62 h, t_{total} 0.68–4.8 h) decreased progressively (graph S13 and spectrum S25, Supporting Information). This may be explained by EMPA accumulation on

Table 1. Degradation Rate of VX on Amberlite IRA 900 F^- Swelled with Different Solvents

run	solvents (molar ratio)[a]	VX[b] (equiv)	$t_{1/2}$[c] (h)	t_{total}[d]
1	ethanol	0.07	2.2	1 d
2	acetonitrile	0.07	0.93	1 d
3	acetonitrile/water (5:2)	0.07	0.75	<2 d
4	acetonitrile/water (1:10)	0.09	0.38	1 d
5	water	0.06	0.26	4 h

[a] Molar ratio of the solvent mixture. [b] VX equivalents per fluoride ion. [c] Half-life time of VX for a pseudo-first-order reaction. [d] Time for total degradation of any toxic agent.

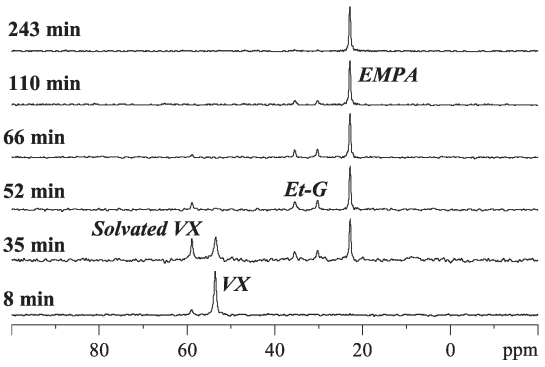


Figure 1. ^{31}P-MAS NMR spectra depicting the degradation profile of VX (0.06 equiv) on Amberlite IRA 900 F^- swelled with water (run 5).

Table 2. Degradation Rate of VX on a Few Amberlite IRA 900 Resins Bearing Different Counterions

run	resin[a]	VX[b] (equiv)	$t_{1/2}$[c] (h)	t_{VX}[d]	t_{total}[e] (h)	products (%) EMPA	products (%) desethyl-VX
6	F^-	0.25	0.17		6.25	100	0
7	F^-	1.25		5 h	6	100	0
8	F^-	6		6.2 d	180	100	0
9	F^-; dry	0.06	0.13		0.68	100	0
10	F^-; dry	4.2		17 d	>18 d	94[f]	0
11	OH^-	0.18	2.7	15 d		92	8
12	OH^-	0.92		>60 d[g]		44[h]	22
13	Cl^-	0.2	92	24 d		86	14

[a] Amberlite IRA 900 bearing the counterion specified below. The resin is swelled with water unless otherwise specified. [b] VX equivalents per fluoride ion. [c] Half-life time of VX for a pseudofirst order reaction. [d] Time for total degradation of VX given only when the reaction is not of first-order. [e] Time for total degradation of any toxic agent. When desethyl-VX or Et-G are left, t_{total} is not specified. [f] Some Et-G (6%) is left. [g] After 2 months VX (34%) is still present. [h] 44% stands for total EMPA (29%) plus MPA (15%) after 2 months.

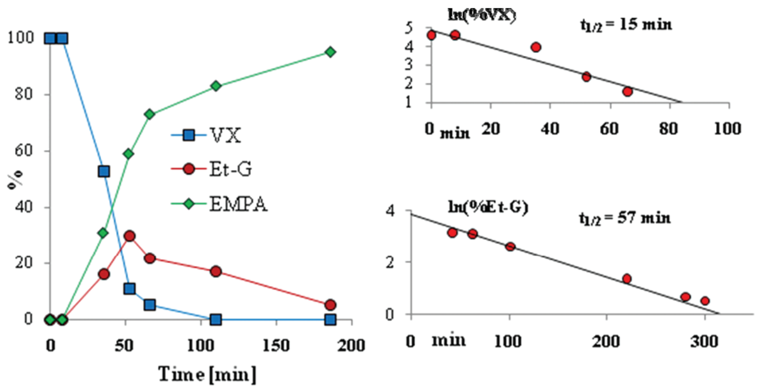
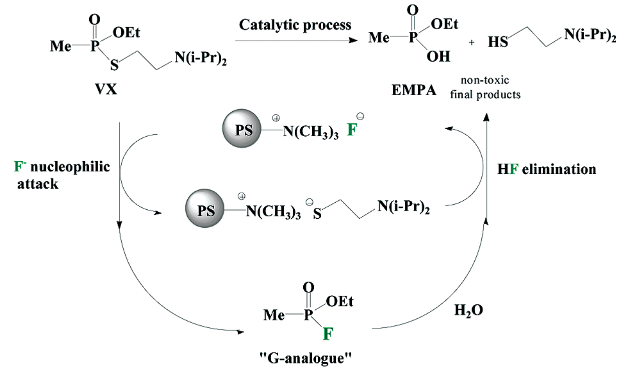


Figure 2. Degradation profiles of VX (0.06 equiv) and of Et-G obtained from VX on the resin swelled with water (run 5).

Scheme 1. Degradation of VX on Amberlite IRA 900 F^-



the surface of the resin (0−0.4 equiv), creating a less "fluid" environment. When an excess of VX (4.2 equiv) was charged on the "dry" resin, the degradation was completed only after 2 weeks, and some Et-G was left, possibly because there was not enough accessible water for the hydrolysis process (Table 2, run 10; spectrum S29, Supporting Information). Despite the fast degradation rates obtained on the "dry" resin with small quantities of VX, it is clear that the water-swelled resin is a better support for the degradation of large amounts of VX.

Control experiments were conducted on the hydroxide and chloride analogues of Amberlite IRA 900 F^-. It takes more than 1 week for VX (0.18 equiv) to totally degrade on Amberlite IRA 900 OH^- (Table 2, run 11). Moreover, some toxic desethyl-VX (8%) is formed together with EMPA. When the amount of loaded VX is close to 1 equiv (0.92 equiv, run 12), 34% is still present two months later along with desethyl-VX (22%). On Amberlite IRA 900 Cl^-, VX undergoes a very slow degradation to desethyl-VX (14%) and EMPA ($t_{1/2}$ 92 h for 0.2 equiv of VX, run 13). The conclusion is that some basic hydrolysis of VX takes place on those resins, with a rate and outcome similar to what is known for the decomposition of VX in basic aqueous medium. The importance of the fluoride ion present in the resin as a nucleophile is now evident. In the absence of fluoride the catalytic process does not occur, and toxic desethyl-VX is formed.

The mechanism proposed for the catalytic degradation of VX on the fluoride resin is detailed in Scheme 1. In the first step, a nucleophilic attack of the fluoride ion on the phosphorus displaces the aminothiolate group from VX and the "G-analogue" is formed. The latter is attacked by water, and the intermediate (not shown in Scheme 1) formed undergoes HF elimination to yield the nontoxic EMPA and aminoethanethiol. Following protonation, fluoride ion is released, returns to the resin-bound ammonium, and is now ready for a new catalytic cycle. The pH of the medium is roughly maintained throughout this process.

Catalytic methods for the destruction of CWAs in solution have been recently reviewed.[28] The iodosocarboxylates or iron-centered tetraamido macrocyclic ligands (Fe-TAML) promoted hydrolysis of OP pesticides by activating hydrogen peroxide.[29,30] However, those ligands catalyze their own decomposition in the presence of hydrogen peroxide. Methanolysis in the presence of Zn^{2+} and La^{3+} catalysts also promotes OP compound destruction, but this technique is limited by the use of methanol as solvent and reactant and also by the sensitivity of these catalysts to moisture.[31] Our method, using commercial Amberlite IRA 900 F^-, seems to be more practical, since this catalyst is stable and can be used in an aqueous environment.

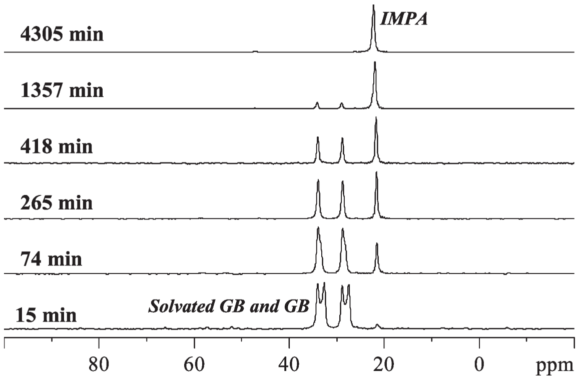


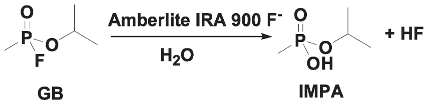
Figure 3. ^{31}P-MAS NMR spectra and degradation profile of GB (0.4 equiv) on the resin swelled with water (run 15) (the second doublet for GB may be attributed to some "solvated" GB).

Table 3. Degradation Rate of GB, Et-G, and Desethyl-VX on Swelled Amberlite IRA 900 F^-

run	compd[a] (equiv)	$t_{1/2}$[b] (h)	t_{total}[c] (d)
14	GB (0.2)	9.6	3
15	GB (0.4)	10.5	3
16	Et-G (0.2)	3.0	2
17	desethyl-VX (0.37)	168	>60

[a] Compound equivalents per fluoride ion. [b] Half-life time of the OP compound for a pseudo-first-order reaction. [c] Time for total degradation of any toxic agent.

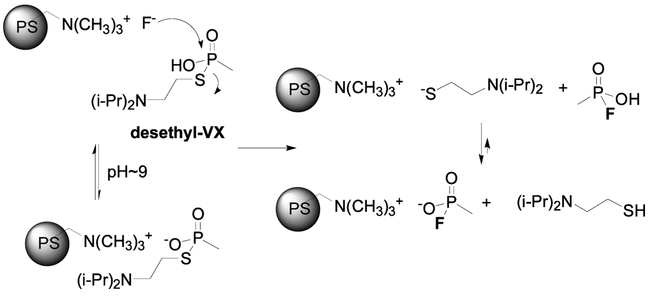
We further investigated the fate of other toxic OP compounds such as GB and desethyl-VX on Amberlite IRA 900 F^-. GB decomposes to isopropyl methylphosphonic acid (IMPA, eq 1) with half-life times of ca. 10 h (Figure 3; Table 3, runs 14 and 15). From the experiments performed with VX, we observed that the half-life time for hydrolysis of Et-G on the resin ($t_{1/2}$ 57 min for VX ≤ 0.5 equiv; Figure 2) was shorter than that found for an authentic sample of Et-G loaded on the resin (Table 3, run 16). A plausible explanation is that during the hydrolysis of GB or Et-G hydrogen fluoride is liberated, and the decrease in pH during the process contributes to a decrease in rate. In the system VX/Et-G/resin, HF is neutralized by the tertiary aminothiolate leaving group as shown in Scheme 1, so that the basic pH ~9 is maintained during the process. In addition, the disparity between GB and Et-G may be explained by the fact that, due to the isopropyl group, GB is more lipophilic and more sterically hindered.



(1)

The degradation of desethyl-VX in the presence of water is an important issue in view of its "inevitable" formation during the decontamination of VX in aqueous media. For this reason, the fate of desethyl-VX on the resin was also studied. Desethyl-VX was loaded onto the resin and slowly ($t_{1/2}$ 168 h) converted to a mixture of fluoromethylphosphonic acid and thiolate. These products are in equilibrium with aminoethanethiol and the fluoromethylphosphonate anion coupled to the ammonium moiety of the resin (Scheme 2). This anion was identified by solid-state and solution ^{19}F and ^{31}P NMR (spectra S34−S35, Supporting Information) due to its characteristic coupling

Scheme 2. Degradation of Desethyl-VX on the Resin (Run 17)



constant (J_{PF} = 956 Hz), different than that found for fluoromethylphosphonic acid or Et-G (J_{PF} = 1045 Hz). The extremely slow rate of degradation of desethyl-VX as compared with VX may be explained by its partial ionization in the basic medium of the resin, which prevents the attack of any nucleophile anion like fluoride or hydroxide.

In conclusion, toxic OP compounds (VX, GB, Et-G, and desethyl-VX) can be degraded on Amberlite IRA 900 F^- resin. The advantage of this resin, in which the ammonium fluoride is covalently bound to the solid support, over the alumina-supported fluoride reagents[8,9] is mainly expressed by its ability to degrade VX in a catalytic mechanism. Moreover, during this catalytic process, the toxic desethyl-VX is not formed in spite of the use of neutral aqueous medium. These results designate this resin as a powerful candidate for the building of active barriers in protective clothes, filters, or column fillers mainly against "V" agents.

EXPERIMENTAL SECTION

Materials. The resin Amberlite IRA 900 F^- ($C_6H_4CH_2N(CH_3)_3F$, also named Fluoride on Amberlyst A-26, cat. no. 338879) and its hydroxide (cat. no. 542571) and chloride (cat. no. 47060) analogues were purchased from a commercial supplier.

NMR. ^{31}P and ^{19}F MAS NMR spectra were obtained at 202 and 471 MHz, respectively, on a 11.7 T (500 MHz) spectrometer, equipped with a 0.4 cm standard CP-MAS probe, using direct polarization (i.e., no cross-polarization (CP) was used). Typical spinning rates were 5−7 kHz. Chemical shifts for ^{31}P and ^{19}F were referenced to external trimethyl phosphate (TMP) and $CFCl_3$, respectively, as 0 ppm. For ^{31}P spectra, the pulse delay was 2 s, which is considered sufficient for relaxation in OP esters on solid matrices. The number of transients per spectrum was 200. For ^{19}F spectra the pulse delay was 2 s, and the number of transients per spectrum varied between 100 and 2000. For comparison purposes, spectra were recorded under identical conditions.

Sample Preparation. *Caution: These experiments should only be performed by trained personnel using applicable safety procedures.* Samples of the appropriate resin (2−32 mg) dry or swelled with the appropriate amount of solvent (deuterated water, water, acetonitrile, or ethanol) were added to the 0.4 cm ZrO_2 rotor, and 0.2−10 μL of the OP compound (VX, GB, Et-G, or desethyl-VX) was applied via syringe to the center of the sample. The rotor was sealed with a fitted Kel-F cap. ^{31}P and ^{19}F MAS NMR spectra were measured periodically to determine remaining starting material and identify degradation products.

The number of equivalents of each reactant was calculated assuming a loading of 0.003 mmol/g fluoride on the resin. The half-life time of any OP compound was calculated only for big excess of fluoride and was derived from the slope of the plot of ln[% OP] as a function of time. The % OP is the molar percentage of the OP in the mixture.

ASSOCIATED CONTENT

Supporting Information. NMR spectra, kinetic data, and plots. This material is available free of charge via the Internet at http://pubs.acs.org/.

AUTHOR INFORMATION

Corresponding Author

*Tel: +972-8-9381453. Fax: +972-8-9381548. E-mail: yossiz@iibr.gov.il; ishayc@iibr.gov.il.

REFERENCES

(1) Wagner, G. W.; Bartram, P. W.; Koper, O.; Klabunde, K. J. *J. Phys. Chem. B* **1999**, *103*, 3225.

(2) Wagner, G. W.; Koper, O.; Lucas, E.; Decker, S.; Klabunde, K. J. *J. Phys. Chem. B* **2000**, *104*, 5118.

(3) Wagner, G. W.; Bartram, P. W. *Langmuir* **1999**, *15*, 8113.

(4) (a) Wagner, G. W.; Procell, L. R.; O'Connor, R. J.; Munavalli, S.; Carnes, C. L.; Kapoor, P. N.; Klabunde, K. J. *J. Am. Chem. Soc.* **2001**, *123*, 1636. (b) Wagner, G. W.; Procell, L. R.; Munavalli, S. *J. Phys. Chem. C* **2007**, *111*, 17564. (c) Saxena, A.; Sharma, A.; Srivastava, A. K.; Singh, B.; Gutch, P. K.; Semwal, R. P. *J. Chem. Technol. Biotechnol.* **2009**, *84*, 1860.

(5) Wagner, G. W.; Chen, Q.; Wu, Y. *J. Phys. Chem. C* **2008**, *112*, 11901.

(6) Prasad, G. K.; Singh, B.; Ganesan, K.; Batra, A.; Kumeria, T.; Gutch, P. K.; Vigayaraghavan, R. *J. Hazard. Mater.* **2009**, *167*, 1192.

(7) Hirakawa, T.; Sato, K.; Komano, A.; Kishi, S.; Nishimoto, C. K.; Mera, N.; Kugishima, M.; Sano, T.; Ichinose, H.; Negishi, N.; Seto, Y.; Takeuchi, K. *J. Phys. Chem. C* **2010**, *114*, 2305.

(8) Gershonov, E.; Columbus, I.; Zafrani, Y. *J. Org. Chem.* **2009**, *74*, 8464.

(9) Zafrani, Y.; Goldvaser, M.; Dagan, S.; Feldberg, L.; Mizrahi, D.; Waysbort, D.; Gershonov, E.; Columbus, I. *J. Org. Chem.* **2009**, *74*, 329.

(10) Bromberg, L.; Hatton, T. A. *Ind. Eng. Chem. Res.* **2005**, *44*, 7991.

(11) Bromberg, L.; Hatton, T. A. *Ind. Eng. Chem. Res.* **2007**, *46*, 3296.

(12) Bromberg, L.; Hatton, T. A. *Polymer* **2007**, *48*, 7490.

(13) Bao, Y. T.; Pitt, C. G. *J. Polym. Sci. A: Polym. Chem.* **1990**, *28*, 741.

(14) Hammond, P. S.; Forster, J. S. *J. Appl. Polym. Sci.* **1991**, *43*, 1925.

(15) Bromberg, L.; Schreuder-Gibson, H.; Creasy, W. R.; McGarvey, D. J.; Fry, R. A.; Hatton, T. A. *Ind. Eng. Chem. Res.* **2009**, *49*, 1650.

(16) Gutch, P. K.; Singh, R.; Acharya, J. *J. Appl. Polym. Sci.* **2011**, *121*, 2250.

(17) Fringuelli, F.; Lanari, D.; Pizzo, F.; Vaccaro, L. *Curr. Org. Synth.* **2009**, *6*, 203.

(18) Sierakowski, T.; Kiddle, J. J. *Tetrahedron Lett.* **2005**, *46*, 2215.

(19) Bellamy, J. *React. Polym.* **1994**, *23*, 101.

(20) The number of VX equivalents are calculated versus the number of fluoride ions in the resin, assuming 3 mmol/g fluoride.

(21) Columbus, I.; Waysbort, D.; Shmueli, L.; Nir, I.; Kaplan, D. *Environ. Sci. Technol.* **2006**, *40*, 3952.

(22) When the amount of fluoride ions is in large excess compared with the CWA, a pseudo-first-order kinetic was assumed for the calculation of the half-life time of the CWA.

(23) The identity of the degradation products (Et-G, EMPA, DEMP, IMPA) was confirmed independently by comparison with NMR of authentic samples.

(24) 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.

(25) Szafraniec, L. J; Szafraniec, L. L.; Beaudry, W. T.; Ward, J. R. ADA-250773, U.S. Army Chemical Research, Development and Engineering Center, Aberdeen Proving Ground, MD, 1990.

(26) The quantities chosen for this experiment were dictated by the volume of the rotor and safety considerations.

(27) The commercial "dry" resin contains 15−20 wt % of water.

(28) Smith, B. M. *Chem. Soc. Rev.* **2008**, *37*, 470.

(29) (a) Moss, R. A; Morales-Rojas, H.; Zhang, H.; Park, B.-D. *Langmuir* **1999**, *15*, 2738. (b) Morales-Rojas, H.; Moss, R. A. *Chem. Rev.* **2002**, *102*, 2497.

(30) Chanda, A.; Khetan, S. K.; Banerjee, D; Ghosh, A.; Collins, T. J. *J. Am. Chem. Soc.* **2006**, *128*, 12058.

(31) Tsang, J. S.; Neverov, A. A.; Brown, R. S. *J. Am. Chem. Soc.* **2003**, *125*, 7602.