Pesticide and Pharmaceutical Photolysis ~ Fate of the Halogens

by

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A thesis submitted in conformity with the requirements
for the degree of Master of Science in Analytical Chemistry

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Abstract

The photolysis of a variety of fluorinated and chlorinated compounds was investigated under actinic radiation. Chloroacetanilide herbicides were irradiated with the intent of identifying the extent of monochloroacetic acid (MCA) production. Conversion of metolachlor to MCA as a result of photolysis increased from 5% during direct photolysis to near 30% conversion during indirect photolysis in a synthetic field water matrix. The photodegradation of alachlor, butachlor and a model chloroacetanilide, 2-chloro-N-methylacetanilide in SFW was also investigated. An investigation involving fluoroanilines (FAs) was conducted with the intent of identifying monofluoroacetic acid (MFA) as a photoproduct. Direct and indirect photolysis revealed the photoproduction of fluoride from 2-FA, 3-FA, 2,4-FA and 2,6-FA, aminophenol from 3-FA and fluoronitrobenzene isomers for each of 2-FA, 4-FA, 2,4-FA and 2,6-FA. Conversion to photoproducts varied with direct vs. indirect photolysis. MFA was not identified as a photoproduct of the fluoroanilines. The photodegradation of flumetsulam, flamprop-methyl and ciprofloxacin were also investigated.
Acknowledgments

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Chapter 1.
Introduction
1.1 Introduction

Although the majority of halogenated organic compounds are either brominated or chlorinated, more often fluorinated organics are being developed and put into use in agriculture, industry and in medicine. For instance, in agriculture approximately 10% of pesticides listed in the Agricultural handbook (2nd ed., Royal Society of Chemistry, 1987) contain fluorine. In medicine, the utility of fluorine as an important structural component for drugs can be illustrated by a few examples that have been the subject of recent public attention. Fluoxetine, better known as Prozac® for example, has revolutionized the face of treatment available for clinical depression. Fluoxetine has chemical characteristics that make it a preferred drug to previous non-fluorinated antidepressants. Another example of the introduction of fluorine to a molecule resulting in an improvement on existing treatments is that of a monofluorinated N-3-substituted imidazoquinazolinone. This compound is thought to be a possible improved alternative to Viagra® (sildenafil) for the treatment of erectile dysfunction, specifically with respect to improved phosphodiesterase selectivity and potency (1). Industry has also been subject to an influx of developments of new and improved products that incorporate fluorine. In fact, predictions included an increase in sales of fluoropolymers from $1.35 billion in 1994 to $1.76 billion by 1999 (2).

The majority of research conducted on the fate of halogenated compounds has focused on brominated and chlorinated organics. The fate of fluorinated compounds has received less attention since as mentioned, they have been utilized to a lesser extent but also because they have been perceived as inert in nature and therefore less harmful biologically and environmentally (3). In the last decade however, the fate of fluorinated organics has become of interest. The presence of fluorinated organics in the blood of the public and of those who work with fluoroorganics (4,
5) together with the identification of trifluoroacetic acid as a breakdown product of HCFC's (6) sparked much of the current research regarding the fate of fluorinated organics.

One class of halogenated organics that pose environmental concern is the carboxylic acids. Haloacetic acids encompass a number of compounds that have been used as industrial or agricultural agents or have been shown as or are suspected to be the breakdown products of larger halogenated precursors. Monochloroacetic acid (MCA) for example, has found its way into the environment through use as a herbicide, as an intermediate in the manufacture of some chemicals such as malonic acid (7) and as a by-product from both the chlorination of drinking water and the contamination of water with chlorinated solvents (8). Two more examples include monofluoroacetic acid (MFA) as a pesticide for the control of vertebrate pests (9), and the identification of trifluoroacetic acid (TFA) as an atmospheric photodegradation product of hydrochlorofluorocarbon (HCFCs) 123, HCFC 124 and hydrofluorocarbon (HFC) 134a (10, 11, 12). Sources are so extensive that almost all of the haloacetic acids, chloro- bromo- and fluoro- have been identified in the aqueous compartment of the environment (13,14).

Photolysis provides an important fate pathway for many environmental pollutants present in aqueous compartments. Often, species that are quite stable or unreactive in an aqueous environment are subject to facile degradation when exposed to sunlight. Photolysis is a term that encompasses a variety of processes responsible for the ultimate loss of a compound. When the excited state of the compound undergoes a reaction resulting in loss of that species, it is referred to as direct photolysis. Indirect photolysis on the other hand involves the interaction of an excited state species with the compound of interest resulting in the loss of the parent compound and the formation of photoproducts. What makes a particular pollutant or natural water constituent susceptible to photolysis is largely based upon physical characteristics. That is,
properties such as water solubility and Henry's Law Constant must be such that once given the opportunity to enter the environment a compound will tend to go to and stay in the aqueous compartment.

The goals of the research herein are to identify monohalogenated photoproducts from various compounds that are used in agriculture, industry or in a pharmaceutical setting with an emphasis on those used in agriculture. In particular this research was initiated with the intent of identifying possible sources of monochloroacetic acid (MCA) and monofluoroacetic acid (MFA). It was also our intention to elucidate the photolytic behaviour of the parent compounds from which the acids are generated, including kinetic and mechanistic information. Such information can then provide a template of information for compounds retaining similar structural features.

The second chapter focuses on the research completed for the identification of chloroacetanilide herbicides as sources of MCA upon irradiation. The topic is introduced by addressing the utility of using such herbicides while at the same time pointing out the detriment of the potential production of MCA. Next, method development for the detection of the acid as well as the conditions of irradiation of the parent compounds, including three herbicides and a model chloroacetanilide are described. The chapter is completed through the discussion of the extent and proposed mechanism for the production of the acid.

Chapter three describes research conducted in the search for a photolytic source of monofluoroacetic acid and to elucidate the photolytic fate of aromatic fluorine. This particular premise was developed throughout the chapter by describing the photolytic behaviour of five fluoroanilines and three commercially used compounds including two pesticides and a pharmaceutical. The focus was to elucidate the fate of fluorine from the parent fluoroaniline
compounds and attempt to relate this behaviour to herbicides and pharmaceuticals that retained a similar structural component.

The final chapter ties in the findings of both projects by addressing the significance of the behaviour identified. Also, possibilities for future work relating to the original objectives of each investigation were discussed in order to provide direction for further research into the photolytic fate of halogenated compounds.

1.2 References
Chapter 2.
Photodegradation of Metolachlor: Isolation, Identification and Quantification of Monochloroacetic Acid

American Chemical Society
2.1 INTRODUCTION

Chloroacetanilides have been under development for use in agriculture since 1952 (Chesters et al., 1989). They are used in Canada and in the United States as pre-emergence herbicides to control annual grass weeds and broadleaf weeds in corn, peanuts, soybeans and beans. This class of herbicides includes metolachlor [2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide], alachlor [2-chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide] and butachlor [2-chloro-N-(2,6-diethylphenyl)-N-(butoxymethyl)acetamide] introduced in 1976, 1969 and 1971 respectively (Hamm 1974). The structure, as the name implies, has been developed around the acetonilide moiety; however, the difference is manifested mainly in the methoxyalkyl side chain. This moiety regulates selectivity, water solubility and other such herbicidal properties (Matolesy et al., 1988). Specifically, chloroacetanilides are detoxified by conjugation with glutathione to the chloroacetyl side chain via glutathione S-transferase (GST) (Lange et al., 1998). Selectivity comes about since corn and other such tolerant species are capable of rapid conjugation while target weeds have reduced GST activity.

Alachlor was withdrawn from general use in Ontario in 1985 (Chesters et al., 1989), resulting in an increase in use of metolachlor. By 1988, metolachlor became the most widely used herbicide in Ontario, with usage exceeding $1.33 \times 10^6$ kg by 1993 (Ontario Ministry of Agriculture, 1993). Estimated United States annual use of alachlor according to Chesters et al. (1989) was approximately $37 \times 10^6$ kg while use of metolachlor was estimated at $22 \times 10^6$ kg.

Contamination of surface water due to pesticide use occurs mainly due to runoff, usually within a few weeks of application. Studies across the United States and Canada have confirmed that chloroacetanilide herbicides do infiltrate ground and surface waters (Chesters et al., 1989;
Kent et al., 1990; Capel et al. 1995; Clark et al., 1999; Kolpin and Nations, 1996; Zacharias et al., 1999; Hatfield et al., 1999). A study of 149 drainage basins across Midwestern United States reported that alachlor and metolachlor are among those herbicides most frequently detected, often in the part-per-billion level (Jaynes et al., 1999). Similarly in Ontario, mean annual concentrations of metolachlor reached 4.1 μg/L at the mouths of the Grand, Saugeen, and Thames Rivers from 1981-1985 (Kochany and Maguire, 1994).

Once in an aqueous environment a pesticide is subject to volatilization, hydrolysis or photolysis. The volatility of the chloroacetanilides is expected to be low due to low values of Henry’s Law Constant, $K_H < 10^{-5}$ (Kent et al., 1990). Alachlor and metolachlor each possess a long hydrolysis half-life (Chiron et al., 1995). Photolysis becomes the most important abiotic degradation pathway for metolachlor under normal conditions in an aqueous environment.

Past investigations regarding the photodegradation of chloroacetanilide herbicides have focused on identifying products resulting from hydroxylation, dehalogenation, oxoquinoline formation and demethylation of the parent compound (Mathew and Khan, 1996), showing that such products are identifiable with little sample preparation using LC/MS or GC/MS. Photoproducts that aren’t easily identifiable however, have often been reported as “unidentified polar products” (Chiron et al., 1995, Kochany and Maguire, 1994; Somich et al., 1988). Studies quantifying photoproducts have only been able to account for 62% (Kochany et al., 1994) and 40% (Chiron et al., 1995) of the degraded parent chloroacetanilide, leaving a significant portion of products unidentified and unaccounted for.

Monochloroacetic acid (MCA) is a polar product that has been identified as a product of chloroacetanilide degradation. Pignatello and Sun (1995) reported MCA as a significant photoproduct of metolachlor resulting from the photoassisted Fenton Reaction during the
investigation of a potential pesticide waste management strategy. Mangiapan et al. (1997) identified MCA as a product of the biodegradation of alachlor incubated in river water for 28 days. Both studies, while valuable, do not provide any information regarding the possibility that direct or indirect photodegradation of chloroacetanilide herbicides could be a source of monochloroacetic acid in the environment.

The presence of haloacetic acids in the environment such as MCA is widespread (Scott and Alaee, 1998); therefore, identification of potential sources is of interest. The chlorination of drinking water (Hirvonen et al., 1996, Wu and Chadik 1998, Kristiansen et al., 1996) is one possible source for haloacetic acids in the environment. Concerns regarding levels of MCA in particular exist since MCA has proven to be highly phytotoxic: the 48 hour effective concentration. 10% (EC10) for the green algae Scenedesmus subspicatus is 7μg/L (Kuhn and Pattard, 1990).

The main objective of this investigation was to use a representative chloroacetanilide herbicide, metolachlor, to investigate the potential for the production of MCA as a photoproduct in various matrices. Further, we hoped to quantify MCA and determine possible conditions leading to maximum production of the acid. Once the conditions producing significant acid were realized, the photolysis of alachlor, butachlor, and a model chloroacetanilide were used to investigate structural factors that may play a role in the production of MCA.

2.2 MATERIALS AND METHODS

Chemicals. Metolachlor, alachlor and butachlor were obtained from Chem-Service (West Chester, Pa). Monochloroacetic acid was of ACS grade obtained from Fischer Scientific (Fair Lawn, NJ). High performance liquid chromatography (HPLC) grade acetonitrile was obtained from J.T. Baker (Phillipsburg, NJ). HPLC grade water was obtained from Caledon Laboratories.
Acetonitrile and water were passed through a 0.45 \( \mu \text{m} \) filter before use. Organic-free water used for photochemical experiments was 18M\( \Omega \) deionized water. Sodium nitrate and sodium bicarbonate used to prepare synthetic field water (SFW) were of reagent grade. Dissolved organic carbon (DOC) used was prepared by pre-ageing a humic acid stock solution in a homemade photosimulator for eight days. Methylaniline and chloroacetyl chloride were purchased from Aldrich Chemical Company (Milw. WI).

**Synthesis.** The propyl ester of MCA was synthesized by refluxing 1g of MCA. 10 mL of 1-propanol and 0.5 mL of concentrated sulfuric acid for two hours. The ester was identified using GC/MS (m/z (abundance) [suggested pathway]): 109(4), 107 (12) [M\(^-\) - C\(_2\)H\(_5\)]; 97 (14). 95 (45) [M\(^-\) - C\(_3\)H\(_3\)]; 79 (32), 77 (100) [M\(^-\) - OC\(_3\)H\(_7\)], 57 (17).

The model chloroacetaldehyde, 2-chloro-\( N \)-methylacetaldehyde, was synthesized by the method of Biechler et al. (1957): 5 g of chloroacetyl chloride was dissolved in 25 mL anhydrous diethyl ether. Dropwise, 3.7 g of methylaniline was added to the solution. The ether layer was washed with water and evaporated. White crystals were obtained upon recrystallization from ethanol-water. The model was identified using GC/MS and \(^1\)H NMR (Varian 400MHz spectrometer with CDCl\(_3\) as solvent). GC/MS: 185 (17), 183 (43) [M\(^+\)], 134 (42) [M\(^-\) - CH\(_2\)Cl]; 107 (46), 106 (100) [M\(^-\) - C(O)CH\(_2\)Cl], 92 (13), 90 (43), 79 (16), 77 (68) [M\(^-\) - CH\(_3\)NC(O)CH\(_2\)Cl]. \(^1\)H NMR (\(\delta\), chemical shift in ppm, s = singlet, m = multiplet): \(\delta\): 7.6-7.2 (m, 5H, H Ar), 3.85 (s, 2H, CH\(_2\)), 3.30 (s, 3H, CH\(_3\)).

**Aqueous stability.** The aqueous stability of monochloroacetic acid was characterized before photochemical experiments. MCA (13 mg/L) solutions were adjusted to pH 7 and pH 9 daily using 0.1N HCl or 0.1N NaOH, and stored in the dark for a twelve day period. Each pH treatment was done in duplicate. At various times MCA levels were analyzed using ion
chromatography.

Photodegradation. The photochemical stability of four chloroacetanilides was tested using a Suntest™ CPS Photosimulator equipped with a xenon arc lamp and a water-cooled tray. Irradiance was set to maximum, 765 W/m² ±10% and included wavelengths from 290 to 800 nm to mimic the intensity distribution of natural light. It has been shown that the behaviour of our photosimulator shows similar irradiance to the sunlight in July in Toronto around midday. For each photolysis experiment, three 80-100 mL samples of 7-12μM chloroacetanilide (consistent concentration within each experiment) were placed in quartz test tubes inside the photoreactor and sealed with rubber stoppers and Teflon tape. Tubes were removed throughout the course of the run, so that three time points in addition to the zero time point were analyzed for each set of photolysis conditions. Samples were stored in bottles wrapped in aluminum foil in the fridge (4°C) until analysis. Plots of ln C/Co (C represents the concentration of the parent chloroacetanilide at time t and Co is the initial concentration) vs. time for each experiment provided pseudo-first-order kinetic data including rate constants and half-lives.

Direct photolysis experiments. Metolachlor was degraded in deionized water adjusted to pH 7 and pH 9. The pH was monitored and adjusted regularly using 0.1N HCl and 0.1N NaOH.

Indirect photolysis conditions. Indirect photolysis of metolachlor was examined using two different matrices chosen for the potential to yield high concentrations of carbonate radical upon irradiation. Metolachlor was degraded in the photosimulator in a solution of 3mM H₂O₂ and 0.092M HCO₃⁻ (pH = 8.23) (Larson and Zepp, 1988). Metolachlor, alachlor, butachlor and 2-chloro-N-methylacetanilide were irradiated in a synthetic field water (SFW) matrix in order to mimic possible environmental sample constituents. SFW consisted of 4.9mM HCO₃⁻, 0.5 mg of C/L DOC, and
0.81 mM NO$_3^-$ (pH = 8.30). Metolachlor was also irradiated in a sample of Don River water (pH = 8.42). The Don River water sample consisted of 3.7 mM HCO$_3^-$, 5.77 mg C/L DOC and 0.44 mM NO$_3^-$. The H$_2$O$_2$/HCO$_3^-$ and SFW treatments were carried out three and four times respectively. All other treatments were performed once.

**Analysis.** Routine HPLC-UV analyses to monitor the photodegradation of the parent chloroacetanilide compound were done by direct aqueous injection into a Waters 600S system with a 486 Variable Wavelength Detector set at 220 nm. The column was a 25 cm × 4.6 mm i.d. reversed phase Alltech Econosil C18, 5U and was preceded by an Alltech All-Guard Cartridge system with an Econosil C18 10U guard cartridge. Various mixtures of acetonitrile and water were used as the mobile phase. The flow rate was 1.0 mL/min for all experiments. Calibration was performed daily using external standards and linear regression analysis.

The aqueous stability of MCA was investigated using ion chromatography including a PE Series 200 pump, Alltech ERIS 1000 HP Autosuppressor and a Waters 712 WISP Autosampler. The column was a 25 cm × 4 mm i.d. Dionex IonPac anion exchange column. The mobile phase and flow rate were 2.1 mM Na$_2$CO$_3$: 0.6 mM NaHCO$_3$ and 1 mL/min respectively. Calibration was performed daily using external standards and linear regression analysis.

The production of MCA was monitored using a PE Autosystem XL gas chromatograph with electron capture detection (ECD). A Simplicity 1701 column (30 m × 0.32 mm i.d., 0.25 μm film thickness) was used to elute the propyl ester of the acid using the following temperature program: hold for 8 min at 45°C, 30°C/min to 250°C. The injector and detector temperatures were 220°C and 300°C respectively. The carrier gas was hydrogen and had a setpoint of 14 psi; the makeup gas was nitrogen at a flow rate of 30 mL/min. Injection mode was splitless and injection
volume was 2.0 µL. Calibration was performed daily using external standards and linear regression analysis.

A PE Autosystem XL gas chromatograph coupled to a PE TurboMass mass spectrometer was used for GC-MS analyses in the electron impact (EI) mode. Full scan EI spectra were obtained at 70 eV. from m/z 50-450 for the propyl ester of MCA and for the model chloroacetanilide 2-chloro-N-methylaniline. Single Ion Monitoring (SIM) EI spectra were obtained for the determination of N-methylaniline in the photolysate of the model compound by monitoring masses 106 and 77. An MDN-5 column (30 m x 0.25 mm, 0.25 µm film thickness) was programmed as follows: MCA propyl ester - 45°C held for 8 min; 30°C/min to 250°C. 2-chloro-N-methylaniline- 60°C held for 2min. 10°C/min to 250°C. N-methylaniline - 70°C held for 1 min 10°C/min to 180°C. 30°C/min to 250°C. The injector temperature and setpoint were 220°C and 8 psi respectively. Injection mode was splitless and injection volume was 1.0 or 2.0 µL.

Photolysate Analysis. Prior to GC-ECD analysis, samples had to be concentrated, derivatised, and extracted in order to analyze monochloroacetic acid as its respective ester. For direct photolysis experiments, the method of Reimann et al. (1996) was used. The method had originally been used for the analysis of MCA in rainwater. A known volume of the photolysate (80-100 mL) was passed through a 3 mL, 500 mg strong anion exchange (SAX) cartridge from either Supelco (Bellefonte, PA), or Varian (Harbor City, CA) via a Vacmaster vacuum manifold (Mid Glamorgan, UK). Cartridges were pre-conditioned with 5 ml of 10% NaCl and washed with 3 mL of 1-propanol once the photolysate had passed. Elution of the acid was achieved via centrifugation for two minutes using 2 mL 1-propanol acidified with 12.5 µL/mL concentrated H₂SO₄. To derivatize MCA, a further 190 µL of conc. H₂SO₄ was added followed by heating in sealed vials at 70°C for two hours. The mixture was then made aqueous by adding 18 mL of
20% NaCl. Extraction with 2 × 0.5 mL pentane followed by a wash of the pentane layer with 9 mL 20% NaCl completed the sample preparation for GC-ECD analysis. Comparison of the derivatized acid with the synthesized ester on GC/ECD and GC/MS confirmed that the ester was made using this method. Solutions of MCA in deionized water were treated using the method in order to obtain standards for all photolysis treatments.

Low recoveries were found in all matrices, excluding the deionized water treatments, using the method established by Reimann et al. Method development to improve recovery included sample pretreatment and variation in the SAX capacity and sample volume. The following variations in the method were tested: (1) acidify to pH 5 using concentrated HCl and degas the photolysate under vacuum prior to sample concentration on the SAX cartridges. (2) acidify, degas, reduce sample volume to 50 mL and use 2500 mg capacity SAX cartridges and (3) acidify, degas and reduce sample volume to 40 mL. Spike and recovery experiments were used to test the efficiency of each variation in the method. All spikes were 25-30 µg/L in MCA in the matrix of interest. Data for these experiments are given in Table II. Results indicated that the most effective modifications were achieved using variation (3). Poor recoveries persisted for the H₂O₂/HCO₃⁻ matrix, however they did reach acceptable levels for the SFW matrix.

The presence of the complementary compound to MCA production from the photolysis of model compound (2-chloro-N-methylacetanilide) was also investigated. Remaining photolysate (around 50 mL) was passed through 500 mg capacity C18 solid phase extraction (SPE) cartridges (Supelco, Bellefonte PA). Ethyl acetate (1 mL) was used to elute the cartridge via centrifugation. After drying, the ethyl acetate was examined for N-methylaniline using GC/MS.
2.3 RESULTS AND DISCUSSION

Aqueous Stability. Over a twelve day period there was no significant decrease in the original MCA present. MCA was considered hydrolytically stable within the time course of all photolysis treatments.

Photodegradation of chloroacetanilides: All treatments were undertaken to elucidate those environmental conditions that may provide a large yield of MCA as a product of chloroacetanilide photodegradation. Regression analysis showed that in all treatments, the photolysis followed pseudo-first-order kinetics with respect to the herbicide concentration (Table I). In deionized water, the photodegradation of metolachlor appeared to be independent of the pH, indicating similar degradation mechanisms. Introduction of naturally occurring species such as nitrate, bicarbonate, hydrogen peroxide, and dissolved organic carbon within the same pH range had a significant kinetic effect. The half-life of metolachlor in \( \text{H}_2\text{O}_2/\text{HCO}_3^- \) treatment decreased by approximately a factor of 30. Dark control experiments show no degradation of the parent compound. In SFW, the half-life of metolachlor decreased by close to a factor of 9 compared to the deionized water treatments.

Sample Preparation. The method of Reimann et al. (1996) proved reliable for the determination of MCA in the deionized water treatments. Several variations of the method were attempted in order to obtain acceptable recoveries for the SFW and \( \text{H}_2\text{O}_2/\text{HCO}_3^- \) treatments. Low recoveries seen for the unmodified derivatization method are believed to be a result of the high levels of carbonate/bicarbonate anions in these two treatments. That is, the anions competed with MCA for active sites on the SAX cartridges. To remedy the competition, each modification was designed to provide more sites on the cartridges for the eluting species. Recovery results and descriptions of each modification are shown in Table II. Reducing the pH to 5 and degassing the
samples should have driven off most of the carbonate as CO$_2$; however, persistent low recovery following modification number could be attributed to competition on the SAX cartridge between MCA and Cl$^-$ (from the HCl used for acidification).

**Table I: Pseudo-first-order kinetic data for the photolysis of chloroacetanilides under various treatments.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Chloroacetanilide</th>
<th>Rate constant (hr$^{-1}$)</th>
<th>Half-life (hours)</th>
<th>Coefficient of Determination ($R^2$)</th>
</tr>
</thead>
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<tr>
<td>pH7</td>
<td>Metolachlor</td>
<td>0.00946</td>
<td>73.3</td>
<td>0.999</td>
</tr>
<tr>
<td>pH9</td>
<td>Metolachlor</td>
<td>0.00942</td>
<td>73.6</td>
<td>0.915</td>
</tr>
<tr>
<td>$\text{H}_2\text{O}_2/\text{HCO}_3^-$</td>
<td>Metolachlor</td>
<td>0.288 ± 0.033 (n = 3)</td>
<td>2.41 ± 0.13 (n = 3)</td>
<td>0.989</td>
</tr>
<tr>
<td>Don River Water</td>
<td>Metolachlor</td>
<td>0.0588</td>
<td>12.4</td>
<td>0.998</td>
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<tr>
<td>Synthetic Field Water (SFW)</td>
<td>Metolachlor</td>
<td>0.0895 ± 0.0014 (n = 4)</td>
<td>7.74 ± 1.2 (n = 4)</td>
<td>0.979</td>
</tr>
<tr>
<td>SFW</td>
<td>Alachlor</td>
<td>0.0708</td>
<td>8.89</td>
<td>0.999</td>
</tr>
<tr>
<td>SFW</td>
<td>Butachlor</td>
<td>0.0618</td>
<td>7.96</td>
<td>0.969</td>
</tr>
<tr>
<td>SFW</td>
<td>2-chloro-$N$-methylacetamide</td>
<td>0.0870</td>
<td>11.2</td>
<td>0.982</td>
</tr>
</tbody>
</table>

The second modification of the method was also unsuccessful in improving the recovery of MCA from photolysate matrices, possibly due to problems with eluting MCA off of the larger capacity cartridge. That is, we found that while they surely provide more sites for the eluting species, the recovery of 2 mL acidified propanol from the 2500 mg cartridges was not quantitative. Returning to the use of the smaller cartridges, and reducing the volume of photolysate extracted (modification number 3) did provide acceptable recoveries (> 80%) for the SFW matrix; however so far, we have been unsuccessful in determining a method that will provide acceptable recoveries for the $\text{H}_2\text{O}_2/\text{HCO}_3^-$ matrix.
Table II: Results from spike and recovery experiments conducted for method development of monochloroacetic acid (MCA) extraction procedure (Frank et al. 1996) from photolysate of chloroacetanilides.

<table>
<thead>
<tr>
<th>Method Description</th>
<th>Treatment</th>
<th>Recovery (%)</th>
<th>Standard Deviation (Range when n = 2)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmodified</td>
<td>pH 7 / pH 9</td>
<td>81.7</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Modified (1):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified (2):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified (3):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified (3):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modified (1):</td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>33.6</td>
<td>2</td>
</tr>
<tr>
<td>Modified (2):</td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>18.2</td>
<td>5</td>
</tr>
<tr>
<td>Modified (3):</td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>82.0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>82.0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>37.5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>37.5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Acidify (pH 5) and degas photolysate</td>
<td>SFW</td>
<td>37.5</td>
<td>2</td>
</tr>
</tbody>
</table>

MCA Analysis. Comparison of the standard curves of each of the derivatized acid and the synthesized ester indicated that the derivatization efficiency of the method was not 100%. Preparing standards according to the same method as photolysate samples accounts for any discrepancy. Table III shows the results from the determination of MCA in each photolysis treatment. MCA, as a percent of the parent chloroacetanilide degraded at each of three time points, was calculated and expressed as an average ± one standard deviation.
Table III: Monochloroacetic acid (MCA) production data from the photolysis of chloroacetanilides under various photolysis treatments. MCA was calculated as percent of the degraded parent chloroacetanilide at each of three time points (n indicates the number of time points) over the course of the photolysis treatment.

<table>
<thead>
<tr>
<th>Chloroacetanilide</th>
<th>Treatment</th>
<th>MCA (% of degraded parent)</th>
<th>Standard Deviation</th>
<th>n (number of time points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metolachlor</td>
<td>pH 7</td>
<td>5.66</td>
<td>0.83</td>
<td>3</td>
</tr>
<tr>
<td>Metolachlor</td>
<td>pH 9</td>
<td>4.38</td>
<td>0.73</td>
<td>3</td>
</tr>
<tr>
<td>Metolachlor</td>
<td>Don River Water</td>
<td>12.6</td>
<td>4.1</td>
<td>3</td>
</tr>
<tr>
<td>Metolachlor</td>
<td>Synthetic Field Water (SFW)</td>
<td>29.3</td>
<td>4.2</td>
<td>3</td>
</tr>
<tr>
<td>Alachlor</td>
<td>SFW</td>
<td>50.5</td>
<td>18.2</td>
<td>2</td>
</tr>
<tr>
<td>Butachlor</td>
<td>SFW</td>
<td>38.9</td>
<td>14.7</td>
<td>3</td>
</tr>
<tr>
<td>2-chloro-N-methylacetamide</td>
<td>SFW</td>
<td>46.8</td>
<td>3.4</td>
<td>3</td>
</tr>
</tbody>
</table>

Direct Photodegradation Experiments. It was found that in pH 7 and pH 9 deionized water, MCA was a minor photoproduct of metolachlor. It is probable that the mechanism for the production of MCA in pH 7 and pH 9 deionized water treatment proceeds via a photo-induced base catalyzed anilide hydrolysis mechanism. The hydrolysis of chloroacetanilides such as metolachlor and alachlor under non-photolytic conditions does not proceed to a significant extent (Chiron et al., 1995). Hydrolysis studies of anilides conducted by Biechler and Taft (1957) suggest that a significant activation energy requirement exists for the decomposition of the tetrahedral intermediate formed upon addition of hydroxide ion to the carbonyl of the anilide. Under photolytic conditions however, MCA is produced thus providing evidence that hydrolysis does occur. Hydrolysis presumably occurs since the absorption of light has created an excited state intermediate which now possesses enough energy to undergo loss of the anilide moiety, disrupting the tetrahedral geometry (Figure 1). It follows that, the similarity in production of MCA at pH 7 and pH 9 arises from the fact that the rate-determining step for the hydrolysis...
mechanism is the degradation of the tetrahedral intermediate (consistent with a high activation barrier), and not initial attack by the hydroxide anion. We have shown that within an environmentally relevant pH range, MCA has the potential to arise as a result of direct photolysis of metolachlor.

**Figure 1.** (a) Structures of the four chloroacetanilides investigated (b) Photo-induced hydrolysis is the proposed mechanism for the production of monochloroacetic acid (MCA) from chloroacetanilides in deionized water at pH 7 and pH 9.
**Indirect Photolysis Experiments.** Naturally occurring species such as nitrate, bicarbonate, hydrogen peroxide and dissolved organic carbon (DOC) are expected to have an effect on the mechanism and the yield of MCA. Each species has a specific contribution to the constitution of natural water. The role of nitrate in natural water has largely been shown as a primary source of the hydroxyl radical (Zepp et al., 1987). Zepp et al. (1987) have claimed that nitrate in naturally occurring water can range from < 0.1 mM up to 10 times in extreme cases where a water body receives large inputs of groundwater rich in nitrate. Hydrogen peroxide also produces hydroxyl radicals upon irradiation but is considered secondary to nitrate in this regard largely based upon the low UV absorption and slow formation rate of H₂O₂ in the environment (Haag and Hoine, 1985).

Bicarbonate and dissolved organic carbon (DOC), the two remaining natural water constituents involved in this investigation, play slightly different roles than nitrate and hydrogen peroxide. Although DOC can produce radicals upon irradiation, bicarbonate and DOC can both act as scavengers of photoproduced radicals. Concentrations greater than 1 mM of carbonate or bicarbonate are considered high carbonate waters (Morel and Hering, 1993) while DOC typically exists in freshwater within the range of 0.5-25 mg of C/L (Larson and Zepp, 1988).

It was our intention to examine the effect of indirect photolysis on the production of MCA from the parent chloroacetanilide. Two matrices were chosen to suit this purpose. First, the H₂O₂/HCO₃⁻ solution was used to provide an extreme case of high carbonate radical in order to survey the effect of this secondary sunlight radical on the overall production of MCA from chloroacetanilides. Upon irradiation, 3 mM H₂O₂ produces hydroxyl radicals that are quickly scavenged by excess bicarbonate (0.092 M) to form the bicarbonate radical. The pH of the solution was 8.23-8.30 while the pKₐ of the carbonate radical has been shown to lie between 7.0
and 8.2 (Eriksen and Lind, 1985), indicating that carbonate radical will dominate in the photolysis matrix. Second, the purpose of using a SFW solution was to provide a matrix high in carbonate radical produced in this case by environmentally realistic concentrations of species likely to be present in a natural water sample. Upon irradiation, nitrate (0.5mM) produces hydroxyl radicals that are scavenged by bicarbonate (3.6mM) to produce the carbonate radical (pH of SFW matrix: 8.3). Table three shows that in SFW the production of MCA is a major pathway for the photodegradation of four chloroacetanilides; however, due to the difficulty of analyzing MCA in H_2O_2/HCO_3 we have not been able to accurately represent the amount of MCA produced in this particular matrix.

We were specifically interested in exposing chloroacetanilides to carbonate radical since Larson and Zepp (1988) and Elango et al. (1984) have postulated that the rate limiting step for the reaction of carbonate radicals with aniline type compounds is electron transfer from the aniline to the carbonate radical. Based on this premise a scheme for the production of MCA from metolachlor has been proposed (Figure 2).

**Figure 2.** Proposed scheme for the production of monochloroacetic acid (MCA) from chloroacetanilides in the presence of carbonate radical.
It is entirely possible that carbonate radical is not the only species responsible for the initial electron transfer; in SFW and in natural water samples. carbonate radicals, hydroxyl radicals and alkylperoxy radicals may all be present and capable of initiating the first step to the production of MCA.

Our proposal for the initial step in going from the chloroacetanilide to MCA has been supported elsewhere; Pignatello and Sun (1995) showed that MCA was a major photoproduct of metolachlor using the photoassisted Fenton reaction. While this type of system is not naturally occurring, the conditions used and results obtained help to provide insight as to the possible mechanism for the production of the acid. That is, the photodegradation of metolachlor was carried out using Fe$^{3+}$/H$_2$O$_2$/u.v. and also using the same conditions without H$_2$O$_2$. In the absence of H$_2$O$_2$, MCA was plotted as a photoproduct and was shown to reach an approximate 40% yield. The reaction of metolachlor under these conditions was thought to be due to charge transfer photolysis of Fe$^{3+}$(aq), which is consistent with our hypothesis. That is, the photodegradation of metolachlor in SFW and using modified photo-Fenton conditions are believed to proceed via an initial photolytically induced electron transfer giving a consistently large yield of MCA throughout the course of the photodegradation.

Evidence to support the initial step of our mechanism is also provided in the work done by Chan et al., (1992) in an experiment investigating the degradation of atrazine by hydroxy radicals. They similarly propose that the fission of N-alkyl groups begins with one-electron oxidation and have conducted a number of experiments that strongly support this hypothesis.

Metolachlor was irradiated in a sample of Don River water. Table 3 shows that in a natural water sample, the production of MCA is intermediate to that in SFW and in deionized water. The results obtained are also consistent with the hypothesis; that is, the natural water
sample contains less nitrate and bicarbonate and close to ten times the amount of DOC. Reduced amounts of nitrate and bicarbonate ultimately result in lower concentrations of carbonate radical. As well, a large increase in DOC concentration may also decrease levels of radical species due to scavenging.

Structural Investigation. Having established that MCA is a major photoprodut of metolachlor in synthetic field water, we attempted to elucidate whether the structure of the chloroacetanilide would be a factor in the yield of MCA. The kinetic data from the photolysis of alachlor, butachlor and a model chloroacetanilide (2-chloro-N-methylacetanilide), as well as the production data for MCA are given in Tables 1 and 3, respectively. Figure 3 allows the comparison of all four chloroacetanilides concerning parent degradation and MCA production. Based on the assumption that all SFW treatments showed similar precision, it appears that metolachlor, alachlor and butachlor all photodegrade at comparable rates. Conversely, the photodegradation of the model chloroacetanilide (2-chloro-N-methylacetanilide) is slower, with a half-life approximately 39% greater than the average of the other three. Table 3 shows that among the four chloroacetanilides, MCA production varies from 29.3% to 50.5% of the parent chloroacetanilide. Only metolachlor and the model were significantly different from one another since the precision for alachlor and butachlor places them rather ambiguously.
Figure 3. Absolute production of monochloroacetic acid and the photodegradation over time of chloroacetanilides. (a) The photodegradation of metolachlor and alachlor and the production of MCA from each. (●) Metolachlor (○) MCA from Metolachlor (▲) Alachlor (△) MCA from Alachlor (b) The photodegradation of butachlor and the model 2-chloro-N-methylacetanilide and the production of MCA from each. (●) Model (○) MCA from model (▲) Butachlor and (△) MCA from Butachlor.
It has been argued that the presence of electron donating substituents on the nitrogen atom of anilines results in a more rapid reaction with the carbonate radical (Larson and Zepp, 1988). In addition, the model compound lacks any type of side chain on the aryl ring, thus decreasing electron donation to the ring. Removal of alkyl side chains will reduce the occasion of several previously established photodegradation products formed from processes such as oxoquinoline formation, ring hydroxylation, and oxidation of aryl side chains (Somich et al., 1988; Schmidt et al., 1995; Moza et al., 1992; Pignatello and Sun 1995). Since there are fewer overall degradation pathways available to the model and the nitrogen atom of the model is less sterically hindered than that of metolachlor, it follows that the overall rate of photodegradation of the model compound is slower and leads to increased MCA production in comparison with metolachlor, alachlor and butachlor.

To support the proposed mechanism for the degradation of chloroacetanilides, we thought it prudent to identify the complementary anilide product (refer to Figure 1b). The model was chosen for this analysis since it had the largest yield of MCA. N-methylaniline was successfully identified in the photolysate of the model using GC/MS.

2.4 CONCLUSIONS
In this study, we have examined the photodegradation of four chloroacetanilides and found that monochloroacetic acid was a major photoproduct in each case following the photodegradation of the parent compound in synthetic field water. The significance of such a finding is that MCA is phytotoxic and under the conditions of this experiment, is more persistent than the parent compound. The matrix in which the photolysis occurs influences the mechanism and extent of production of the acid. Certain structural features may also play a role in the yield of MCA. This investigation supports the premise that photolysis of chloroacetanilide herbicides has the
potential to be a significant source of MCA in the natural environment.

Acknowledgements. This work was funded by the National Science and Engineering Research Council (NSERC). The authors would also like to acknowledge Perkin Elmer for their contribution to the creation of the Analytical Laboratory for Environmental Science Research & Training (ANALEST), used significantly in this investigation.

2.5 References


Kolpin, D.W.; Nations, B.K.; Goolsby, D.A.; Thurman, E.M. Acetochlor in the Hydrologic


Chapter 3.
The Photolytic Fate of Aromatic Fluorine in Drugs and Pesticides
3.1 Introduction

The presence of haloacetic acids in the environment is widespread (1,2). In particular, monofluoroacetic acid (MFA) has been identified in various locations in the Canadian aqueous environment, including lake (surface and subsurface), ground and tap water at sub ppb levels (2). Therefore, identification of potential sources of MFA is of interest. Environmental concerns regarding MFA exist since it has proven to be a strong mammalian toxicant with an oral lethal dose of 2-5 mg/kg. MFA is a strong acid whose mode of action is thought to be conversion to fluorocitrate, which then inhibits the TCA cycle in animals (3). MFA is also known as compound 1080 and has been used as a vertebrate pesticide for the control of rabbits, dingoes, pigs and foxes; most extensively in New Zealand and Australia, for more than 40 years (4,5,6).

Exposure to halogenated aniline derivatives has been a concern in industrial settings because of their use in the production of dyes, pharmaceuticals and agrochemicals. Extensive use of such compounds can also lead to exposure to low or moderate levels of halogenated aniline derivatives due to environmental exposure to industrial waste. For example, one major concern among environmentalists is the presence of such compounds in industrial wastewater generated from colourization processes during the preparation of azo dyes (7). The analysis of effluent from dye manufacturing plants has indicated that some waste treatment processes are unsuccessful in removing the dyes and the constituents used to produce them (8), namely aromatic amines, diazotized aromatic amines and phenols. While the majority of halogenated azodyes and the respective starting materials are chlorinated, the recent increase in incorporation of fluorine into all aspects of industrial products (9, 10) indicate that an ever increasing percentage of the environmental contaminants from the above described process would be fluorinated in nature.
Exposure to halogenated anilines, including both fluorinated and chlorinated results in toxic endpoints dependent on whether exposure is acute or chronic. Acute effects include methemoglobinemia (11) and nephrotoxicity (12) the latter of which is most often linked to the formation of aminophenols during the degradation of the aniline (10,13). Chronic exposure has been reported to result in anemia, hypoxia, and cutaneous lesions (11).

Anilines and their fluorinated derivatives are also an integral structural feature of many agrochemicals. In our study, we have focused on those containing monofluorinated aniline type moieties. Specifically we have investigated flamprop-methyl (FPM) and flumetsulam (FLU). Flamprop-methyl [Methyl 1-N - benzoyl-N-(3-chloro-4-fluorophenyl)-DL-alaninate] (Figure 1a) is an herbicide used mainly for wild oats and has recently shown moderate success in controlling volunteer flax in wheat (14). Flamprop-methyl has a low Henry's Law Constant ($K_H < 10^{-5}$) and a water solubility of approximately 35 mg/L (15). These characteristics indicate that flamprop-methyl will be found in the aqueous compartment of the environment, making it susceptible to photolytic degradation. Very little data are available regarding the photolytic character of this pesticide however, it is reported as stable to light and heat (16).

Flumetsulam [$N$-(2,6-difluorophenyl)-5-methyl-[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide] (Figure 1b) is a sulfonamide acetolactate synthase (ALS) inhibiting herbicide that has a broad spectrum activity on many broad leaf weeds and good crop selectivity (17). This herbicide also has a low value of $K_H ( < 10^{-5})$ and a high water solubility (49 mg/L) (18) making it a candidate for photolytic degradation in the natural environment. Information regarding the photolysis of flumetsulam is limited, the only literature available indicates high persistence. That is, half-lives in an aqueous environment and in soil are reported as 6-12 mos. and 3 mos. respectively, however no insight regarding the conditions of these experiments are given (16).
Figure 1. Chemical structures of (a) flamprop-methyl, (b) flumetsulam and (c) ciprofloxacin
Fluoroquinolones constitute a class of antibacterial agents that have been under development since the discovery of nalidixic acid in the 1960s. Progress has resulted in antibiotics that have a broad spectrum of activity against both gram-positive and –negative bacteria. A few of these compounds incorporate a fluoroaniline type moiety into their structure, one of which includes ciprofloxacin (Figure 1c). Ciprofloxacin (CPX) is one of the most widely used fluoroquinolones in human medicine because of its breadth and intense activity against Gram negative bacteria including, *Mycoplasma* spp., *Chlamydia* spp. and *Rickettsia* spp.. As well, recent studies have examined the use of CPX for use in food producing animals (20).

It is well documented that photoxicity is a class effect (21) of fluoroquinolone antibacterial agents, that is they are able to induce photosensitivity in the skin of those treated (22). Specifically, fluoroquinolone derivatives with no substituent at the C-8 position or those with a fluorine substitution in this position are unstable when irradiated within the actinic region of the electromagnetic spectrum (23). The mechanism responsible for such a reaction remains unknown: therefore information about the photolytic behavior in a variety of environments will add to the knowledge lacking in this area.

The majority of research conducted on the fate of halogenated compounds has focused on brominated and chlorinated organics. The fate of fluorinated compounds has received less attention since as mentioned, they have been utilized to a lesser extent but also because they have been perceived as inert in nature and therefore less harmful biologically and environmentally (24). The perception is likely attributed to the fact that the C-F bond is among the strongest found in nature with a value of 116 kcal/mol (25), therefore presumably making it more resistant to degradation into harmful intermediates.

Previously, we have shown that the photolysis of chloroacetanilide pesticides is one potential source of monochloroacetic acid (26). It was the hypothesis of the present research that the
photolysis of pesticides and pharmaceuticals, namely CPX, FLU and FPM, containing a fluoroaniline-type moiety may yield MFA as a photodegradation product. The objectives that followed from the original hypothesis included 1) the elucidation of the photolytic behaviour of fluoroanilines (FAs) and related pesticides and pharmaceuticals and 2) the identification of fluorinated photoproducts, specifically aiming to determine the factors affecting the fate of aromatic fluorine with respect to the perceived strength of the C-F bond.

3.2 Materials and Methods

Chemicals. 2-fluoroaniline, 3-fluoroaniline, 4-fluoroaniline, 2,4-fluoroaniline and 2,6-fluoroaniline were acquired from Lancaster, distributed by Caledon Laboratories Ltd. (Georgetown ON) with purities of 97% or greater. Chemical intermediates of photodegradation mentioned hereafter were purchased from Aldrich (Milw. WI) with purities of 97% or greater. Flamprop-methyl was of Pestanal® grade obtained from Riedel-de-Haën. flumetsulam was a gift from Dow AgroSciences LLC (Indianapolis IN) and ciprofloxacin was obtained as a 0.2% ready-for-use 100 mL infusion solution in 5% Dextrose Injection. Ciprofloxacin was extracted from the i.v. solution by incrementally increasing the pH of the solution using 0.1M NaOH until the faint to light yellow crystals began to precipitate. Crystals were then filtered from the mother liquor using a 0.22 μm nylon filter and dried in a vacuum desiccator for three days. The purity of the antibiotic was confirmed using 1H NMR (500MHz, DMSO d6 as solvent) and UV/VIS - see Appendix A and B for the spectra. High performance liquid chromatography (HPLC) grade acetonitrile and water were obtained from J.T. Baker (Phillipsburg, NJ). Acetic acid and triethylamine used for the HPLC mobile phase were obtained from Aldrich with purities of 99% or greater. All mobile phase solvents were passed through a 0.45 μm filter before use. Organic-free water used for photochemical experiments was 18MΩ deionized water. Sodium nitrate and sodium bicarbonate used to prepare synthetic field water (SFW) were of reagent grade.
Dissolved organic carbon (DOC) used was prepared by pre-aging a humic acid stock solution in a homemade photosimulator for eight days.

**Stability of MFA.** The aqueous stability of monofluoroacetic acid was characterized before photochemical experiments. The stability of MFA was tested in organic free water at about 26°C in the dark over a 12-day period. At various times MFA levels were analyzed using ion chromatography. The photolytic stability of MFA was characterized using $^19$F NMR. The acid was irradiated for periods of time equal to or longer than the irradiation times of the fluoroanilines in deionized water and in a matrix consisting of 30mM H$_2$O$_2$.

**Photolysis.** The photochemical stability of five fluoroanilines, two pesticides and one pharmaceutical was tested using a Suntest CPS Photosimulator equipped with a xenon arc lamp and a water-cooled tray. Irradiance was set to maximum, 765 W/m$^2$ ± 10% and included wavelengths from 300 to 800 nm to mimic the intensity distribution of natural light. For each photolysis experiment 30-40 mL samples of 9-15 μM parent compound (consistent concentration within each experiment) were placed in quartz test tubes inside the photoreactor and sealed with rubber stoppers and Teflon tape, each experiment was run in triplicate. Tubes were removed throughout the course of the photodegradation, so that four time points in addition to the zero point were analyzed for each set of photolysis conditions; samples were analyzed immediately. Concentrations on the order of 10 μM were chosen to maintain environmental relevance and also since preliminary investigations indicate that photolysis of fluoroanilines at 100 μM did not follow pseudo-first order kinetics. Plots of Ln C/Co (C represents the concentration of the parent chloroacetanilide at time t and Co is the initial concentration) vs. time for each experiment provided pseudo-first-order kinetic data including rate constants expressed in min$^{-1}$ or h$^{-1}$ and half-lives in min or h. For those photoproducts that were identified, the percent conversion of the parent compound to the product were calculated by dividing the number of moles of
photoprodut produced at time t, by the number of mols of parent degraded at time t. For each value expressed, percent conversion was calculated at a given time point during the course of the photodegradation, and each photodegradation was repeated three times.

Direct photolysis experiments. Each of 2-FA, 3-FA, 4-FA, 2,4-FA, 2,6-FA, flamprop-methyl, flumetsulam and ciprofloxacin were degraded in deionized water adjusted to pH 7 or pH 9. The pH was monitored and adjusted regularly using 0.1N HCl and 0.1N NaOH.

Indirect photolysis conditions. Indirect photolysis of each fluoroaniline was examined in a matrix containing 30 mM H$_2$O$_2$. The indirect photolysis of 4-FA was also investigated in three matrices that contained common bicarbonate and dissolved organic carbon (DOC) levels. 0.40 mM and 1 mg C/L respectively, and varying levels of nitrate including 0.40 mM, 0.81 mM and 0.081 mM. Indirect photolysis of all the fluoroanilines, both pesticides and the pharmaceutical was conducted in two synthetic field water matrices, heretofore referred to as SFW1 and SFW2. SFW1 contained 0.40 mM nitrate, 0.40 mM bicarbonate and 1 mg C/L of DOC while SFW2 contained 0.81 mM nitrate, 4.95 mM bicarbonate and 25 mg C/L DOC.

Analysis. UV/VIS. UV/VIS spectra were obtained for five fluoroanilines 2-, 3- and 4-fluoronitrobenzene, 2-, 3-, and 4-aminophenol. flamprop-methyl, flumetsulam and ciprofloxacin on a Perkin Elmer single beam Lambda 11 Spectrometer. Please refer to Appendix B for all UV/VIS spectra.

High Performance Liquid Chromatography (HPLC). Routine HPLC analyses to monitor the photodegradation of the parent fluoroaniline compound were done by direct aqueous injection into a Waters 600S system with a 486 Variable Wavelength Detector, or a 996 Photodiode Array Detector (PDA). The PDA was set at 200-400 nm to analyze UV spectra. Either a 25 cm x 4.6 mm i.d. reversed phase Alltech Econosil C18, 5U or a 25 cm x 4.6 mm i.d. reversed phase Alltech Alltima, 5U column was used. The columns were preceded by an Alltech All-Guard
Cartridge system with an Econosil C18 10U guard cartridge. The mobile phase consisted of various mixtures of acetonitrile and water for the five fluoroanilines and flamprop-methyl, with the detector set at 230 nm for all. The detector (PDA) was also set to extract at 274 nm during fluoroaniline photolysis in order to quantify the fluoronitrobenzenes. Formation of aminophenols (APs) or fluoronitrobenzenes (FNBs) were confirmed through HPLC retention times and UV/VIS spectra as compared to authentic standards. 2.4-FNB and 2.6-FNB were quantified from 4-FNB and 2-FNB respectively since authentic standards were unavailable. Acetonitrile: 0.5% acetic acid (50:50) was used for flumetsulam with the detector set at 250 nm and acetonitrile: 0.5% acetic acid/0.2% triethylamine (20:80) was used for ciprofloxacin with the detector set at 280 nm. The flow rate was 1.0 mL/min for all experiments. Calibration was performed daily using external standards and linear regression analysis.

**Ion Chromatography (IC).** The aqueous stability of MFA and the formation of fluoride was investigated using ion chromatography including a PE Series 200 pump, Alltech ERIS 1000 HP Autosuppressor and a Waters 712 WISP Autosampler. The column was a 25 cm × 4 mm i.d. Dionex IonPac anion exchange column. The mobile phase and flow rate were 2.1 mM Na₂CO₃: 0.6 mM NaHCO₃ and 1 mL/min respectively. Method validation for the quantification of fluoride was performed by conducting spike and recovery experiments at three concentrations; 0.7 µM, 5 µM and 12 µM respectively (n=4 for each concentration); the recoveries were 113.0 ± 12.2%, 78.1 ± 2.9% and 83.1 ± 5.3% respectively. The limit of detection for fluoride, defined as three times the standard deviation of the blank (27), was found to be 0.41 µM (8 ppb). Calibration was performed daily using external standards and linear regression analysis.

**NMR.** All ¹⁹F spectra were obtained at 25 °C on a Varian Unity 500. 3-channel spectrometer operating at 470.297 MHz and equipped with a 5-mm Nalorac 19F proton decoupling probe (refer to Appendix A for all spectra, including parameter details). Chemical shifts were recorded
relative to CFCl$_3$ (0.000ppm) and hexafluorobenzene was used as an internal standard.

Acquisition time for spectra taken of the photolysate of the fluoroanilines was approximately twelve hours. The photolysate of each fluoroaniline was analyzed without concentration with one exception: the photolysate of 4-FA in Matrix A/SFW1 (60 mL) was concentrated onto a C18 Solid Phase Extraction (SPE) cartridge, eluted into deuterated acetonitrile followed by analysis of the eluent by $^{19}$F NMR. Quantitation of the yield of fluoride from MFA during the photolysis stability study was conducted using a three point standard curve for each of MFA and fluoride. Acquisition time was approximately 25 minutes or 640 transients per sample. Quantitation was performed based on the S/N ratio.

3.3 Results and Discussion

Fluoroanilines.

Direct Photolysis. The relative rates of photolysis at both pH7 and pH9 decreased in the order 4-FA $>$ 2.4-FA $>$ 3-FA $>$ 2-FA $>$ 2.6-FA and all followed pseudo-first order kinetics with $R^2$ values of 0.95 or greater. half lives are given in table I. The relative rates are understandable on the basis of absorbance characteristics and molecular structure. Based upon the value of molar absorptivity, symbolized by $\varepsilon$, one would not expect that the photolysis of 2.6-FA would proceed as slowly as it does. Considering nearly identical values of $\varepsilon$, it is also unexpected that the relative rate of photolysis of 2-FA should be greater than that of 3-FA. During direct photolysis, loss of the parent compound is attributed to the degradation of the excited state of the species of interest. Without data for the quantum yield of degradation of the parent and a quantum yield value for the photoproduction of fluoride, it is difficult to speculate upon reasons for the unexpected differences since the efficiency of the processes involved in excited state degradation are unknown. However, there is evidence in the literature to suggest that intramolecular hydrogen bonding of the type N–H⋯F exists when a fluorine is in a position ortho to the NH$_2$ on
an aniline (28, 29). Also, it has been shown that excited state interaction between the amino group and the ring results in a significant increase in negative charge at the N, C₂ and C₆ atoms (30), therefore making loss of the parent compound by nucleophilic displacement of the fluorine atoms highly unfavorable. The combined effects of ‘protection’ of the fluorine atoms through hydrogen bonding and repulsion of nucleophiles by the carbon atoms attached to the fluorine atoms provides some explanation for the resistance of 2-FA and 2,6-FA to direct photodegradation.

The degradation of the parent compound as the formation of selected photoproducts was followed in order to determine the fate of fluorine during photolysis. A typical profile for the loss of fluoroaniline and evolution of photoproducts during direct photolysis is given for 2-FA in Figure 2 and the conversion of fluoroanilines to photoproducts is listed in Table I. The remainder of the photolytic profiles for the fluoroanilines can be found in Appendix C. Only 2-FA was observed to have significantly different photolysis rates under the two direct photolysis conditions, with half-lives of 210 and 173 minutes at pH7 and pH9 respectively. The observation of significant amounts of fluoride at each pH value from the onset of irradiation suggests that the strength of the C-F bond is significantly reduced in the excited state making the loss to fluoride more facile than in the dark where no loss of 2-FA or production of fluoride was observed. The production of 2-FNB was also observed at both pH values to the extent that the two photoproducts accounted for all of the fluorine lost through degradation of the parent. The observation of 2-FNB as a main photoprodut resulting from the photolysis of 2-FA in aqueous solution is analogous with the behaviour of 2-chloroaniline (31). The photolysis profile of 2-FA suggests that at least two competing mechanisms for the degradation of 2-FA were occurring simultaneously. That is, the oxidation from amino- to nitro- occurs as one photodegradation process while at the same time the scission of the C-F bond occurs.
Table 1. Photolysis data for five fluoroanilines (FAs), including half-lives, molar absorptivities, and values for percent conversion to photoproducts at pH7/9 and in synthetic field water (SFW). Percent conversion to photoproducts is calculated in triplicate and given with error estimates of one standard deviation.

<table>
<thead>
<tr>
<th></th>
<th><strong>F</strong>-</th>
<th><strong>FNB</strong></th>
<th><strong>AP</strong></th>
<th>t₁/₂/min</th>
<th>% conversion to photoproduct</th>
<th>% conversion to photoproduct</th>
<th>% conversion to photoproduct</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>F</strong>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-FA</td>
<td>1076</td>
<td>210</td>
<td>173</td>
<td>133</td>
<td>68.7 ± 8.5</td>
<td>40.2 ± 5.5</td>
<td>46.0 ± 0.2</td>
</tr>
<tr>
<td>3-FA</td>
<td>920</td>
<td>90.0</td>
<td>91.6</td>
<td>81.5</td>
<td>101 ± 10.8</td>
<td>106 ± 2.0</td>
<td>94.5 ± 3.9</td>
</tr>
<tr>
<td>4-FA</td>
<td>2829</td>
<td>4.90</td>
<td>4.00</td>
<td>3.69</td>
<td>45.5 ± 4.0</td>
<td>61.7 ± 3.3</td>
<td>42.8 ± 3.9</td>
</tr>
<tr>
<td>2,4-FA</td>
<td>3120</td>
<td>52.9</td>
<td>52.3</td>
<td>48.8</td>
<td>58.0 ± 7.2</td>
<td>32.2 ± 5.3</td>
<td>50.0 ± 3.3</td>
</tr>
<tr>
<td>2,6-FA</td>
<td>1410</td>
<td>1780</td>
<td>1960</td>
<td>173</td>
<td>60.4 ± 4.5</td>
<td>38.2 ± 1.5</td>
<td>25.8 ± 1.4</td>
</tr>
<tr>
<td></td>
<td><strong>E</strong></td>
<td><strong>F</strong>-</td>
<td><strong>FNB</strong></td>
<td><strong>AP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Molar absorptivity/(M) cm⁻¹</td>
<td>Fluoride</td>
<td>Fluoro nitrobenzene and aminophenol respectively</td>
<td>Represents % conversion of 2-FA to photoproducts at pH7. Represents % conversion of 2-FA to photoproducts at pH9.</td>
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Figure 2. The photolysis profiles for the photodegradation of 2-fluoroaniline at pH 7, pH 9 and in two synthetic field water (SFW) matrices.
As the irradiation of 2-FA progresses at pH 9, there is loss of 2-FNB. Nitroaromatic compounds are relatively stable in an aerobic environment due to their highly oxidized state, however in an excited state reactions such as nucleophilic substitution become much more facile (32). This is especially true in the case nitro substituents existing in a position ortho or para to a halogen. We hypothesize that loss of the 2-FNB results in the production of the hydrolysis products, namely nitrophenol and fluoride. A proposed pathway for the direct photodegradation of 2-FA is shown in scheme 1 where $k_1$ refers to the oxidation of excited state 2-FA to 2-FNB, $k_2$ refers to the photonucleophilic substitution of 2-FNB to 2-nitrophenol and fluoride, while $k_3$ refers to the scission of the C-F bond of 2-FA to form fluoride. The process possessing the lowest activation energy would then govern the behaviour observed during the loss of the parent compound. The photonucleophilic substitution reaction in this case must be bimolecular in nature since the loss of FNB is visible at pH 9 and not at pH 7, implying that the rate limiting step has dependence on

Scheme 1. Proposed pathway for the direct photodegradation of 2-Fluoroaniline.

![Scheme 1](image)

the concentration of OH, which is also consistent with the increased rate of degradation at the greater pH value. The behaviour observed can be explained from this mechanism indicating that the activation barrier associated with $k_2$ is less than for either of $k_1$ or $k_3$. Such an observation is
consistent with the proposal that hydrogen bonding poses a significant barrier for the oxidation process and the C-F scission process.

The profile (see Appendix C) and the conversion to photoproducts seen for 4-FA (table I) indicate that the loss of 4-FNB occurs in an analogous fashion to the loss of 2-FNB. However, because there is no difference observed at the two pH values, the evidence suggests that either $k_1$ or $k_3$ govern the observed behaviour of 4-FA. It is more likely that since the conversion of 4-FA to 4-FNB is greater than the conversion to fluoride, that the dominant process is the formation of 4-FNB, a process that is independent of pH. This observation is consistent with the fact that the excited state of 4-FA is quinoid-like (27, 33) lending double bond character to C-F and therefore making it more resistant to C-F scission than 2-FA or 3-FA.

It may seem inconsistent then that the behaviour of 2,6-FA and perhaps even 2,4-FA do not follow that of 2-FA: however, there is no difference in either the rates or percent conversion to photoproducts for 2,4-FA or 2,6-FA at the different pH values. Based on our previous discussion, independence of rate on pH indicates that either $k_1$ or $k_3$ represents the process with the lowest activation barrier. The percent conversion to fluoride and fluoronitrobenzene (table I) are similar to each other with approximately 60% conversion to fluoride indicating approximately equivalent C-F bond strengths, and approximately 40% conversion to FNB isomers. Unlike 2-FA at pH 9 and 4-FA, no loss of FNB is observed for either 2,4-FA or 2,6-FA, directing us to believe that the majority of fluoride is coming from the direct scission of a weaker C-F bond than exists for 2-FA. Literature suggests that when an aromatic compound is disubstituted with fluorine atoms, it becomes much more reactive during nucleophilic substitutions than its monofluorinated counterpart (34), and in fact the strongest electron acceptor is a fluorine meta to the other fluorine. It follows then that the lowest activation barrier for both 2,4-FA and 2,6-FA, which have two fluorine atoms meta to one another, is $k_3$ - provided
that the scission of the C-F bond occurs as a result of a unimolecular nucleophilic displacement. Therefore independent of pH, the first step in the nucleophilic displacement is the heterolytic scission of the C-F bond to form fluoride. The product of nucleophilic displacement is presumably the short-lived hydroxylated product, which was not identified during our experiments.

The behaviour of 3-FA during direct photolysis does not resemble that of any of the other fluoroanilines in that 3-FA goes quantitatively to fluoride and aminophenol, indicative of photohydrolysis i.e. heterolytic substitution of F by OH involving a molecule of water. 3-chloroaniline, 3-chlorobenzene and 3-chlorophenol have all been shown to undergo a similar transformation in aqueous solution (35, 36, 37). The 3-fluorophenol also shows nearly quantitative conversion to the photohydrolysis product, resorcinol (38). Because there is no difference at the two pH values, it seems that the rate-limiting step (RLS) of the mechanism cannot include the nucleophile, and must first consist of scission of the C-F bond. The behaviour of 3-FA is consistent with the variation of charge distribution for exited state fluoroanilines. That is, the carbon atom at the C-F bond is considerably more delta positive for 3-FA than it is for either of 2-FA or 4-FA (27). The result is that in reference to scheme 1, the activation barrier for \( k_3 \) becomes so much less than either of \( k_1 \) or \( k_2 \) that \( k_3 \) is the only mechanism to occur.

The results from direct photolysis suggest that the conversion to fluoride from the parent compound gives some indication of the relative excited state strengths of the C-F bond. The bond appears to be influenced by charge redistribution that occurs following irradiation due to the interaction of both the amino and the fluorine atoms with the aromatic ring. Ultimately, what is seen is that 4-FA is most resistant to fluoride formation followed by 2-FA, then 2,4-FA and 2,6-FA and finally to 3-FA which possesses the weakest C-F bond in comparison to the other fluoroanilines.
**Indirect Photolysis.** The use of $^{19}$F NMR to screen the photolysate of the fluoroanilines was appealing for several reasons. Firstly, we were interested primarily in the fate of fluorine resulting from the irradiation of the parent compound. Secondly, it is a relatively sensitive method due to the fact that the $^{19}$F isotope is 100% abundant. Finally, the large spectral window afforded by this technique provides the opportunity to identify fluorinated products despite similarities in structure. $^{19}$F NMR is a technique that has been recognized as extremely advantageous for environmental or biological analyses (39, 40, 41, 42) because of the above-mentioned reasons, creating an analysis technique that requires little or no sample clean-up/preparation. The limit of detection for MFA during a 12 hour acquisition was estimated based upon the previous work of a colleague (26) to be approximately 80 ng/L therefore giving us the potential to identify a 0.01% conversion of fluoroaniline to MFA.

Initially a matrix was chosen that, while it was not likely to be found in the environment, would give some indication regarding the potential for MFA to be produced from the photolysis of the fluoroanilines. It was believed that in the presence of excess hydroxyl radicals, hydroxylation of the aromatic ring would occur in such a fashion as to create a diol. The diol would ultimately yield the acid as the most probable pathway to MFA. Evidence exists to support the formation of the 2,3-\textit{cis}-diol precursor when a 1,4-disubstituted benzene derivative (1=Me and 4=F) is exposed to an environment where hydroxylation will occur (43). The yield of the \textit{cis}-diol was 21%. The premise for the hypothesis of MFA formation was based largely upon the nature of the C-F bond. we believed that this unusually strong bond would resist attack therefore permitting the above mechanism to occur leaving the C-F bond intact.

Examination of the $^{19}$F NMR spectra for each fluoroaniline in the 30 mM $\text{H}_2\text{O}_2$ matrix revealed that the only fluorinated photoproduct was fluoride in each case (please refer to Appendix A for all $^{19}$F NMR spectra). The results indicated, contrary to our predictions, that
MFA was unlikely to be produced under the conditions described and that in fact the C-F bond, under these circumstances, was not strong enough to withstand such a matrix. To eliminate the possibility that the 30 mM H₂O₂ matrix was too harsh a matrix for the photoproduction of anything but fluoride, we chose to irradiate 4-fluoroaniline using three different matrices with environmentally relevant concentrations of 3 field water constituents.

Each matrix contained bicarbonate, dissolved organic carbon and nitrate. They were designed such that hydroxyl radical would remain the primary transient responsible for photodegradation of the parent compound. In each matrix dissolved organic carbon and bicarbonate were kept constant and at low concentrations of 0.40 mM and 1 mg C/L respectively. At these levels dissolved organic carbon (DOC), the major sink for hydroxyl radical and also a possible source of reactive radical species, was environmentally realistic but kept the scavenging of hydroxyl radical to a minimum. When DOC is low and bicarbonate is present at levels greater than 1 mM, bicarbonate becomes competitive in scavenging hydroxyl radicals thus leading to the production of carbonate radicals (44, 45). Such an occurrence was undesirable since it is unlikely that the formation of carbonate radical will lead to the photoproduction of MFA. That is, carbonate radicals have been shown through positive Hammet plot correlation to selectively react at the nitrogen of aniline type compounds through an electron transfer process as the primary reaction (46, 47). For these reasons, the concentration of bicarbonate was kept less than 1 mM. The level of hydroxyl radical was varied by changing the level of nitrate, a field water constituent with the primary role of producing hydroxyl radicals upon irradiation. The concentrations chosen range from low to high within environmentally realistic levels.

The half-lives in each matrix varied from 3.7 to 4.0 minutes and the conversion of 4-FA to fluoride ranged from 43 to 48%. Figure 3 illustrates the profile showing loss of the parent compound and photoproduction of fluoride in each matrix indicating that there is no significant
difference among the three matrices. It appears that altering the level of hydroxyl radical in the matrix has no significant effect on the mechanism of photodegradation. Other fluorinated photoproducts were determined through the use of $^{19}$F NMR on the concentrated ($\times 60$) photolysate of the medium level nitrate matrix. The only fluorinated product observed, besides fluoride, was 4-fluoronitrobenzene, confirmed by comparison with the spectrum of an authentic standard.

From the investigation of fluoroaniline photolysis in the presence of hydroxyl radical we can conclude that varying the level of nitrate from high to low while keeping bicarbonate and DOC concentrations to a minimum has no effect on the mechanism of photolysis of 4-FA. We can also conclude that MFA will not be a photoproduct. This statement is supported by both the absence of MFA in the photolysate of the fluoroanilines and from the results of our control experiments. Control experiments regarding the aqueous stability of MFA show that over a twelve day period there was no significant decrease in the original amount of acid present. In terms of photolytic stability, in deionized water, no loss of monofluoroacetic acid was detected based upon the values of S/N determined from the main peak of the MFA triplet located at approximately $-215$ ppm. MFA showed a $22\%$ conversion to fluoride after 140 minutes of photolysis in $30\, \text{mM} \, \text{H}_2\text{O}_2$. The time of irradiation corresponded to approximately $20 \times$ the longest half-life ($7.5\text{-min}$ for 2,6-FA) among the fluoroanilines in this particular matrix. Of all the indirect photolysis matrices investigated, $30\, \text{mM} \, \text{H}_2\text{O}_2$ was considered the most harsh in terms of the persistence of photoproducts for analysis. We have shown then, had MFA been a photoproduct of any of fluoroanilines under indirect photolysis conditions it would have been detected during the 12-hour acquisitions.
Figure 3. The production of fluoride from the photolysis of 4-fluoroaniline in matrices varying in the concentration of nitrate.
Having sufficiently disproved the potential for MFA photoproduction from the fluoroanilines, the remainder of the discussion regarding indirect photolysis experiments will focus on determining the fate of the fluorine following the irradiation of fluoroanilines in two synthetic field water matrices. SFW1 is identical in constitution to the matrix described above that contained a medium level of nitrate and low values for both bicarbonate and DOC, while SFW2 contained the highest environmentally relevant levels of each of nitrate, bicarbonate and DOC. As discussed previously, bicarbonate and DOC are kept low in SFW1 in order to maintain hydroxyl radical as the primary reactive transient to be responsible for the degradation of the fluoroanilines. SFW2 however, contains high levels of each constituent creating a more complex matrix in which a variety of scenarios can occur. That is, there exists opportunity for other reactive intermediates such as singlet oxygen, organic peroxy radicals and carbonate radicals to form as well as the hydroxy radical. In fact, with the levels of bicarbonate and DOC so high, it is expected that because it is such a reactive and unselective radical, hydroxyl radicals would be consumed within a few microseconds of production (48) by both bicarbonate and DOC. The role of dissolved organic carbon is complex in sunlit surface waters; humic materials are capable of inducing behaviour that may not occur in the absence of DOC. Photoinduced reactions that can occur due to DOC include photosensitization reactions, photoxidations and photoreductions along with the radical reactions mentioned previously (49).

Table I gives pseudo-first order half lives for the indirect photodegradation of the fluoroanilines in both SFW1 and SFW2. The term “indirect” implies that irradiation causes the excitation of some species other than the fluoroaniline which results in the formation of a reactive transient. Then the photoproduced transient reacts with presumably the ground state fluoroaniline resulting in its degradation. It is however, still possible and likely that excitation of the fluoroaniline does occur resulting in an additional pathway for degradation. For each
fluoroaniline, the rate of photolysis is significantly increased in SFW2 as compared to SFW1; with the exception of 4-FA for which the opposite is true.

SFW1. In SFW1 the order of reactivity decreases as 4-FA>2,4-FA>3-FA>2-FA>2,6-FA, identical to the relative reactivities seen during direct photolysis. However, as expected due to the presence the reactive transients mentioned above combined with the antioxidant nature of anilines, the half-lives are significantly reduced in each case. The most marked change occurs for 2-FA and for 2.6-FA. 2-FA is 1.5× more reactive in SFW1 while 2.6-FA. it is approximately 11× more reactive in SFW1 than during direct photolysis. Accompanying these increased rates of reactivity is a change in the percent conversion to photoproducts, the observed photoproducts only account for 51% and 26% of the fluorine lost during photodegradation of 2-FA and 2.6-FA respectively which contrasts direct photolysis where identified photoproducts accounted for ~100% of degraded fluorine. 2.4-FA shows similar behaviour in that only 73% of fluorine that can be accounted for however, unlike 2-FA and 2.6-FA there are not marked changes in the rate of reactivity. The data in table one suggest that in SFW1, 2-FA and 2.6-FA and 2.4-FA have been subject to a change in the pathway/mechanisms responsible for their degradation. Specifically, the fact that each experiences a decrease in the conversion to fluoride as compared to direct photolysis, suggests that the excited state is probably not solely responsible for the loss of the parent compound. That is, the decrease is an indication that some of the fluoroaniline is degraded through the ground state, which has a stronger C-F bond compared to its excited state (as established through direct photolysis behaviour). 3-FA and 4-FA degrade only slightly faster in SFW1 and yield the same distribution of fluorinated photoproducts as seen during direct photolysis, indicative of the conclusion that both are still photodegrading through the excited state. During the photolysis of 3-FA in SFW1 there is a change (with respect to direct
photolysis) in the percent conversion to 3-aminophenol from the parent, most likely attributable to the degradation of the photoprodut in the presence of reactive SFW1 transients.

Overall, based upon the conversion to fluoride, the C-F bond of 3-FA remains the most labile while 4-FA, 2-FA and 2,4-FA appear to have C-F bonds of comparable strength. The strength of 2,6-FA C-F bonds however appears to be much increased since the production of fluoride is decreased indicating that other processes with lower energy requirements are responsible for the degradation of 2,6-FA.

SFW2. The relative rates of photolysis in SFW2 decrease as 4-FA>2,6-FA>2,4-FA>2-FA>3-FA. almost no relation to the behaviour observed during direct photolysis or in SFW1. SFW2 is a complex matrix with high levels of each of bicarbonate, DOC and nitrate. The dynamic occurring in this matrix would be complicated. due to the presence of a variety of reactive radical transients. As listed in Table 1, all of the fluorine can be accounted for during the photolysis of each of 4-FA, 3-FA and 2,4-FA. Only 76% and 23% of fluorine has been identified as fluorinated photoproducts for each of 2-FA and 2,6-FA.

The conversion to fluoride in SFW2 indicates that there has been little change in the relative C-F bond strengths among the fluoroanilines as compared to SFW1. All the fluoroanilines show similar C-F bond scission behaviour with the exception of 2,4-FA which increases significantly in the production of fluoride. The conclusion drawn is that a larger proportion of 2,4-FA is degrading through the excited state therefore reducing the overall C-F bond strength in SFW2 as compared to SFW1.

The photoproduction of fluoronitrobenzenes was reduced in several cases in both SFW1 and SFW2. The presence of bicarbonate in the solution can lead to the production of carbonate radicals following the scavenging of hydroxyl radicals produced as a result of the irradiation of nitrate. It has been shown that in the presence of anilines, the carbonate radical will undergo an
electron transfer reaction from the aniline to the carbonate radical (39, 44, 50). Data for the reactivity of the carbonate radical toward aromatic compounds in aqueous solution, including aniline, show that \( \rho \) values associated with Hammett plots for the reaction of carbonate radicals with substituted benzenes correlate well with radical reactions as well as electrophilic aromatic substitutions (44, 51). Thus decreasing the amount of parent compound able to undergo oxidation to the nitro compound, since it most likely that the fluorine becomes subject to incorporation into coupled type products as has been observed for chloroanilines, as well as into electrophilic aromatic substitution products such as ring hydroxylated species.

Literature regarding the photolysis of chloroanilines suggests that coupled products form as a result of radical pathways including hydrogen abstraction from the N atom and homolytic scission of the C-Cl bond (52, 53). It is likely that this could become a mechanism for the loss of fluoroanilines in irradiated SFW matrices where radical species are present to facilitate such a pathway.

*The Role of DOC.* Many of the observed changes upon going from direct to indirect photolysis can be explained when the role of DOC is examined. For example, physical effects such as shielding from light can occur when organic pollutants sorb to dissolved or colloidal humic material. Also, there may be a marked change in the UV/VIS spectrum of the sorbed species that ultimately will result in the exhibition of differences in photoreaction distribution (39). It appears as though both effects are observed during the photolysis of 4-FA in SFW2 since the 2-fold decrease in reactivity is also accompanied by a change in the distribution of observed photoproducts as compared to direct photolysis.

The interaction of anilines with humic materials has been the subject of much attention; literature suggests that an important pathway for aromatic amines in aquatic ecosystems is covalent binding with natural organic matter, including dissolved organic carbon. It has been
suggested that binding occurs in two phases (54), the first of which is extremely rapid and reversible in aqueous solution therefore preventing the isolation of the product. Phase one in particular involves the formation of imines by the reaction of the amine with the carbonyl functionality found in quinone type structures present in DOC. Phase two is thought to be a slow 1,4-nucleophilic addition of the amino group onto a quinone ring.

We observed that there is a direct relationship between the relative rate of photolysis and the decreased amount of fluorine accounted for during photolysis in SFW1. That is, for each of 2,4-FA, 2-FA and 2,6-FA the percent of unaccounted for fluorine increases as the half-life increases. That is the half lives are 48, 133 and 173 minutes corresponding to 27%, 49% and 74% (2.4-FA, 2-FA and 2,6-FA respectively) of fluorine that cannot be accounted for as photoproducts. The evidence suggests that interaction may be occurring between DOC and these three fluoroanilines, but we are unable to define to which phase or to what extent interaction has occurred. However, the nature of the excited state of fluoroanilines lends support to the occurrence of phase two type interactions. That is, as discussed previously, upon excitation, as a result of interaction between the amino group and the aromatic ring, the N, C2 and C6 atoms become significantly more negatively charged (27). An increase in negative charge to the N atom of the fluoroaniline would certainly provide favorable conditions for a 1,4-nucleophilic addition of the amino group onto a quinone ring found within the humic material.

Even though there is 25× more DOC present than in SFW1, and 2-FA and 2,6-FA still had significant portions of unaccounted for fluorine, there did not appear to be any direct correlation between rate of reactivity and the percent of unaccounted for fluorine. This seems to be contradictory to the previous argument however, the complexity of SFW2 makes it extremely difficult to isolate an observation to a single variable, i.e. as well as binding to fluoroanilines, the DOC and other water constituents are likely undergoing several competing mechanisms. This is
in contrast to SFW1 in which, as discussed previously, the matrix was designed such that hydroxyl radical would be the only significant reactive transient present.

*Environmental Significance.* During both direct and indirect photolysis, we have been able to identify photoproducts that should be of concern when proven to be potential environmental contaminants. Fluoronitrobenzene isomers have been identified for all five fluoroanilines except for 3-FA. Nitroaromatic compounds are already among the most abundant of environmental pollutants. Sources of nitroaromatics are largely attributed as military ordinance compounds and as precursors for monomer synthesis. Concern regarding their presence exists because many have toxic potential, have been proven to be quite stable thus leading to persistence, and most importantly, have the potential to lead to the formation of much more toxic compounds (i.e., azo, azoxy, and nitroso compounds).

Aminophenol was identified as a photoproduct of 3-FA. The potential for this type of compound to be released into the environment is also of concern. That is, much of the toxic effects attributed to exposure to anilines are attributed to the formation of aminophenol metabolites (55).

Probably the most significant environmental finding is that the C-F bond is not as strong and resistant to degradation as may be believed. That is, more often fluorinated compounds are being developed for use in industry, agriculture and in medicine because of their perceived resistance to degradation. However, it appears as though while this may hold true during the commercial uses of the products which may not involve exposure to sunlight; it is certainly not the case when the compound is present in the aqueous compartment of the environment where is it subject to photodegradation.
Pesticides and Pharmaceuticals

Flamprop-methyl (FPM), flumetsulam (FLU) and ciprofloxacin (CPX) were all chosen for this study in order to investigate whether the photolytic behaviour would in any way mirror that seen for the fluoroanilines. Flamprop-methyl has a fluorine para to the amine functionality. Flumetsulam is 2,6-difluorinated to the amine functionality, while ciprofloxacin is ortho fluorinated. Both pesticides and the pharmaceutical were subject to the same four treatments as the fluoroanilines, namely direct photolysis at pH7 and pH9 and indirect photolysis in SFW1 and SFW2.

FLU, FPM and CPX all follow pseudo-first order kinetics at pH 7 and pH 9 and in SFW1 and SFW2. The relative rates of photolysis decrease as CPX > FLU > FPM during direct photolysis and as CPX > FPM > FLU during indirect photolysis. During direct photolysis the pattern observed could be expected based upon the molar absorptivity of each (see Table II). Each of FPM, CPX and FLU produced significant amounts of fluoride during each photolysis treatment, representative profiles for the degradation of flamprop-methyl and the evolution of fluoride at pH7 and at pH9 and in SFW1 and SFW2 can be found in Figure 4; the remainder of the profiles for CPX and FLU can be found in Appendix C. As with the fluoroanilines, fluoride was quantified at each of the time points taken over the course of the photoreaction. The percent conversion of the parent compound was calculated for n=3 for each of FLU, FPM and CPX and can be found in Table II.

Flumetsulam. Unlike 2,6-FA, flumetsulam does exhibit a difference in rate of photolysis at each pH value. An increase in the pH is observed to increase the rate of photodegradation of the parent compound, that is the half-life at pH9 is approximately 30% less than at pH7. The percent conversion of flumetsulam to fluoride appears to decrease with increasing pH, from approximately 100% conversion to fluoride at pH9 to approximately 65% at pH7. The fluoride
value at each pH has a large margin of error associated with it, indicating that there are several mechanisms responsible for the formation of fluoride from the photolysis. As for 2,6-FA, scission of the C-F bond appears to be a major photodegradation pathway for flumetsulam. It is also worth noting that hydrogen bonding is possible for only one of the fluorine atoms of flumetsulam, and also that 2-FA shows pH dependence and exhibits a decrease in percent conversion to fluoride at pH 9 as compared to pH 7. The ability to hydrogen bond may play some role in the photolytic behaviour, as it seems that the direct photolysis of flumetsulam may show similarity to 2-FA.

The reactivity of flumetsulam increases in SFW matrices as compared to direct photolysis. flumetsulam is more reactive in SFW1 than SFW2. All of the photodegraded fluorine can be accounted for as fluoride in both SFW1 and SFW2. This is much in contrast to 2,6-FA which we propose is interacting with DOC and/or forming coupled products to account for 75% of fluorine which does not occur as fluoride. It is most likely that flumetsulam cannot participate in DOC interaction due to both steric inhibition and due to the presence of the SO$_2$ group. That is, the nucleophilicity of the amino functionality is decreased making interaction with quinones in the DOC unfavorable and C-F scission more favorable.
Table II. Photolysis data for ciprofloxacin (CPX), flumetsulam (FLU) and flamprop-methyl (FPM), including half-lives, molar absorptivities, and values for percent conversion to fluoride at pH7/9 and in synthetic field water (SFW). Percent conversion to photoproducts is calculated in triplicate and given with error estimates of one standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>Direct</th>
<th></th>
<th></th>
<th>Photolysis Treatment</th>
<th></th>
<th></th>
<th>SFW1</th>
<th></th>
<th>SFW2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t₁/₂/hour</td>
<td>% conversion to fluoride</td>
<td>t₁/₂/hour</td>
<td>% conversion to fluoride</td>
<td>t₁/₂/hour</td>
<td>% conversion to fluoride</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPX</td>
<td>29860</td>
<td>0.0230</td>
<td>0.0269</td>
<td>78.1 ± 3.2</td>
<td>61.7 ± 11.0</td>
<td>0.0324</td>
<td>65.9 ± 5.5</td>
<td>0.0956</td>
<td>17.9 ± 0.5</td>
<td></td>
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<tr>
<td>FLU</td>
<td>6233</td>
<td>52.5</td>
<td>68.6</td>
<td>99.2 ± 27.9</td>
<td>64.9 ± 4.2</td>
<td>14.6</td>
<td>96.5 ± 1.9</td>
<td>17.7</td>
<td>95.9 ± 3.4</td>
<td></td>
</tr>
<tr>
<td>FPM</td>
<td>305</td>
<td>110</td>
<td>124</td>
<td>65.3 ± 10.6</td>
<td>66.8 ± 2.0</td>
<td>10.3</td>
<td>75.9 ± 6.4</td>
<td>13.7</td>
<td>46.5 ± 0.9</td>
<td></td>
</tr>
</tbody>
</table>

* ε = Molar absorptivity/M·cm⁻¹.
Figure 4. Profiles of the photolytic behaviour of flamprop-methyl during direct photolysis at pH7 and pH9 and during indirect photolysis in SFW1 and SFW2.
Flamprop-methyl. Flamprop-methyl was extremely persistent, having half-lives of greater than one hundred hours at both pH7 and pH9. The kinetic data for FPM indicate that there is no significant difference in the rate of reactivity at either pH value. Reactivity is increased in SFW as compared to direct photolysis and flamprop-methyl is more reactive in SFW1 than in SFW2. The production of fluoride is the same within error at each pH and in SFW1. However percent conversion to fluoride in SFW2 decreased. The behaviour of flamprop-methyl shows similarity to that of 4-FA in that under each photolysis treatment. FPM shows a significant yield of fluoride. However, unlike 4-FA, FPM shows an increase in the production of fluoride in SFW1 as compared to direct photolysis and a decrease in the production of fluoride in SFW2. Much of the reactivity of FPM must be attributed to the ground state since; unlike 4-FA FPM has been shown to be sensitive to the constituents of the photolysis matrix. Much of the excited state character of 4-FA is attributed to the amino group. It follows then, that the presence of the benzoyl and the alkyl-ester groups present on the N atom of FPM have significantly altered the molecule. i.e. the excited state is no longer important during the loss of fluorine by photolysis. However, the underlying fluoroaniline structure still leads to the production of fluoride as a major degradation pathway.

Ciprofloxacin. Ciprofloxacin was photolytically labile with half-lives at pH7 and pH 9 of 82.8 and 96.8 seconds respectively. The margins of error on replicate experiments indicate that there is no difference between the kinetics for CPX at pH7 and pH9 or in SFW1. Conversion to fluoride for this compound is slightly higher at pH7 than at pH9 or in SFW1. The rate of reactivity of CPX in SFW2 is decreased with respect to the other three treatments and the conversion to fluoride is substantially reduced. The photodefluorination of CPX is a major photodegradation pathway, as is the case for 2-FA, such behaviour is contrary to literature which states that ciprofloxacin does not defluorinate (56). There does not appear to be any other
correlation between the photolytic behaviour of CPX and 2-FA in terms of rates or patterns of photoproduct distribution. CPX has no opportunity to participate in the hydrogen bonding that 2-FA does, therefore removing the barrier to photodegradation. As well, the remainder of the CPX molecule results in a very different absorption profile (see Appendix B for the UV/VIS spectra of each) including a molar absorptivity that is 27× greater than of 2-FA. The data suggest then, that the fluoroaniline moiety contributes to the determination of C-F bond strength however, plays an insignificant role in the determination of the actual photolytic characteristics of CPX such as rate constants or absolute photoproduct amounts.

In conclusion, we have been able to elucidate the photolytic behaviour, direct and indirect, of five fluoroanilines. 2-fluoroaniline, 3-fluoroaniline, 4-fluoroaniline, 2,4-difluoroaniline and 2,6-difluoroanilines. All five follow pseudo-first order kinetics at pH7 and pH9 as well as in two synthetic field water matrices that contain varying levels of three natural water constituents, nitrate, bicarbonate and dissolved organic carbon. Only 2-FA exhibited differences in behaviour at the two pH values. All fluoroanilines exhibited an increase in the rate of photolysis in SFW1 and SFW2 as compared to direct photolysis, with the exception of 4-FA which experienced a decrease in photolysis rate in SFW2 and no difference in SFW1. The fate of fluorine during each photolysis investigation was examined and found largely to be as fluoride. The fate of aromatic fluorine and the strength of the C-F bond on an aniline was shown to be dependent on a number of factors including whether or not degradation was occurring through the excited state, the number of fluorine atoms on the ring and the ability of the fluorine to hydrogen bond. The common photoproduct was fluoride; fluoronitrobenzene was found for all but 3-FA for which photohydrolysis appeared to be the main reaction available. The significance for the behaviour deduced for all the fluoroanilines lies in the fact that photoproducts are generated that pose significant concern as environmental contaminants.
Flumetsulam, flamprop-methyl and ciprofloxacin were also photolysed in each of the above mentioned matrices with the intent of investigating the potential of the fluoroanilines to predict the behaviour of compounds containing a similar moiety. Overall it appears as though the contribution of the fluoroaniline moiety is to provide some lability to the C-F bond resulting in the production of fluoride as a major photoproduct.

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3.4 References


Chapter 4.
Conclusions and Future Work
4.1 Conclusions

Photolysis provides an important pathway for the degradation of many environmental contaminants. The overall objective of this research was to establish whether or not photolysis was a realistic pathway for the production of monohalogenated acids from the degradation of halogenated organic compounds with very specific structural features. The first investigation involving the photolysis of chloroacetanilides was successful in identifying this extremely useful class of herbicides as a significant source of MCA following irradiation under a number of photolysis conditions. In addition, a modified method for the extraction/analysis of the acid from an aqueous matrix was developed that proved superior to those found in the literature.

The significance of the results lies not only in the obvious utility of the development of an improved method, but also that the conditions used for photolysis were designed to mimic the constitution of natural waters. More importantly, of all the conditions investigated it was in synthetic field water that the maximum yield of the acid for all the chloroacetanilides investigated was observed. The fact also that a photoproduct is generated that is more phytotoxic than the parent compound presents serious issues that need to be addressed in terms of regulation of the herbicides themselves.

Our investigation for a photolytic source of MFA was unsuccessful in that the acid was not observed even under conditions designed to provide the most favorable circumstances for acid production. The investigation was however, successful in elucidating the photolytic behaviour of five fluoroanilines, specifically investigating factors affecting the fate of the aromatic fluorine atoms and the strength of the C-F bond. As with the chloroacetanilide study, significant results included the determination of somewhat persistent and potentially harmful photoproducts, including the fluoronitrobenzene and aminophenol isomers from the respective
fluoroanilines, under environmentally relevant conditions. It was also the intention of the investigation to determine what role the fluoroaniline moiety may play in the photolytic fate of the aromatic fluorine in structurally similar commercial compounds. Of those that were investigated namely flumetsulam (FLU), flamprop-methyl (FPM) and ciprofloxacin (CPX), it appears as though the primary degradation pathway for the loss of the fluorine is through scission of the C-F bond, much the same as for the fluoroanilines themselves.

Overall, both investigations provide a template of information for compounds retaining similar structural features to the fluoroanilines and the chloroacetanilides. The information gained during the described research should provide a good basis for the determination of sources of various environmental contaminants of structural similarity to those described. In addition, insight into the photolytic persistence of compounds resembling fluoroanilines or chloroacetanilides has been made available.

4.2 Future Work

Useful research that could supplement what has been found during the investigation of chloroacetanilides includes further investigation into the factors that affect the production of the acid. Specifically, in order to prove that the carbonate radical is the species responsible for initiating the pathway to MCA experiments could be performed. The first step would be to determine the actual reactivity of the pesticide with the carbonate radical using a competition kinetic method whereby carbonate radical would be generated without the use of light (1) to eliminate the possibility of competing reactions. Following the determination of the reactivity with carbonate radical, the matrix should be analyzed for the acid and intermediates leading to it. Such an investigation would provide further support for the proposed pathway described in chapter two.
Two separate investigations that would provide further useful information into the photolytic behaviour of fluoroanilines including: 1) the determination of quantum yields for both the degradation of the parent compound and for the photoproduction of fluoride and 2) an investigation into the incorporation of fluoroanilines into dissolved organic carbon, in particular humic materials, following irradiation.

The first investigation would involve the use of a monochromatic light system since it has been shown that when the light intensity, extinction coefficient and pathlength are known, one can use the slope of a pseudo-first order plot to determine the quantum yield of direct photolysis in a dilute aqueous environment (2). Such information would provide further support for the arguments describing the differences observed in the relative reactivities and photoproduct distribution for each of the five fluoroanilines.

Research into the interaction of anilines with humic materials in an irradiated system would not only provide concrete support for the theories describing the observed behaviour of the fluoroanilines, but would also be novel in nature. That is, although extensive work has been done to investigate the interaction of anilines with humic material (3, 4, 5, 6) no literature to date has looked at the influence of light on the nature of the interaction.

4.3 References

Appendix A.
UV/VIS Spectra
Appendix B.
NMR Spectra
$^1$H NMR - Chloro-$$N$$-methyl acetanilide
$^{19}F$ NMR – Monofluoroacetic acid, dark control.
\(^{19}\text{F NMR} - \text{Monofluoroacetic acid irradiated in 30 mM H}_2\text{O}_2 \text{ for 140 minutes.}\)
$^{19}$F NMR - ~ 10 μM 2-fluoroaniline photoysed in 30mM H$_2$O$_2$. 
$^{19}$F NMR -- 10 µM 3-fluoroaniline photolysed in 30mM H$_2$O$_2$. 
$^{19}$F NMR – ~ 10 $\mu$M 4-fluoroaniline photolysed in 30mM H$_2$O$_2$. 
$^{19}$F NMR -- $\sim 10 \mu M$ 2,4-difluorobenzaldehyde photolyzed in 30mM $H_2O_2$
$^{19}$F NMR – ~ 10 μM 2,6-difluoroaniline photolyzed in 30mM $\text{H}_2\text{O}_2$
$^{19}$F NMR – Concentrated 4-fluoroaniline ($\times$ 60) in SFW1.
$^1$H NMR - Ciprofloxacin.
Appendix C – Photolysis Profiles
Direct Photolysis
Direct Photolysis
Synthetic Field Water I.
Synthetic Field Water 1.

![Graph 1](image1)

![Graph 2](image2)

![Graph 3](image3)
Synthetic Field Water 2.
Synthetic Field Water 2.