DERIVATIZATION OF SMALL ACIDS TO ENHANCE SENSITIVITY IN GAS CHROMATOGRAPHY MASS SPECTROMETRY AND GAS CHROMATOGRAPHY VACUUM ULTRAVIOLET SPECTROSCOPY

By

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THESIS

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ABSTRACT

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The University of Texas at Arlington, 2016

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Disinfection by-products (DBPs) are a significant concern in drinking water quality. Haloacetic acids, which are generated from disinfection processes, are one of the major groups in disinfection by-products. Because they induce potential harmful effects for human health, the US government has already established regulations to control the levels of haloacetic acids in drinking water. In order to control the presence of haloacetic acids in drinking water and monitor other potential harmful compounds, an appropriate analytical method is needed. In this study, a gas chromatography (GC) method was developed for detecting haloacetic acids in water. Three different derivatization reagents were compared for sensitivity enhancement in conjunction with mass spectrometry (MS) and vacuum ultraviolet (VUV) detection. A model study was first performed using acetic acid and then the study was extended to haloacetic acids. The sensitivity of GC-MS and GC-VUV had been increased after the derivatization. However, it also had many shortcomings and challenges that needed to be overcome: (1) the efficiency of derivatization was low; (2) the benzyl alcohol derivatization caused many side reactions in complex samples and generated high intensities of

interference noises. Further study will need to modify the GC-MS and GC-VUV methods, especially for the detection of brominated trihaloacetic acids.

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CHAPTER ONE

Introduction

1. Disinfection by-products (DBPs)

Water is the most important chemical for humans and other creatures. Sources of safe drinking water become more important as the population grows; thus, it is a common practice to filter and disinfect water in order to drink safely. Disinfection by-products are produced as a result of these processes.[1]

Disinfection by-products are the by-products that are produced during the water disinfection process.[2] In order to prevent the occurrence of water-borne diseases, chlorinated disinfection agents are used during the drinking water treatment processes.[3] Chlorinated disinfection agents not only destroy pathogenic bacteria, but also react with nature organic matter.[4] And then it form disinfection by-products such as trihalomethanes (THMs), haloacetic acids (HAAs), and chlorite.[5,6,7]

In 1970, the US Environmental Protection Agency (EPA) determined that organic compounds, which did not appear in original water source, were present after chlorination water treatment.[8] And then in 1974, Rook also found that drinking water contained THMs after the chlorinated disinfection treatment. Therefore, he named the compounds “disinfection by-products” since they were generated through the sterilization process.[9]

THMs and HAAs are the major products produced during the drinking water chlorination process.[10] THMs account for 20% of disinfection by-products. They are the most important water disinfection by-products and they

are also the most common water pollutant.[11] On the other hand, HAAs account for up to 10-13% of disinfection by-products.[12] Generally speaking, the concentration of these two types of disinfection by-products can be the representative index of all chlorinated disinfection by-products produced by the water treatment process.[13]

However, THMs can be removed by heating because boiling points of THMs is about 60 ℃. In contrast, HAAs have boiling points greater than 180 ℃.[14] Therefore, it is difficult to remove HAAs by boiling the water. Humans consume about 2 liters of water every day, so it is easy to be exposed to water containing THMs and HAAs.[15] Therefore, due to the difficulty of removing HAAs, the amount of HAAs present in water becomes an important issue in this day and age.

2. Haloacetic acids

According to US EPA, nine haloacetic acids that contain chlorine and bromine have been detected in water.[16] These are chloroacetic acid (CAA), dichloroacetic acid (DCAA), trichloroacetic acid (TCAA), bromoacetic acid (BAA), dibromoacetic acid (DBAA), tribromoacetic acid (TBAA), bromochloroacetic acid (BCAA), bromodichloroacetic acid (BDCAA), and chlorodibromoacetic acid (CDBAA). Figure 1 shows the structures of the haloacetic acids.

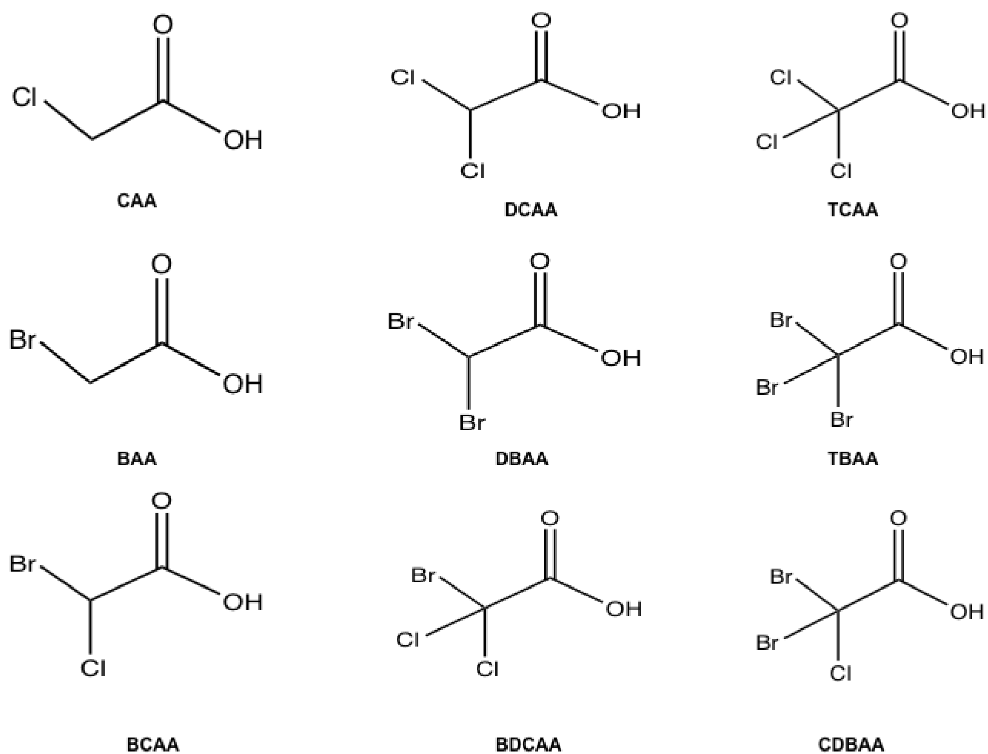


Figure 1. The structures of nine haloacetic acids.

Haloacetic acids are polar, hydrophilic, and nonvolatile molecules.[15] Table 1 shows the pKa value and boiling points for the nine haloacetic acids. The pKa values of haloacetic acids are low. In the typical water environment (pH> 6), they are completely dissociated (>99.9%) and exist primarily in the form of an acetate halide ion.[12]

.

Table 1. The pKa and boiling temperature of haloacetic acids.[14]

Name	pKa	Boiling points (℃)
Bromochloroacetic acid	1.39	215
Bromodichloroacetic acid	0.05	210
Chlorodibromoacetic acid	0.13	234
Dibromoacetic acid	1.48	232
Dichloroacetic acid	1.37	194
Bromoacetic acid	2.73	208
Chloroacetic acid	2.65	189
Tribromoacetic acid	0.22	245
Trichloroacetic acid	0.09	195.5

Because these compounds could cause potential harmful effects for human health, the U.S. EPA have established a maximum contaminant level (MCL) of 60 μg/l for the sum of five HAAs (CAA, DCAA, TCAA, BAA, DBAA) in the first stage of the Disinfectants and Disinfection Byproducts Rules (DDBR).[17] The World Health Organization (WHO) also set MCLs for DCAA (50 μg /l) and TCAA (100 μg /l) in drinking water.[18]

Dichloroacetic acid and trichloroacetic acid can both cause severe irritation in human eyes and skin at high concentration.[19] According to Integrated Risk Information System (IRIS), haloacetic acids are classified as a Group 2B cancer classification (possibly oncogenic to humans) because of the evidence for oncogenic in animal experiment.[20,21]

In research observing long-term toxicity, haloacetic acids were shown to

cause liver tumors in mice exposed to drinking water containing DCAA and TCAA.[22] Moreover, DCAA was a neurotoxic to adult rats when administered through drinking water than when administered by gavage.[23] Therefore, there could be an increasing risk of cancer if one experiences long-term consumption of water with levels of HAAs that exceed the MCL published by the EPA.[24,25]

Analysis of HAAs can be quite difficult. First, HAAs are polar and thermally labile.[26-30] To be analyzed by gas chromatography (GC), HAAs must be derivatized to esters first so that they are volatile enough for GC analysis.[28] Second, the concentration of HAAs in environmental waters is very low. It is difficult to detect the HAAs without improving the sensitivity.[29] Therefore, they cannot be directly injected into GC without derivatization.

The common way to analyze haloacetic acids is based on US EPA Method 552, *Determination of Haloacetic Acids in Drinking Water by Liquid-Liquid Extraction, Derivatization*, *and Gas Chromatography with Electron Capture Detection (ECD) (1990)*, and US EPA Method 552.2, *Determination of Haloacetic Acids and Dalapon in Drinking Water by Liquid-Liquid Extraction, Derivatization and Gas Chromatography with Electron Capture Detection (1995)*. In EPA Method 552.2, water samples are extracted by liquid - liquid extraction, and then derivatize by acidified methanol. The pre-processing steps are complex and time-consuming. Therefore, researchers are trying to find alternate ways to improve upon the traditional methods.

In general, the analysis of haloacetic acids requires a gas chromatograph with an ECD. However, these instrumental techniques have some disadvantages such as the requirement of derivatization, long analysis time,

and susceptible to chromatographic interference.[31] As a result, other analytical methods for the analysis of haloacetic acids have been developed by researchers. These have included instrumental methods incorporating the use of capillary zone electrophoresis, liquid chromatography, and electrochemical analysis.

A) Capillary zone electrophoresis

Capillary electrophoresis (CE) is a sensitive separation technique and is useful in the analysis of small molecules.[32] Capillary zone electrophoresis (CZE) is one of CE method.[33] The extraction method for capillary electrophoresis was off-line liquid-liquid extraction method. However, this method had many disadvantages, such as toxic chemical, inflammable solvent uses, time-consuming extraction time, and poor limits of detection.[34, 35] Therefore, in order to increase the sensitivity in CE, electrokinetic injection had been applied to increase the concentrate of analyte.[36]

B) Liquid chromatography

This method applied ion-pair reversed-phase liquid chromatography with indirect ultraviolet spectrometer to measure HAAs.[37] By applying a C18 column and adding ultraviolet absorbing ions to the mobile phase, HAAs can be measured. However, the report shown that the sensitivity of haloacetic acids was less than GC-ECD in EPA Method 552.[38]

C) Electrochemical analysis[39]

Ion sensors, which are made from conducting polymers, can be used to perform qualitative analysis to identify HAAs based on the different stripping potentials of different analytes.[38] In addition, the current generated is proportional to the concentration of the analyte, so the current can be used for

quantitative analysis.[40]

3. Mass spectrometry and electron capture detector

Mass spectrometry (MS) is a powerful detector and it can be coupled with GC. MS has already been developed over 100 years, so the sensitivity of MS is very high.[41] The mass spectrometer can be divided by two parts: ionization and mass analyzer. Ionization of MS is to utilize electron ionization (EI) or chemical ionization (CI) to ionize the analyte. The mechanism of EI is to bombard the analyte with energetic electrons to produce ions.[42] EI is considered a hard ionization method, because it produces high fragmentation that is helpful for identifying unknown compounds. The mechanism of CI is to generate ions through the impact of analyte with reagent gas.[43] Compared to EI, CI is considered a soft ionization method because it generates less fragmentation that is helpful for the determination of molecular mass. Negative chemical ionization (NCI) and electrospray ionization (ESI) are also CI method and can be used for HAAs.[40,44] Then, ions pass through the electric or magnetic field and are separated, basing on the analyte a mass to charge ratio (m/z). There are many different types of mass analyzers have been using today. Quadrupole mass spectrometer is one type of mass analyzers and has been widely used.[45] It contains four parallel metal rods, which were applied voltage. So, by changing the voltage, only the certain m/z ions can reach the detector.[46] Ion trap mass spectrometer is another type of mass analyzers. Ion trap works similar to quadrupole mass analyzer, but ions are trapped in the quadrupole radio frequency field and ejected consecutive.[47]

On the other hand, electron capture detector is also a common detector

coupled with GC.[48] The mechanism of ECD is to attach electrons on the analyte by electron capture ionization and detect electron-absorbing components. ECD use radionuclide ^{63}Ni to collide with make-up gas (usually nitrogen) and generate free electrons. The electrons generate the background current. When the analyte is carried into the detector, highly electronegative compounds capture the electron and the background current decreases.[49] Therefore, ECD is very sensitive to highly electronegative compounds, such as halogenated compounds.

4. Vacuum Ultraviolet (VUV) detector

To overcome the limitation of GC-MS and to improve the efficiency and capability for the application of GC, a novel vacuum ultraviolet (VUV) technique has been recently developed.[50]

The spectral range for vacuum ultraviolet (VUV) light is from 115 nm to 185 nm. In this range, photons are able to probe the excitation of molecular species and chemical bond, especially $\sigma \rightarrow \sigma^*$ and short wavelength high probability $\pi \rightarrow \pi^*$. The compound which is not able to be detected in traditional UV/vis absorption spectroscopy can be detected by VUV detector. Because lacking appropriate light sources that emit high intensity and successive radiation and lacking detectors that produce linear signal responses in the VUV region, the previous application for VUV absorption spectral measurement was limited to synchrotron facilities.

Now, analytical measurements in this wavelength range have been a recent development. The general schematic of the VUV instrument and operation principles of the GC-VUV instrument is shown on Figure 2.

Through a heated transfer line (usually 300 ℃) that contains a deactivated stainless steel capillary that is thermally insulated, the VUV detector can be connected to any standard GC system because the analyte has already been vaporized. After eluting from the GC column, the analyte enters the heated transfer line. At the end of transfer line, make-up gas is introduced.

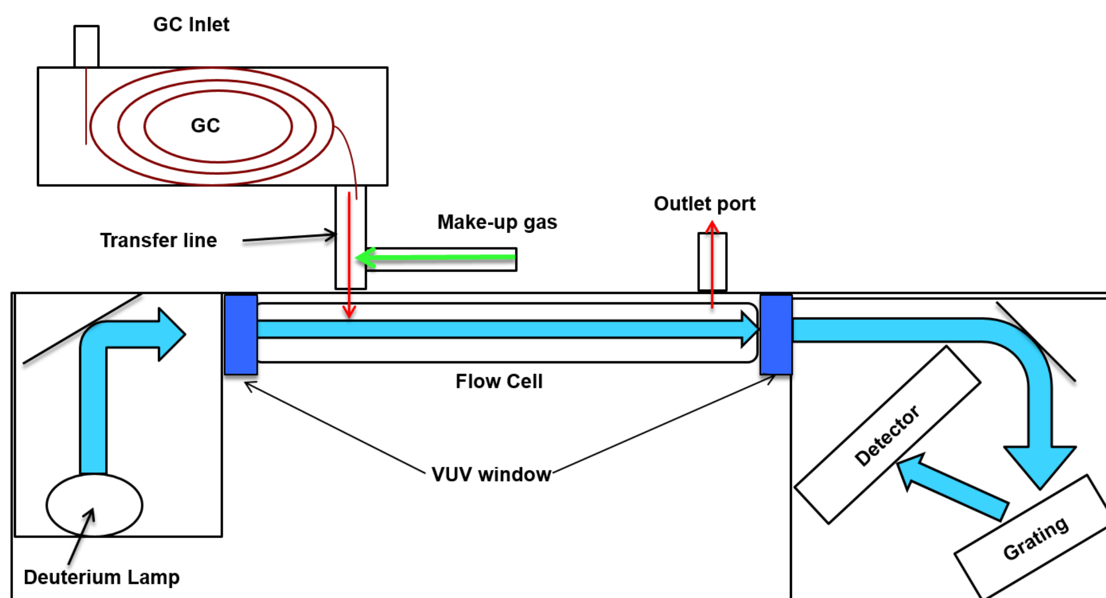


Figure 2. The scheme of GC coupled with VUV detector.[50]

The detector response is proportional to the amount of analyte per unit time since the VUV detector is mass-sensitive. Therefore, the sensitivity of detector can be improved by adjusting the residence time of analyte in the flow cell. A make-up gas can be argon or nitrogen. The flow rate of make-up gas can be adjusted in order to change the residence time of analyte in the flow cell and to enhance the sensitivity. For higher concentration analytes, a higher make-up flow is applied in order to avoiding detector saturation. In contrast, a lower make-up flow can be used for weaker absorbing (or lower concentration) compounds. Through allowing more molecules to be detected per unit time, the sensitivity of analyte can be improved. Moreover, introducing

make-up gas into the flow cell also avoids potential band broadening generated by the large volume flow cell.

The analyte vapor enters the VUV flow cell (10 cm path length; 80 μL volume) where it absorbs VUV (and some UV) light. A deuterium lamp is used as light source and the VUV windows are made from MgF_2. The VUV window can let higher than 115 nm wavelengths to pass through. The key to have the ability of collecting high quality VUV (and some UV) absorption data between 115-240 nm from the flow cell is to use specially coated reflective optics and a back-thinned charged coupled device (CCD) light path monitor. The CCD is similar to photodiode array (PDA). It have many acceptors and can detect the different wavelength from the grating simultaneously. Therefore, it can simultaneously evaluate absorption features across the spectrum for peaks eluting from the GC column.

When each run begins, the detector collects dark and background scan at the same time in order to carry out background subtraction. Data acquisition rate for the GC-VUV can be as fast as 100 Hz, making measurements compatible with fast GC applications. After passing through the flow cell, following analyte come out through the outlet port. Absorption data are sent to the data station for data analysis.

In this study, vacuum ultraviolet (VUV) technique has been applied to the application for the analysis of haloacetic acids. The VUV detector is suitable for many of the limitations for haloacetic acids analysis. First, unlike the electron capture detector, the VUV detector is a universal detector. It can provide fast measurement of absorption spectra from 115 to 240 nm, where

almost all chemical species can absorb. Second, the VUV detector can perform excellent qualitative and quantitative analysis for haloacetic acids. The quantitation of VUV analysis follows standard Beer-Lambert law principles, and the absolute amount (i.e., the number of molecules) in the detector cell can be determined if an absorption cross-section for the chemical compound is known. Third, the VUV detector can also be applied to analyze labile compounds that cannot be analyzed by MS because it does not need ionization.

5. Derivatization

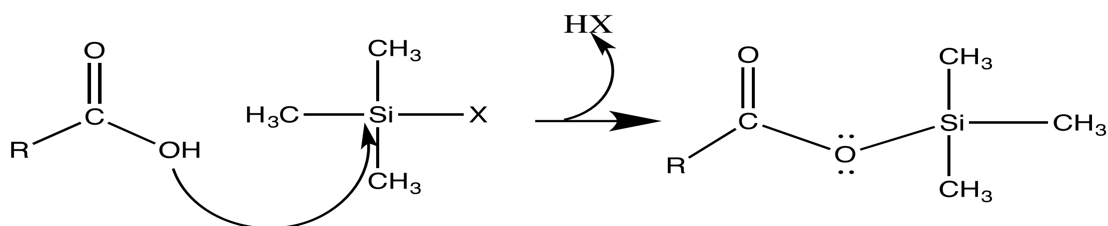
Derivatization in GC analysis can be defined as pre-processing techniques that primarily changes analyte functional group in order to increase the efficiency of GC analysis.[51] The analyte will be modified through derivatization reaction and will increase the volatility so that the analyte can elute at reasonable temperatures with no thermal decomposition. In GC analysis, samples containing functional groups, such as -OH, -NH, -SH, and –COOH, are the primary issue to be considered because these functional groups tend to interact with each other and form intermolecular hydrogen bonds.[52] These intermolecular hydrogen bonds affect the inherent volatility of compounds. It also interacts with column packing materials and analyte itself. Therefore, by modifying the functional group, derivatization process can increases the volatility of the compound. It also can reduce analyte adsorption in the GC system, improve detector sensitivity and peak symmetry.[53]

Generally speaking, the goal of the derivatization is to improve the stability, efficiency, and detectability in GC. In this study, there are two type of

derivatization mechanism base on the generated product have been applied: silylation and alkylation. These general processes are discussed below.

a. Silylation

Silylation is the most widely used derivatization method because it can easily increase the volatility of the analyte. The silylation reaction is a nucleophilic attack reaction. The mechanism of silylation reaction is to replace the active hydrogen (in -OH, -COOH, $-NH_2$, and -SH groups) with a trimethylsilyl (TMS) group. The mechanism is shown below. X is the leaving group.

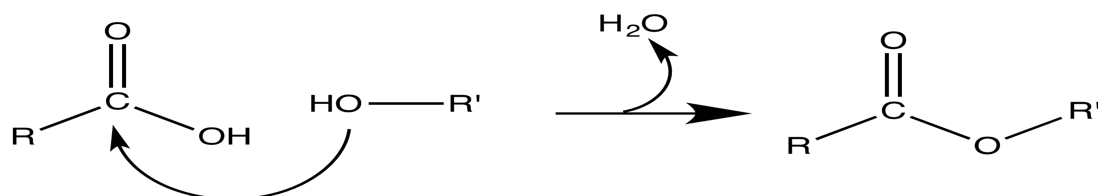


The derivatization products from silylation are more volatile and can generate narrow and symmetrical peaks. In this paper, N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) had been considered as silylation derivatization reagent. It has similar reactivity as Bistrimethylsilylacetamide (BSA) and Bistrimethylsilyltrifluoroacetamide (BSTFA). MSTFA is more volatile than BSA or BSTFA but with similar silylation strength.[54] It is useful in the analysis of volatile trace compound and in preparation of volatile and thermally stable derivatives for GC and MS analysis.

b. Alkylation

Alkylation is usually used for protecting active hydrogen in analyte or first step of further derivatization.[51] The mechanism of alkylation reaction involves

the replacement of active hydrogen by an aliphatic or aliphatic-aromatic (e.g., benzyl) group. The general reaction is shown below.



The alkylation reaction in GC analysis mostly converts organic acids into esters, especially methyl esters. By doing this derivatization reaction, the volatility of analyte will increase and it can provide better chromatograms than free acids when using GC analysis. For analytical work, esterification is better reacted in the presence of a volatile catalyst such as hydrogen chloride or thionyl chloride, which can be removed along with excess alcohol. Hydrogen chloride is the favored catalyst because of its acid strength and it is readily removed.

In this study, trimethylanilinium hydroxide in methanol (TMPAH) and benzyl alcohol (BnOH) had been considered as alkylation derivatization reagents. Through these two mechanisms, highly polar materials such as haloacetic acids can be suitable for GC analysis by increasing their volatility and sensitivity.

CHAPTER TWO

Detection of Acetic Acid and Haloacetic Acids in Water

In this study, the advantages of GC-VUV detection and derivatization reactions had been combine. Derivatization reagents had been investigated for their potential to enhance the sensitivity for haloacetic acids determination. Acetic acid had been used as an initial model analyte. The results obtained using gas chromatography - mass spectrometry and gas chromatography - vacuum ultraviolet spectroscopy were compared.

2.1 Experimental for Acetic Acid

Initial experiments were performed using acetic acid to develop the methods and perform an initial comparison of GC-MS and GC-VUV performance. Three different derivatization reagents were tested and evaluated based on their efficiency to derivatize the target compounds, as well as to provide enhanced sensitivity.

2.1.1 Reagents and Chemicals

All solutions were prepared from analytical reagent grade chemicals. Acetic acid (100%, ACS grade) and hydrochloric acid (ACS grade) were purchased from EMD Millipore (Billerica, MA). Methyl acetate (99%) was purchased from MCB reagents (Cincinnati, OH). Derivatization reagent N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) and trimethylanilinium hydroxide (TMPAH) in methanol solution were purchased from Restek Corporation (Bellefonte, PA). Benzyl alcohol (99%) and benzyl acetate (99%) were purchased from Alfa Aesar (Haverhill, MA).

2.1.2 Sample Preparation and Derivatization

10 μL of acetic acid was transferred to a sample vial for GC-MS and then diluted with 990 μL of methanol (capillary GC grade, ≥99.9%). This solution was then injected in GC-MS and GC-VUV to provide a signal for the underivatized analyte as a basis for comparison.

The acetic acid was then derivatized by the following reagents:

Derivatization with N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA)

10 μL of acetic acid was transferred to a sample vial for GC-MS and 300 μL of N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) reagent was added. 30 μL of hydrochloric acid was then added as a catalyst to drive the reaction.

The vial was sealed and shaken for 2 min. It was heated up to 60 ℃ for 1 hour and then cooled down to room temperature. Finally 660 μL of methyl tert-butyl ether (MTBE) as solvent was added and the resulting solution was injected in GC-MS and GC-VUV.

The product must be injected before 24 hours to avoid degradation.[53]

Derivatization with Trimethylanilinium hydroxide (TMPAH) in methanol solution

10 μL of acetic acid was transferred to a sample vial for GC-MS and 300 μL of trimethylanilinium hydroxide (TMPAH) in methanol solution was added. The vial was sealed and shaken for 2 min. It was heated to 70 ℃ for 30 minutes and then cooled down to room temperature. 690 μL of MTBE as

solvent was added and the solution was injected into the GC-MS and GC-VUV systems.

The product must be injected within 24 hour.[53]

Derivatization with Benzyl alcohol

10 μL of acetic acid was transferred to a sample vial for GC-MS and 960 μL of benzyl alcohol was added as derivatization reagent. 30 μL of hydrochloric acid was added as a catalyst to drive the reaction. In order to drive the esterification reaction, water has to be removed when it formed. The vial was sealed, shaken for 2 min, heated to 60 ℃ for 3 hours and then cooled down to room temperature. At last, the solution was injected into GC-MS and GC-VUV.

The product must be injected within 24 hour.

2.1.3 Instrumentation

GC-MS Analysis

For GC-MS analysis, a GCMS-TQ8030 from Shimadzu Scientific Instruments, Inc. (Columbia, MD) was used for analyzing acetic acid and acetic acid derivatized products. An AOC-20s autosampler from Shimadzu was used for injection sample and a 30 m x 0.25 mm x 0.25 μm film thickness Stabilwax-DA capillary column from Restek Corporation was used.

The injector temperature was 250 ℃ and the transfer line was maintained at 250 ℃. The carrier gas was helium and the linear velocity was set to 50 cm/s and held constant through the analysis. 0.2 μL of sample was injected with a split ratio of 100:1. The temperature program was as shown in Table 2.

Table 2. The temperature program for analysis of acetic acid and its derivatives for GC-MS

Temperature Program	Initial temperature(℃)	Rate (℃/min)	Final temperature (℃)
Acetic acid	40, hold 0.7 min	10	120, hold 5 min
Acetic acid with TMPAH	40, hold 0.7 min	10	120, hold 5 min
Acetic acid with MSTFA	40, hold 0.7 min	10	120, hold 5 min
Acetic acid with BnOH	40, hold 0.7 min	10	200, hold 5 min

For the setting of MS, the ion source temperature was 250 ℃ and the electron ionization energy was 70 eV. The Mass Spectrometer Detector was operated in the electron ionization mode. Positive fragment ions were analyzed by using SCAN mode at range over 40–400 m/z. Select ions were then monitored using selected ion monitoring (SIM) mode in order to achieve better sensitivity and better quantitation.

For the TMPAH derivatization, the fragments 59 m/z, $[COOCH_3]^+$ were chosen corresponding to the methyl-ester derivatives of acetic acid. For the MSTFA derivatization, the fragments 73 m/z, $[Si(CH_3)_3]^+$, values were chosen corresponding to the silylation derivatives of acetic acid.[55] For the BnOH

derivatization, the fragment 91 m/z, $[C_7H_7]^+$ values were chosen corresponding to the benzylation derivatives of acetic acid.

GC-VUV Analysis

For GC-VUV, VUV absorption spectra were recorded on a VGA-100 VUV detector from VUV Analytics, Inc., (Cedar Park, TX), which was coupled to a Shimadzu GC-2010 gas chromatograph. An AOC-20s autosampler from Shimadzu was used for sample injection and a 30 m x 0.25 mm x 0.25 μm film thickness Stabilwax-DA capillary column from Restek Corporation was used.

The temperature of the GC injector was 250 ℃. The temperature of the VUV transfer line and the flow cell was 275 ℃. The pressure of makeup gas was set to 0.25 psi throughout the experiments. Helium was used as the GC carrier gas and nitrogen was used as makeup gas. The linear velocity was set to 30 cm/s and held constant through the analysis. 0.5 μL of sample was injected with a split ratio of 50: 1. The temperature program was as shown in Table 3.

Table 3. The temperature program of acetic acid and its derivatives by using GC-VUV.

Temperature Program	Initial temperature(℃)	Rate (℃/min)	Final temperature (℃)
Acetic acid	40, hold 2 min	10	120, hold 5 min
Acetic acid with TMPAH	40, hold 2 min	10	150, hold 5 min
Acetic acid with MSTFA	40, hold 2 min	10	150, hold 5 min
Acetic acid with BnOH	40, hold 2 min	10	150, hold 5 min

2.1.4 Results and Discussion

Figure 3 showed chromatograms of acetic acid and all three derivatives by GC-MS. The Figure 4 showed chromatograms of acetic acid and all three derivatives by GC-VUV. From chromatograms, it was apparent that the peak shape of analyte was improved. Moreover, after the derivatization, acetic acid became more volatile and eluted faster than in its underivatized form, as expected. The alkylation derivative (TMPAH) and silylation derivative was eluted faster than underivatized products, which mean the derivatization reduced the analysis time.

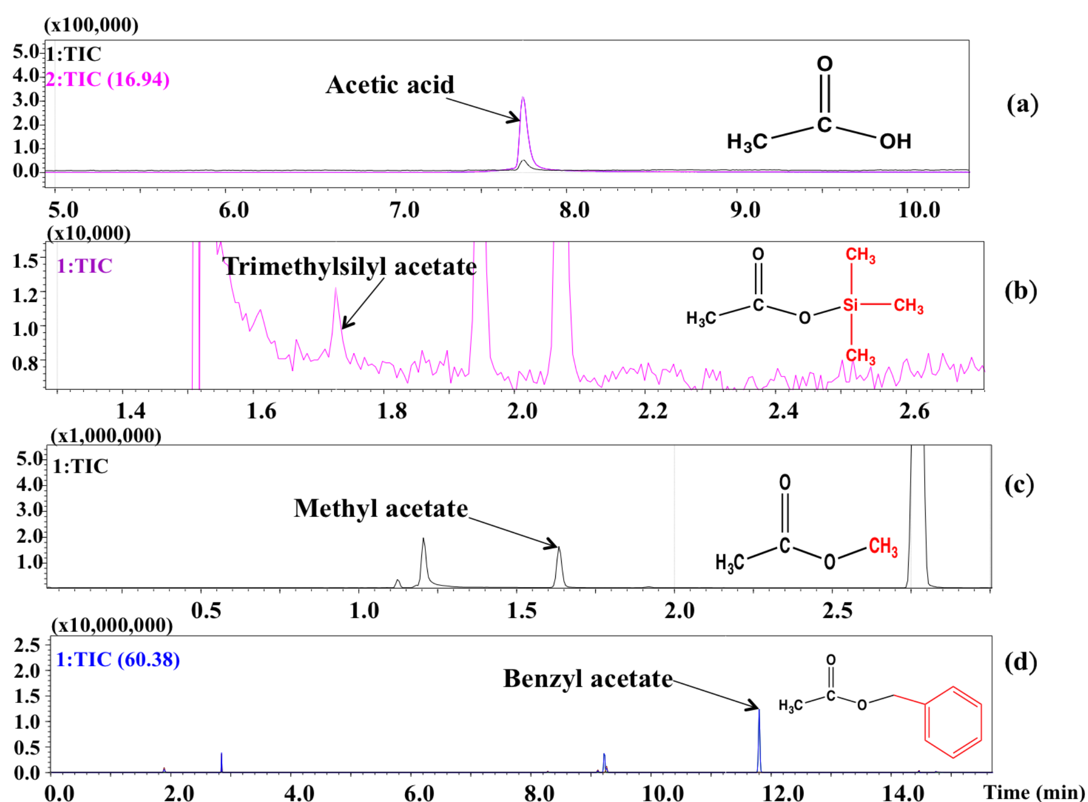


Figure 3. Chromatograms by GC-MS (a) acetic acid. (b) acetic acid with TMPAH derivatization. (c) acetic acid with MSTFA derivatization. (d) acetic acid with BnOH derivatization.

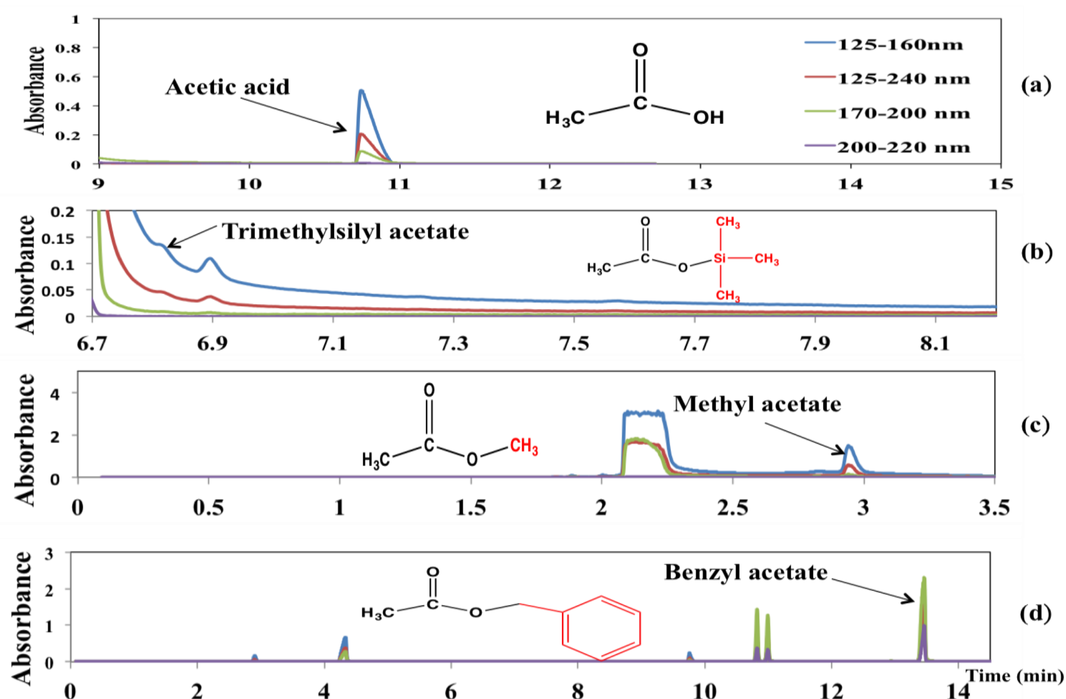


Figure 4. Chromatograms by GC-VUV (a) acetic acid. (b) acetic acid with MSTFA derivatization. (c) acetic acid with TMPAH derivatization. (d) acetic acid with BnOH derivatization.

Figure 5 showed the VUV spectra of standards for acetic acid, methyl acetate, and benzyl acetate. The concentration of each standard compounds was 0.1 M. Benzyl acetate was shown the highest absorption in GC-VUV because the benzyl-group is a strong chromophore and will enhance the absorption of VUV/UV light.

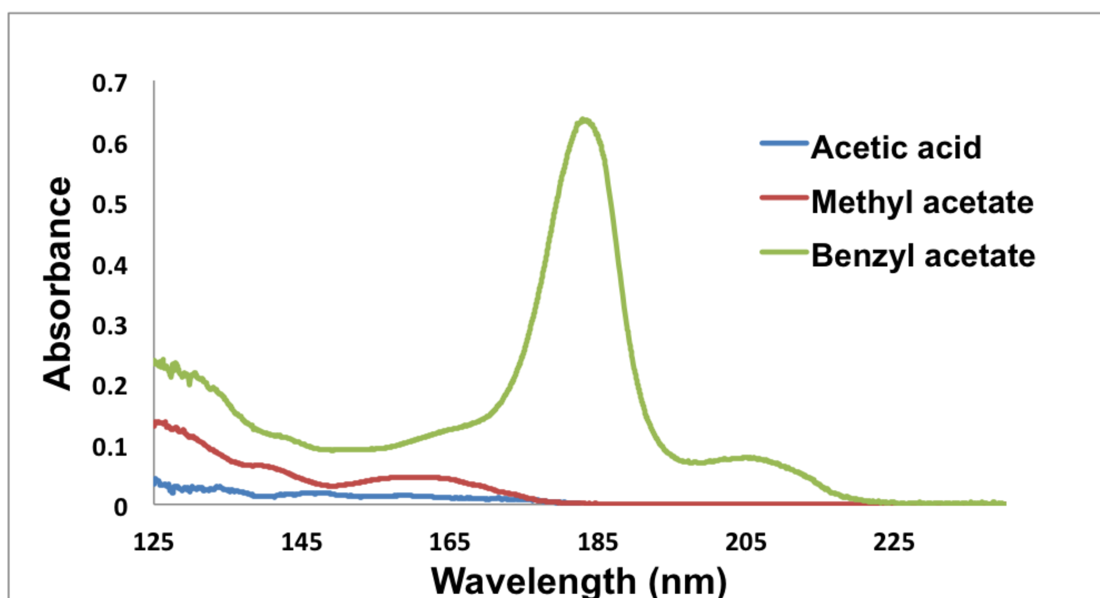


Figure 5. The VUV spectra of standard compounds for acetic acid, methyl acetate, and benzyl acetate. The concentration of each standard compounds was 0.1 M.

Figure 6 showed the signal to noise ratio (S/N) from different wavelength filters in the VUV detector. The value of S/N for acetic acid and it derivatives were shown in Table 4. After applying 157-162 nm wavelength filters, the S/N of acetic acid was 1.38 times higher and the S/N of methyl acetate was 1.82 times higher than 125-160 nm wavelength filters. The 157-162 nm was a low noise filter because the lamp exhibited the greatest output in this range. According to Figure 6, methyl acetate was shown high absorption in 125-160 nm but the output of the deuterium lamp was low in that region; on the other hand, the absorption of methyl acetate in 157-162 nm was lower than in 125-

160 nm. However, the deuterium lamp showed the strongest output in that region. As a result, the S/N of acetic acid and methyl acetate in GC-VUV can be optimized by applying the 157-162 nm wavelength filters.

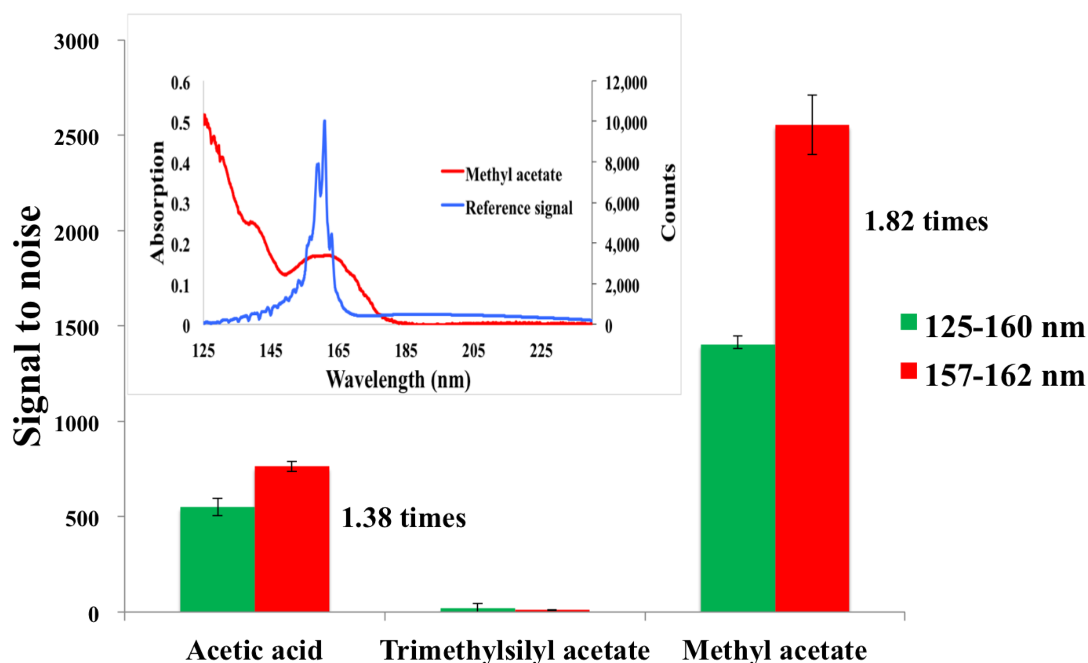


Figure 6. The S/N of acetic acid and methyl acetate increased after applied 157-162 nm wavelength filters in GC-VUV.

Table 4. The S/N of acetic acid and methyl acetate from different wavelength filters by GC-VUV.

Signal to Noise	125-160 nm	157-162 nm
	Average	Average
Acetic acid	551±46	764±26
Trimethylsily acetate	22±23	10.5±3.4
Methyl acetate	1405±45	2560±160

After the S/N for VUV detection was optimized, the S/N of acetic acid before and after derivatization was compared using both GC-MS and GC-VUV detectors. The results were shown in Figure 7. The result of MSTFA derivatization showed low sensitivity in both GC-MS and GC-VUV. The derivatization from MSTFA generated many by-products, which caused more intense interferences.56 And more importantly, MSTFA derivatives were susceptible to moisture and this negatively affected the efficiency of derivatization. However, it was apparent that the S/N of methyl acetate and benzyl acetate increased significantly relative it's the underivatized acetic acid. The S/N of methyl acetate was 1.86 times higher in GC-MS and 3.34 times higher in GC-VUV. The S/N of benzyl acetate was 10.40 times higher in GC-MS and >11.8 times higher in GC-VUV. Because the absorption signal of benzyl acetate in GC-VUV was saturated at certain wavelengths, the S/N was estimated using a fit method.

When n analytes were simultaneously present in the flow cell, as was the case of coelution, the absorption for each component may be solved using the following linear combination

$$A = \Sigma f_i A_{i,ref},\ i = 1 \text{ to } n$$

A was the calculated absorbance spectrum and f_i were the fit parameters to be optimized while $A_{i,ref}$ were the basic functions (library spectra).[60] The model absorbance spectrum was usually applied to calculate the deconvolution of analytes, but it also can be used to calculate wavelength regions that were saturated, i.e. when the absorbance exceeded 1.1. In this case, the above equation reduced to a simple, single component equation where f was determined for the non-saturated portion of the signal. By knowing this

constant, f, the entire signal may be recovered. However, there was a caveat, and that was that the greater the degree of signal saturation was, the worse this fit method will work since there will be fewer wavelength regions available to calculate f.

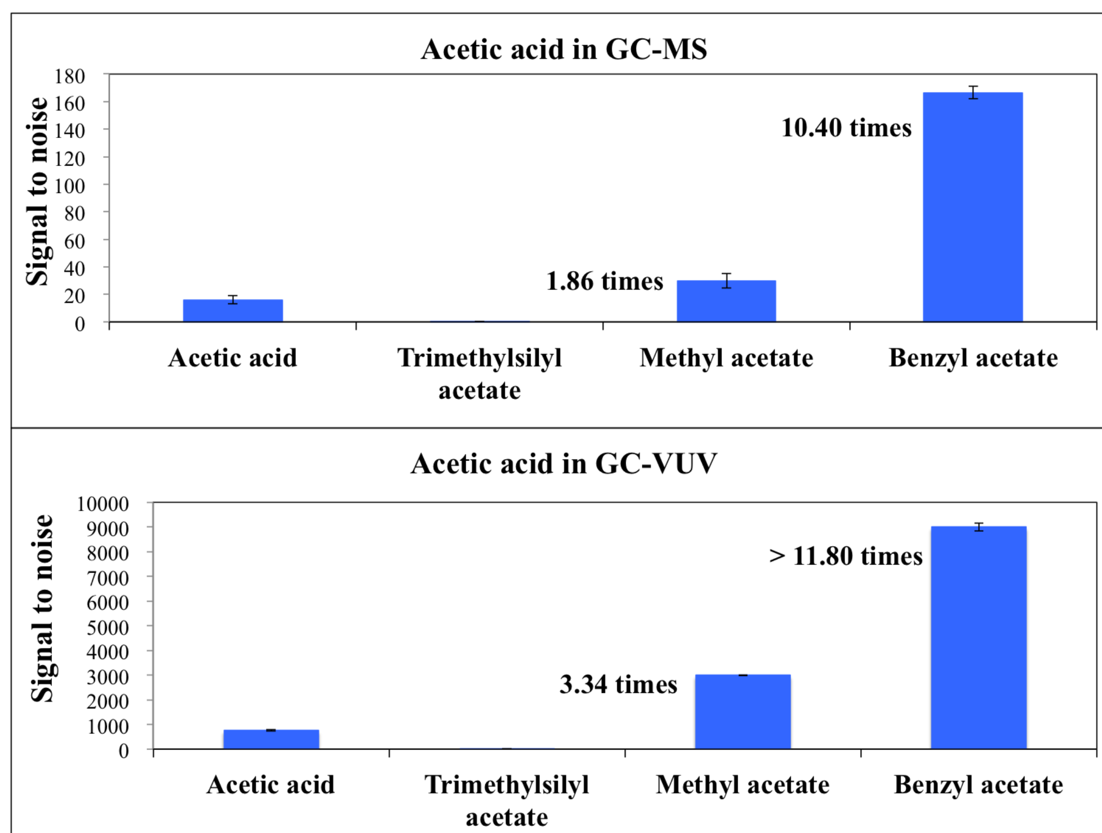


Figure 7. The signal to noise of acetic acid and its derivatized products in GC-MS and GC-VUV

Table 5 summarized the three different derivatization processes. Compared to the others, the alkylation derivatization (TMPAH) requires less reaction time and has fewer side reactions. TMPAH can provide convenient, fast, quantitative alkylation derivatization. The benzyl alcohol derivatization had shown many advantages. First, although the benzylation derivatization required the longest reaction time and analysis time, the intensity of benzylation product was higher than others reactions. Second, the

benzylation product can be preserved longer time than other derivatives. Third, the aromatic group will not only prevent the formation of intermolecular hydrogen bonds, but also enhance the sensitivity of VUV because aromatic groups are known to be strong chromophores for absorption in the VUV and UV range of light.

Table 5. The comparison of three different derivatization reagents.

	TMPAH	MSTFA	Benzyl alcohol
Reaction time	30 min	60 min	180 min
Analysis time	15 min	15 min	20 min
Advantage	Reaction fastest	Intensity lowest	Intensity highest

Further step was to apply the developed method in the study of haloacetic acid in water. The TMPAH reagent and benzyl alcohol were chosen to derivatize the analyte because of the reasons, which were discussed above.

2.2 Experimental for Haloacetic Acids and Real Sample Analysis

After the testing of acetic acid, the previous method for acetic acid was improved and applied in analysis of haloacetic acids; ideally, in order to increase the sensitivity for their determination in water.

2.2.1 Reagents and Chemicals

ACS grade H_2SO_4 was purchased from EMD Millipore. $CuSO_4$ and Na_2SO_4 were purchased from Sigma-Aldrich (Saint Louis, MO). MTBE was purchased from ACROS (99%, extra dry) without further purification. A HAAs standard mixture was purchased from Restek. The standard contained nine HAAs with different concentrations in MTBE (Table 6). The water sample to be tested for the presence of HAAs was collected from a laboratory tap at U.T. Arlington.

Table 6. Different concentration of HAAs standard.

Name	Concentration
Bromochloroacetic acid	400 ppm
Bromodichloroacetic acid	400 ppm
Chlorodibromoacetic acid	1000 ppm
Dibromoacetic acid	200 ppm
Dichloroacetic acid	600 ppm
Bromoacetic acid	400 ppm
Chloroacetic acid	600 ppm
Tribromoacetic acid	2000 ppm
Trichloroacetic acid	200 ppm

2.2.2 Preparation and Derivatization of Tap Water Sample

The sample preparation was based on EPA method 552.2.[16]

40 mL of water sample was placed into a 50-mL amber glass vial with a polypropylene screw cap and PTFE-faced septum. The sample was allowed to equilibrate to room temperature. 1 mL of concentrated sulfuric acid was added to adjust pH < 0.5.

2 g of copper II sulfate pentahydrate was quickly added and the mixture was shaken until the salt dissolved. The reason why copper II sulfate pentahydrate was added was to make the aqueous phase blue, so it can easily be distinguished from the organic phase when performing the microextraction. With the help of heat generated from sulfuric acid, the

anhydrous sodium sulfate quickly dissolved in solution. 1 mL of MTBE was added as extractant. 4 g of anhydrous sodium sulfate was quickly added. Sodium sulfate was added to increase the ionic strength of the aqueous phase and thus further drive the haloacetic acids into the organic phase. The vial was sealed, shaken for 2 min, and allow the organic layer to separate from the water phase for a minimum of 10 minutes. 0.75 mL of the upper MTBE phase was then transferred to a 1 mL vial.

The extract was derivatized by the following reagents:

Derivatization with Trimethylanilinium hydroxide (TMPAH) in methanol solution

50 μL of extract was transferred to a sample vial and 500 μL of trimethylanilinium hydroxide (TMPAH) in methanol solution was added. In order to drive the esterification reaction, water had to be removed when it formed. Thus, 1 g of sodium sulfate was added to the sample. The sodium sulfate did not completely dissolve

The vial was sealed and shaken for 2 minutes. It was heated to 70 ℃ for 15 minutes and then cooled to room temperature. At last, 450 μL of MTBE was added as solvent and the solution was injected into the GC-MS and GC-VUV instruments. The product must be injected within 24 hour.

Derivatization with Benzyl alcohol

50 μL of the tap water extract was transferred to a sample vial and 920 μL benzyl alcohol was added as derivatization reagent. To this mixture, 30 μL of hydrochloric acid was added as catalyst to drive the reaction. In order to

drive the esterification reaction, water has to be removed when it formed. Water was removed by adding 1 g of sodium sulfate to the sample.

The vial was sealed and shaken for 2 minutes. It was heated to 60 ℃ for 3 hours and then cooled to room temperature. The sample was then injected into the GC-MS and GC-VUV instruments. The product must be injected within 24 hour.

2.2.3 Instrumentation

GC-MS Analysis

GCMS-TQ8030 from Shimadzu was applied for analyzing nine haloacetic acids detection. An AOC-20s autosampler from Shimadzu was used for sample injection and Stabilwax-DA capillary column (30 m x 0.25 mm x 0.25 μm film thickness) from Restek Corporation was used.

The injector temperature was 250 ℃ and the transfer line was maintained at 250 ℃. The carrier gas was helium and the linear velocity was set to 50 cm/s and held constant through the analysis. The temperature program was as shown in Table 7.

Table 7. The temperature program of haloacetic acids and derivatizes in GC-MS. 1 μL of sample was injected with split ratio of 10:1.

Temperature Program	Initial temperature(℃)	Rate(℃/min)	Final temperature (℃)
Haloacetic acids	30, hold 0.7 min	4	120, hold 5 min
Haloacetic acids with TMPAH	30, hold 0.7 min	4	130, hold 5 min
Haloacetic acids with BnOH	30, hold 0.7 min	10	220, hold 10 min
Water sample	30, hold 0.7 min	4	130, hold 5 min

The ion source temperature was 250 ℃ and the electron energy was 70 eV. Positive fragment ions were analyzed by using SCAN mode at a range over 50-400 m/z. SIM mode was used in order to achieve the better sensitivity for quantitative assessments.

For the TMPAH derivatization, the fragment of 59 m/z, $[COOCH_3]^+$, and 49 m/z, $[CH_2Cl^{35}]^+$, values were chosen corresponding to the methyl-ester derivatives of the haloacetic acids.[57] For the BnOH derivatization, the fragment of 91 m/z values, $[C_7H_7]^+$, were chosen corresponding to the benzylation derivatives of haloacetic acids.

GC-VUV Analysis

For GC-VUV analysis, VUV absorption spectra were recorded on a VGA-100 VUV detector, which was coupled to a Shimadzu GC-2010 gas chromatograph. An AOC-20s autosampler from Shimadzu was used for sample injection and a 30 m x 0.25 mm x 0.25 μm film thickness Stabilwax-DA capillary column from Restek Corporation was used.

The temperature of the GC injector was 250 ℃. The temperature of the VUV transfer line and the flow cell was 300 ℃ and 275 ℃, respectively. The pressure of makeup gas was set to 0.25 psi throughout the experiments. Helium was used as the GC carrier gas and nitrogen was used as makeup gas. The linear velocity was set to 30 cm/s and held constant through the analysis. The temperature program was as shown in Table 8.

Table 8. The temperature program for analysis of haloacetic acids and their derivatives by GC-VUV. 1 μL of sample was injected in splitless mode.

Temperature Program	Initial temperature(℃)	Rate (℃/min)	Final temperature (℃)
Haloacetic acids	30, hold 2 min	4	130, hold 5 min
Haloacetic acids with TMPAH	30, hold 2 min	4	130, hold 5 min
Haloacetic acids with BnOH	30, hold 5 min	10	220, hold 5 min
Water sample	30, hold 2 min	4	200, hold 5 min

2.2.4 Results and Discussion

The Figure 8 showed the chromatogram of haloacetic acids and the derivatized products by GC-MS. The Figure 9 showed the chromatogram of haloacetic acids and it derivatized product by GC-VUV. For the underivatized haloacetic acids, eight had been observed and transformed to halomethanes, based on the GC-MS result. Although the CAA and BAA had low intensity, other haloacetic acids were separated well and had good sensitivity. However, BCAA was difficult to detect during this method. Perhaps, it was caused due to the decomposition of BCAA or its coelution with the solvent peak. In GC-VUV, only five HAAs (TCAA, DBAA, BDCAA, CDBAA, and TBAA) had been observed and transformed to halomethanes. BDCAA, CDBAA, and TBAA had high intensity peak and were separated well. Because other four haloacetic acids eluted fast, it will be covered by the solvent peak.

After HAAs derivatized with TMPAH, five of the HAAs derivatives (CA-OMe, BCA-OMe, DCA-OMe, DBA-OMe, and TCA-OMe) had been observed by GC-MS. The intensity of each peak increased after the derivatization and BCAA, which could not be detected before the derivatization, was now observed. The unsuccessful derivatization for other haloacetic acids can be caused by the decarboxylation reactions.[30] The decarboxylation reactions of haloacetic acids were influenced by the electronegativity of the halide group. The haloacetic acids will transform to halomethane and will affect the derivatization efficiency. Therefore, because of the decarboxylation, brominated trihaloacetic acids had very low yield in derivatization. For GC-VUV, there were four HAAs (CA-OMe, DCA-OMe, TCA-OMe, and BCA-OMe) had been observed. The signal of DBA-OMe was not observed by GC-VUV.

This can be caused by the high intensities of interference signals. The reasons for other missing peaks were as discussed above.

After the benzylation derivatization, only three of the HAAs (CA-OBn, BA-OBn, and DCA-OBn) had been detected in the benzyl derivatized form by GC-MS. One of the reasons was that the derivatization reaction was hindered due to the steric effect, since the benzyl-group was very bulky functional group.[58] Another reason was that the benzylation derivatization will cause many side reactions and generate lot of by-products.[59] Therefore, the interference noises were very high. For the SIM mode in GC-MS, the fragment of 91 m/z values, $[C_7H_7]^+$, was not very selective. Other more selective ion should be studied in order to minimize the interference noises. For GC-VUV, only two of the HAAs (CA-OBn and BA-OBn) had been observed. Although BnOH derivatization increased the intensity of analyte, it also increased the interference noises. Moreover, it was difficult to identify unknown compounds using the VUV detector, because they were not in the VUV spectral library. Therefore, optimization of the wavelength filters should be studied in order to increase the sensitivity.

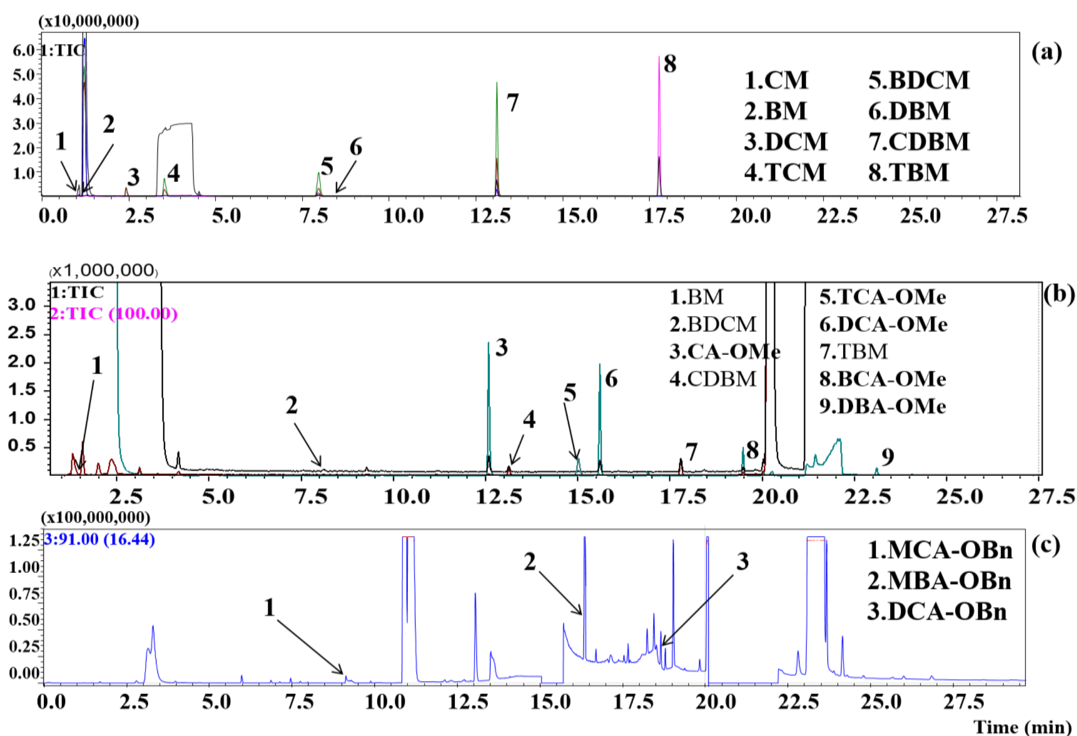


Figure 8. Chromatograms by GC-MS (a) underivatized HAAs standard. (b) HAAs standard with TMPAH derivatization. (c) HAAs standard with BnOH derivatization.

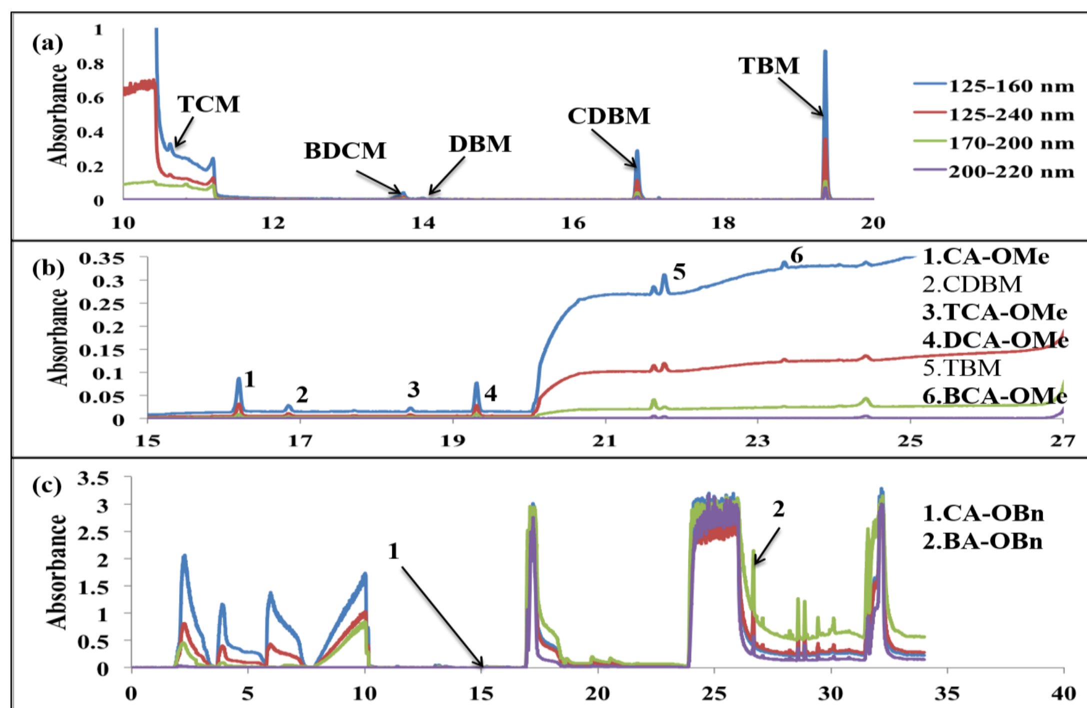


Figure 9. Chromatograms by GC-VUV (a) underivatized HAAs standard. (b) HAAs standard with TMPAH derivatization. (c) HAAs standard with BnOH derivatization.

Figure 10 showed the sensitivity of HAAs standard before and after the TMPAH derivatization in GC-MS and GC-VUV. For GC-MS, the S/N of CAA was 3486 times higher, the S/N of DCAA was 275 times higher, the S/N of DBAA was 468 times higher, and the S/N of TCAA was 10 times higher after derivatization. BCAA can be detected after derivatization. For GC-VUV, the wavelength range of 125-160 nm was chosen for HAAs underivatized and TMPAH derivatized because it provided the better signal to noise ratio. After the derivatization, CAA, DCAA, TCAA, and BCAA can be detected and showed high S/N.

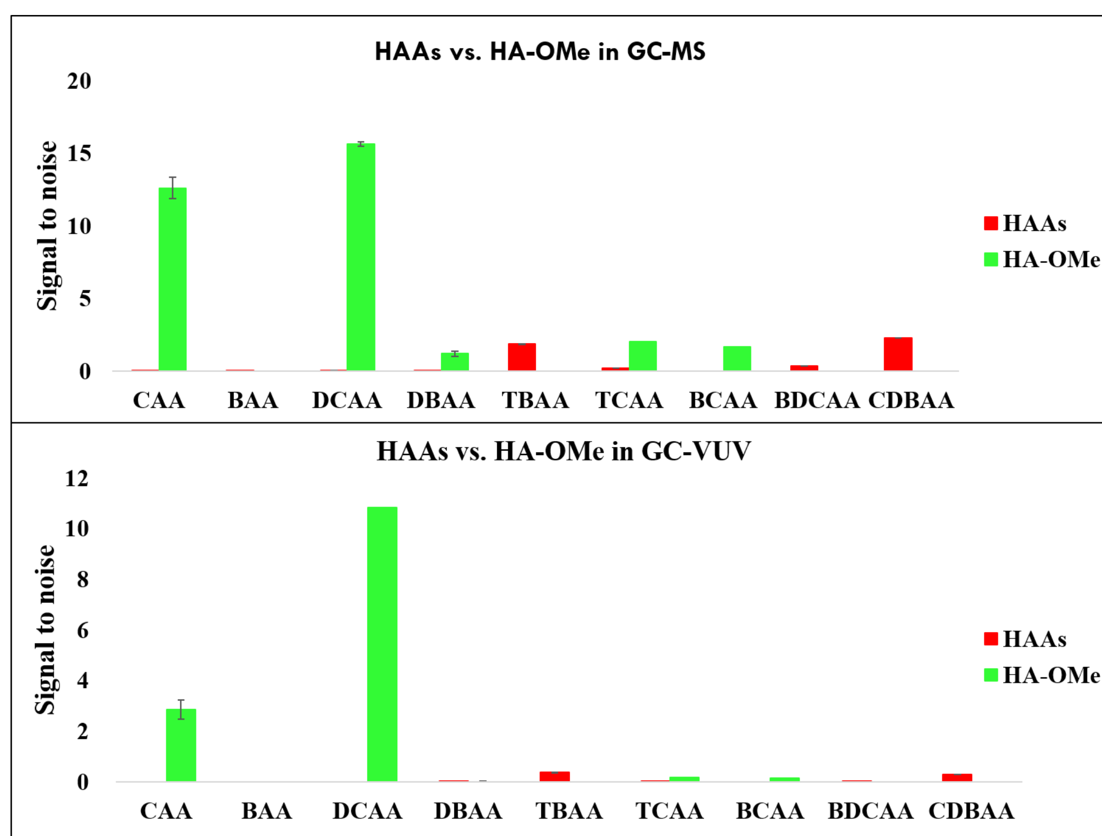


Figure 10. The S/N of HAAs before and after the TMPAH derivatization by GC-MS and GC-VUV.

Figure 11 compared the signal to noise ratio of GC-MS and GC-VUV in the detection of HAAs and it derivatives. It was apparent that the sensitivity of MS was much higher than VUV. Although the method of GC-MS had less

amount of injection, it still provided higher S/N than the GC-VUV. Also, VUV detector was difficult to analysis unknown compounds because of lacking database.[50] In comparison with the EPA method 552.2, the GC-MS and GC-VUV method which had been developed in this study provided shorter analysis time.[16] However, the derivatization reaction was unsuccessful. Although the unsuccessful HAAs derivatives are not regulated by U.S. EPA, this method must be optimized.[17] Perhaps enhancing the derivatization efficiency or minimizing the decarboxylation can improve the sensitivity of brominated trihaloacetic acids. Maybe it can be achieved by increasing the heating time or adding catalyst in TMPAH and BnOH derivatization.

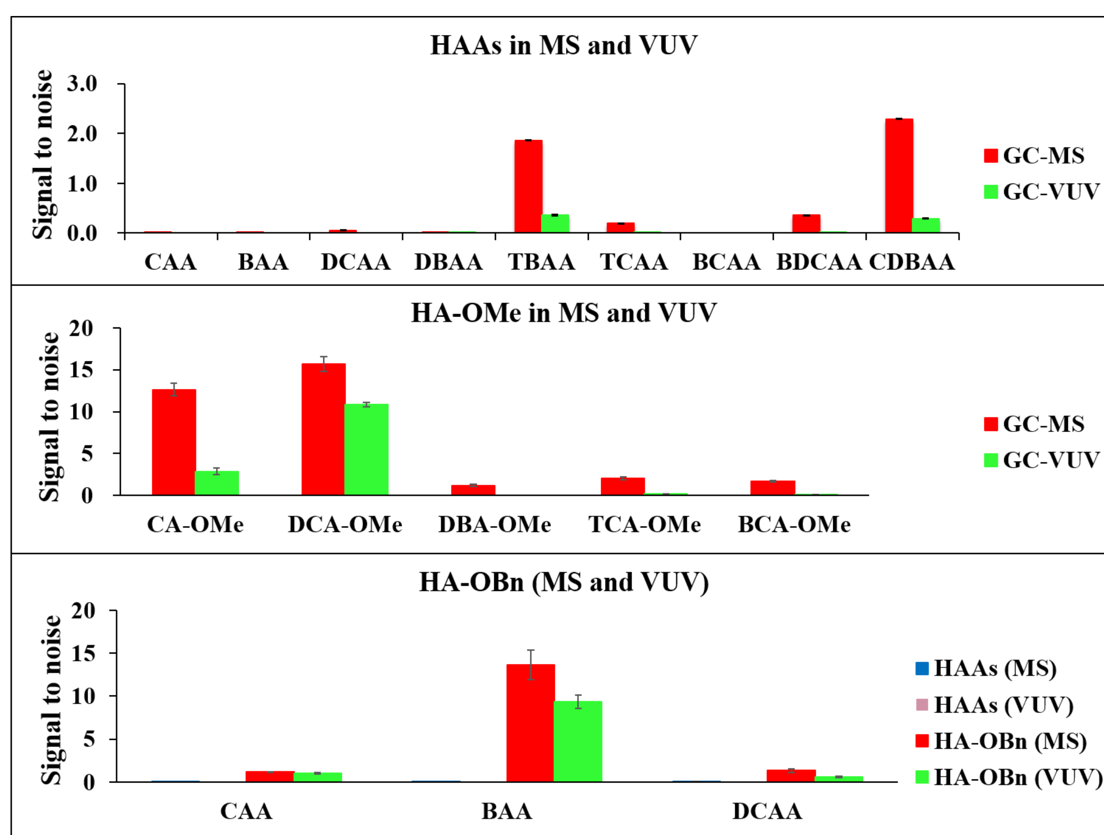


Figure 11. The comparison of HAAs and its derivatives by GC-MS and GC-VUV.

The water sample was collected from a laboratory tap at U.T. Arlington and had been observed in the presence of haloacetic acids. Chromatograms were shown in Figure 12 and the S/N of haloacetic acids by GC-MS were shown on Figure 13. Haloacetic acids were not observed by using GC-VUV because the concentration was too low. The derivatization reactions in water sample were unsuccessful. Therefore, this method needed to be improved.

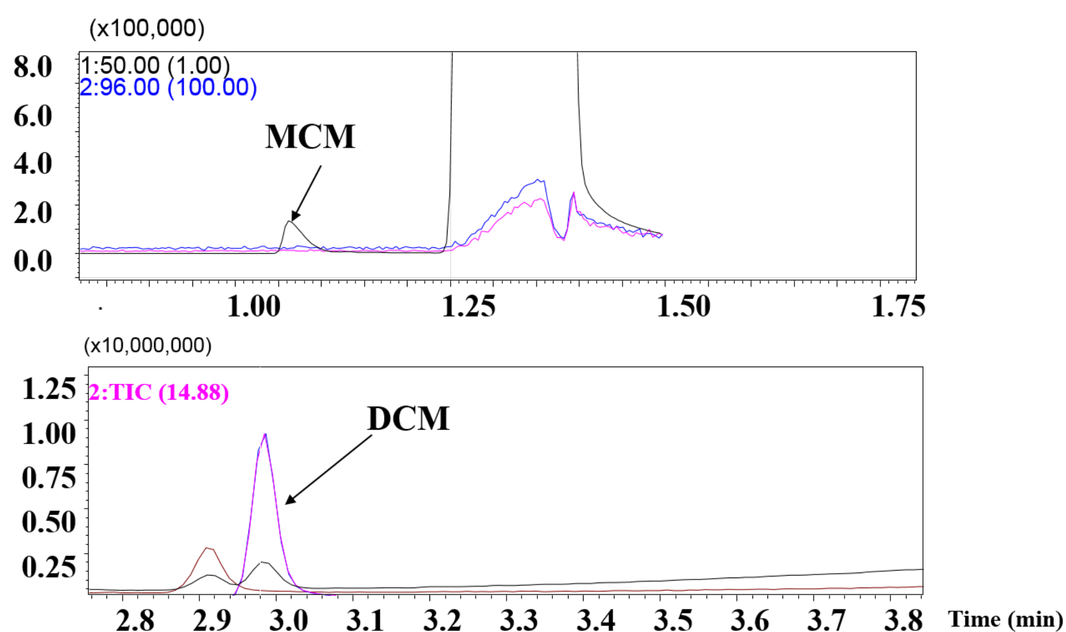


Figure 12. Chromatograms of HAAs in water sample by GC-MS.

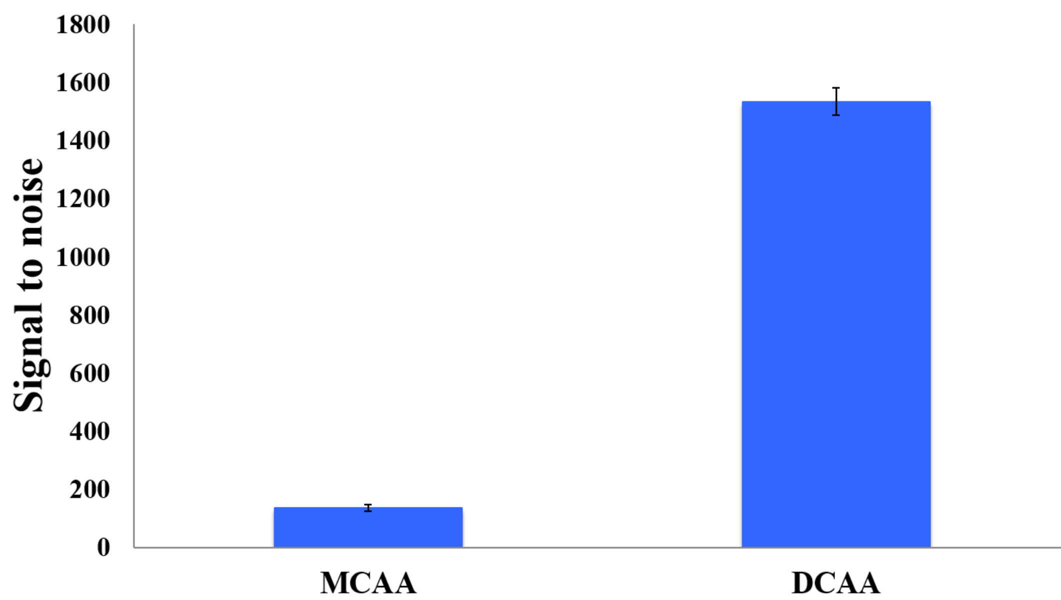


Figure 13. The S/N of HAAs in water sample by GC-MS.

CHAPTER THREE

Conclusion and Future Perspectives

In this study, GC-MS and GC-VUV were evaluated for determining haloacetic acids in drinking water. Different derivatization reagents were tested and the results obtained using GC-MS and GC-VUV were compared.

The sensitivity increased in both GC-MS and GC-VUV after the derivatization. However, this method also had many shortcomings and challenges that needed to be overcome: (1) the VUV detector was difficult to identify unknown compounds; (2) although the benzyl alcohol derivatization can increase the intensity of analyte, it also caused many side reactions in complex samples and generated high intensities of interference noises; (3) the efficiency of derivatization was low.

In future study, the methods of GC-MS and GC-VUV will need to be modified in order to determining nine of haloacetic acids. The different catalysts should be studied in order to increase the efficiency of derivatization. Also, the selective ions for benzyl alcohol derivatization should be studied to minimize the interference signal. The different wavelength filters in VUV should also be tested in order to improve the sensitivity of VUV. After methods have been developed, it should be able to apply to real sample. GC-MS and GC-VUV should be capable of applying in the qualitative and quantitative analysis of haloacetic acids in water.

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