***N*-nitrosodimethylamine (NDMA) Formation from the Ozonation of Model Compounds**

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Abstract:

Nitrosamines are a class of toxic disinfection byproducts commonly associated with chloramination, of which several were included on the most recent U.S. EPA Contaminant Candidate List. Nitrosamine formation may be a significant barrier to ozonation in water reuse applications, particularly for direct or indirect potable reuse, since recent studies show direct formation during ozonation of natural water and treated wastewaters. Only a few studies have identified precursors which react with ozone to form *N*-nitrosodimethylamine (NDMA). In this study, several precursor compound solutions, prepared in ultrapure water and treated wastewater, were subjected to a 10 molar excess of ozone. In parallel experiments, the precursor solutions in ultrapure water were exposed to gamma radiation to determine NDMA formation as a byproduct of reactions of precursor compounds with hydroxyl radicals. The results show six new NDMA precursor compounds that have not been previously reported in the literature,

including compounds with hydrazone and carbamate moieties. Molar yields in deionized water were 61-78% for 3 precursors, 12-23% for 5 precursors and <4% for 2 precursors. Bromide concentration was important for three compounds (1,1-dimethylhydrazine, acetone dimethylhydrazone and dimethylsulfamide), but did not enhance NDMA formation for the other precursors. NDMA formation due to chloramination was minimal compared to formation due to ozonation, suggesting distinct groups of precursor compounds for these two oxidants. Hydroxyl radical reactions with the precursors will produce NDMA, but formation is much greater in the presence of molecular ozone. Also, hydroxyl radical scavenging during ozonation leads to increased NDMA formation. Molar conversion yields were higher for several precursors in wastewater as compared to deionized water, which could be due to catalyzed reactions with constituents found in wastewater or hydroxyl radical scavenging.

Keywords: *N*-Nitrosodimethylamine; NDMA; ozone; nitrosamine; disinfection byproduct; potable reuse

1. Introduction

Nitrosamines, particularly *N*-Nitrosodimethylamine (NDMA), have received a great deal of attention as harmful nitrogenous disinfection byproducts. NDMA is classified as a B2 carcinogen by the U.S. Environmental Protection Agency, it is listed on the third Contaminant Candidate List (US EPA, 2012), and it was part of the Unregulated Contaminant Monitoring Rule 2 (US EPA, 2013). Although no federal regulations have been established for NDMA, the California Department of Public Health has set a drinking water notification level of 10 ng/L (CPDH, 2013). The E-6 (1 in 1,000,000) cancer risk level for drinking water is 0.7 ng/L (US EPA IRIS, 2012). In addition to many direct anthropogenic sources (e.g., rubber manufacturing, circuit board manufacturing and rocket fuel production), NDMA is formed as a disinfection byproduct (DBP) in drinking water and wastewater treatment (Mitch et al. 2003).

As potable water demands and shortages rise, more communities are considering reuse of wastewater as an option for increasing the overall water supply. Ozone is effective for treating pathogens and trace organic contaminants and, therefore, is a promising treatment technology for potable water reuse applications. Its treatment versatility for pre- and post-disinfection, decolorizing, taste and odor removal, coagulation assistance, and zero residual are some of the other advantages. However, the formation of ozone byproducts, such as NDMA, could be a barrier to the use of ozone in potable water reuse.

NDMA formation is commonly associated with chloramination (Mitch et al. 2003, Choi and Valentine 2002), but recent studies indicate that direct formation during ozonation also occurs (Andrzejewski et al. 2008, von Gunten et al. 2010, Oya et al. 2008,

Kosaka et al. 2009, Schmidt and Brauch 2008, Nawrocki and Andrzejewski 2011, Pisarenko et al. 2012, Padhye et al. 2013, Hollender et al. 2009). Initially, the chloramination pathway was thought to involve nucleophilic substitution between monochloramine and a secondary amine (Choi and Valentine 2002, Mitch and Sedlak 2002). This reaction resulted in unsymmetrical dimethylhydrazine (UDMH), which was subsequently oxidized by chloramines to form NDMA. The modified pathway involves the reaction of dichloramine and a model secondary amine, dimethylamine (DMA), which forms chlorinated unsymmetrical dimethylhydrazine (Cl-UDMH) as an intermediate. Dissolved oxygen oxidizes Cl-UDMH to NDMA (Schreiber and Mitch 2006). On the other hand, very little is known about the NDMA formation pathway and any intermediates that are formed with ozonation. Von Gunten et al. (2010) proposed a mechanism for NDMA formation from dimethylsulfamide (DMS), which is a degradation product of the fungicide tolylfluanid. The mechanism is bromide-catalyzed and results in the loss of $-SO_2$ as a leaving group and N-N bond formation. While UDMH conversion to NDMA is an oxidation reaction, additional pathways for other precursors' reactions with ozone have not been identified.

In order for NDMA to form as a disinfection byproduct from ozonation, certain compounds must be present in the water. Beside DMS and other metabolites of tolylfluanid, a few other precursors have been identified, including daminozide, 1,1-dimethylhydrazine (UDMH), dimethyldithiocarbamate, methylene blue, *N,N*-Dimethyl-*p*-phenylenediamine (DMPD), 1,1,1',1'-Tetramethyl-4,4'-(methylenedi-*p*-phenylene)disemicarbazide (TMDS), 4,4'-hexamethylenebis(1,1-dimethylsemicarbazide) (HDMS) and poly(diallyldimethylammoniumchloride) (polyDADMAC). The chemical

structures of these compounds include hydrazines, semicarbazides, sulfamides, and tertiary amines with a dimethylamine functional group (abbreviated as dimethylamine). In particular, compounds with dimethylamine bonded directly to a nitrogen atom or separated with a good leaving group (e.g., -SO₂) form NDMA with significant molar conversion yields (i.e., 10-80%) (von Gunten et al. 2010, Kosaka et al. 2009, Schmidt and Brauch 2008). Precursors with the dimethylamine and no additional nitrogen may also form NDMA upon ozonation, but the yields are <0.01% (Oya et al. 2008, Padhye et al. 2013, Padhye et al. 2011).

In more complex water matrices, certain factors have been shown to impact NDMA formation with ozone, including dissolved ions and pH. For example, bromide ions catalyze the reaction of DMS with ozone (von Gunten et al. 2010). Oya et al. (2008) found that NDMA formation by ozonation of dimethylamine dyes increased in river water compared to deionized water. They also noticed increased NDMA formation with increased pH; however, this was attributed to changes in the reaction mechanism at different pH. Dissolved molecular ozone and hydroxyl radicals can be involved in both formation (Andrzejewski et al. 2008, Schmidt and Brauch 2008) and destruction of NDMA (Mezyk et al. 2004, Lee et al. 2007a), but the extent of each oxidant's role is not well understood.

The goal of this study was to identify specific organic structures that may contribute to the direct formation of NDMA by ozonation. Only a few precursors have been identified in literature and there is much to gain in understanding which compounds lead to NDMA formation. If model precursors can be identified, then specific strategies

could be utilized to identify them and remove the precursors prior to ozonation and limit the production of DBPs.

2. Materials and Methods

2.1 Tested Waters and Equipment

The tested waters included ultrapure water and pilot-scale membrane bioreactor treated wastewater (0.032 MGD). Ultrapure water was buffered at neutral pH with phosphate buffer (1 mM or 5 mM final concentration). The neutral pH (6.7-7.1) wastewater came from a municipal source with treatment consisting of primary sedimentation with ferric chloride addition, biological secondary treatment with partial nitrification, and tertiary membrane microfiltration (0.40 μ m nominal pore size). Table S3 contains water quality information and key treatment parameters. No additional filtration was performed and wastewater was stored at 4 °C for preservation prior to bench-scale work.

Ozonated water was generated using an oxygen-fed generator (model CFS-1A, Ozonia North America, Inc., Elmwood Park, NJ, USA) to diffuse ozone into ultrapure water as described previously (Wert et al. 2009). The ozone stock solution was typically between 65 and 85 mg/L. Aliquots of the ozonated water were measured in a graduated cylinder and quickly poured into the container with the test water. The containers were sealed and shaken to mix the water. Dilution factors based on addition of the ozone stock aliquots were accounted for in all results.

2.2 Analytical Methods and Reagents

A more detailed description can be found in the Supplementary Information. Briefly, neat standards of the precursors were individually dissolved in ultrapure water and/or acetonitrile (for solubility). Precursors were individually spiked into the test water at 100 μ M in amber glass bottles. Bromide, hydrogen peroxide, parachlorobenzoic acid (pCBA) or tert-butyl alcohol (tBA) spikes were added to the samples next, as appropriate. Ozonated water was added to give a final concentration of approximately 1 mM (48 mg/L), which is at least a 10-fold molar excess. Samples were sealed and mixed after ozone addition and left undisturbed at room temperature (23 °C) overnight in the dark. Based on an ozone decay curve for ultrapure water, the ozone residual (1.52 mM initially) was less than 1.67×10^{-2} mM after three hours. Therefore, leaving the bottles to sit overnight was sufficient to eliminate the ozone residual. Ozone concentration was measured using the indigo method (Rakness et al. 2010).

Chloramine NDMA formation potential was evaluated based on a previously published method (Mitch et al. 2003). As before, ozonated samples were allowed to sit overnight to ensure there was no ozone residual prior to chloramination. Samples were spiked with preformed monochloramine at 2 mM (140 mg/L) as Cl_2 , stored at room temperature (23 °C) in the dark, and quenched after ten days.

Radiolysis tests were conducted to isolate the impact of hydroxyl radicals on NDMA formation. Phosphate buffered (1 mM) ultrapure water was saturated with nitrous oxide (N_2O gas) for one hour. Aqueous electrons and $\cdot\text{OH}$ are formed by direct gamma radiolysis of the water (Peller et al. 2003). Aqueous electrons are scavenged by N_2O to form N_2O^- , which decomposes to N_2 and $\text{O}^{\cdot-}$. The $\text{O}^{\cdot-}$ is subsequently protonated by water to form $\cdot\text{OH}$. Samples were shipped overnight on ice in amber glass containers to

the Radiation Laboratory at the University of Notre Dame. The samples were subjected to gamma irradiation (1.93 Gy/min) with a Shepard 109-68 ⁶⁰Co source for specific time lengths (2-20 min) corresponding to different hydroxyl radical concentrations (Peller et al. 2003).

NDMA analysis was performed by direct injection with liquid chromatography tandem mass spectrometry (LC-MS/MS) using isotope dilution with d6-NDMA. The mass spectrometer was operated via multiple reaction-monitoring in positive-ion mode with a source temperature of 375 °C. Two transitions were monitored for NDMA (75/43 and 75/58) and d6-NDMA (81/46 and 81/64). The reporting limit (0.34 μM or 25 μg/L) was set at greater than five times the signal to noise ratio and was based on the instrument detection limit (n=12, concentration=25 μg/L). There was no matrix suppression for the phosphate buffer. Recovery for the wastewater matrix spike was 102% and NDMA in the ozonated ambient wastewater was below the reporting limit.

Individual precursors were analyzed by direct injection with LC-MS/MS and monitoring corresponding mass transitions for: TMDS (371.17/285.2), Daminozide (161/143.1), DMS (124.9/107.9), 2-F-DMH (139/96.1), DMC-phenyl (223.1/105), DMTC-phenyl (210.1/108), DMC-dithio (312/223.1), UDMH (60.9/45) and DMA (46/31.1). An external calibration with 7 points for each precursor (0.005 to 0.25 μM) was used. R² values of 0.995 or better were observed for all compounds. Reporting limits were set at greater than five times the signal to noise ratio and were based on the instrument detection limit (n=12) for individual precursors. There was no matrix suppression for the phosphate buffer.

2.3 *Selection of model NDMA precursors*

The literature suggests that certain structures are more likely to form NDMA by ozonation, as mentioned in the introduction. Therefore, the search for model precursors was based on structural moieties, such as a dimethylamine group, hydrazine, sulfamide, hydrazone and carbamate. The selected compounds contain the dimethylamine group and at least one other nitrogen, which forms the building block for NDMA. In some compounds, the building block is located on the end of the structure (e.g., DMSC) and for other compounds it is more centrally located (e.g., Atazanavir). In most compounds, the dimethylamine (DMA) is bonded to an additional nitrogen; however, the carbamates have a -CO₂ group separating the nitrogens. The precursors were identified using online structure search tools (e.g., eMolecules, Sigma-Aldrich and Ryan Scientific substructure search, ChemSpider structure search and DrugBank ChemQuery) for compounds available for purchase, which is not necessarily an indication of commercial or industrial use. Table 1 lists the abbreviations and structures of the new precursors selected in this study, as well as other studies on NDMA formation with ozone. More details about the precursors are available in the Supplementary Information (Table S2).

3. **Results and Discussion**

3.1 *Molar Yields in Buffered Ultrapure Water*

Each of the selected precursor compounds were individually reacted with a 10-fold molar excess of ozone in 5 mM phosphate buffered ultrapure water. Figure 1 shows the molar yields of NDMA formed. Molar yields (mol NDMA / mol calculated precursor amount) varied widely, from 0-78%. There was no NDMA formation observed for

203 atazanavir, dacarbazine and streptozocin. Ozone may react with these compounds, but not
204 in a manner that results in NDMA. As expected, DMS and DMA did not result in NDMA
205 formation. The reaction between ozone and DMS is catalyzed by bromide (von Gunten et
206 al. 2010), which was not present in ultrapure water solutions. DMA reacts with
207 dichloramine to form NDMA, but ozonation of amines mainly results in the formation of
208 aldehydes (Munoz and von Sonntag 2000). Very low molar yields (<0.4%) for ozonation
209 of DMA have been reported (Andrzejewski et al. 2008, Yang et al. 2009), but the
210 reaction may be due to nitrosation rather than ozonation.

211 Several of the model compounds formed NDMA upon ozonation. The
212 hydrazones, Acetone-DMH and 2-F-DMH, are similar to the known precursor UDMH.
213 However, these compounds have a double bond which makes them potentially more
214 reactive with ozone (e.g., ozonolysis reaction). DMSC and DMTC-phenyl are similar to
215 the known precursor TMDS. DMC-phenyl and DMC-dithio are related to DMS in that
216 the nitrogen atoms are separated by a good leaving group (e.g., -SO₂, -CO₂). These
217 carbamate compounds differ from dimethyldithiocarbamate (DMDTC) precursors
218 previously reported (Padhye et al. 2013, Sedlak et al. 2005). Although the mechanism for
219 NDMA formation with ozone is not fully understood, it seems rearrangement with the
220 loss of a small molecule, CO₂, results in the nitrogen-nitrogen bond. Consequently, other
221 dimethylcarbamate compounds may potentially be precursors.

222 Acetone-DMH was found to be unstable in water. Through LC-MS/MS analysis,
223 it was confirmed that Acetone-DMH degraded rapidly to UDMH, which explains the
224 very similar results between these two compounds. In addition, UDMH slowly degraded
225 in water and calibration standards were prepared fresh every two weeks. No other

compounds showed short-term instability in water; however, NDMA was detected in old stock solutions (>1 yr) for 2-F-DMH, UMDH, and TMDS. NDMA was present in a fresh solution of 2-F-DMH prepared in acetonitrile, which suggests there may be residual NDMA from synthesis. DMA was detected in old stock solutions for 2-F-DMH, UMDH, DMC-dithio, DMC-phenyl and DMS, which may be due to slow hydrolysis of these precursors.

3.2 Influence of Bromide on Molar Yields

The ozonation bench-scale experiments in 5 mM phosphate buffered ultrapure water were repeated with two different bromide spikes (Figure 1). As seen in the figure, molar yields for some compounds (DMS, UDMH, and Acetone-DMH) are enhanced by bromide, while others remain constant. Although there is a slight decrease in molar yield for 2-F-DMH, daminozide, and TMDS, this is probably the effect of an increased ozone demand caused by the bromide spike at 1250 ppb. A greater ozone demand could result in lower NDMA formation.

In agreement with work by von Gunten et al. (2010), there was considerably more NDMA formed in solutions of DMS containing bromide. Bromide concentration was also significant for NDMA formation in solutions of UDMH and Acetone-DMH. DMC-phenyl and DMC-dithio, which have the $-\text{CO}_2$ leaving group, did not show increased formation with bromide. This suggests that the reaction pathway for these compounds is different than the bromide-catalyzed, $-\text{SO}_2$ leaving reaction for DMS. It appears that there are multiple reaction pathways for NDMA precursors that react with ozone which need further investigation.

249

250 **3.3 *Effect of Hydrogen Peroxide Addition and Ozone Dose***

251 The effects of hydrogen peroxide and ozone dose on NDMA formation were
252 investigated for two compounds (TMDS and 2-F-DMH) in 5 mM phosphate buffered
253 ultrapure water at pH 7. These compounds were chosen to represent different structural
254 classes (i.e., semicarbazide and hydrazone). Hydrogen peroxide was added at O₃:H₂O₂
255 mg/L ratios of 1:0.25 and 1:0.50 (or mM ratios 1:0.35 and 1:0.70). As seen in Figure 2,
256 the addition of hydrogen peroxide had minimal impact on NDMA level. This was also
257 seen by Oya et al. (2008).

258 The two precursor compounds were individually reacted with ozone at doses
259 ranging from 0.1 to 1.5 mM O₃ in buffered ultrapure water. Initial ozone dose affected
260 the extent of NDMA formation. For 2-F-DMH, NDMA formation increased from 0.1 to
261 0.5 mM O₃ and then leveled off (Figure 3). The maximum molar conversion yield was
262 70%. Likely, increasing the ozone dose above 0.5 mM did not cause more NDMA
263 formation because the precursor had reacted completely to form NDMA and other
264 transformation products. In the case of TMDS, there was a linear correlation ($R^2 = 0.98$)
265 between NDMA formation and ozone dose in the tested range. No maximum molar
266 conversion yield was achieved at these ozone doses.

267

268 **3.4 *Chloramination Formation Potential***

269 Chloramine NDMA formation potential (NDMA-FP) is a test to quantify
270 precursors that react with chloramine to form NDMA. At a high chloramine dose, the test
271 serves as a way to determine the maximum formation potential for NDMA. In this study,

NDMA-FP for the targeted precursors was investigated through ten day tests in 5 mM phosphate buffered ultrapure water before and after ozonation. Experimental parameters were kept the same for comparison to previous tests. One set of samples was spiked with preformed monochloramine (140 mg/L as Cl₂). The other set of samples was ozonated and allowed to react for 24 hours before spiking with preformed monochloramine.

NDMA formation in buffered ultrapure water after ozonation only and after chloramination only can be seen in Figure 1. The NDMA molar conversion yields are summarized in Table 2. With the exception of DMA, all yields for chloramination were below 3% and most were below 1.5%. These precursors have a much higher NDMA formation with ozone as compared to chloramines, making these precursors distinctly different from other dimethylamine-containing compounds. As expected, DMA had the highest molar conversion yield with chloramines. NDMA-FP decreased after ozonation for DMA (data not shown), which agrees with previous research that ozonation can reduce NDMA-FP associated with chloramination (Pisarenko et al. 2012).

Molar yields for UDMH and Acetone-DMH increased slightly for chloramination following ozonation (Figure 4). This suggests that transformation products from the ozonation reaction may be NDMA chloramination precursors. Ozonation of tertiary amines can result in DMA formation (Lee et al. 2007b), which would result in NDMA with subsequent chloramination.

3.5 Comparison of molecular ozone and $\cdot$ OH as oxidants for NDMA formation

To determine the potential $\cdot$ OH oxidation involved in ozonation processes, samples of 1 mM buffered ultrapure water spiked with precursors (DMTC-phenyl, 2-F-

DMH and TMDS) were subjected to gamma irradiation and analyzed for NDMA formation, as well as precursor degradation. These compounds were chosen to represent different structural classes (i.e., carbamate, hydrazone and semicarbazide). Buffered ultrapure water spiked with NDMA was irradiated in parallel and destruction due to $\bullet\text{OH}$ was measured. The results for the gamma radiation experiments are a combination of NDMA formation from the precursors reacting with $\bullet\text{OH}$ and potentially subsequent NDMA destruction by $\bullet\text{OH}$. Due to low NDMA concentration, samples underwent solid phase extraction and GC-MS/MS analysis (Holady et al. 2012). NDMA was formed by all three precursors at low molar yields (0.2-4.3%), which were calculated based on the amount of precursor that degraded after 20 min (38.6 Gy). More details are provided in the Supplementary Information. Based on bench-scale experiments using pCBA as a probe, $[\bullet\text{OH}]$ from gamma irradiation was similar to what was produced during ozonation. Since radiolysis resulted in low NDMA formation, molecular ozone is the main oxidant responsible, while the $\bullet\text{OH}$ may play a minor role in NDMA formation for these model precursors.

The presence of hydroxyl radicals may be more likely to hinder NDMA formation than to increase it because of side reactions and increased ozone decay. For example, hydroxyl radical quenching with tBA was shown to increase NDMA formation from DMS by reducing $\bullet\text{OH}$ reactions that either formed products other than NDMA or resulted in bromate formation, which limited bromide catalysis (von Gunten et al. 2010). Similarly, parallel ozonation tests for the precursors in buffered ultrapure water with and without tBA resulted in greater molar yields when $\bullet\text{OH}$ were scavenged (Figure 5).

3.6 *Molar Yields in a Secondary Wastewater Matrix*

NDMA formation was examined in wastewater by dissolving each precursor compound individually in the tertiary-treated wastewater and reacting with a 10-fold molar excess of ozone using the same procedure as the buffered ultrapure water. NDMA formation was affected by the water matrix for a few compounds. It was anticipated that the ozone demand presented by the wastewater would decrease the ozone concentration available for reaction with the precursor compounds, and therefore lower NDMA molar conversion yields were expected. However, the opposite was observed. For four compounds (UDMH, Acetone-DMH, TMDS and DMSC), the NDMA molar conversion yield was significantly greater in the wastewater matrix compared to phosphate buffered ultrapure water (Figure 1). This trend was also seen by a group of researchers comparing NDMA formation by ozonation of two dyes in river water and deionized water matrices at pH 7 (Oya et al. 2008). They measured higher NDMA formation in the river water matrix that contained bromide and nitrite, but at a concentration too low to account for this increase. At this time, specific constituents in the wastewater responsible for the increased formation have not been determined. Another explanation for the increased molar yields in wastewater is through $\cdot\text{OH}$ scavenging. Effluent organic matter in wastewater can scavenge $\cdot\text{OH}$. As demonstrated in the previous section, $\cdot\text{OH}$ scavenging is associated with increased NDMA formation.

3.7 *Practical implications of the research*

As shown in this research, compounds with a general structure of $(\text{H}_3\text{C})_2\text{N-N-R}$ or $(\text{H}_3\text{C})_2\text{N-L-N-R}$, where L is a good leaving group like $-\text{SO}_2$ or $-\text{CO}_2$, have a high

likelihood of forming NDMA with ozonation. While previously reported precursors UDMH, DMS, TMDS and daminozide have been reported in groundwater or are known products in use, the new precursors reported in this study were selected by structure only and have not been quantified in wastewater, surface water or groundwater.

According to the results of this study, the ozone dose for treating wastewater may strongly affect NDMA formation. Treatment plants operating at high ozone doses for color removal or chemical contaminant removal could experience much greater NDMA formation compared to treatment plants using low ozone doses for final disinfection. In addition, precursors may be removed through treatment steps, such as reverse osmosis, biotreatment, and oxidation, leading to less NDMA formation when ozonation occurs at the end of a treatment train. Consequently, one should consider both the dose and placement within the treatment train when determining an appropriate ozone application.

Bench-scale ozonation testing with ultrapure water may not demonstrate the full potential of the precursors to form NDMA. Wastewater constituents can increase NDMA formation, such as by bromide catalysis or hydroxyl radical quenching (von Gunten et al. 2010). Therefore, further study is needed to understand the influence of the matrix on NDMA formation and to develop possible mitigation strategies.

Chloramination may follow ozonation when a chlorine residual is necessary. The combined disinfection could have varying results. If the source water contains mostly NDMA precursors that react with chloramine, then pre-ozonation may reduce NDMA formation potential (Pisarenko et al. 2012). However, if the source water contains NDMA precursors that react with ozone, then the initial ozonation may form NDMA, as well as additional chloramination precursors via degradation products (i.e., from UDMH).

Without an analytical method to quantify NDMA precursors for either oxidant, it is necessary to experimentally determine NDMA formation potential for each source water in order to determine the optimal disinfection strategy.

4. Conclusions

Experiments with known and potential NDMA precursors resulted in the following findings on NDMA formation by ozonation:

- Out of 9 compounds selected based on structural characteristics, six new compounds were identified as NDMA precursors. Two are hydrazones, two are semicarbazides, and two are carbamates.
- Bromide concentration was significant for NDMA formation in solutions of dimethylsulfamide (DMS), unsymmetrical dimethylhydrazine (UDMH) and acetone dimethylhydrazone. Other compounds showed no enhancing effect of bromide on NDMA formation.
- Although all the precursors tested contain a dimethylamine that reacts with chloramine to form NDMA, the reaction with ozone results in significantly higher NDMA formation. This group of precursors is distinctly different than other dimethylamine-containing compounds.
- Transformation products from the ozonation of UDMH may be NDMA chloramination precursors.
- Molecular ozone was confirmed as the main oxidant responsible for NDMA formation for the model precursors.

- Higher NDMA formation was observed in wastewater than ultrapure water for several precursors. Wastewater may contain constituents that promote NDMA formation.
- Hydroxyl radical scavenging and a greater ozone dose lead to increased NDMA formation for the model precursors, while the addition of hydrogen peroxide had no significant effect on NDMA formation.

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References

Andrzejewski, P., Kasprzyk-Hordern, B. and Nawrocki, J. (2008) N-nitrosodimethylamine (NDMA) formation during ozonation of dimethylamine-containing waters. *Water Research* 42(4-5), 863-870.

407 California Department of Public Health (2013). Drinking Water Notification Levels.
 408 Retrieved November 12, 2013, from [http://www.cdph.ca.gov/certlic/](http://www.cdph.ca.gov/certlic/drinkingwater/Pages/NotificationLevels.aspx)
 409 [drinkingwater/Pages/NotificationLevels.aspx](http://www.cdph.ca.gov/certlic/drinkingwater/Pages/NotificationLevels.aspx).
 410 Choi, J. and Valentine, R.L. (2002) Formation of N-nitrosodimethylamine (NDMA) from
 411 reaction of monochloramine: A new disinfection by-product. Water Research
 412 36(4), 817-824.
 413 Durant, J.L., Jacobs, B. and Shanahan, P. (2008) Historical inputs of N-
 414 nitrosodimethylamine to the public drinking water supply in Wilmington,
 415 Massachusetts, p. Environmental and Water Resources Institute of ASCE,
 416 American Society of Civil Engineers, Honolulu, HI, United states.
 417 Holady, J.C., Trenholm, R.A. and Snyder, S.A. (2012) Use of automated solid-phase
 418 extraction and GC-MS/MS to evaluate nitrosamines in water matrices. American
 419 Laboratory 44(3), 25-30.
 420 Hollender, J., Zimmermann, S.G., Koepke, S., Krauss, M., McArdell, C.S., Ort, C.,
 421 Singer, H., von Gunten, U. and Siegrist, H. (2009) Elimination of Organic
 422 Micropollutants in a Municipal Wastewater Treatment Plant Upgraded with a
 423 Full-Scale Post-Ozonation Followed by Sand Filtration. Environmental Science &
 424 Technology 43(20), 7862-7869.
 425 Kosaka, K., Asami, M., Konno, Y., Oya, M. and Kunikane, S. (2009) Identification of
 426 antiyellowing agents as precursors of N-nitrosodimethylamine production on
 427 ozonation from sewage treatment plant influent. Environmental Science and
 428 Technology 43(14), 5236-5241.
 429

430 Lee, C., Yoon, J. and Von Gunten, U. (2007a) Oxidative degradation of *N*-
 431 nitrosodimethylamine by conventional ozonation and the advanced oxidation
 432 process ozone/hydrogen peroxide. *Water Research* 41(3), 581-590.

433 Lee, C., Schmidt, C., Yoon, J. and von Gunten, U. (2007b) Oxidation of *N*-
 434 Nitrosodimethylamine (NDMA) Precursors with Ozone and Chlorine Dioxide:
 435 Kinetics and Effect on NDMA Formation Potential. *Environmental Science &*
 436 *Technology* 41(6), 2056-2063.

437 Lee, C., Lee, Y., Schmidt, C., Yoon, J. and Von Gunten, U. (2008) Oxidation of
 438 suspected *N*-nitrosodimethylamine (NDMA) precursors by ferrate (VI): Kinetics
 439 and effect on the NDMA formation potential of natural waters. *Water Research*
 440 42(1-2), 433-441.

441 Mezyk, S.P., Cooper, W.J., Madden, K.P. and Bartels, D.M. (2004) Free Radical
 442 Destruction of *N*-Nitrosodimethylamine in Water. *Environmental Science &*
 443 *Technology* 38(11), 3161-3167.

444 Mitch, W.A. and Sedlak, D.L. (2002) Formation of *N*-nitrosodimethylamine (NDMA)
 445 from dimethylamine during chlorination. *Environmental Science and Technology*
 446 36(4), 588-595.

447 Mitch, W.A., Gerecke, A.C. and Sedlak, D.L. (2003a) A *N*-Nitrosodimethylamine
 448 (NDMA) precursor analysis for chlorination of water and wastewater. *Water*
 449 *Research* 37(15), 3733-3741.

452 Mitch, W.A., Sharp, J.O., Trussell, R.R., Valentine, R.L., Alvarez-Cohen, L. and Sedlak,
 453 D.L. (2003b) N-nitrosodimethylamine (NDMA) as a drinking water contaminant:
 454 A review. *Environmental Engineering Science* 20(5), 389-404.
 455 Mitch, W.A. and Sedlak, D.L. (2004) Characterization and Fate of *N*-
 456 Nitrosodimethylamine Precursors in Municipal Wastewater Treatment Plants.
 457 *Environmental Science & Technology* 38(5), 1445-1454.
 458 Munoz, F. and von Sonntag, C. (2000) The reactions of ozone with tertiary amines
 459 including the complexing agents nitrilotriacetic acid (NTA) and
 460 ethylenediaminetetraacetic acid (EDTA) in aqueous solution. *Journal of the*
 461 *Chemical Society, Perkin Transactions 2* 0(10), 2029-2033.
 462 Nawrocki, J. and Andrzejewski, P. (2011) Nitrosamines and water. *Journal of Hazardous*
 463 *Materials* 189(1-2), 1-18.
 464 Oya, M., Kosaka, K., Asami, M. and Kunikane, S. (2008) Formation of *N*-
 465 nitrosodimethylamine (NDMA) by ozonation of dyes and related compounds.
 466 *Chemosphere* 73(11), 1724-1730.
 467 Padhye, L., Luzinova, Y., Cho, M., Mizaikoff, B., Kim, J.-H. and Huang, C.-H. (2011)
 468 PolyDADMAC and dimethylamine as precursors of *N* -nitrosodimethylamine
 469 during ozonation: Reaction kinetics and mechanisms. *Environmental Science and*
 470 *Technology* 45(10), 4353-4359.
 471 Padhye, L.P., Kim, J.-H. and Huang, C.-H. (2013) Oxidation of dithiocarbamates to yield
 472 *N*-nitrosamines by water disinfection oxidants. *Water Research* 47(2), 725-736.

473 Peller, J., Wiest, O. and Kamat, P.V. (2003) Mechanism of Hydroxyl Radical-Induced
 474 Breakdown of the Herbicide 2,4-Dichlorophenoxyacetic Acid (2,4-D). Chemistry
 475 – A European Journal 9(21), 5379-5387.

476 Pisarenko, A.N., Stanford, B.D., Yan, D., Gerrity, D. and Snyder, S.A. (2012) Effects of
 477 ozone and ozone/peroxide on trace organic contaminants and NDMA in drinking
 478 water and water reuse applications. Water Research 46(2), 316-326.

479 Rakness, K.L., Wert, E.C., Elovitz, M. and Mahoney, S. (2010) Operator-Friendly
 480 Technique and Quality Control Considerations for Indigo Colorimetric
 481 Measurement of Ozone Residual. Ozone-science & Engineering 32(1), 33-42.

482 Schmidt, C.K. and Brauch, H.-J. (2008) N,N-dimethylsulfamide as precursor for N-
 483 nitrosodimethylamine (NDMA) formation upon ozonation and its fate during
 484 drinking water treatment. Environmental Science and Technology 42(17), 6340-
 485 6346.

486 Schreiber, I.M. and Mitch, W.A. (2005) Influence of the order of reagent addition on
 487 NDMA formation during chloramination. Environmental Science and Technology
 488 39(10), 3811-3818.

489 Schreiber, I.M. and Mitch, W.A. (2006) Occurrence and fate of nitrosamines and
 490 nitrosamine precursors in wastewater-impacted surface waters using boron as a
 491 conservative tracer. Environmental Science and Technology 40(10), 3203-3210.

492 Sedlak, D.L., Deeb, R.A., Hawley, E.L., Mitch, W.A., Durbin, T.D., Mowbray, S. and
 493 Carr, S. (2005) Sources and fate of nitrosodimethylamine and its precursors in
 494 municipal wastewater treatment plants. Water Environment Research 77(1), 32-
 495 39.

496 U.S. Environmental Protection Agency (2012). Integrated Risk Information System: *N*-
 497 Nitrosodimethylamine (CASRN 62-75-9). Retrieved January 21, from
 498 <http://www.epa.gov/iris/subst/0045.htm#quaoral>.
 499 U.S. Environmental Protection Agency (2012). Contaminant Candidate List 3. Retrieved
 500 November 12, 2013, from [http://water.epa.gov/scitech/drinkingwater/](http://water.epa.gov/scitech/drinkingwater/dws/ccl/ccl3.cfm)
 501 [dws/ccl/ccl3.cfm](http://water.epa.gov/scitech/drinkingwater/dws/ccl/ccl3.cfm).
 502 U.S. Environmental Protection Agency (2013). Unregulated Contaminant Monitoring
 503 Rule 2. Retrieved November 12, 2013, from [http://water.epa.gov/lawsregs/](http://water.epa.gov/lawsregs/rulesregs/sdwa/ucmr/ucmr2/index.cfm)
 504 [rulesregs/sdwa/ucmr/ucmr2/index.cfm](http://water.epa.gov/lawsregs/rulesregs/sdwa/ucmr/ucmr2/index.cfm).
 505 von Gunten, U., Salhi, E., Schmidt, C.K. and Arnold, W.A. (2010) Kinetics and
 506 Mechanisms of *N*-Nitrosodimethylamine Formation upon Ozonation of *N,N*-
 507 Dimethylsulfamide-Containing Waters: Bromide Catalysis. *Environmental*
 508 *Science & Technology* 44(15), 5762-5768.
 509 WaterReuse Foundation. Removal and Destruction of NDMA and NDMA Precursors
 510 during Wastewater Treatment; project WRF-01-002; 2006.
 511 Wert, E.C., Rosario-Ortiz, F.L. and Snyder, S.A. (2009) Effect of ozone exposure on the
 512 oxidation of trace organic contaminants in wastewater. *Water Research* 43(4),
 513 1005-1014.
 514 Yang, L., Chen, Z., Shen, J., Xu, Z., Liang, H., Tian, J., Ben, Y., Zhai, X., Shi, W. and Li,
 515 G. (2009) Reinvestigation of the nitrosamine-formation mechanism during
 516 ozonation. *Environmental Science and Technology* 43(14), 5481-5487.

Table 1

Table 1. Structures of precursors investigated for NDMA formation with ozonation.

o

p

q

r

s

t

u

v

w

x

y

z

aa

ab

ac

ad

ae

a: DMA	b: UDMH	c: acetone DMH	d: 2-F-DMH	e: dacarbazine	f: daminozide
g: HDMS	h: TMDS	i: DMSC	j: DMTC-phenyl	k: atazanavir	l: streptozocin
m: DMC-phenyl	n: DMC-dithio	o: DMS	p: tolylfluanid	q: DMST	r: 3-OH-DMST
s: OH-methyl-DMST	t: COOH-DMST	u: 2-OH-DMST	v: methylene blue	w: NDAB	x: NPDP
y: methyl orange	z: methyl violet B	aa: auramine	ab: brilliant green	ac: DMF	ad: polyDADMAC
ae: DMDTC					

Table 2

Table 2. NDMA precursors and molar yields for NDMA formation with different oxidants in different water matrices.

Compound Name or Abbreviation	Molar Yield (%) Chloramination, ultrapure water [Br ⁻]	Molar Yield (%) Ozonation, ultrapure water	Molar Yield (%) Ozonation, ultrapure water + [Br ⁻]	Molar Yield (%) Ozonation, drinking water	Molar Yield (%) Ozonation, wastewater [Br ⁻]
Dimethylamine	7.5 ^a <1 ^g 1.32 ^l	<0.3 ^a <0.4 ^d 0.011 ^h	<0.3 ^a [1250 ppb]	<0.05 ^b	<0.3 ^a
UDMH	<0.3 ^a	16 ^a	34 ^a [1250 ppb]	80 ^b	54 ^a
Acetone DMH	0.3 ^a	22 ^a	35 ^a [1250 ppb]	--	53 ^a
2-F-DMH	2.6 ^a	61 ^a	55 ^a [1250 ppb]	--	66 ^a
Dacarbazine	<0.3 ^a	<0.3 ^a	<0.3 ^a [1250 ppb]	<0.05 ^b	<0.3 ^a
Daminozide	0.5 ^a	78 ^a	69 ^a [1250 ppb]	55 ^b	83 ^a
4,4-Hexamethylene bis(1,1-dimethyl semicarbazide), HDMS	N/A ^c	10 ^c	--	--	--
TMDS	0.7 ^a N/A ^c	23 ^a 27 ^c	19 ^a [1250 ppb]	--	47 ^a
DMSC	1.5 ^a	64 ^a	60 ^a [1250 ppb]	--	90 ^a
DMTC-phenyl	0.8 ^a	12 ^a	10 ^a [1250 ppb]	--	14 ^a
Atazanavir	<0.3 ^a	<0.3 ^a	<0.3 ^a [1250 ppb]	--	<0.3 ^a
Streptozocin	<0.3 ^a	<0.3 ^a	<0.3 ^a [1250 ppb]	--	<0.3 ^a
DMC-phenyl	1.4 ^a	15 ^a	13 ^a [1250 ppb]	--	14 ^a
DMC-dithio	0.8 ^a	3.8 ^a	3 ^a [1250 ppb]	--	2 ^a
DMS	<0.3 ^a <0.3 ^a [250 ppb]	<0.3 ^a	20 ^a [1250 ppb] 54 ⁱ [15-20 ppb]	52 ^b	<0.3 ^a 2.5 ^a [250 ppb]
Tolylfluanid	--	--	--	9 ^b	--
N,N-dimethyl-N'-p-tolylsulfamide, DMST	--	--	--	15 ^b	--
3-OH-DMST	--	--	--	25 ^b	--
OH-methyl-DMST	--	--	--	22 ^b	--
COOH-DMST	--	--	--	18 ^b	--

2-OH-DMST	--	--	--	27 ^b	--
Methylene blue	--	$8.3 \times 10^{-3 f}$	--	--	--
N,N-dimethyl aminobenzene, NDAB	--	$6.4 \times 10^{-3 f}$	--	--	--
N,N-dimethyl-p-phenylenediamine, NDPD	--	$4.3 \times 10^{-2 f}$	--	--	--
Methyl orange	--	$7.2 \times 10^{-3 f}$	--	--	--
Methyl violet B	--	$1.2 \times 10^{-2 f}$	--	--	--
Auramine	--	$1.3 \times 10^{-2 f}$	--	--	--
Brilliant green	--	$<1.0 \times 10^{-4 f}$	--	--	--
N,N-dimethylformamide, DMF	$6.3 \times 10^{-2 m}$	$3.5 \times 10^{-4 f}$	--	--	--
poly(diallyldimethylammoniumchloride), polyDADMAC	N/A ^k	N/A ^j	--	--	--
Dimethyldithio-carbamate, DMDTC	0.008 ^e	0.008 ^e	--	--	--

^aThis paper, ^bSchmidt and Brauch 2008, ^cKosaka et al. 2009, ^dAndrzejewski et al. 2008, ^ePadhye et al. 2013, ^fOya et al. 2008, ^gMitch et al. 2002,

^hYang et al. 2009, ⁱvon Gunten et al. 2010, ^jPadhye et al. 2011, ^kPark et al. 2009, ^lBond and Templeton 2011, ^mMitch and Sedlak 2004; --: not tested, N/A: molar yield not available

Figure 1

Figure 1. Molar yield of NDMA formed by ozonation ($O_3 = 1 \text{ mM}$) of precursors in buffered ultrapure water at pH 7 with and without bromide addition (0, 50, 1250 ppb), by ozonation in wastewater, and by chloramination (140 mg/L or 2 mM as Cl_2) in buffered ultrapure water at pH 7. Error bars represent one standard deviation ($n=2$).

Figure 2

Figure 2. Effect of hydrogen peroxide addition on NDMA formation by ozonation ($O_3 = 1\text{ mM}$) in buffered ultrapure water at pH 7. Error bars represent one standard deviation ($n=2$).

Figure 3

Figure 3. Effect of ozone dose on NDMA formation by ozonation ($O_3 = 1\text{ mM}$) in buffered ultrapure water at pH 7. Error bars represent one standard deviation ($n=2$).

Figure 4

Figure 4. Comparison of NDMA formation with ozonation only ($O_3 = 1 \text{ mM}$) and ozonation/chloramination ($O_3 = 1 \text{ mM}$; $140 \text{ mg/L as } Cl_2$) in buffered ultrapure water at pH 7. Error bars represent one standard deviation ($n=2$).

Figure 5

Figure 5. Comparison of NDMA formation after ozonation ($O_3 = 1\text{ mM}$) in buffered ultrapure water at pH 7 with and without tert-butyl alcohol (tBA) for scavenging hydroxyl radicals. Error bars represent one standard deviation ($n=2$).