**Formation of *N*-nitrosamines by chloramination or ozonation of amines
listed in Pollutant Release and Transfer Registers (PRTRs)**

Suchul Yoon*, Hiroaki Tanaka

Research Center for Environmental Quality Management, Kyoto University, 1-2 Yumihama,
Otsu, Shiga 520-0811, JAPAN

*Corresponding author. Tel: +81 77 527 6223; Fax: +81 77 524 9869

E-mail addresses: yoons@biwa.eqc.kyoto-u.ac.jp, tigerchulman@gmail.com (S.C. Yoon)

Abstract

We determined whether or not the chloramination or ozonation of amines and hydrazines listed in Pollutant Release and Transfer Registers (PRTRs) results in the formation of *N*-nitrosamines when reacted in secondary wastewater effluent. We selected 12 primary, 2 secondary, 2 tertiary amines and 3 hydrazines from the PRTRs of Japan, the USA, and Korea. In this study, based on the assumption that there is a production of *N*-nitrosamines by not only the original selected amines and hydrazines but also the intermediate products in case of chloramination and ozonation, it was examined whether precursors were identified by selected amines and hydrazines based on the gap of the *N*-nitrosamines formation potential between day 0 and day 10 rather than analyzing the contribution depending on the concentration of selected amines and hydrazines. Many of the primary amines (notably 2,6-xylidine) and all of the secondary and tertiary amines produced *N*-nitrosodimethylamine (NDMA) by chloramination. Furthermore, the primary amines 2,6-xylidine, 3,3'-dimethylbenzidine, 4,4'-methylenebis(2-chloroaniline), 4-aminoazobenzene, *p*-chloroaniline, and *p*-cresidine produced more NDMA than did the secondary amines. The secondary amines produced mainly NDMA. Ozonation produced NDMA only from the hydrazine 1,1-dimethylhydrazine, and at a higher concentration than by chloramination. We identified 2,6-xylidine, 3,3'-dimethylbenzidine, 4,4'-methylenebis(2-chloroaniline), 4-aminoazobenzene, *p*-chloroaniline, *p*-cresidine, 1,1-dimethylhydrazine, diethylamine, 4,4'-methylenebis(*N,N*-dimethyl)benzenamine, and chinomethionat as warranting further study.

Key words: N-nitrosamines, N-nitrosamines precursors, chloramination, ozonation, Pollutant Release and Transfer Registers (PRTR)

1. Introduction

N-nitrosamines, including *N*-nitrosodimethylamine (NDMA), are carcinogenic (Richardson et al., 2007). Studies of how NDMA forms (Mirvish 1975; Schreiber and Mitch, 2006) have identified dimethylamine (DMA) as a precursor during chemical disinfection (Choi and Valentine, 2002; Mitch and Sedlak, 2002). However, DMA alone cannot account for all of the NDMA formed (Mitch et al., 2003; Mitch and Sedlak, 2004; Chen and Valentine, 2007; Padhye et al., 2009). Hence, efforts to identify other precursors and

formation pathways are critical to developing strategies to minimize NDMA formation during water and wastewater treatment (Krasner et al., 2009; Padhye et al., 2010). Cationic amine-based water treatment polymers containing DMA moieties form NDMA upon chlorination or chloramination (Najm and Trussell, 2001; Kohut and Andrews, 2003; Park et al., 2009). Accordingly, *N*-nitrosamines have been frequently detected in treatment plants using quaternary amine-based polymers such as poly (diallyldimethylammonium chloride) (poly-DADMAC) (Wilczak et al., 2003; Mitch 2009; Russell et al., 2010). Mechanisms of NDMA formation via the chloramination of poly-DADMAC and polyamines—amine-based polymers most commonly used in potable water treatment—have also been reported (Park et al., 2009). However, the reaction of these polymers with disinfectants other than chlorine or chloramines is unknown.

The concentration of NDMA formed as a byproduct of chloramination appears to depend on the chloramine dose. In a 2001 study (Najm et al., 2001), it was found that increasing the chloramine dose from 1 to 5 mg L⁻¹ more than doubled the resultant NDMA concentration. The findings suggested that chloramine doses in the ranges generally used for drinking water treatment might result in NDMA formation in the range of the potential regulatory window.

Regarding ozonation, studies conducted relating to NDMA was mainly on its reduction rather than on its formation as oxidation by-product. For example, it was reported that reaction rate constants of NDMA with ozone and HO• were $(5.2 \pm 0.16) \cdot 10^{-2}$ and $(4.5 \pm 0.21) \cdot 10^8 \text{ M}^{-1} \text{ s}^{-1}$, respectively, and NDMA were dominantly decomposed by HO• during ozonation (Lee et al., 2007b). Lee et al. (2007a) reported that when selected NDMA precursors were pre-ozonated, the NDMA FP_{NH₂Cl} by chloramination were decreased. We defined the formation potential (FP) of *N*-nitrosamines by chloramination (FP_{NH₂Cl}) as the increase in *N*-nitrosamine concentration during 10 d chloramination. More recently, however, several studies of NDMA formation by ozonation have been reported. Andrzejewski et al. (2008) reported that NDMA is formed by DMA ozonation. NDMA was found in high concentrations (>100 ng L⁻¹) in some German drinking waters after ozonation (Schmidt and Brauch, 2008). This was unexpected because NDMA is typically only formed in the low ng L⁻¹ range as an ozonation byproduct (Richardson et al., 2007; Andrzejewski et al., 2008; Oya et al., 2008; Hollender et al., 2009). The NDMA precursor was determined to be *N,N*-dimethylsulfamide (DMS), a previously unknown metabolite of the fungicide tolylfluanide (Schmidt and Brauch, 2008). A survey in Germany showed DMS concentrations as high as

18 $\mu\text{g L}^{-1}$ in groundwaters (Schmidt and Brauch, 2008). Because this metabolite is transformed to NDMA with high yields (29-52%) during ozonation of real waters, concentrations of 2-310 ng L^{-1} of NDMA were found post-ozonation. These observations led to a suspension of tolylfluanide in Germany and other European countries.

In addition to their formation as disinfection byproducts, *N*-nitrosamines are formed unintentionally in various industrial processes in which amines get into contact with nitrogen oxides, nitrous acid, or nitrite. Their formation during rubber manufacturing and processing, leather tanning, metal casting, metalworking using semisynthetic cutting fluids, and food processing has been recognized (Ducos et al., 1998; WHO 2002). *N*-Nitrosamines might also be present in rocket fuels based on *N,N*-dimethylhydrazine, and in antifreeze, pesticides, and metal-complexing agents (WHO 2002; Orange County Sanitation District 2002).

Various countries maintain Pollutant Release and Transfer Registers (PRTRs), environmental databases or inventories of potentially hazardous chemical substances or pollutants released to the environment or transferred off-site for treatment or disposal. National PRTRs may vary in terms of the chemicals included, the industry or business categories that must report, and the types of releases (<http://www.prtr.net/en/about>). In this study, using secondary effluent of wastewater treatment plant (WWTPs), we determined whether or not the chloramination or ozonation of amines listed in the PRTRs of Japan, the USA, and Korea results in *N*-nitrosamines.

2. Materials and Methods

2.1. Analytical chemicals

NDMA, *N*-nitrosomethylethylamine (NMEA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodi-*n*-propylamine (NDPA), *N*-nitrosopyrrolidine (NPYR), *N*-nitrosopiperidine (NPIP), *N*-nitrosomorpholine (NMOR), and *N*-nitrosodi-*n*-butylamine (NDBA) were purchased from Supelco (Bellefonte, PA, USA). Deuterated *N*-NDMA (NDMA- d_6), NDPA (NDPA- d_{14}), and NPYR (NPYR- d_8) were used as internal standards, and toluene- d_8 was used an injection internal standard; these chemicals were purchased from CDN Isotopes (Pointe-Claire, PQ, Canada). As isotope-labeled analogs were not available for some of the compounds, we used NDPA- d_{14} for quantification of NDBA, and NPYR- d_8 for NMEA, NDEA, NPIP, and NMOR. Individual stock solutions of the standards were prepared at 1 mg L^{-1} in dichloromethane

(DCM) and stored at -20 °C. Working standard mixtures (10 to 250 µg L⁻¹) of the compounds were prepared daily and used in standard curve preparation. GC-MS-grade DCM was obtained from Wako Pure Chemical Industries (Osaka, Japan). Ultrapure water (Milli-Q) was obtained from Milli-Q-Plus (Millipore, Billerica, MA, USA). The detailed information of characteristics of target *N*-nitrosamines is shown in Table 1.

(Insert Table 1)

2.2. Sample collection and preservation for method optimization

For tests of FP, secondary effluent samples were collected from a WWTP (conventional activated sludge treatment, 94,900 m³ d⁻¹, 108,000 population equivalents) located in a residential area of city O in Japan. All the samples were collected as grab samples and were filtered with a glass fiber filter (GF/B, pore size: 1.0 µm, Whatman, Osaka, Japan), which was washed with acetone before use. All samples were collected in 1-L amber glass bottles, held in the dark at 4 °C, and analyzed within 10 h.

2.3. Amines analyzed

We selected 12 primary, 2 secondary, 2 tertiary amines and 3 hydrazines from the PRTRs of Japan and Korea and from the Toxics Release Inventory of the USA.

Primary amines; 2,4-toluenediamine, 2,6-xylylidine, 3,3'-dimethylbenzidine, 3,3'-dichlorobenzidine, 4,4'-diaminodiphenylmethane, 4,4'-methylenebis(2-chloroaniline), 4-aminoazobenzene, aniline, *o*-anisidine, *p*-chloroaniline, *p*-cresidine, and toluidine (*o*-toluidine) (Fig. 1) were purchased from Wako and Sigma-Aldrich Japan (Tokyo, Japan). All were of analytical grade (purity > 95%).

(Insert Figure 1)

Secondary amines; diethylamine, and dimethylamine (Fig. 2) were purchased from

Wako and Sigma-Aldrich Japan. All were of analytical grade (purity > 95%).

(Insert Figure 2)

Tertiary amines; 4,4'-Methylenebis(*N,N*-dimethyl)benzenamine, and chinomethionat (Fig. 3) were purchased from Wako. All were of analytical grade (purity > 95%).

(Insert Figure 3)

Hydrazines; monomethylhydrazine, anhydrous hydrazine, and 1,1-dimethylhydrazine (Fig. 4) were purchased from Wako. All were of analytical grade (purity > 95%).

(Insert Figure 4)

2.4. Tests of FP

2.4.1. *N*-Nitrosamine FP_{NH_2Cl} by chloramination

The test for *N*-nitrosamine FP_{NH_2Cl} followed Mitch et al. (2003) with a minor modification (Yoon et al., 2011).

A 20 mM stock solution of monochloramine (NH_2Cl) was prepared for chloramination. Unfiltered wastewater samples from the secondary effluent (900 mL) in WWTP O with pH adjusted to 6.9 with 10 mM phosphate buffer were dosed with 100 mL of stock solution (final concentration of 2.0 mM, or 142 mg L^{-1} as Cl_2), and the samples were stored for 10 d at 20 °C. The concentrations of NH_2Cl were analyzed every day by *N,N*-diethyl-*p*-phenylenediamine colorimetry (Eaton et al., 1998). Organic matter (OM) in the form of suspended solids in the wastewater contained substantial concentrations of *N*-nitrosamine precursors. The water samples were not filtered, so as to retain the OM. The NH_2Cl stock solution was added intermittently to react with any *N*-nitrosamine precursors present in the OM. The rate of NH_2Cl consumption revealed the concentration of initial *N*-nitrosamine precursors present in the samples. The *N*-nitrosamine FP_{NH_2Cl} concentrations were adjusted

for the values of controls (analysis without spiking of any amines).

The residual concentration at the end of each test was approximately 0.14 mM (10 mg L⁻¹ as Cl₂), implying that the NH₂Cl concentration was sufficient for NDMA formation throughout the chloramination process. Therefore, the formation of *N*-nitrosamines under these conditions can be used as a surrogate for *N*-nitrosamine FP_{NH₂Cl}.

2.4.2. *N*-Nitrosamine FP_{O₃} by ozonation

We defined the FP of *N*-nitrosamines by ozonation (FP_{O₃}) as the increase in *N*-nitrosamine concentration at pH 9, temperature 20 °C, ozone feed rate 5 mg L⁻¹ min⁻¹, and retention time 20 min, at which the *N*-nitrosamine FP_{O₃} was maximized. Concentrations were adjusted for the values of blanks (analysis without spiking).

2.4.3. Contributions of precursors to *N*-nitrosamines by chloramination and ozonation

We selected several amines and hydrazines as *N*-nitrosamine precursors via chloramination or ozonation. We carried out batch experiments which are the test of *N*-Nitrosamine FP by chloramination or ozonation with these amines and hydrazines to determine FP_{NH₂Cl} and FP_{O₃}. In this study, based on the assumption that there is a production of *N*-nitrosamines by not only the original selected amines and hydrazines but also the intermediate products in case of chloramination and ozonation, it was examined whether precursors were identified by selected amines based on the gap of the *N*-nitrosamines FP between day 0 and day 10 rather than analyzing the contribution depending on the concentration of selected amines and hydrazines.

2.5. Extraction and pre-treatment procedure

First, 200 mL of each collected sample was filtered with a GF/B glass fiber filter. Then the deuterated forms of NDMA (NDMA-*d*₆; CDN Isotopes, Pointe-Claire, Canada), NDPA (NDPA-*d*₁₄; CDN Isotopes), and NPYR (NPYR-*d*₈; CDN Isotopes) were added to all filtrate samples as internal standards and the *N*-nitrosamines in the filtrate were concentrated in a Sep-Pak NH₂ cartridge (as a sample clean-up step) and an AC-2 cartridge at a rate of 10 mL

min⁻¹. Use of the NH₂ cartridge (silica-based polar-bonded phase with basic character) substantially reduces the amount of co-extracted acidic interferences. The cartridges were conditioned in advance with 5 mL of DCM, 5 mL of methanol, and 5 mL of Milli-Q water. After concentration, only the AC-2 cartridge was dried, using a pneumatic pump (Ulvac, DA-6-S, Osaka, Japan), for 2 h, in order to remove the remaining water in the cartridge. *N*-nitrosamines were eluted from the dehydrated cartridge with 2 mL of DCM. The eluate was further concentrated with a gentle stream of N₂ gas at 35 °C just before dryness. The residue was reconstituted in 200 µL of DCM and subjected to *N*-nitrosamine quantification by GC-MS/MS. To correct for fluctuations in the GC-MS/MS apparatus, an injection internal standard (toluene-*d*₈: CDN Isotopes) was added just before injection of the samples into the system (Yoon et al., 2012).

2.6. Measurement by GC-MS/MS

The eight *N*-nitrosamines, their three internal standards, and the injection internal standard were analyzed on a Varian 300 triple-quadrupole mass spectrometer (Varian, Tokyo, Japan) coupled to a Varian 450 GC (Yoon et al., 2012). Chromatographic separation was achieved in a FactorFour VF-17 ms capillary column (Varian; 30 m length, 0.25 mm id, and 0.25 µm film thickness). Specific information details of GC-MS/MS, and optimized analytical MS parameters are given in Table 2.

(Insert Table 2)

An optimization process was performed for each analyte to optimize data acquisition under multiple reaction monitoring (MRM) mode. Positive chemical ionization (CI) mode was used as ionization mode. This process was performed by injecting 1 mg L⁻¹ of individual standard solutions without using a column. Collision energy and ionization mode were optimized for each analyte in order to obtain maximum sensitivity with the greatest amount of product ions available, and the most sensitive MRM transitions were determined for each analyte (Table 1). The MS parameters are summarized in Table 1.

238

239 3. Results and discussion

240 3.1. Limit of detection (LOD) and limit of quantification (LOQ)

241 The LOD and LOQ of this method were estimated by measuring standard solutions with
242 *N*-nitrosamine concentrations of 5, 10, 20, 50, and 100 $\mu\text{g L}^{-1}$ by GC-MS/MS. From values
243 measured five times for each solution, the average value and standard deviation (SD) value
244 for each *N*-nitrosamine were calculated and then used for acquiring a coefficient of variation
245 (CV), which is defined as the ratio of SD value as compared to the average value. Based on
246 the SD (σ) of the solution with the lowest concentration and a CV of less than 20%, the LOD
247 (3σ) and LOQ (10σ) were calculated. The LOD of the eight *N*-nitrosamines was in the range
248 of 0.1 to 1.0 ng L^{-1} and the LOQ was in the range of 0.4 to 3.3 ng L^{-1} . Detail information on
249 the LODs and LOQs of the eight *N*-nitrosamines is given in Table 3.

250

251 (Insert Table 3)

252

253

254 3.2. Production of *N*-nitrosamines by chloramination

255 Chloramination produced notable concentrations of four *N*-nitrosamines (NDMA,
256 NDEA, NPYR, and NMOR) from each amine (Fig. 5). All secondary and tertiary amines
257 produced NDMA (Fig. 5a), as reported previously in relation to secondary amines (Tanaka et
258 al., 1998; Mitch and Sedlak, 2002) and recently in relation to tertiary amines (Lee et al.,
259 2008; Le Roux et al., 2011; Shen and Andrews, 2011). Many primary amines also produced
260 NDMA, among which 2,6-xylylidine produced the most ($\text{FP}_{\text{NH}_2\text{Cl}} = 0.74 \text{ nmol NDMA nmol}^{-1}$
261 2,6-xylylidine). This reaction has not been reported before. Furthermore, the primary amines *p*-
262 chloroaniline and *p*-cresidine produced more NDMA than the secondary amines (Fig. 5a).
263 The primary amines produced more NDEA and NPYR than the secondary and tertiary
264 amines, albeit at low concentrations (Fig. 5b and 5c). Some of the primary amines produced
265 more NMOR also than the secondary and tertiary amines (Fig. 5d). The $\text{FP}_{\text{NH}_2\text{Cl}}$
266 concentrations of the other *N*-nitrosamines were very low (ranging from below the detection
267 limit to 12 ng L^{-1}).

268

269 (Insert Figure 5)

3.3. Production of *N*-nitrosamines by ozonation

Ozonation produced notable concentrations of four *N*-nitrosamines (NDMA, NDEA, NMOR, and NDBA) from each amine (Fig. 6). NDMA was produced only from the secondary amine 1,1-dimethylhydrazine (Fig. 6a), and at a higher concentration than by chloramination. NDMA is formed by ozonation of DMA (Andrzejewski et al., 2008) and of a plant growth regulator (daminozide), its decomposition product (1,1-dimethylhydrazine), a fungicide (tolylfluanide), and its decomposition products (*N,N*-dimethyl-*N'*-*p*-tolylsulphamide and dimethylsulfamide) (Schmidt and Brauch, 2008; Gunten et al., 2010). Although NDMA was produced from 1,1-dimethylhydrazine, as in several previous studies (Mitch et al., 2003), it was not produced from DMA here. NDEA was produced at the greatest concentration from *p*-chloroaniline, although the concentration was low (Fig. 6b). NMOR was produced from the primary amines 2,6-xylidine and 3,3'-dimethylbenzidine (Fig. 6c). NDBA was produced from the primary amines 2,6-xylidine, 3,3'-dimethylbenzidine, and 4,4'-diaminodiphenylmethane (Fig. 6d). The FP_{O₃} concentrations of the other *N*-nitrosamines were very low (ranging from below the detection limit to 9 ng L⁻¹).

(Insert Figure 6)

3.4. Contributions of precursors to *N*-nitrosamines by chloramination and ozonation

Several amines contributed to the production of NDMA by chloramination (Fig. 7a), of which one contributed also by ozonation (Fig. 7b). Of these, we identified three primary (2,6-xylidine, *p*-chloroaniline, *p*-cresidine), two secondary (1,1-dimethylhydrazine, diethylamine), and a tertiary amines (chinomethionat) as warranting further study. We omitted dimethylamine, as it has been found to be the most effective organic nitrogen precursor of NDMA formation by chloramination. Detail information of the concentrations and contribution of *N*-nitrosamines FP by chloramination and ozonation are given in Table SM-1 and SM-2 in Supplementary Material (SM).

(Insert Figure 7)

4. Conclusions

In this study, using secondary effluent of wastewater treatment plant (WWTPs), we determined whether or not the chloramination or ozonation of amines listed in the PRTRs of Japan, the USA, and Korea results in *N*-nitrosamines. The more specific conclusions are follows:

Many of the 12 primary amines and all of the 2 secondary, 2 tertiary amines and 3 hydrazines produced NDMA by chloramination. Two primary amines (*p*-chloroaniline and *p*-cresidine) produced more NDMA than did the secondary amines. NDEA and NPYR were produced more by the primary amines than by the secondary and tertiary amines, but the production was low (20–30 ng L⁻¹).

Ozonation produced NDMA only from a hydrazine (1,1-dimethylhydrazine), and by more than by chloramination. Ozonation also produced NDEA from *p*-chloroaniline, and NMOR and NDBA from primary amines.

The contributions of precursors to NDMA FP_{NH2Cl} were 0.74 nmol NDMA FP_{NH2Cl} nmol⁻¹ 2,6-xylydine, 0.50 nmol NDMA FP_{NH2Cl} nmol⁻¹ 3,3'-dimethylbenzidine, 0.84 nmol NDMA FP_{NH2Cl} nmol⁻¹ 4,4'-methylenebis(2-chloroaniline), 0.42 nmol NDMA FP_{NH2Cl} nmol⁻¹ 4-aminoazobenzene, 0.54 nmol NDMA FP_{NH2Cl} nmol⁻¹ *p*-chloroaniline, 0.64 nmol NDMA FP_{NH2Cl} nmol⁻¹ *p*-cresidine, 0.25 nmol NDMA FP_{NH2Cl} nmol⁻¹ 1,1-dimethylhydrazine, 0.30 nmol NDMA FP_{NH2Cl} nmol⁻¹ diethylamine, 0.87 nmol NDMA FP_{NH2Cl} nmol⁻¹ 4,4'-methylenebis(*N,N*-dimethyl)benzenamine, and 0.93 nmol NDMA FP_{NH2Cl} nmol⁻¹ chinomethionat⁻¹.

Acknowledgments

This study was partially supported by the CREST project, which is funded by the Japan Science and Technology Agency and the Ministry of land, Infrastructure, Transport and Tourism of Japan. We thank the staff of WWTP N for their cooperation. We especially thank Dr. Norihide Nakada of the Research Center for Environmental Quality Management at Kyoto University for his painstaking help with this research work. We also thank Mr.

Yasuhiro Kato of Metawater Co., Ltd for their valuable cooperation.

References

- Andrzejewski, P., Kasprzyk-Hordern, B., Nawrocki, J., 2008. *N*-Nitrosodimethylamine (NDMA) formation during ozonation of dimethylamine containing water. *Water Res.* 42, 863–870.
- APHA, 1998. *Standard Methods for the Examination of Water and Wastewater*. American Public Health Association, Washington, DC.
- Chen, Z., Valentine, R.L., 2007. Formation of *N*-nitrosodimethylamine (NDMA) from humic substances in natural water. *Environ. Sci. Technol.* 41, 6059–6065.
- Choi, J., Valentine, R.L., 2002. Formation of *N*-nitrosodimethylamine (NDMA) from reaction of monochloramine: A new disinfection byproduct. *Water Res.* 36, 817–824.
- Ducos, P., Gaudin, R., Maire, C., Mavelle, T., Bouchikhi, B., Debry, G., 1998. Occupational exposure to volatile nitrosamines in foundries using the Ashland core-making process, *Environ. Res.* 47, 72–78.
- Gunten, V., Salhi, E.C., Schmidt, K., Arnold, W.A., 2010. Kinetics and mechanisms of *N*-Nitrosodimethylamine formation upon ozonation of *N,N*-Dimethylsulfamide-containing waters: bromide catalysis. *Environ. Sci. Technol.* 44, 5762–5768.
- Hollender, J., Zimmermann, S.G., Koepke, S., Krauss, M., McArdell, C.S., Ort, C., Singer, H., Von Gunten, U., Siegrist, H., 2009. Elimination of organic micropollutants in a municipal wastewater treatment plant upgraded with a full-scale post-ozonation followed by sand filtration. *Environ. Sci. Technol.* 43, 7862–7869.
- Kohut, K.D., Andrews, S.A., 2003. Polyelectrolyte age and *N*-Nitrosodimethylamine formation in drinking water treatment. *Water Qual. Res. J. Can.* 38, 719–735.
- Krasner, S.W., Westerhoff, P., Chen, B., Rittmann, B.E., Amy, G., 2009. Occurrence of disinfection byproducts in United States wastewater treatment plant effluents. *Environ. Sci. Technol.* 43, 8320–8325.
- Lee, C., Lee, Y., Schmidt, C., Yoon, J., Von Gunten, U., 2008. Oxidation of suspected *N*-Nitrosodimethylamine (NDMA) precursors by ferrate (VI): kinetics and effect on the NDMA formation potential of natural waters. *Water Res.* 42, 433–441.
- Lee, C., Yoon, J., Von Gunten, U., 2007b. Oxidative degradation of *N*-nitrosodimethylamine by conventional ozonation and the advanced oxidation process ozone/hydrogen peroxide.

Water Res. 41, 581–590.

Lee, C., Schmidt, C., Yoon, J., Von Gunten, U., 2007a. Oxidation of *N*-Nitrosodimethylamine (NDMA) precursors with ozone and chlorine dioxide: kinetics and effect on NDMA formation potential. Environ. Sci. Technol. 41, 2056-2063.

Le Roux, J., Gallard, H., Croué, J.P., 2011. Chloramination of nitrogenous contaminants (pharmaceuticals and pesticides): NDMA and halogenated DBPs formation. Water Res. 45, 3164–3174.

Mirvish, S.S., 1975. Formation of *N*-nitroso compounds-Chemistry, kinetics, and invivo occurrence. Toxicol. Appl. Pharmacol. 31, 325–351.

Mitch, W.A., Gerecke, A.C., Sedlak, D.L., 2003. *N*-Nitrosodimethylamine (NDMA) precursor analysis for chlorination of water and wastewater. Water Res. 37, 3733–3741.

Mitch, W.A., Krasner, S.W., Westerhoff, P., Dotson, A., 2009. Occurrence and Formation of Nitrogenous Disinfection By-Products; Water Research Foundation, Denver, CO, 2009.

Mitch, W.A., Sedlak, D.L., 2002. Formation of *N*-nitrosodimethylamine (NDMA) from dimethylamine during chlorination. Environ. Sci. Technol. 36, 588-595.

Mitch, W.A., Sedlak, D.L., 2004. Characterization and fate of *N*-nitrosodimethylamine precursors in municipal wastewater treatment plants. Environ. Sci. Technol. 38, 1445–1454.

Najm, I., Trussell, R.R., 2001. NDMA formation in water and wastewater, J. Am. Water Works. Ass. 93(2), 92-99.

Orange County Sanitation District, 2002. Sources of *N*-Nitrosodimethylamine in the Orange County Sanitation District Surface Area. Report. Source Control Division, Orange County Sanitation District, California.

Oya, M., Kosaka, K., Asami, M., Kunikane, S., 2008. Formation of *N*-Nitrosodimethylamine (NDMA) by ozonation of dyes and related compounds. Chemosphere 73, 1724-1730.

Padhye, L., Tezel, U., Mitch, W.A., Pavlostathis, S.G., Huang, C.H., 2009. Occurrence and fate of nitrosamines and their precursors in municipal sludge and anaerobic digestion systems. Environ. Sci. Technol. 43, 3087–3093.

Padhye, L., Wang, P., Karanfil, T., Huang, C.H., 2010. Unexpected role of activated carbon in promoting transformation of secondary amines to *N*-nitrosamines. Environ. Sci. Technol. 44, 4161–4168.

Park, S.H., Wei, S., Mizaiakoff, B., Taylor, A.E., Favero, C.d., Huang, C.H., 2009. Degradation of amine-based water treatment polymers during chloramination as *N*-

400 Nitrosodimethylamine (NDMA) precursors. Environ. Sci. Technol. 43, 1360–1366.
 401 PRTR, Net, <http://www.prtr.net/en/about/>.
 402 Richardson, S.D., Plewa, M.J., Wagner, E.D., Schoeny, R., DeMarini, D.M., 2007.
 403 Occurrence, genotoxicity, and carcinogenicity of regulated and emerging disinfection by-
 404 products in drinking water: A review and roadmap for research. Mutation Res. 636, 178–
 405 242.
 406 Russell, C., Blute, N., Chowdhury, Z., Wu, X., Via, S., 2010. Nitrosamine occurrence in the
 407 U.S. regulatory impacts and treatment considerations. In Water Quality Technology
 408 Conference and Exposition, Savannah, GA, 2010.
 409 Schmidt, C.K., Brauch, H.J., 2008. *N,N*-Dimethylsulfamide as precursor for *N*-
 410 Nitrosodimethylamine (NDMA) formation upon ozonation and its fate during drinking
 411 water treatment. Environ. Sci. Technol. 42, 6340–6346.
 412 Schreiber, I.M., Mitch, W.A., 2006. Nitrosamine formation pathway revisited: The
 413 importance of chloramine speciation and dissolved oxygen. Environ. Sci. Technol.
 414 40(19), 6007–6014.
 415 Shen, R., Andrews, S., 2011. Demonstration of 20 pharmaceuticals and personal care
 416 products (PPCPs) as nitrosamine precursors during chloramine disinfection. Water Res.
 417 45, 944–952.
 418 Tanaka, K., Hayatsu, T., Negishi, T., Hayatsu, H., 1998. Inhibition of *N*-nitrosation of
 419 secondary amines in vitro by tea extracts and catechins. Mutation Res. 412, 91–98.
 420 WHO, 2002. Concise International Chemical Assessment Document, 38, World Health
 421 Organization, Geneva, *N*-Nitrosodimethylamine.
 422 Wilczak, A., Assadi-rad, A., Lai, H.H., Hoover, L.L., Smith, J.F., Berger, R., Rodigati, F.J.,
 423 Beland, W., Lazzelle, L.L., Kincannon, E.G., Baker, H., Heaney, C.T., 2003. Formation
 424 of NDMA in chloraminated water coagulated with DADMAC cationic polymer. J. Am.
 425 Water Works. Ass. 95(9), 94–106.
 426 Yoon, S.C., Nakada, N.H., Tanaka, H.A., 2011. Occurrence and removal of NDMA and
 427 NDMA formation potential in wastewater treatment plants. J. Hazard. Mater. 190, 897-
 428 902.
 429 Yoon, S.C., Nakada, N.H., Tanaka, H.A., 2012. A new method for quantifying *N*-
 430 nitrosamines in wastewater samples by gas chromatography - triple quadrupole mass
 431 spectrometry, Talanta 97, 256-261.

Table 1Characteristics of target *N*-nitrosamines.

No.	<i>N</i> -nitrosamine	CAS number	Molecular weight	Corresponding internal standard
1	<i>N</i> -nitrosodimethylamine (NDMA)	62-75-9	74.08	NDMA- <i>d</i> ₆
2	NDMA- <i>d</i> ₆ (internal standard)	17829-05-9	80.12	.
3	<i>N</i> -nitrosomethylethylamine (NMEA)	10595-95-6	88.11	NPYR- <i>d</i> ₈
4	<i>N</i> -nitrodiethylamine (NDEA)	55-18-5	102.14	NPYR- <i>d</i> ₈
5	<i>N</i> -nitrosodi- <i>n</i> -propylamine (NDPA)	621-64-7	130.22	NDPA- <i>d</i> ₁₄
6	NDPA- <i>d</i> ₁₄ (internal standard)	93951-96-3	145.20	.
7	<i>N</i> -nitrosopyrrolidine (NPYR)	930-55-2	100.11	NPYR- <i>d</i> ₈
8	NPYR- <i>d</i> ₈ (internal standard)	1219802-09-1	109.12	.
9	<i>N</i> -nitrosopiperidine (NPIP)	100-75-4	114.15	NPYR- <i>d</i> ₈
10	<i>N</i> -nitrosomorpholine (NMOR)	59-89-2	116.10	NPYR- <i>d</i> ₈
11	<i>N</i> -nitrosodi- <i>n</i> -butylamine (NDBA)	924-16-3	158.24	NDPA- <i>d</i> ₁₄

CAS, Chemical Abstracts Service.

Table 2

Detailed analytical parameters for GC-MS/MS.

Gas chromatograph (Varian 450 GC)	
Capillary column	FactorFour VF-17 ms, 30 m × 0.25 mm i.d., 0.25 µm film thickness
Flow rate	1 mL min ⁻¹
Oven program	40 °C, hold 1 min; to 80 °C at 5 °C min ⁻¹ ; to 280 °C at 20 °C min ⁻¹ , hold 3 min
Injector temperature	250 °C
Interface temperature	280 °C
Injection mode	Splitless, hold 1 min
Injection volume	2 µL
Mass spectrometer (Varian 300 MS)	
Ionization mode	positive chemical ionization
Detector range	600 to 2000 V
Ion source temperature	220 °C
Transfer line temperature	250 °C
Carrier gas	helium, constant 50 kPa, 1.5 mL min ⁻¹
Chemical ionization gas	methane, 1Pa
Filament current	50 µA
Ionization energy	70 eV
Acquisition mode	– MRM ^a mode – Selected ions: NDMA (75 ^b , 43 ^c , 58 ^c), NDMA- <i>d</i> ₆ (80 ^b , 46 ^c , 64 ^c), NMEA (89 ^b , 43 ^c , 61 ^c), NDEA (103 ^b , 56 ^c , 75 ^c), NDPA (131 ^b , 43 ^c , 89 ^c), NDPA- <i>d</i> ₁₄ (145 ^b , 97 ^c), NPYR (101 ^b , 55 ^c , 70 ^c), NPYR- <i>d</i> ₈ (109 ^b , 62 ^c), NPIP (115 ^b , 41 ^c , 69 ^c), NMOR (117 ^b , 57 ^c , 87 ^c), NDBA (159 ^b , 57 ^c , 103 ^c)

^a Multiple reaction monitoring. ^b Parent ion. ^c Daughter ion.**Table 3**LODs and LOQs of the *N*-nitrosamines studied.

	NDMA	NMEA	NDEA	NDPA	NPYR	NPIP	NMOR	NDBA
LOD (ng L ⁻¹)	0.1	0.4	1.0	0.9	0.4	0.5	1.0	0.9
LOQ (ng L ⁻¹)	0.4	1.3	3.2	2.9	1.3	1.5	3.3	2.9

Fig. 1. Chemical structures of selected primary amines.

Dimethylamine

Diethylamine

Fig. 2. Chemical structures of selected secondary amines.

**4,4'-methylenebis
(N,N-dimethyl)benzenamine**

Chinomethionat

Fig. 3. Chemical structures of selected tertiary amines.

Monomethylhydrazine

Hydrazine, anhydrous

1,1-dimethylhydrazine

Fig. 4. Chemical structures of selected hydrazines.

Fig. 5. FP_{NH2Cl} concentrations of 4 *N*-nitrosamines by chloramination of 400 ng L⁻¹ of each amine and hydrazine in secondary effluent.

Fig. 6. FP_{O3} concentrations of 4 *N*-nitrosamines by ozonation of 400 ng L⁻¹ of each amine and hydrazine in secondary effluent.

Fig. 7. Contribution of 400 ng L⁻¹ of each amine and hydrazine to *N*-nitrosamine FP by (A) chloramination and (B) ozonation.