Contamination, decomposition, and formation of

N-nitrosodimethylamine in water samples at the ng/L level of
determination

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Abstract

An ultra-sensitive analytical system that can determine the concentration of N-nitrosamines at the ng/L level without preconcentration was used to investigate the contamination, decomposition, and formation of N-nitrosodimethylamine (NDMA) and other N-nitrosamines in water samples during general analytical procedures. A preliminary experiment was performed to estimate the NDMA concentrations in ambient air. As the air samples contained NDMA at concentrations in the range of 2.0–10.7 ng/m³, ambient air was identified as the source of NDMA contamination in water samples. We directly confirmed that the concentration of aqueous 10-ng/L NDMA samples stored in clear glass bottles decreased upon exposure to sunlight. Thus, to maintain the N-nitrosoamine concentration, such samples must always be protected from sunlight during sampling. The existence of N-nitrosamines in experimental reagents, such as ranitidine and sodium hypochlorite solutions, was also confirmed, as was the formation of NDMA on an activated carbon solid-phase extraction cartridge.

Keywords: N-nitrosodimethylamine (NDMA), air, sunlight, reagent, contamination, decomposition, formation
1. Introduction

$N$-Nitrosodimethylamine (NDMA) and other $N$-nitrosamines are known potent carcinogens that are present in food, beverages, tobacco, cosmetics, and rubber products\textsuperscript{1-3}. It has been confirmed during the last two decades that $N$-nitrosamines are formed as byproducts of tap water and wastewater disinfection\textsuperscript{4,5}. Therefore, $N$-nitrosamine levels in recycled water intended for potable reuse are of emerging concern\textsuperscript{6}, and so NDMA levels in potable water are being increasingly regulated in many parts of the world. For example, California (USA) has set a notification level of 10 ng/L for NDMA in potable water\textsuperscript{7}, while Australia has set a guideline level of 10 ng/L for NDMA in recycled water intended for indirect potable water reuse\textsuperscript{8}.

$N$-Nitrosamines present at the ng/L level in water samples are typically determined by gas or liquid chromatography coupled with mass spectrometric detection after an up to 1,000-fold preconcentration using solid-phase extraction (SPE) techniques\textsuperscript{5,9}. The US Environmental Protection Agency method 521 (EPA method 521) states that an activated carbon (AC) absorbent should be used for SPE in $N$-nitrosamine determination\textsuperscript{10}. However, recent studies have demonstrated that AC surfaces provide effective sites for the formation of NDMA through the reaction of dimethylamine with nitrite ions in water\textsuperscript{11}. Therefore, the NDMA formed during SPE procedures is a cause for concern. Furthermore, although these analytical methods have been successfully implemented for the accurate quantification of $N$-nitrosamines in water, they require labor-intensive pretreatment procedures and large sample volumes. Therefore, it is easy to overlook the effects of contamination, decomposition, and the formation of $N$-nitrosamines at ng/L levels during such analytical procedures.

Recently, an ultra-sensitive $N$-nitrosamine analysis system based on HPLC
separation followed by in-line matrix removal, the photochemical conversion of \( N \)-nitrosamines to peroxynitrite, and luminol-based chemiluminescence detection (HPLC-AEM-PR-CL) has been developed \(^{12,13}\). This system can measure NDMA at sub-ng/L levels in water samples without preconcentration using a sample injection volume of only 200 \( \mu \)L. A validation study was also recently performed for this system for the determination NDMA in advanced-treated recycle water, drinking water, and waste water \(^{14}\). The usefulness of this system has been demonstrated in several recent studies, including surveys of tap water and its source water \(^{15,16}\), and evaluations of reverse osmosis membranes and disinfectants \(^{17-21}\). As this system is currently the only method capable of directly detecting NDMA in water samples at ng/L levels, it has revealed that sample analyses are widely subject to contamination by \( N \)-nitrosamines and their decomposition.

Accordingly, in the current study, we investigate the contamination of water samples with \( N \)-nitrosamines from ambient air. In addition, some previously reported data on NDMA decomposition and formation are rechecked at the ng/L level without using analytical processes that potentially lead to contamination by (or the formation of) NDMA. We expect that this study will provide highly useful information for analysts that routinely use other methodologies for the determination of \( N \)-nitrosamines.

2. Experimental

2.1. Reagents and solutions

Certified 100 mg/L NDMA, \( N \)-nitrosomorpholine (NMOR), \( N \)-nitrosomethylethylamine (NMEA), and \( N \)-nitrosopyrrolidine (NPYR) solutions in methanol were purchased from Agilent (RI, USA). A stock solution of each compound was prepared at a concentration
of 10 ng/mL in methanol and stored at −15 °C in the dark. A working standard solution of each compound was also prepared at a concentration of 10 ng/mL in ultrapure water. Luminol (5-amino-2,3-dihydro-1,4-phthalazinedione) was purchased from TCI (Tokyo, Japan). A luminol stock solution was prepared at a concentration of 20 mM by dissolving luminol (0.355 g) in sodium carbonate buffer (100 mL, 0.5 M, pH 10.0). The luminol stock solution was stored at 4 °C in the dark. All chemicals used in this study were of analytical reagent grade or higher, and were used without further purification. The ultrapure water used in this study was obtained using an Elix 5 UV water purification system (Millipore, Tokyo, Japan) followed by a Milli-Q Advantage system (Millipore, Tokyo, Japan).

2.2. Instrumentation

The HPLC-AEM-PR-CL system is shown in Fig. S1. The instrument comprises of LC-10ADvp HPLC pumps (Shimadzu, Kyoto, Japan), an SIL-20AC autosampler (Shimadzu), an electrochemically regenerated anion exchange module (AEM) (Nichiri Mfg., Chiba, Japan); an AEM-photochemical reactor (PR) control unit equipped with a peristaltic pump dedicated to the AEM washing solution and two inline degassers (Nichiri Mfg., Chiba, Japan), a CTO-20AC column oven (Shimadzu) containing the AEM, a PR, and an InertSustain C18-AQ column (5 μm, 250 mm length; 4.6 mm i.d., GL Sciences, Tokyo, Japan), a CLD-8020 CL detector (Nichiri Mfg., Chiba, Japan), and a Chromato-PRO data processor (Runtime Instruments, Kanagawa, Japan). The PR installed in the column oven was equipped with a low-pressure mercury lamp (OFS-221XB, Miyata Elevam Inc., Yokohama, Japan) and a reaction coil composed of a perfluoroalkoxy alkane tube (1/16” o.d. × 0.5 mm i.d., active length = 100 cm) in an aluminum tube.
The impinger method was used for N-nitrosamine analysis in air. Two serially connected impingers were used to trap NDMA from the air samples. The impingers were charged with 25 mL of ultra-pure water as the trap solvent and air was aspirated using an MP-W5 air-pump (SIBATA, Saitama, Japan) at a rate of 0.50 L/min for approximately 30 min through the impingers (Fig. S2). The ultra-pure water in the first impinger was analyzed with the HPLC-AEM-PR-CL system to confirm the presence of NDMA in the air.

A UV Light Meter TM-208 (Tenmars Electronics Ltd., Taipei, Taiwan) was used to measure the solar irradiance.

2.3. Analytical conditions for the HPLC-AEM-PR-CL system

Analysis using the HPLC-AEM-PR-CL system was performed by feeding the eluent (1 mM phosphate buffer-methanol, 95:5, v/v, pH 6.9) at a flow rate of 1.5 mL/min. Water samples (except for ultra-pure water) were pre-filtered through a 0.45-μm hydrophilic PTFE filter and injected into the HPLC-AEM-PR-CL system. The sample injection volume was 200 μL unless otherwise stated. The AEM was operated at a constant current of 100 mA, and the UV lamp intensity was kept constant by automatic adjustment of the voltage through a UV intensity feedback system equipped on the AEM-PR control unit. The temperature in the oven (containing the column, AEM, and PR) was maintained at 40 °C. The anode compartment of the AEM was continuously flushed with a cleaning solution (ultra-pure water) at 0.5 mL/min to remove anions that permeated through the anion exchange membrane. A 0.05-mM luminol solution was fed to the HPLC-AEM-PR-CL system at a flow rate of 0.50 mL/min.
2.4. Decomposition and stability test procedures

To confirm the decomposition of NDMA in glass vessels by sunlight, the following procedure was employed. Amber and clear autosampler vials (1.5 mL volume, glass thickness, 1 mm; i.d., 1 cm) were used as test vessels. A sample of the NDMA solution (1 mL, 10 ng/L in ultrapure water) was fed into the vial and the cap was tightened. The prepared vials were placed under sunlight for the desired times. After exposure to sunlight, the vials were set in an autosampler and the residual NDMA concentrations were measured.

Stability tests for the N-nitrosamines present in the water samples were carried out over 30 d as follows. Three N-nitrosamine solutions (10 ng/L) were prepared using tap water, tap water containing 2 mM sodium thiosulfate, and tap water containing 2 mM sodium sulfite, after which aliquots (1 mL) of the solutions were fed into 1.5-mL amber polypropylene (PP) autosampler vials and their caps closed tightly. Thirty vials were prepared for each solution, with 15 of each stored at 4 or 25 °C in the dark for 0, 3, 7, 14, and 30 d and then immediately stored in a freezer. At the end of the static period, all samples (a total of 90 vials) were defrosted and then measured in the same set.

3. Results and discussion

3.1 NDMA contamination from laboratory air

We observed that NDMA was consistently detected in the ultra-pure water after exposure to the atmosphere. Typical chromatograms obtained from the ultra-pure water allowed to stand in a glass beaker for 0, 6, and 24 h are shown in Fig. 1, which indicates that NDMA contamination of the ultra-pure water was caused by the ambient air. However, literature information regarding the concentrations of N-nitrosamines in ambient air is scarce.\textsuperscript{22,23}
although one previous study demonstrated that the concentrations of NDMA in air
sampled from around industrial plants such as lubber plants were at μg/m³ levels. Therefore, a preliminary experiment was performed to estimate the NDMA concentrations in air samples.

Table 1 shows the NDMA concentrations in the air samples obtained from various locations. The air samples obtained from the analytical laboratories (Rooms A and B) contained NDMA at a level of 10 ng/m³. Although no NDMA was detected in the atmospheric air, it is possible that this formed through decomposition under solar irradiation. It was also found that the living space air contained NDMA at levels of a few ng/m³. As this study employed a single air-sampling system in addition to serial sampling, the obtained values may reflect the time distribution of NDMA in the room. Indeed, the source and behavior of NDMA in the air appears particularly interesting, and so further research will be conducted in this area. In the case of our study, we have confirmed that exposure to air after water sampling is the main source of NDMA contamination at the ng/L level. We also confirmed that the ultra-pure water in the second impinger did not contain NDMA. Therefore, the NDMA in the air samples was collected in the ultra-pure water while passing through the first impinger, suggesting that NDMA contamination from ambient air is efficiently removed upon its passage through water. We previously installed an air-washing system in the HPLC-PR-CL system to prevent the contamination of nitrate and nitrite from ambient air to an eluent, since these anions are also detected by the HPLC-PR-CL system and cause background CL. In this study, we also confirmed the possibility the NDMA and N-nitrosamines present in ambient air result in the contamination of an eluent. Therefore, the air-washing system was installed in the HPLC-AEM-PR-CL system as shown in Fig. S1.
3.3 Decomposition of NDMA in glass vessels by sunlight

N-Nitrosamines have two absorption wavelengths, namely 230 and 330 nm. To date, a number of studies have addressed the decomposition and detection of N-nitrosamines by photochemical excitation at 230 nm\textsuperscript{25-27}, and the detection methodology proposed herein also employs photochemical cleavage of the N–NO bond with UV irradiation from a low-pressure mercury lamp (254 nm)\textsuperscript{12}. However, the sunlight that reaches the Earth’s surface contains radiation with a wavelength of 330 nm, while the 230 nm region of the sunlight spectrum is absorbed by the atmosphere. We also note that the photochemical attenuation of NDMA in surface water by natural sunlight has been previously demonstrated\textsuperscript{28}, where direct photolysis under solar irradiation at 765 W/m\textsuperscript{2} was found to degrade NDMA at a half-life of 16 min. In addition, light with a wavelength of 330 nm is known to pass through glassware, and so EPA method 521 also states that water samples should be stored in amber bottles prior to analysis\textsuperscript{10}. Since our method can directly measure the degradation of ng/L levels of NDMA in glassware, the decomposition of NDMA in glassware was also investigated.

More specifically, Fig. 2(a) shows the result of the decomposition test, whereby the NDMA present in the clear glass vial was easily decomposed by sunlight. Indeed, N-nitrosamines have been reported to decompose readily upon exposure to sunlight, even in high-matrix water samples such as treated wastewater\textsuperscript{28}. We also confirmed that N-nitrosamines decompose in ultra-pure water, tap water, and treated wastewater samples (Table S1, Fig. S3); however, the N-nitrosamines stored in the amber glassware did not decompose. Figure 2(b) shows the relationship between the residual concentration of NDMA and average solar irradiance after 20 min exposure. As indicated, the residual
NDMA concentration in the clear glass vials decreased upon increasing the average solar irradiance, thereby confirming the decomposition of N-nitrosamines by direct sunlight. We confirmed that N-nitrosamines do not decompose when the samples are stored in amber glass vials. Therefore, to maintain the concentration of N-nitrosamines in a water sample, it must not be exposed to sunlight, even for a short time such as that encountered during sampling in the field. Conversely, we also confirmed that N-nitrosamines do not decompose even in clear glass vials under indoor lighting conditions.

3.4 Stabilities of N-nitrosamines in water samples during storage

In general, a water sample volume of >250 mL is required for a single NDMA analysis at the ng/L level by conventional liquid and gas chromatography methods. Therefore, large volumes of sample must be stored until the preconcentration step is performed. In addition, residual chlorine in the water sample can result in the formation of NDMA during storage. Thus, the preservation of NDMA at the ng/L level in water samples during storage is important, but is difficult to achieve through conventional methods. Although analysis following the EPA method 521 protocol has demonstrated the stability of dechlorinated water samples stored at <6 °C for two weeks, our proposed method greatly facilitates such testing, since the volume of sample required for a single measurement is particularly small (<1 mL). Therefore, we can easily confirm the stability of N-nitrosamines in water.

Thus, we initially checked the long-term stabilities of the 10 ng/L solutions of N-nitrosamines prepared using ultra-pure water and maintained in glass autosampler vials in the refrigerator (4 °C), the results of which are shown in Fig. 3. The concentrations of the N-nitrosamine solutions were found to be stable for over one year. Slight variations
in concentration were likely introduced during the dilution process, in which the standard
certified concentration (100 mg/L) solution was diluted 10,000,000-fold to prepare the 10
ng/L solutions.

Subsequently, we performed stability tests for the N-nitrosamine-spiked water
samples. Although no decrease in the N-nitrosamine concentration was observed even at
25 °C after 30 d (Fig. S4), the NDMA concentrations tended to slightly increase over time
in the tap water samples. We therefore speculated that the NDMA formed from the matrix
components in the tap water sample during storage, despite the removal of residual
chlorine with reducing agents (sodium thiosulfate and sodium sulfite). However, the
NDMA concentration was also observed to increase in the same experiment when sample
solutions were prepared with ultra-pure water (Fig. S5). In these experiments, to avoid N-
nitrosamine decomposition and to measure all samples in the same set, we freeze-stored
the samples, which required the use of PP vials as glass vials can break upon freezing.

However, we noticed that the PP vials sealed inconsistently owing to variations in the
molding process used in their manufacture (Fig. S6). Thus, the increase in NDMA
composition is likely to have been caused by contamination from ambient air.

Although we must consider the biodegradation of N-nitrosamines in unsterilized
water, ng/L-level N-nitrosamine solutions are stable; however, these results must be
verified using a range of water samples. Nevertheless, we have demonstrated that it is of
key importance to ensure the integrity of the storage container to avoid NDMA
contamination from ambient air.

3.5 Determining the NDMA contents in reagents, and its formation under various
conditions
Recent studies have demonstrated that NDMA can be present in pharmaceutical products. The formation of NDMA during food processing and in the stomachs of humans is also well-known, and the formation of N-nitrosamines in older cosmetic products has also been reported. The majority of previous research on N-nitrosamine precursors in water was based on formation potential analysis. The findings of these previous studies indicated that NDMA is generated by the reaction of secondary amines with nitrite ions in acidic media, and/or through the oxidation of amines. Accordingly, in the current study, the concentrations of N-nitrosamines in the reagents that are used in formation potential testing, such as amines, disinfectants, and reducing agents, were evaluated, and the results are presented in Table 2.

The highest concentration of NDMA found in the four analyzed opened sodium hypochlorite solutions was 1.55 μg/L. Although these reagent bottles were stored in the same refrigerator, the NDMA concentrations detected in these bottles showed no relationship with the storage period. These results indicate that the solutions were contaminated with NDMA and/or an NDMA precursor in the manufacturing process and not during storage. In addition, the dimethylamine (DMA) hydrochloride sample was found to contain 40 μg/kg of NDMA, despite being a solid. We expected that NDMA would be formed in the ranitidine sample during storage, since the formation efficiency of NDMA is particularly high in the presence of oxidizing agents. However, the concentrations of NDMA in the 100 mM ranitidine hydrochloride solution stored for over one year in the refrigerator and that in the solution newly prepared from the solid reagent were essentially comparable. In addition, we purchased fresh batches of ranitidine hydrochloride of the same brand and found that the NDMA concentrations in these two samples were different, as shown in Table 2. These results suggest that NDMA is not
formed during the decomposition of ranitidine during storage, but instead is formed and/or introduced through contamination during the synthetic process.

AC surfaces have been reported to be effective sites for the reactions of secondary amines and nitrite ions in water to form N-nitrosamines $^{11,36}$. Therefore, the formation of NDMA during conventional SPE procedures was considered. Our proposed method eliminates the requirement for preconcentration and can confirm NDMA formation at each step of the conventional process. Thus, a solution of 1 mM DMA and 1 mM NaNO$_2$ in 10 mM phosphate buffer (pH 6.8) was confirmed to contain 8.0 ng/L of NDMA, as shown in Table 3, while the 1 mM DMA solution contained 3.3 ng/L of NDMA as shown in Table 2. Therefore, the net production of NDMA upon the mixing of DMA and NaNO$_2$ was 4.7 ng/L. This result suggests that nitrosation occurs under neutral conditions, despite being rather inefficient. In general, nitrosation between a secondary amine and a nitrite occurs under acidic conditions $^{37}$. Further, 2.5 mL of this mixed solution was passed through an SPE cartridge, dried with N$_2$ gas for 10 min at a gas flow rate of 0.5 L/min, and then back-flushed with 5 mL of methanol as the eluent. The NDMA concentration of this methanol solution was 3.7 μg/L (Table 4), and so the NDMA concentration of the resultant solution was over 1,000-times higher than that of the mixed solution. For an SPE cartridge drying, N$_2$ or O$_2$ gas, which were confirmed to be NDMA-free using the developed impinger method, were employed due to the fact that ambient air for cartridge drying contains ng/m$^3$ levels of NDMA, as indicated in Table 1. Therefore, it is clear that the formation of NDMA occurs on the AC SPE cartridge.

Moreover, no differences in the NDMA formation concentrations were observed for O$_2$ gas drying and N$_2$ gas drying of the mixed solution of 1 mM DMA and 1 mM NaNO$_2$. However, it has also been reported that NDMA can be formed from secondary
amines and from the active oxygen and nitrogen species generated from atmospheric/dissolved O$_2$ and N$_2$ on AC surfaces $^{38}$. In our study, it was confirmed that the feeding of a 1 mM DMA solution alone into the SPE cartridge followed by O$_2$ drying results in NDMA formation. Thus, we added 10 mM sodium sulfite to the mixed solution to reduce the quantity of dissolved O$_2$, resulting in the formation of NDMA being approximately halved, as indicated in Table 4. However, this phenomenon was also observed for the mixed solution, as shown in Table 3. Thus, since the sulfite ions not only reduce the quantity of dissolved O$_2$, they also suppress the nitrosation reaction. As a result, we were unable to evaluate the effect of dissolved O$_2$ on AC surfaces using the sulfite ion.

In this study, the retention conditions of the feed compounds in the SPE cartridge were unknown. Furthermore, the different effects of atmospheric/dissolved N$_2$ and O$_2$ gas on AC surfaces should be considered. Moreover, a high-matrix water, such as treated wastewater, contains various compounds, and these compounds also have the potential to form N-nitrosamines on AC surfaces during the SPE preconcentration step. Consequently, further detailed studies are required to provide a better understanding of these results.

4. Conclusions

We herein reported the contamination, decomposition, and formation of N-nitrosodimethylamine (NDMA) and other N-nitrosamines in water samples. Our analyses demonstrated that, for ng/L-level NDMA analyses, NDMA contamination from ambient air during sample handling and storage must be avoided. In addition, this study reconfirmed the photodecomposition of NDMA in glassware by sunlight, and the stability of NDMA at low-ng/L concentrations in solution. Moreover, the formation and contamination of NDMA in reagents and its formation during analytical procedures were
also confirmed. Our developed system based on HPLC separation followed by in-line matrix removal, the photochemical conversion of N-nitrosamines to peroxynitrite, and luminol-based chemiluminescence detection (HPLC-AEM-PR-CL) can therefore be considered an excellent tool for rapidly confirming the concentrations of N-nitrosamines in reagents and solutions, as well as confirming artefact formation and contamination by N-nitrosamines during analytical procedures.

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| Air sample* | NDMA (ng/L) | Sampling volume (m³) | NDMA (ng/m³)*b |
|-------------|-------------|----------------------|----------------|
| Atmospheric air - 1 | nd | 0.0281 | nd |
| Atmospheric air - 2 | nd | 0.0274 | nd |
| Atmospheric air - 3 | nd | 0.0528 | nd |
| Living space air - 1 | 1.1 | 0.0128 | 2.2 |
| Living space air - 2 | 2.8 | 0.0297 | 2.4 |
| Living space air - 3 | 2.1 | 0.029 | 1.8 |
| Laboratory air (Room A) - 1 | 8.3 | 0.0253 | 8.2 |
| Laboratory air (Room A) - 2 | 10.8 | 0.0327 | 8.2 |
| Laboratory air (Room A) - 3 | 7.3 | 0.0251 | 7.3 |
| Laboratory air (Room B) - 1 | 8.8 | 0.0179 | 12.3 |
| Laboratory air (Room B) - 2 | 8.8 | 0.0222 | 10.0 |
| Laboratory air (Room B) - 3 | 10.1 | 0.0255 | 9.9 |

nd: not detected

* All air sampling was serially-conducted at each sampling site by the sampling system outlined in Fig. S1. The number allocated to each sample name indicates the order of sampling.

*b NDMA concentration: NDMA amount (ng) / Sampling volume (m³).

NDMA amount: NDMA concentration of trap solvent (ng/L) × trap solvent volume (0.025 L).
Table 2. NDMA concentrations in various reagents, and confirmation of NDMA formation during storage

| Prepared solution** | NDMA concentration in reagent bottle | Description |
|---------------------|-------------------------------------|-------------|
| Sodium hypochlorite solution* | 0.6 0.03 μg/L | Brand A, unopened (October 2019) |
| Sodium hypochlorite solution | 8.3 0.42 μg/L | Brand A, unopened (October 2018) |
| Sodium hypochlorite solution 50 times-diluted (+ 10 mM Sodium sulfite) | 9.0 0.45 μg/L | Brand A, used (April 2018) |
| Sodium hypochlorite solution | 31.1 1.55 μg/L | Brand A, used (January 2017) |
| Sodium hypochlorite solution | 6.8 0.34 μg/L | Brand A, used (March 2015) |
| Sodium hypochlorite solution | 0.5 0.02 μg/L | Brand B, used (January 2017) |
| Ammonium chloride 10 mM | nd | - |
| Sodium sulfite 10 mM | nd | - |
| Sodium thiosulfate 10 mM | nd | - |
| Sodium nitrite 1 mM | nd | - |
| Dimethylamine hydrochloride 1 mM | 3.3 0.040 mg/kg | Purchased in 2017 from brand C |
| Trimethylamine hydrochloride 1 mM | nd | - |
| | 1 mM | nd | Stored as 100 mM in methanol solution over 1-year |
| N,N-dimethylbenzylamine 1 mM | 32.9 0.244 mg/kg | Stored as 100 mM in methanol solution over 1-year |
| Ranitidine hydrochloride 1 mM | 364 1.03 mg/kg | Purchased in 2017 from brand C |
| | 1 mM | 408 1.15 mg/kg | Stored as 100 mM in methanol solution over 1-year |
| Ranitidine hydrochloride 1 mM | 169 0.476 mg/kg | Newly purchased in 2019 from brand C |

nd: not detected

*a All solutions were prepared at a concentration of 100 mM using water or methanol and then diluted with water.
*b All sodium hypochlorite solutions obtained from different batches were stored in the same refrigerator.
Table 3. NDMA concentrations of mixed reagent solutions

| Prepared mix solution*<sup>a</sup> | NDMA (ng/L) in solution |
|----------------------------------|-------------------------|
|                                 | mean | sd (n = 3) |
| 1 mM DMA and 1 mM NaNO<sub>2</sub> | 8.0  | 0.2       |
| 1 mM DMA, 1 mM NaNO<sub>2</sub>, and 10 mM NaSO<sub>3</sub> | 5.4  | 0.6       |

Triplicate measurements were performed for each solution; sd: standard deviation.

**<sup>a</sup> All solutions were prepared using 10 mM phosphate buffer (pH 6.8) and the results for a single compound solution are presented in Table 2.

Table 4. NDMA concentrations in eluting solutions after SPE using an AC SPE cartridge

| Added mixed solution on SPE (2.5 mL)*<sup>a</sup> | Drying method of SPE | NDMA (μg/L) in eluting methanol*<sup>b, c</sup> |
|-----------------------------------------------|----------------------|-----------------------------------------------|
|                                               |                      | mean | sd (n = 3) |
| 1 mM DMA and 1 mM NaNO<sub>2</sub>            | N<sub>2</sub> gas     | 3.7  | 0.2       |
| 1 mM DMA, 1 mM NaNO<sub>2</sub>, and 10 mM NaSO<sub>3</sub> | N<sub>2</sub> gas     | 1.5  | 0.2       |
| 1 mM DMA and NaNO<sub>2</sub>                 | O<sub>2</sub> gas     | 3.5  | 0.3       |
| 1 mM DMA                                       | O<sub>2</sub> gas     | 0.09 | 0.01      |
| 1 mM NaNO<sub>2</sub>                          | O<sub>2</sub> gas     | nd   | -         |
| 10 mM Phosphate buffer (pH 6.8, blank solution)| O<sub>2</sub> gas     | nd   | -         |

nd: not detected.

SEP cartridge: Supelclean Coconut Charcoal SPE tube (bed wt., 2 g; volume, 6 mL; Supelco).

**<sup>a</sup> All sample preparation procedures were serially performed, triplicate experiments were performed for each condition, and all solutions were prepared using 10 mM phosphate buffer (pH 6.8).

*<sup>b</sup> Back-flushed with 5 mL methanol as an eluting solution.

*<sup>c</sup> Injection volume of the sample solution = 20 μL (1/10 sensitivity).
Figure captions

Fig. 1. Typical chromatograms showing the NDMA contamination of ultra-pure water caused by experimental room air. a) 10 ng/L N-nitrosamines standard solution, b) ultra-pure water, c) ultra-pure water after 6 h, and d) ultra-pure water after 24 h. Peak identification: 1; NDMA, 2; NMOR, 3; NMEA, 4; NPYR.

Fig. 2. Decomposition of NDMA upon exposure to sunlight. (a) Decreasing NDMA concentration with exposure time. (b) The relationship between the average solar irradiance (20 min) and the residual NDMA concentration. All points (mean ± standard deviation) were obtained from the results of three vials subjected to the same conditions.

Fig. 3. Long-term stabilities of four N-nitrosamines standard solutions at concentrations of 10 ng/L and stored at 4 °C. Values are means of two determination results from two different vials. Error bars show standard deviations.
Fig. 1
Fig. 2
Fig. 3
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