# Quaternary Amines As Nitrosamine Precursors: A Role for Consumer Products?

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Nitrosamine formation has been associated with wastewater-impacted waters, but specific precursors within wastewater effluents have not been identified. Experiments indicated that nitrosamines form in low yields from quaternary amines, and that the nitrosamines form from the quaternary amines themselves, not just lower order amine impurities. Polymeric and benzylated quaternary amines were more potent precursors than monomeric quaternary alkylamines. Pretreatment of quaternary amines with ozone or free chlorine, which deactivate lower order amine impurities, did not significantly reduce nitrosamine formation. The nitrosamine formation pathway is unclear but experiments indicated that transformation of quaternary amines to lower order amine precursors via Hofmann elimination was not involved. Experiments suggest that the pathway may involve quaternary amine degradation by amidogen or chloramino radicals formed from chloramines. Quaternary amines are significant constituents of consumer products, including shampoos, detergents, and fabric softeners. Although quaternary amines may be removed by sedimentation during wastewater treatment, their importance should be evaluated on a case-by-case basis. The high loadings from consumer products may enable the portion not removed to serve as precursors.

## Introduction

Nitrosamines, such as *N*-nitrosodimethylamine (NDMA), form during disinfection of drinking waters (*1*), wastewaters (*2*), and recreational waters (*3*), particularly during chloramine disinfection (*4*). Their formation has caused considerable concern, because the U.S. EPA has classified several nitrosamines as probable human carcinogens and placed them on the Contaminant Candidate List 3.

Nitrosamines have been particularly important for facilities using quaternary amine-based treatment polymers. Final effluent NDMA concentrations in a survey of U.S. drinking water treatment plants were correlated to the dosage of quaternary amine-based poly(diallyldimethylammonium chloride) coagulant (polyDADMAC) (Figure 1) (*5*). Wilczak et al. (*6*) also observed a correlation between polyDADMAC dose and NDMA formation in pilot- and full-scale plants employing chloramination. A utility employing anion exchange exhibited the highest effluent NDMA concentration

in another drinking water plant survey (*7*). Most anion exchange resins are constituted from quaternary amine-based polymers.

NDMA precursors correlate strongly with degree of wastewater impact, rather than total dissolved organic nitrogen. Application of large monochloramine doses for extended times (i.e., a formation potential analysis) produced ~300−1300 ng/L NDMA when applied to secondary wastewater effluents (*8*), but a maximum of 58 ng/L for eutrophic waters not impacted by wastewater (*1*). NDMA precursors accumulated along a river due to wastewater effluent inputs (*9*). Specific precursors within wastewater effluents responsible for NDMA formation have not been identified. Although dimethylamine (*10*) and trimethylamine (*11*) are human waste constituents, previous research indicated that the dimethylamine present in effluents accounted for <12% of NDMA precursors (*8*), while trimethylamine was not detected (*12*).

The association of NDMA precursors with municipal wastewater effluents suggests a role for consumer products, rather than organic nitrogen-rich biomolecules. Application of a nitrosamine formation potential analysis to nitrogenous biomolecules and even pure bacterial cultures formed no significant NDMA (*8*). Quaternary amine monomers are widely used in antibacterial soaps and mouthwashes, while polymers are used in shampoos, detergents, and fabric softeners. Interestingly, nitrosamines were detected in toiletries, even in the absence of disinfectant exposure (*13*).

How nitrosamines form from quaternary amines is unclear. Previous research indicated that nitrosamine formation during chloramination could be explained by an initial nucleophilic substitution reaction between dichloramine and the electron lone pair of secondary amines (*14*). Electrophilic transfer of chlorine from chlorine or chloramines to the electron pair of tertiary amines rapidly released secondary amines, with subsequent nitrosamine formation during chloramination (*12*). However, the lack of electron lone pairs in quaternary amines precludes these pathways.

One possibility is that nitrosamine formation arises from lower order amine impurities, particularly within polymers, where purity analysis is difficult. Although dimethylamine was an impurity in polyDADMAC (*15*), and both dimethylamine and trimethylamine were impurities in anion exchange resins (*16*), these unbound impurities could not account for NDMA formation. Another possibility is that tertiary amine impurities become incorporated into polymers. For example, allyldimethylamine (ADMA), a likely impurity during synthesis of diallyldimethylammonium chloride (DADMAC) monomer, could be incorporated within polyDADMAC (Scheme 1). The order of NDMA formation during chloramination of equivalent concentrations (by weight) was DADMAC < polyDADMAC < ADMA, suggesting that such impurities could be responsible for NDMA formation (*15*). However, the addition of increasing ADMA concentrations to a DADMAC solution prior to cyclopolymerization only modestly increased NDMA formation during subsequent chloramination.

Alternatively, quaternary amines themselves could form nitrosamines. Wilczak et al. (*6*) observed no difference in NDMA formation during chloramination of polyDADMAC collected from 5 drinking water plants. Because differences in impurity prevalence might be expected among different manufacturers and batches, these results indicate that quaternary amines form NDMA. Park et al. (*15*) suggested that polyDADMAC's quaternary amine could form a tertiary amine via base-promoted Hofmann elimination (Scheme

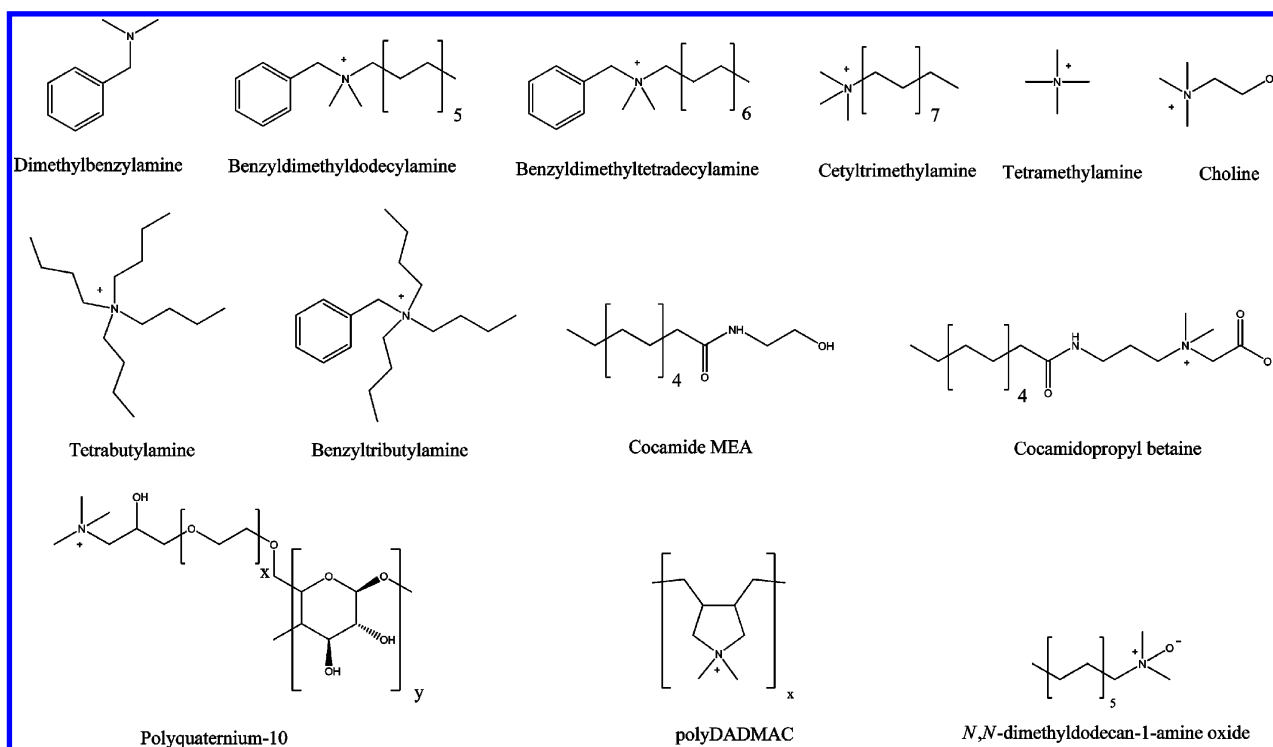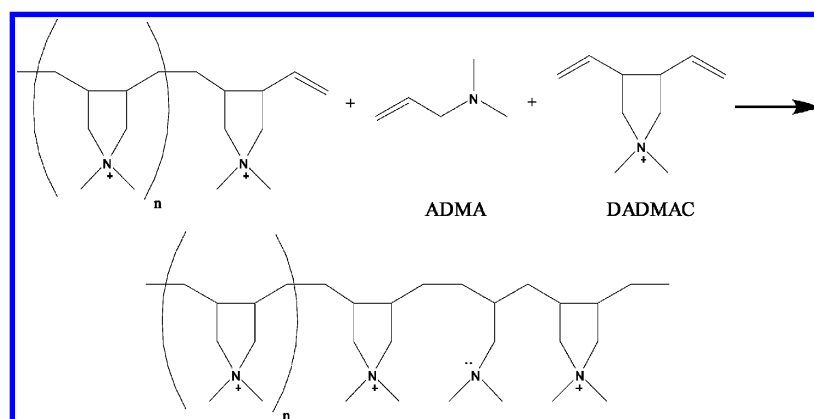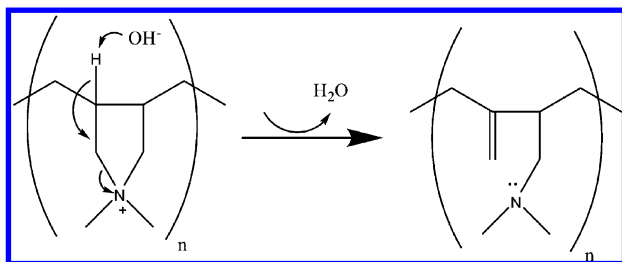* Corresponding author phone: (203) 432-4386; fax: (203) 432-4387; e-mail: william.mitch@yale.edu.

**FIGURE 1. Structures of model compounds.**

## SCHEME 1



## SCHEME 2



2). Following dialysis of the polymer to remove dimethyl-amine, dimethylamine formed during chloramination, suggesting polymer degradation (*15*). However, the dimethylamine yield was ~0.05%, and dimethylamine would be a likely product from the degradation of any tertiary amine impurities (*12*) incorporated into the polymer (Scheme 1).

Whether nitrosamine formation arises from impurities or from quaternary amines is important. If the former, formation could be minimized by improving synthesis to reduce impurities. Alternatively, polymers could be treated with oxidants to deactivate impurities prior to use. Previous research indicated that application of chlorine (*17*), ozone, or chlorine dioxide (*18*) prior to chloramination deactivated NDMA precursors. However, if quaternary amines form nitrosamines, then alternative cationic functional groups to quaternary amines should be evaluated. This study provides an initial evaluation of quaternary amines in consumer products as NDMA precursors. Another objective was to investigate the effectiveness of oxidative destruction of lower order amine impurities in polymers prior to use. Finally, we assessed whether quaternary amines themselves serve as precursors, and initiated an investigation into responsible pathways.

## Materials and Methods

**Materials.** Material sources and purity and nitrosomethyl-benzylamine synthesis are provided in the Supporting Information (SI). With the exception of cetyltrimethylam-monium chloride, benzalkonium chloride, and cocamide MEA, monomeric quaternary amines purities were ≥97%. Benzalkonium chloride was a mixture of C12 (benzyldi-

**TABLE 1**. Nitrosamine Formation Potential Results

| compound | category | precursor concentration (μM) | NDMA concentration[a] (ng/L) | NDMA molar yield[a] (%) |
|---|---|---|---|---|
| model monomers | | | | |
| tetramethylamine | quaternary alkylamine | 10 | 0 (0) | 0 (0) |
| tetrabutylamine[b] | quaternary alkylamine | 10 | 1420 (160) | 0.09 (0.02) |
| cetyltrimethylamine | quaternary alkylamine | 10 | 200 (5) | 0.03 (0.001) |
| choline | quaternary alkylamine | 10 | 1230 (80) | 0.16 (0.01) |
| benzyltributylamine[b] | benzyltrialkylamine | 10 | 4050 (490) | 0.26 (0.1) |
| dimethylbenzylamine | benzyldialkylamine | 0.1 | 4760 (620) | 64 (8) |
| monomeric constituents of personal care products | | | | |
| cocamide MEA | amide | 10 | 0 (0) | 0 (0) |
| cocamidopropyl betaine | quaternary alkylamine | 10 | 1200 (340) | 0.16 (0.05) |
| benzyldimethyldodecylamine | benzyltrialkylamine | 10 | 2080 (290) | 0.28 (0.04) |
| benzyldimethyltetradecylamine | benzyltrialkylamine | 10 | 1910 (360) | 0.26 (0.05) |

| compound | category | precursor concentration (mg/L) | NDMA concentration (ng/L) | NDMA mass yield (%) |
|---|---|---|---|---|
| polymers and polymeric constituents of personal care products | | | | |
| polyDADMAC | quaternary alkylamine | 2 | 3810 (670) | 0.19 (0.03) |
| polyquaternium-10 | quaternary alkylamine | 1.9 | 190 (40) | 0.01 (0.002) |
| bulk personal care products | | | | |
| Dawn dishwashing hand soap | see text | 200 | 2520 (50) | 0.0013 ($2.4 \times 10^{-5}$) |
| Cheer laundry detergent | see text | 200 | 0 (0) | 0 (0) |
| Pantene shampoo | see text | 200 | 0 (0) | 0 (0) |
| Suave shampoo | see text | 200 | 100 (7) | $5 \times 10^{-5}$ ($3 \times 10^{-6}$) |

[a] Parentheses indicate the standard deviation of duplicate measurements. [b] Nitrosamine analyzed is NDBA in place of NDMA.

methyldodecylammonium chloride), C14 (benzyldimethylte-tradecylammonium chloride), C16, and C18 homologues. The C12 homologue was obtained by purification via fraction collection using HPLC-MS (see SI). Polymeric quaternary amines purities were unspecified. The SI details preparation and standardization of stock solutions.

Municipal wastewater effluent grab samples were collected in fluorinated containers from the final effluents of the Southington (CT), Wallingford (CT), and New Haven (CT) treatment plants for analysis of benzalkonium chloride. Final effluents samples (1 L) were filtered through 0.7-$\mu m$ nominal pore size glass fiber filters that had been baked at 400 °C to remove contaminants. Extraction and analysis details are provided in the SI. For analysis of shampoo biotransformation, a grab sample of activated sludge was collected in a fluorinated container from the activated sludge tank of the New Haven treatment plant. The SI provides background information regarding the activated sludge system.

**Analyses.** Total residual chlorine was measured by the DPD colorimetric method and residual ozone by UV spectrophotometry (*19*). Following derivatization, formaldehyde was measured by HPLC-UV (*12*), and primary and secondary amines were measured by gas chromatography mass spectrometry (GC/MS) (*20*). Nitrosamines and nitrosomethylbenzylamine were analyzed using EPA method 521 by GC/MS (see SI). Benzalkonium chloride, dimethylbenzylamine, methylbenzylamine, benzaldehyde, tetrabutylamine, and tributylamine were analyzed by HPLC-MS (see SI).

## Results and Discussion

**Quaternary Amines As Nitrosamine Precursors.** The tendency of quaternary amines to serve as nitrosamine precursors was evaluated using a nitrosamine formation potential test (*20*). This test employs the nitrosamine concentration formed following exposure to a large monochloramine dose (2 mM) for an extended reaction time (10 d) to materials dissolved in deionized water buffered at pH 7 with 20 mM

phosphate buffer as a surrogate for total nitrosamine precursors. The nitrosamine concentration in the untreated sample was subtracted from the treated sample.

Similar to previous research with amides (*8*), cocamide MEA, an amide monomer in consumer products, yielded no NDMA (Table 1 and Figure 1). Among model quaternary alkylamines, tetramethylamine formed no significant NDMA. With longer alkyl substituents, NDMA (or for tetrabutylamine, nitrosodibutylamine (NDBA)) molar yields ranged from 0.03 to 0.16%. Similarly, cocamidopropyl betaine, a quaternary alkylamine monomer in consumer products, yielded 0.16% NDMA. These yields are ~1−6% of the 2.6% NDMA molar yield observed from dimethylamine (*8*).

For benzyltributylamine, the NDBA yield increased to 0.26%. Similar NDMA molar yields were observed for benzyldimethyldodecylamine and benzyldimethyltetradecylamine, the monomeric C12 and C14 constituents of benzalkonium chloride. The benzyl substituent appeared to double nitrosamine yields. Interestingly, for benzyldimethyltetradecylamine, the molar yield of nitrosomethylbenzylamine (NMBA) was only 0.016% (±0.001% standard deviation).

Previous research indicated that nitrosamine yields from tertiary amines containing benzyl or similar (e.g., furan) substituents were far higher than those from dimethylamine (*21*). Similarly, when we applied the nitrosamine formation potential analysis to dimethylbenzylamine (Figure 1), the NDMA yield was 64%, but that of NMBA (~4%) was similar to the NDMA yield from dimethylamine (2.6%) or trimethylamine (2%) (*8*).

Nitrosamine formation potential analyses were applied to two polymeric quaternary amines: a polyDADMAC coagulant polymer, and polyquaternium-10, a consumer product constituent (Figure 1 and Table 1). Because these materials are polymeric, NDMA yields were reported on a mass basis. The NDMA yields were ~0.01% for polyquater-

nium-10, but ~0.2% for polyDADMAC. Note that polyDAD-MAC features higher nitrogen content by weight (Figure 1).

Finally, the nitrosamine formation potential assay was applied to 4 consumer products (Table 1). After initial mixing, the vials were not mixed during the formation potential assay. The surfactant concentrations in these materials were not specified. To assess whether the concentrations employed had exceeded solubilities, we applied the assay to increasing product concentrations (e.g., Figure SI-2), and selected concentrations within the linear range of response. Although constituent concentrations were not provided, their relative concentrations generally follow their order on the ingredients list (22). Nitrosamine concentrations in nonchloraminated controls were relatively insignificant. Dawn dishwashing soap featured the highest NDMA mass yield (0.0013%); C12−14−16 dimethylamine oxide was the fourth ingredient. Suave shampoo exhibited a much lower NDMA mass yield ($5 \times 10^{-5}$ %); cocamidopropyl betaine and guar hydroxypropyltrimonium chloride, a quaternary amine-based polymer, were the third and twelfth ingredients. Despite containing polyquaternium-10 as the eleventh ingredient, Pantene shampoo yielded no NDMA. Cheer laundry detergent yielded no NDMA, but ingredients were unspecified.

The concentrations of benzalkonium chloride (BAC), a quaternary amine biocide in consumer products, ranged between 120 and 149 ng/L in 3 wastewater effluents (Table SI-1). Previous research had found BAC concentrations of ~30−600 ng/L in Austrian wastewater effluents (23). The concentrations of the C12 and C14 homologues were approximately equal, with the C16 and C18 homologues less important. Approximately 60% of BAC was removed using 0.7-$\mu$m glass fiber filters. Applying the 0.28% and 0.26% NDMA molar yields applicable to the C12 and C14 homologues (Table 1), the effluent BAC concentrations would form only 103−124 pg/L of the ~300−500 ng/L NDMA typically observed from nitrosamine formation potential analyses of wastewater effluents (8).

During wastewater treatment, the positive charge on quaternary amines renders them likely to adhere to activated sludge flocs, which are predominantly negatively charged. Quaternary amines are likely either to be removed by sedimentation with microorganisms within secondary clarifiers, or possibly to be biotransformed into more potent, soluble nitrosamine precursors that could proceed to disinfection. Unfortunately, analysis of polymeric quaternary amines is difficult due to varying polymer chain lengths. We evaluated the impact of a simulated activated sludge treatment on the NDMA formation potential of Suave shampoo. After 1-L aliquots of activated sludge were either spiked or not spiked with 10 mL of shampoo, the solutions were bubbled with air for 6 h, filtered through 0.7-$\mu$m glass fiber filters, and subjected to the formation potential analysis. No significant difference was observed in NDMA formation for the activated sludge samples spiked (667 ± 124 ng/L) or unspiked (729 ± 62 ng/L) with shampoo.

Although our results are insufficient to draw firm conclusions regarding their importance, we suggest that future research evaluate quaternary amines employed in consumer products as contributors to the association of NDMA formation with chloramination of wastewater-impacted waters (9). Previous research had indicated that dimethylamine and trimethylamine, although constituents of human waste (10, 11), were not significant precursors in wastewater effluents (8, 12). In contrast to other potential anthropogenic amine-based microconstituents in wastewaters, such as pharmaceuticals, quaternary amines serve as major constituents in an array of widely used consumer products.

Suave shampoo, which contained cocamidopropyl betaine as the third ingredient, yielded NDMA at $5 \times 10^{-5}$ % by weight during the nitrosamine formation potential test.

The GNHWPCA wastewater treatment plant, serving 213,000 people, treats 1.3 m³/s of sewage. Assuming 80% of people use 13 mL of Suave shampoo daily (24), the shampoo would contribute 9.5 ng/L of NDMA precursors. As typical effluents form 300−500 ng/L NDMA in a nitrosamine formation potential analysis (8), the shampoo would contribute 2−3% of the total precursor loading.

Our calculations are highly preliminary. Consumer products exhibited a range of tendencies to serve as precursors during chloramination, and it is unlikely that any one compound would account for the majority of nitrosamine formation. Certain products, including the Cheer laundry detergent and Pantene shampoo, did not form nitrosamines. However, the NDMA mass yield from Dawn dishwashing detergent was 26 times greater than that for Suave shampoo.

Although biotransformation to soluble precursors capable of passage to the disinfection system was not important for Suave shampoo, biotransformation potential should be evaluated on a case-by-case basis. Previous research indicated that activated sludge treatment converted alkyltrimethylammonium compounds to lower order amine precursors of NDMA (25). Even where biotransformation is insignificant, it is important to evaluate nitrosamine formation from particle-bound quaternary amines, as unfiltered effluents can have up to 30 mg/L total suspended solids. We had previously found that usage of a tertiary amine-based coagulant for sludge thickening resulted in particle-associated NDMA precursors that doubled NDMA formation in these plants (8). NDMA formation was linearly correlated to polyDADMAC dosage in a survey of drinking water plants (5); particle-bound polyDADMAC captured on filters may be exposed to oxidants applied upstream for biofilm control. A similar situation may pertain in wastewater recycling facilities, where nitrosamine formation is of particular concern (4), because chlorine injection for biofilm control upstream of filters leads to chloramine formation in non-nitrified wastewaters, and potential reactions with filter-bound particle-associated quaternary amines.

**Evaluation of Impurities.** Where possible, we had employed reagents with >97% purity (Table 1). However, secondary and tertiary amines are likely impurities; synthesis of quaternary amines often involves the nucleophilic attack on an alkyl halide by a tertiary amine. Because nitrosamine yields from quaternary amines (~0.03−0.3% (Table 1)) were 1−2 orders of magnitude lower than yields from secondary and tertiary amines (2−2.6% (8)), it was conceivable that lower order amine impurities might account for nitrosamine formation. Benzyltributylammonium chloride, a 98% pure monomer, was further purified via preparative HPLC (see SI). The yield of NDBA upon application of the nitrosamine formation potential test to 10 $\mu$M of benzyltributylammonium chloride declined from 4150 ng/L (±490 ng/L standard deviation) to 3220 ng/L (±330 ng/L standard deviation) upon purification. The slight decline indicates that quaternary amines themselves, rather than impurities, were the dominant nitrosamine precursors.

Due to varying polymer lengths, it was not feasible to further purify polymers of incorporated impurities (e.g., Scheme 1) using a similar preparative HPLC system. We evaluated the importance of impurities by assessing whether pretreatment with free chlorine or ozone reduced nitrosamine formation; previous research indicated that free chlorine (17) and ozone (18) deactivate secondary and tertiary amines precursors. Ten $\mu$M as monomer of polyDADMAC (i.e., 1.6 mg/L) or polyquaternium-10 was added to deionized water buffered at pH 7. Three oxidant conditions were evaluated: free chlorine, ozone, and ozone with tert-butanol. Ozone can impact precursors via two pathways: direct oxidation by ozone, or formation of hydroxyl radical (26). To distinguish these pathways, 10 mM tert-butanol was added to lower the

steady-state hydroxyl radical concentration by factors of 100−1000 based on the rate constant of a potential unprotonated tertiary amine impurity reacting with hydroxyl radical and the theoretical molar nitrogen concentration as a surrogate for monomer concentration (27). After 3 h, two 100-mL aliquots were withdrawn and quenched with 200 mg of thiosulfate for dimethylamine analysis. To initiate formation potential assays, 500-mL aliquots subjected to chlorination were immediately treated with 2 mM monochloramine. Because ozone consumption was complete within 10 min, aliquots subjected to ozone alone were not quenched prior to monochloramine addition. For ozonated aliquots treated with tert-butanol, residual ozone was quenched with cinnamic acid prior to monochloramine addition.

For both polymers, NDMA and dimethylamine formation were similar with or without preoxidation for up to 5 mg/L as $Cl_2$ free chlorine (Figure 2). Application of 3.4 mg/L ozone did not affect NDMA formation from polyDADMAC, but modestly reduced NDMA formation from polyquaternium-10. Ozonation did not affect dimethylamine formation from polyquaternium-10, but increased dimethylamine formation to 80,000 ng/L (1.8 $\mu$M), ~20% of the 10 $\mu$M of polyDADMAC monomer units. Due to the elevated ozone to dimethylamine molar ratio, NDMA formation from ozonation of dimethylamine was likely negligible (28).

Tert-butanol did not affect dimethylamine formation, but decreased NDMA formation by an order of magnitude for both polyDADMAC and polyquaternium-10, even without ozonation. We evaluated NDMA yields as a function of tert-butanol concentration for cetyltrimethylamine, a monomer, and polyDADMAC (Figure SI-3). Increasing tert-butanol reduced NDMA formation from polyDADMAC, but modestly reduced NDMA formation from cetyltrimethylamine.

For polyDADMAC, we evaluated whether oxidant treatments could damage its coagulant properties. PolyDADMAC (42 $\mu$M as monomer or 6.7 mg/L) was added to deionized water containing 1 mM phosphate buffer, and was treated with the same oxidants. Oxidant quenching was similar, except that chlorine was quenched with a slight excess of ammonia. A model surface water was prepared containing 7 mg/L dissolved organic carbon of Aldrich humic acid, 372 mg/L sodium bicarbonate, 33 mg/L sodium chloride, and 37 mg/L sodium sulfate in deionized water at pH 8. The synthetic water was treated with 3.7 mg/L as iron of ferric chloride and 5 mg/L of polyDADMAC or preoxidized polyDADMAC. The solutions were mixed at 35 rpm for 1 min using an EC Engineering (Alberta, Canada) model CLM6 Compact Laboratory Mixer. An aliquot was withdrawn for measurement of solution absorbance at 254 nm. The solutions were subjected to mixing at 350 rpm for 1 min, followed by mixing at 35 rpm for 45 min. After settling for 1 h, another aliquot was measured for UV absorbance at 254 nm. Humic acid removal was evaluated by comparing the initial and final UV absorbance. Although the percentage reduction in UV absorbance by Aldrich humic acid may not correlate directly to percentage NOM removal by polyDADMAC to be anticipated in a real water, it should indicate whether oxidative treatments interfere with its coagulant properties. Although the nature of any coagulant transformations occurring during oxidative treatments requires further study, certain oxidative treatments reduced coagulation. However, treatment with as low as 2.4 mg/L ozone halted coagulation. The addition of even 1 mM of tert-butanol impeded coagulation by polyDADMAC, even without ozonation. Preoxidation with 17.5 mg/L as $Cl_2$ chlorine did not impact coagulation (Figure 2C).

Our experiments with purified benzyltributylamine and preoxidant applications to polymeric quaternary amines indicated that nitrosamine formation is associated with quaternary amines, rather than just lower order amine impurities. Accordingly, improved purification during manu-
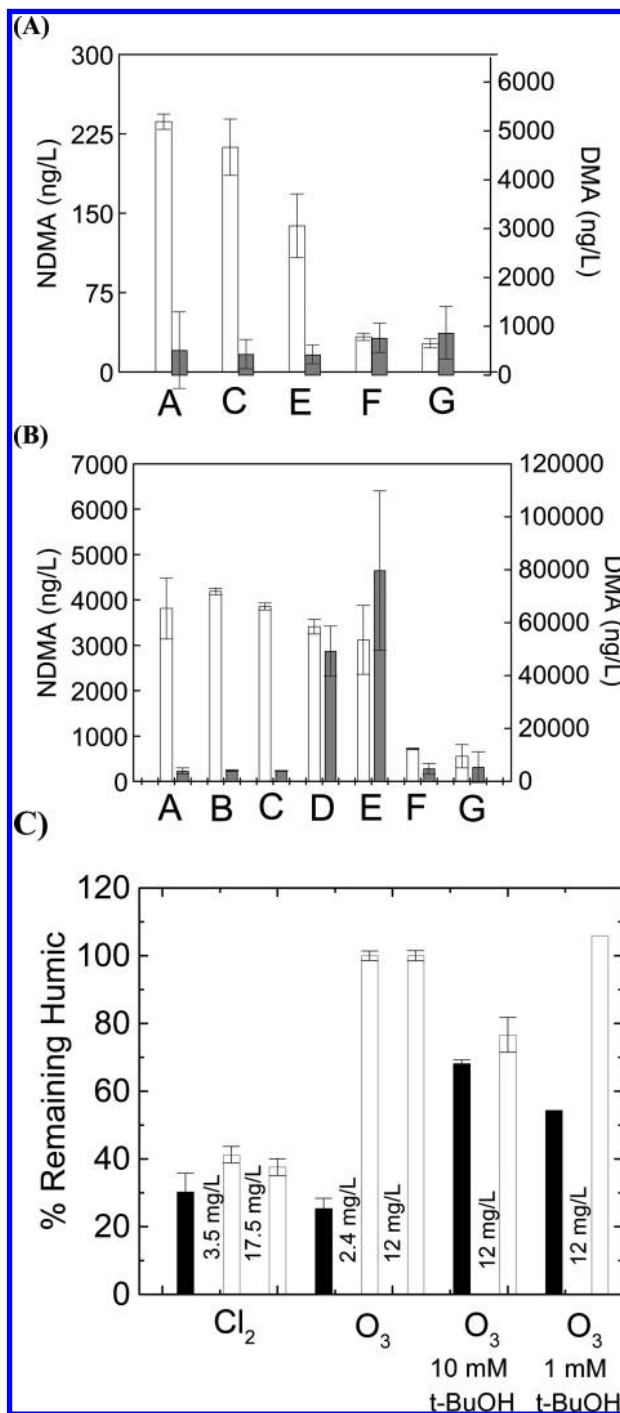


FIGURE 2. Nitrosamine formation potentials of preoxidized Polyquaternium-10 (A). Nitrosamine formation potentials (B) and coagulation properties (C) of preoxidized polyDADMAC. For (A) and (B) white bars = NDMA; gray bars = DMA. Concentrations of polymers were 10 $\mu$M as monomer. A = No preoxidation. B = 1 mg/L $Cl_2$. C = 5 mg/L $Cl_2$. D = 0.68 mg/L $O_3$. E = 3.4 mg/L $O_3$. F = 10 mM tert-butanol. G = 10 mM tert-butanol and 3.4 mg/L $O_3$. For figure (C) black bars = no oxidant; white bars = oxidant applied. Humic acid was coagulated within synthetic water. Concentration of polyDADMAC was 5 mg/L. Error bars represent the standard deviation of experimental replicates ($n = 2$); otherwise $n = 1$.

facturing may improve, but not eliminate, nitrosamine formation. Application of oxidants to deactivate impurities was not effective, and in the case of polyDADMAC ozonation, destroyed its coagulant capabilities. Given that nearly all

cationic surfactants employed in consumer products, and coagulants and anion exchange resins used for water treatment, are based upon quaternary amines, alternative designs for cationic groups should be sought.

**Reaction Pathway Investigations.** Previous researchers suggested that base-promoted Hofmann eliminations could convert quaternary amines, including polyDADMAC, to lower order amine precursors (15). To test this hypothesis, we employed tetrabutylamine as a model quaternary amine, because its lower order amine degradation products are commercially available. We evaluated yields from tetrabutylamine of tributylamine (from 1 mM tetrabutylamine), dibutylamine, and butylamine (both from 100 $\mu$M tetrabutylamine) in deionized water with 20 mM phosphate buffer at either pH 7 or adjusted to pH 11 with sodium hydroxide. No significant increases in amine concentrations were observed over 12 d, even at pH 11, indicating that a Hofmann elimination is unlikely to be important for quaternary amines.

Dibutylamine and butylamine were measured during application of either 1 mM chlorine or monochloramine to 100 $\mu$M tetrabutylamine in deionized water buffered at pH 7 with 20 mM phosphate buffer. Because tertiary amines degrade nearly instantaneously to secondary amines during free chlorination (12), tributylamine was not measured. No significant dibutylamine or butylamine formation was observed with chlorine over 12 d. However, with monochloramine, dibutylamine increased over 4 d to reach 500–1000 nM (~1% molar yield). Lastly, 360 nM ($\pm$160 nM standard deviation) dibutylamine and 9 nM ($\pm$1 nM standard deviation) NDBA were measured after applying a nitrosamine formation potential analysis to 10 $\mu$M tetrabutylamine. Amines were more reactive with chloramines than chlorine even though chlorine is a stronger oxidant.

We sought to further evaluate the particular reactivity of chloramines with quaternary amines, and the higher nitrosamine yields from quaternary amines bearing benzyl substituents. Because the low nitrosamine, secondary and tertiary amine yields from quaternary amines inhibit mass balance calculations, we assessed product yields from chlorination and chloramination of dimethylbenzylamine, a benzylated tertiary amine. Previously, we evaluated the transformation of tertiary alkylamines during chlorination and chloramination (12). Chlorine transfer to the nitrogen electron pair, followed by hydrochloric acid elimination and hydrolysis of the resulting imine yielded an aldehyde and a secondary amine. No preferential substituent loss (i.e., regioselectivity) was observed. Here, we applied 200 $\mu$M free chlorine to 50 $\mu$M dimethylbenzylamine in deionized water at pH 7 (Figure 3A). As with tertiary alkylamines, dimethylbenzylamine decay was complete within 5 min. The formaldehyde and methylbenzylamine yields were ~3.3 times higher than benzaldehyde and dimethylamine yields, indicating only modest regioselectivity in favor of methyl substituent loss. When 200 $\mu$M monochloramine was applied to 50 $\mu$M dimethylbenzylamine, dimethylbenzylamine decay occurred over 1 day (Figure 3B). Formaldehyde and methylbenzylamine yields were ~3.9 times higher than benzaldehyde and dimethylamine yields, indicating a slight preference for methyl substituent loss. However, after 21 h the NDMA yield was ~60%. Applying the 2.6% NDMA yield from dimethylamine (8), the dimethylamine concentration could not account for the NDMA formed. For both chlorination and chloramination, combined nitrogen and carbon mass balances were ~100%.

With dimethylbenzylamine, NDMA yields during chloramination were far higher than could be explained by chloramination of the dimethylamine produced. These results indicate a potential for nitrosamine formation via direct
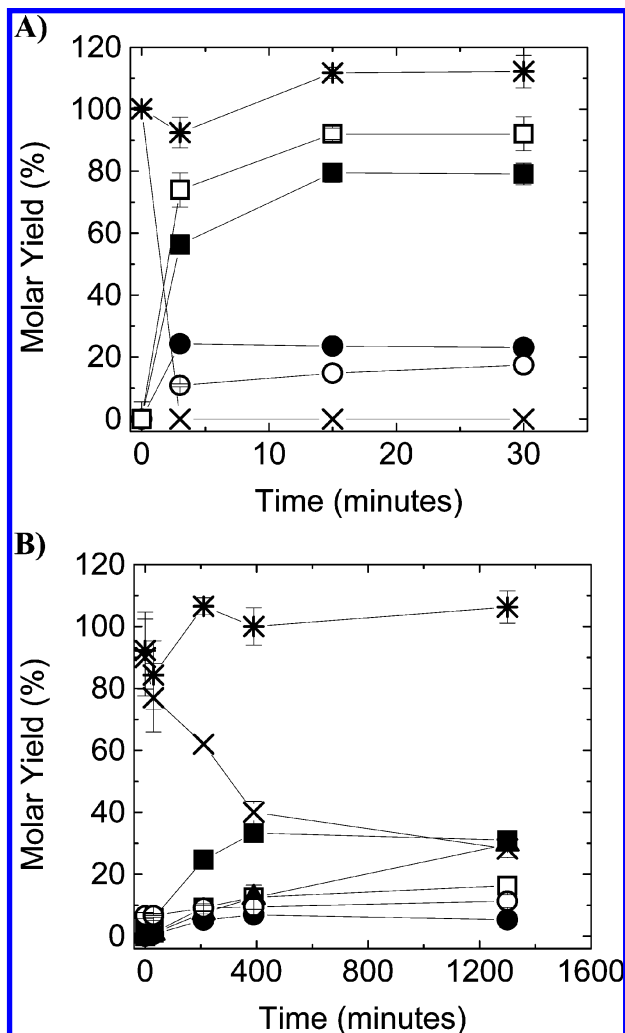


**FIGURE 3. Reaction of 200 $\mu$M dimethylbenzylamine with 50 $\mu$M of (A) free chlorine or (B) monochloramine in deionized water buffered at pH 7 with 20 mM phosphate buffer: $\times$ = dimethylbenzylamine, ■ = formaldehyde, □ = methylbenzylamine, • = benzaldehyde, ○ = dimethylamine, ▲ = NDMA, * = mass balance. Error bars represent the standard deviation of experimental duplicates.**

reaction between chloramines and dimethylbenzylamine. Interestingly, the lack of a dramatic shift in the regioselectivity of amine and aldehyde product formation both between alkyl tertiary amines (12) and benzylated tertiary amines (Figure 3), as well as between chlorination and chloramination of benzylated tertiary amines (Figure 3), indicates that such an additional pathway would co-occur with other pathways previously identified (e.g., chlorine transfer to the nitrogen, followed by hydrochloric acid elimination and imine hydrolysis) (12).

Previous research indicated that inorganic chloramines can form amidogen or chloramino radicals (29), particularly in the presence of reduced iron (30). To evaluate a potential role for these radicals, we applied the nitrosamine formation potential analysis to 10 $\mu$M cetyltrimethylamine. NDMA formation was similar in the absence (200 ng/L $\pm$ 5 ng/L standard deviation) and presence (280 ng/L $\pm$ 60 ng/L standard deviation) of 0.09 mg/L of ferric chloride as a source of Fe(III), a concentration relevant to natural waters. However, with 0.09 mg/L of ferrous sulfate as a source of Fe(II), NDMA formation increased to 330 ng/L ($\pm$40 ng/L standard deviation).

Although our results are insufficient to define such a new pathway, they suggest a novel pathway associated with chloramines. Nitrosamine formation increased in the presence of Fe(II), but tert-butanol decreased nitrosamine formation, particularly with polymeric quaternary amines. Although tert-butanol may have distorted the reaction system, because it interfered with the coagulation properties of polyDADMAC even without ozonation, tert-butanol can scavenge amidogen radicals (*31, 32*). Previously, we had employed tert-butanol to significantly reduce NDMA formation from dimethylamine during chloramination at a chlorine to ammonia molar ratio of ~1.7, where breakpoint reactions are maximized (*33*). Although the nature of the chloramine decay reactions occurring during breakpoint chlorination is incompletely defined, formation of radicals is a strong possibility. While maximized at a chlorine to ammonia molar ratio of ~1.7, breakpoint chlorination reactions occur at slower rates even at the 0.7−1 molar ratios typically employed during drinking water chloramination (*34*).

For both dimethylbenzylamine and benzyldimethyltetradecylamine, NDMA formation was strongly favored over nitrosomethylbenzylamine. The lack of shift in regioselectivity between tertiary alkylamines and dimethylbenzylamine indicates that this preference does not arise from preferential release of dimethylamine and benzaldehyde via previously identified pathways (*12*). It is noteworthy that benzyl radicals are more stable than alkyl radicals. If radicals are involved, the stabilization of a benzyl radical leaving group might explain both the elevated NDMA yields and the preference of NDMA formation over nitrosomethylbenzylamine. For benzyldimethyltetradecylamine, dimethyltetradecylamine could be an intermediate that could form NDMA during chloramination. Further research would be needed to evaluate the possible involvement of benzyl radicals and tertiary amine intermediates.

Lastly, there were indications that polymerization of quaternary amines may promote nitrosamine formation. Although our results indicated that polymeric quaternary amines, such as polyDADMAC and polyquaternium-10, exhibit a greater tendency than monomers to react with chloramines (Table 1), we had used a technical grade polyDADMAC stock that may have contained trace metal catalysts among other impurities. To have better control over purity, we synthesized polyDADMAC (see SI). The nitrosamine formation potential analysis of 10 $\mu$M DADMAC yielded 1370 ng/L ($\pm$40 ng/L standard deviation), whereas 10 $\mu$M as monomer polyDADMAC produced 5000 ng/L ($\pm$1700 ng/L standard deviation).

The significantly higher NDMA yield from polyDADMAC indicated that polymerization may promote nitrosamine formation. NDMA formation from both polyDADMAC and polyquaternium-10 was more affected by tert-butanol than was monomeric cetyltrimethylamine. Previously, application of 100 $\mu$M monochloramine to 100 $\mu$M of a tertiary amine-based cationic coagulation polymer yielded 930 times more NDMA over 4 h than did trimethylamine, its monomeric analogue (*8*). Further research would be needed to explain the polymerization effect, and to confirm and delineate a role for radicals in reactions between chloramines and quaternary amines.

## Acknowledgments

## Supporting Information Available

Additional details of the materials and methods, and additional figures and tables. This material is available free of charge via the Internet at http://pubs.acs.org.

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