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Formation of carbonaceous and nitrogenous disinfection by-products during monochloramination of oxytetracycline including N-Nitrosodimethylamine

Fu-xiang Tian[a], Bin Xu[a,*], Kang-ning Tian[a], Chen-yan Hu[b], Sheng-ji Xia[a], Nai-yun Gao[a], Tao Ye[a]

[a]*State Key Laboratory of Pollution Control and Resources Reuse, Key Laboratory of Yangtze River Water Environment, Ministry of Education, College of Environmental Science and Engineering, Tongji University, Shanghai 200092, P.R. China, Tel. +86 13918493316; email: tjwenwu@gmail.com*
[b]*College of Environmental and Chemical Engineering, Shanghai University of Electric Power, Shanghai 200090, P.R. China*

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ABSTRACT

Formation of typical volatile carbonaceous and nitrogenous disinfection by-products (C-DBPs and N-DBPs) during aqueous monochloramination of oxytetracycline (OTC) was investigated in this study. Impact factors including reaction time, pH, monochloramine (NH_2Cl) dosages, and bromide concentrations were examined. The results showed that six DBPs including chloroform, dichloroacetonitrile, trichloronitromethane, 1,1-dichloropropanone, 1,1,1-trichloropropanone, especially extreme toxic N-Nitrosodimethylamine were found. Formation of these DBPs increased over time and monochloramine dosages with maximum yields given as 14.2, 4.3, 0.8, 2.1, 0.7, and 4.1 μg/mg at pH 7, respectively (μg/mg represents DBPs yields per mg of OTC). Solution pH exerted significant influence on the formation of all the DBPs species. Peak yields were found under circumneutral conditions. Production of bromine-substituted DBPs increased in the presence of bromide. Removal of presented OTC in waters should be implemented before chloramination disinfection process in drinking water treatment.

Keywords: Carbonaceous disinfection by-products (C-DBPs); Nitrogenous disinfection by-products (N-DBPs); N-Nitrosodimethylamine (NDMA); Monochloramination; Oxytetracycline (OTC)

1. Introduction

Oxytetracycline (OTC) is one of the most widely used tetracyclines, which are applied extensively to treat infections and diseases in protecting animal health during the feeding cycle [1]. Residues of OTC can be transported to the aquatic environment from the discharges of pharmaceutical manufacturers, livestock, poultry production, and wastewater treatment plant [2]. As a result, OTC has been widely detected in surface waters and the effluents of wastewater treatment in many regions such as Canada [3], Europe [4], and the USA [5]. As reported, the concentrations of OTC frequently detected are 0.07–1.34 μg/L in surface water samples, 86–199 μg/kg in soils, and 3 μg/L in farm lagoons [6,7]. In a runoff from a manure-applied field, the concentration was detected to be 71.1 μg/L [8]. Since antibiotics pose a serious threat to

*Corresponding author.

aquatic ecosystems and jeopardize human health consequences, fate and removal of antibiotics in the environments received particular attention recently [8,9].

OTC was found to be strongly soil-adsorbed by cation ion exchange [10], regardless of the types of soil [11], and the adsorption identity turned to be reversible under certain conditions [12]. Multiwalled carbon nanotubes can also effectively remove OTC by adsorption [13]. The degradation rate of OTC by permanganate is relatively slow (with $k_{app} = 52.6\ M^{-1}\ s^{-1}$) [14]. The oxidation kinetics of OTC by ClO_2 and free chlorine are very rapid (with large apparent second-order rate constants $k_{app} = 1.24 \times 10^6\ M^{-1}\ s^{-1}$ with ClO_2 and $k_{app} = 1.78 \times 10^6\ M^{-1}\ s^{-1}$ with free chlorine at pH 7.0) [9]. Data indicated that many kinds of by-products can be generated during the oxidation of OTC, which shows far more dangerous than the parent compound [14]. Although monochloramination as an alternative disinfection process has been widely used in water treatment plants (WTPs), little is known about the fate of tetracyclines during monochloramination in drinking water treatment plants (DWTPs).

It is well documented that disinfection with monochloramine generates less regulated carbonaceous disinfection by-products (C-DBPs), such as trihalomethanes (THMs) and haloacetic acids (HAAs), than chlorination. However, more emergent nitrogenous disinfection by-products (N-DBPs) including nitrosodimethylamine (NDMA), haloacetonitriles (HANs), and halonitromethanes (HNMs) are formed, which pose far greater threat to human health [15–17]. For example, NDMA shows significant carcinogenic characteristics with a theoretical 10^{-6} lifetime cancer risk level at exposures of 0.7 ng/L and has been classified in group B2 list as probable human carcinogen by USEPA [18].

Studies on N-DBPs formation and control during disinfection process have been of particular concern these days. DBPs formation during monochloramination of diuron [19], chlortoluron [20], isoproturon, trifluralin, and ranitidine [21], as well as algae organic matters of *Microcystic aeruginosa* [22] has been investigated. Our previous studies have reported formation of volatile halogenated by-products during the chlorination of OTC [23]. OTC monochloramination is subjected to hydroxylation and Cl-substitution, and many DBPs can be formed [24]. However, DBPs formation during monochloramination of OTC has not been studied in detail yet. The aim of the present study is to investigate the formation of C-DBPs and N-DBPs during monochloramination of OTC including NDMA. Impact factors including reaction time, pH, monochloramine dosages, and bromide concentrations were then examined in detail.

2. Materials and methods

2.1. Chemicals and reagents

Chromatographical purity of OTC hydrochloride (>97%) was purchased from Dr Ehrenstorfer (Germany) and used without further purification. The physico-chemical properties of OTC can be found elsewhere [23]. Analytical grade reagents including KH_2PO_4, CH_3COONH_4, CH_3COOH, NaOH, NH_4Cl, and H_2SO_4 were purchased from Sinopharm Chemical Reagent Co., Ltd (Shanghai, China) without being further purified.

Halogenated volatiles mixed standard solutions including chloroform (CF), bromodichloromethane, dibromochloromethane, bromochloroacetonitrile (BCAN), dibromoacetonitrile (DBAN), dichloroacetonitrile (DCAN), 1,1-dichloro-2-propanone (DCP), 1,1,1-trichloroacetone (TCP), trichloroacetonitrile (TCAN), and trichloronitromethane (TCNM) were purchased from Sigma–Aldrich (St Louis, MO, USA). NDMA standard (>99.5%) and NDMA-d6 (used as internal standard) were obtained from Chem Service, Inc. (Westchester, PA, USA) and Cambridge Isotope Laboratories, Inc. (MA, USA). All the solutions were prepared with ultra-pure water produced from a Milli-Q water purification system (Millipore, USA). HPLC grade methanol and methyl tert-butyl ether (MTBE) were obtained from J.T. Baker (USA).

NH_2Cl solution was made daily by adding NaOCl solution gently into a stirred NH_4Cl solution with the Cl:N molar ratio at 1:1.2 to prevent breakpoint chlorination due to local excess of OCl^- [25], and the pH was kept at around 8.5 to avoid the disproportionation of NH_2Cl to $NHCl_2$ [26].

2.2. Experimental plans

All experiments were carried out in batch reactors, which were fixed in a thermostatic culture oscillator with controlled temperature at 25 ± 1°C. The experiments of OTC monochloramination were conducted in duplicate under headspace-free conditions in 40-mL glass screw-cap vials with PEFE-lined septa. For experiments on violated DPBs formation, a typical run involving monochloramine dose (0.75 mM as Cl_2, mass ratio of Cl_2/C=10) was applied to OTC solutions (0.02 mM) with phosphate buffer (10 mM) for 3 d reaction [23]. The investigation time was controlled at 2 h, 8 h, 1 d, 2 d, 3 d, 4 d, 5 d, and 7 d. The range of pHs conducted in the formation experiments was from 5 to 9. Phosphate buffer solution was used at pH 6–8, carbonate buffer solution at 9, and acetate buffer solution at 5. KBr was added to OTC solution in order to make

batch of experiments containing Br^-. At scheduled time, NH_4Cl was added 1.5 times the initial molar concentration of chloramine to quench any residual disinfectants [20].

The NDMA formation experiments were conducted using the method developed by Mitch et al. [26] with the typical monochloramine dosage as 2 mM. Reacting samples were incubated in dark in batch reactors at controlled temperature (25 ± 1 ℃) for 2 h, 7 h, and 1–7 d. The solution pH was buffered from 4 to 9 as described above. At scheduled time, ascorbic acid (50 mM) was used to quench the reaction.

2.3. Analytical methods

Chlorine and monochloramine concentrations were analyzed using the N,Ndethyl-p-phenylenediamine (DPD) colorimetric method [27]. pH was measured using a pH-meter (module PHS-3B, Shanghai LEICI Analysis Instrument Factory, China), which was calibrated on a regular basis using standard pH 4, 6.86, and 9.18 buffers.

C-DBPs and N-DBPs were analyzed following the USEPA method of 551.1 [28]. Samples were extracted with MTBE, and the extracts were then analyzed by a gas chromatograph (GC-2010, Shimadzu, Japan) equipped with an electron capture detector (ECD) and a fused silica capillary column (HP-5, 30 m × 0.25 mm ID, 1 μm film thickness). The column temperature program was 35 ℃ (5 min), 35–50 ℃ (4 ℃/min), 50–250 ℃ (30 ℃/min), and 250 ℃ (5 min), with temperature of the injector and ECD at 200 and 290 ℃, respectively.

NDMA was analyzed using UPLC-ESI-MS (ESI source, TSQ Quantum, Thermo Fisher Scientific Inc., USA) with a Thermos Hypersil GOLD C8 column (150 × 2.1 mm I.D, 3 μm film thickness, Thermo Fisher Scientific Inc., USA). Methanol (solvent A) and 2 mM ammonium acetate buffer in Milli-Q water (solvent B) were used as the mobile phase with a flow rate of 0.15 mL min^{-1}. The detailed method was described in our previous study [20].

3. Results and discussion

3.1. Effect of reaction time

In order to find the volatile DPBs and NDMA yields of OTC monochlorination, reactions were kept up to 7 d with monochloramine in excess [24]. The time-dependent formation of C-DBPs and N-DBPs after monochloramination of OTC at pH 7 is presented in Fig. 1.

As shown in Fig. 1, six DBPs including CF, DCAN, TCNM, DCP, TCP, and NDMA were detected and

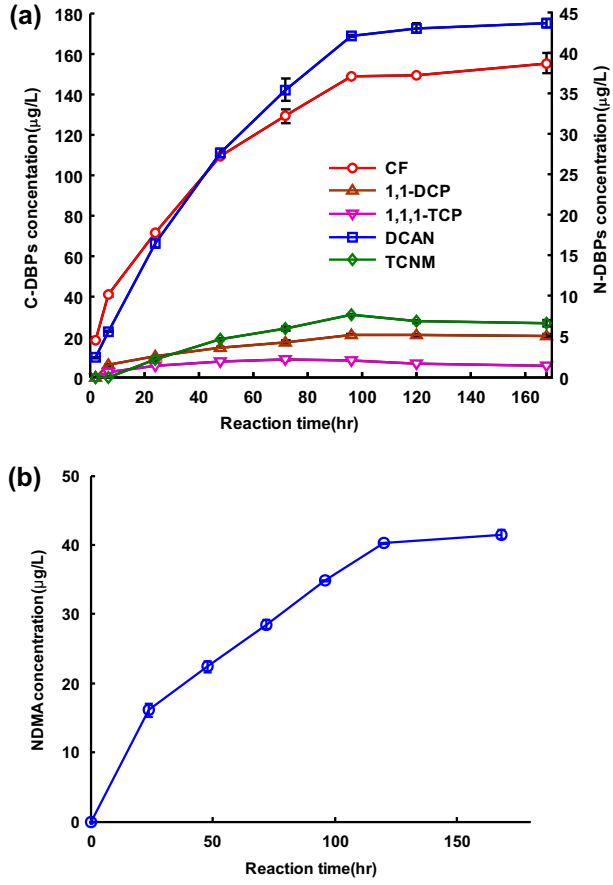

Fig. 1. Time-dependent formation of (a) volatile DBPs ($[NH_2Cl]_0 = 0.75$ mM as Cl_2, $[OTC]_0 = 0.02$ mM) and (b) NDMA ($[NH_2Cl]_0 = 2$ mM as Cl_2, $[OTC]_0 = 0.04$ mM) during monochloramination of OTC at 25 ± 1 ℃ and pH 7. Error bars represent the difference between maximum and the minimum value of replicate measurements.

their generation increased with reaction time. CF and DCAN were the most abundant DBP formed and followed by NDMA, TCNM, and DCP. Limited concentration of TCP was obtained at the level of several μg/L. Among these DBPs, particular concern should be focused on highly carcinogenic NDMA. Relatively high yield of NDMA was found during OTC monochloramination. OTC can be regarded as important precursor of NDMA, which generated more NDMA than chlortoluron during monochloramination [20].

The concentrations of CF and DCAN increased rapidly from 18 to 2 μg/L at 2 h to 142 and 43 μg/L at 7 d, respectively. The maximum yields were calculated as 14.2 and 4.3 μg/mg with initial concentrations of NH_2Cl and OTC as 0.75 and 0.02 mM at pH 7, respectively (μg/mg represents DBPs yields per mg of OTC). TCNM, DCP, and TCP reached the maximum values by 96 h and then decreased as the reaction time

increased. Compared to volatile DBPs yields after 7 d, over 70% of all species were formed within 72 h, which indicated OTC reacted rapidly with monochloramine and formed DBPs. The patterns of DBPs yields were similar to the results of monochloramination of natural organic matters in Yang's study [25]. However, the patterns exited a bit difference from the OTC chlorination [23]. CF is usually the end product during both monochloramination and chlorination; thus, highest concentrations of CF were found during both processes [23]. DCP was detectable during monochloramination and absent in chlorination at pH 7 [23], which can be explained by the consecutive model proposed by Reckhow and Singer [29]. DCAN increased to a maximum and then gradually decreased during chlorination due to the hydrolysis in the presence of chlorine [23], which did not happen during monochloramination.

As shown in Fig. 1(b), formation of NDMA increased gradually and reached a maximum of 41 μg/L at 7 d. Use of monochloramination greatly increases NDMA formation, while no significant NDMA was found during OTC chlorination [23]. The results are consistent with other investigated precursors including diuron [19], chlortoluron [20], ranitidine [21], and so on. As our previous report, dimethylamino structure of OTC inclined to release form the parent molecule during monochloramination [24]. Thus, NDMA was generated by UMDH pathways from dimethylamine (DMA) or chlorinated DMA in the presence of monochloramine [24]. Stable NDMA concentrations were observed after 120 h in this study, which indicated formation rate of NDMA was generally slower than violated DBPs. Similar results were also obtained in our previous study on chlortoluron monochloramination [20].

3.2. Effect of monochloramine dosage

Effect of monochloramine dosage on violate DBPs formation was investigated with mass NH_2Cl (as Cl_2)/C ratio of 1–10, reaction time of 3 d, and initial OTC concentration of 0.02 mM, and the results are shown in Fig. 2(a) and (b).

It is obvious that all the violate DBP species increased greatly with the increase in monochloramine concentration. CF, DCAN, and DCP were formed even at very low monochloramine concentrations (Cl_2/C=1), while TCP and TCNM were found at higher monochloramine concentrations (Cl_2/C > 2). CF and DCAN were the most abundant volatile DBPs and kept increased with increasing monochlorine concentration.

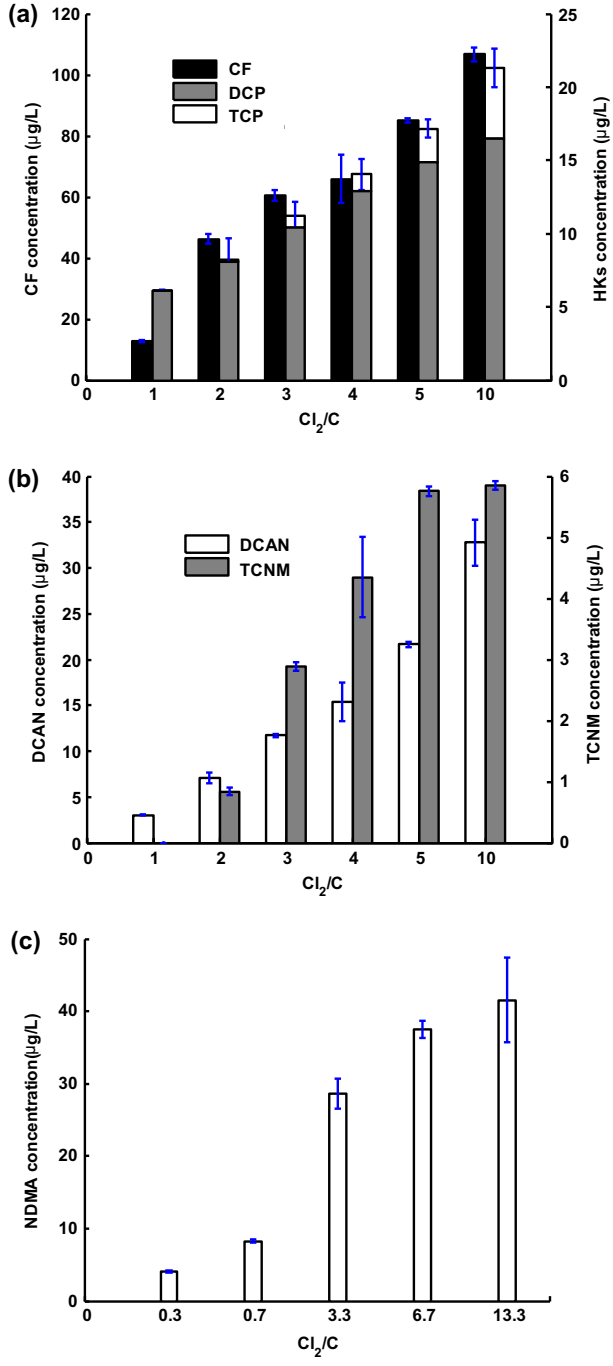

Fig. 2. Formation of (a) volatile C-DBPs and (b) volatile N-DBPs ($[OTC]_0$ = 0.02 mM, reaction time = 3 d), (c) NDMA ($[OTC]_0$ = 0.04 mM, reaction time = 3 d) during monochloramination of OTC as functions of monochloramine dosage at 25 ± 1 ℃ and pH 7. The Cl_2/C value represents mass ratio of NH_2Cl (as Cl_2) and dissolved organic carbon (DOC) in solution. Error bars represent the difference between maximum and the minimum value of replicate measurements.

However, the increase in DCP and TCNM gradually slowed down at $Cl_2/C > 5$. TCP formation was significant prompted while high monochloramine dosage applied. As reported, unstable DBPs including DCAN and DCP tend to undergo decomposition and hydrolysis reactions in the presence of excess oxidant like chorine [23]. However, it was not happened during OTC monochloramination in this study. The phenomena also found others literature reports, which implied that DCP and DCAN became more stable with monochloramine than chlorine [25,30,31].

Since monochloramine can contribute nitrogen source for the nitroso-group in NDMA, the concentrations of NDMA increased with increasing monochloramine concentration in Fig. 2(c), and the increase gradually slowed down at $Cl_2/C > 6.7$. Similar pattern was also found in monochloramination of diuron and chlortoluron [20,32]. The NDMA formation potential was observed as high as 41.6 μg/L while 2 mM monochloramine applied. The NDMA yield of OTC was calculated as 13.3 μM/mM, which is 4.2 times higher than that of chlortoluron [20]. Compounds containing heterocyclic ring seemed to generate more NDMA than that having aromatic rings [32].

3.3. Effect of pH

It is well documented that auto-decomposition reactions of monochloramine and OTC dissociation are highly related to pH value of the solution as well as the halogenation and hydrolysis reactions for DPBs [23]. Effect of solution pH on the formation of C-DBPs and N-DBPs during OTC monochloramination is presented in Fig. 3.

As shown in Fig. 3, solution pH exerted a great influence on the formation of all detected DBPs. All the DBPs concentration increased from pH 4 to 7 and then decreased to pH 9. The peak concentration of CF, DCAN, NDMA, DCP, TCP, and TCNM was 118, 36.7, 41.2, 18.2, 5.96, and 8.5 μg/L at pH 7, respectively. The effect of pH on DBPs formation could be explained by NH_2Cl auto-decomposition, and the major reaction was listed reactions (Eqs. (1)–(3)), which results in multiple chlorinated oxidants to coexist, including NH_2Cl, $NHCl_2$, OCl^-, and hypochlorous acid (HOCl) [24].

$$NH_2Cl + H_2O \rightarrow HOCl + NH_3 \quad (1)$$

$$HOCl + NH_2Cl \rightarrow NHCl_2 + H_2O \quad (2)$$

$$NH_2Cl + NH_2Cl \rightarrow NHCl_2 + NH_3 \quad (3)$$

Due to the dominant presence of NH_2Cl in the solution and faster hydrolysis reaction (Eq. (1)) from

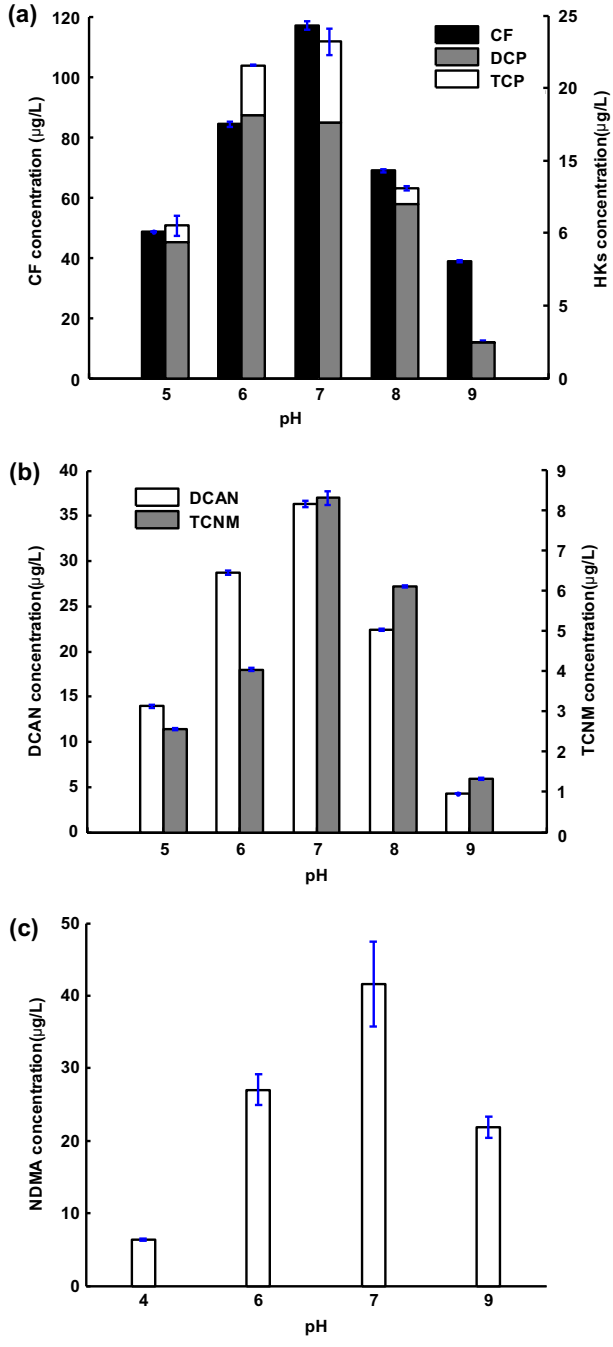

Fig. 3. Formation of (a) volatile C-DBPs and (b) volatile N-DBPs ($[NH_2Cl]_0 = 0.75$ mM as Cl_2, $[OTC]_0 = 0.02$ mM), (c) NDMA ($[NH_2Cl]_0 = 2$ mM as Cl_2, $[OTC]_0 = 0.04$ mM) during monochloramination of OTC as functions of solution pH at 25 ± 1°C. Error bars represent the difference between maximum and the minimum value of replicate measurements.

NH_2Cl to HOCl at neutral pH, peak yields of all DBPs were observed under circumneutral conditions as a result [24]. On the other hand, OTC pKa values are 3.27, 7.32, and 9.11 [23]; the reactivity of OTC between

multiple chlorinated oxidants is highly pH-dependent too and thus affected DBPs formation.

Solution pH can also affect the stability of DBPs including DCAN, DCP, and TCP, which subjected to base-catalyzed decomposition. CF was a common product from hydrolysis of DCP and TCP [33,34]. This might explain the unstable DBPs concentration decrease at solution pH > 7.

Peak yield for NDMA was also found at neutral pH. Acidic and alkaline conditions both reduced NDMA formation. The results were also consistent with the reports in the monochloramination of amitriptyline, diuron, and chlortoluron [20,32,35].

3.4. Effect of bromide

As previous findings have confirmed, introduction of bromide would increase the bromine-substituted DBPs and suppress the regular chlorine-contained DBPs [36–38]. Experiments on various concentrations of bromide were carried out to assess the influence of Br^- on the formation of DBPs. Fig. 4 shows the effect of bromide on the formation of violated DBPs during monochloramination of OTC.

As shown in Fig. 4, as $[Br^-]/[Cl]$ grew from 0.002 to 0.2, CF and DCAN decreased while DBAN and BF increased significantly. The yields of total THMs and HANs reached the maximum when $[Br^-]/[Cl]$ was 0.2. The significant increase in total yields of DBPs could be interpreted as addition, substitution and oxidation reaction between OTC and Hypobromous acid (HOBr) or bromochloramine [39]. Due the transformation of brominated chlorinated analogs, it was also observed that TCP and TCNM both vanished as $[Br^-]/[Cl] > 0.1$. When $[Br^-]/[Cl]$ exceeded 0.1, only 1,1-DCP can be detected, and its concentration reduced to a relatively low level.

HOBr can be formed easily from NH_2Cl when bromide was present in solution. Furthermore, HOBr would react with monochloramine to form bromochloramine [40,41]. Bromochloramine was proved to play an important role in the formation of bromine-substituted DBPs due to the labile and reactive bromine atom in the molecule structure [21,34]. Bromamine decomposition model has been proposed by Lei et al. [42] and bromochloramine's formation and decay reactions are developed by other researchers [38,39,43]. Information on bromochloramine formation, decay, and acid catalysis effect was so far limited. The complex relationship between bromochloramine and DBPs formation should be further studied.

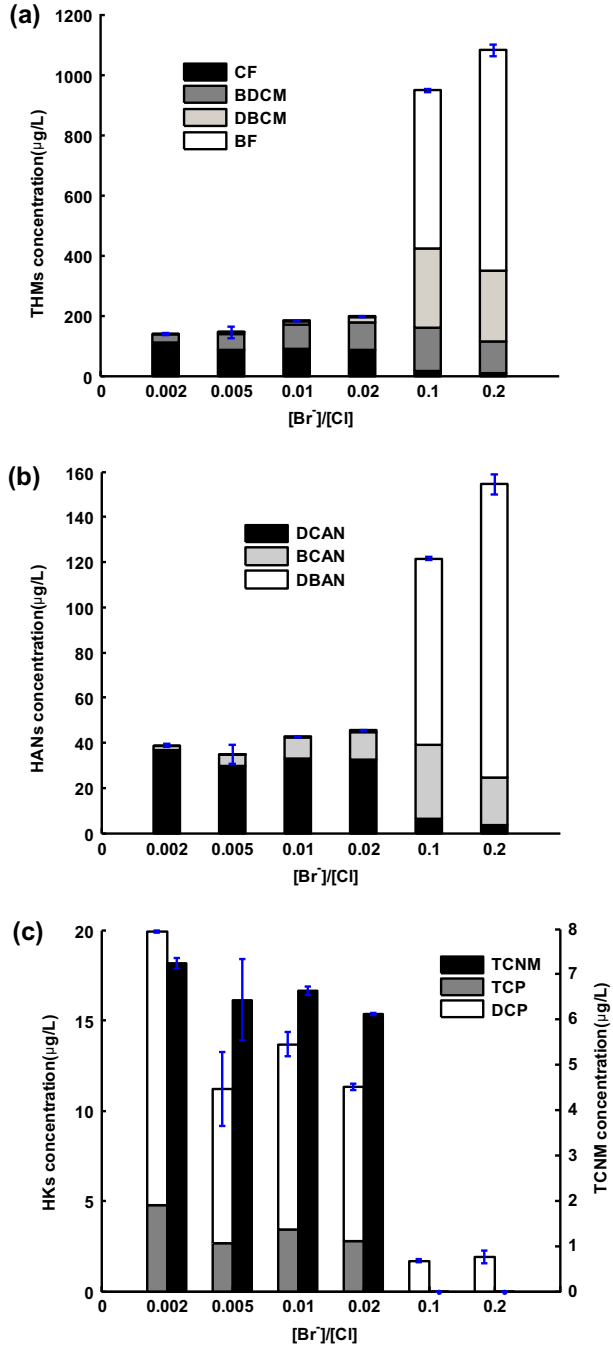

Fig. 4. Influence of bromide on (a) THMs, (b) HANs (c) HKs and TCNM formation during monochloramination of OTC at 25 ± 1°C and pH 7 ($[NH_2Cl]_0 = 0.75$ mM as Cl_2, $[OTC]_0 = 0.02$ mM). $[Br^-]/[Cl]$ value represents mole ratio of bromide and NH_2Cl (as Cl_2) in solution. Error bars represent the difference between maximum and the minimum value of replicate measurements.

4. Conclusions

(1) Six DBPs including CF, DCAN, TCNM, DCP, TCP, especially NDMA were found during monochloramination of OTC.
(2) Solution pH and monochloramination dosage exerted significant influence on the formation of all detected DBPs. Peak yields of all DBPs species were found under circumneutral conditions during monochloramination of OTC. All the DBP species increased greatly with the increase in monochloramine concentration. Formation rate of NDMA was generally slower than violated DBPs.
(3) Formation of bromine-substituted DBPs increased accordingly in the presence of bromide. It was believed that bromochloramine formed in the reaction of HOBr and monochloramine played an important role.
(4) Considering the high conversion of OTC to six kinds of toxic and hazardous DBPs including CF, DCAN, TCNM, DCP, TCP, and NDMA, removal of presented OTC in waters should be implemented before chloramination disinfection process in drinking water treatment.

Acknowledgments

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