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Formation pathways of brominated products from benzophenone-4 chlorination in the presence of bromide ions

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ABSTRACT

The brominated products, formed in chlorination treatment of benzophenone-4 in the presence of bromide ions, were identified, and the formation pathways were proposed. Under disinfection conditions, benzophenone-4 would undertake electrophilic substitution generating mono- or di-halogenated products, which would be oxidized to esters and further hydrolyzed to phenol derivatives. The generated catechol intermediate would be transformed into furan-like heterocyclic product. The product species were pH-dependent, while benzophenone-4 elimination was chlorine dose-dependent. When the chlorination treatment was performed on ambient water spiked with benzophenone-4 and bromide ions, most of brominated byproducts could be detected, and the acute toxicity significantly increased as well.

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Introduction

UV filters are widely used in pharmaceuticals, insecticides, agricultural chemicals and personal care products (Roelandts et al., 1983; Stenback, 1977; Tomson et al., 1981). As main ingredients of these products, UV filters have a great chance to enter the environment through swimming, bathing, and leaching of land and house coating (Poiger et al., 2004; Giokas et al., 2007; Plagellat et al., 2006). Benzophenone-type chemicals (BPs) are a primary member in the UV filter family. BP-3 (2-hydroxy-4-methoxy-BP) and BP-4 (2-hydroxy-4-methoxy-5-sulfonic acid-BP) have been approved by the European Legislation to be used in sunscreens (Shaath, 2007). The maximum concentration range permitted for BP-4 in cosmetics is from 5% to 10% in Japan, Australia, USA, EU and China (MHLW, 2000; TGA, 2003; FDA, 1999; EC, 1976; MOH, 2007). Due to its higher polarity, BP-4 was mainly detected within the water phase (Zener et al., 2008). The residual concentrations of BP-4 were at hundreds of ng/L level in river and sea water, and ranged from 237 to 1481 ng/L in wastewater samples (Rodil et al., 2008). However, many studies showed that BP-4 had no significant deduction in conventional biodegradation processes (Rodil et al., 2008; Kasprzyk-Hordern et al., 2008), bringing the risks to fish and other aquatic organisms through interruption of their sexual hormone system (Zucchi et al., 2011). For example, BP-type chemicals exhibited multiple adverse biological effects, such as uterotrophic effects in vivo, estrogenic activity in the yeast two-hybrid assay (Kawamura et al., 2003), stimulating the proliferation of MCF-7 breast cancer cells, and increasing the secretion of the tumor marker pS2 in vitro (Schlumpf et al., 2001). Benzophenone has been classified as “chemicals suspected of having endocrine disrupting effects” by Japanese Ministry of Environment (NIES, 1998).

Disinfection with free available chlorine (FAC, HOCl/OCl−) is a necessary process for drinking water, swimming pool water and wastewater reclamation treatment. During these processes, residual UV-filters may react with disinfectant to form chlorinated,

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oxidized, and fragmented byproducts (Deborde and Gunten, 2008; DellaGreca et al., 2009; Yang and Shang, 2004; Dodd and Huang, 2004; Pinkston and Sedlak, 2004; Hu et al., 2003; Buth et al., 2007). Negreira et al. (2008) studied the stability of three UV-filters under chlorination conditions and identified up to 8 byproducts for BP-3. Sakkas et al. (2003) detected mono-chlorinated byproducts of octyl-dimethyl-p-aminobenzoic in swimming pool water.

Except for dissolved organic materials, some inorganic ions, such as Br\(^{-}\), I\(^{-}\), and SO\(_4\)\(^{2-}\) in ambient water bodies, would also affect the chlorination process (Deborde and Gunten, 2008). It was reported that Br\(^{-}\) in natural water was around 100 μg/L in the USA, and it could reach as high as 2000 μg/L in some regions of the world (Richardson et al., 2003). Deborde and Gunten (2008) concluded the reaction of chlorine with bromide. During chlorination, bromide was oxidized by hypochlorous acid and hypo-chlorite, due to chlorine and bromide standard redox potentials. First, a BrCl-type intermediate would be formed via the transfer of Cl\(^{-}\) from hypochlorous acid to the bromide (Br\(^{-}\)). Then the BrCl-type intermediate was hydrolyzed and lead to OBr\(^{-}\) (reactions (1) and (2)) (Kumar et al., 1986; Kumar and Margerum, 1987; Johnson and Margerum, 1991).

\[
\text{HOCl} + \text{Br}^- \rightarrow \text{BrCl} + \text{OH}^- \quad (1)
\]

\[
\text{BrCl} + 2\text{OH}^- \rightarrow \text{OBr}^- + \text{Cl}^- + \text{H}_2\text{O} \quad (2)
\]

The small amount of chemically active bromine would be formed during traditional chlorination process (Gallard et al., 2003; Acero et al., 2005), leading to brominated byproducts (Gallard et al., 2003; Acero et al., 2005; Hu et al., 2006). Gallard et al. (2003) studied the kinetics of bromination based on ortho- and para-substituted phenols, and found that the reaction rate was about 1000-fold higher than that of chlorination in drinking water treatment conditions. Besides, brominated disinfection byproducts usually exhibited more significant toxicity than their chlorinated analogs (Richardson et al., 2007), causing more safety concerns in this regard (Xiao et al., 2012).

In our previous study on the transformation characteristics of BP-4 in chlorination process, 13 transformation products were identified, and the possible transformation mechanisms were proposed (Xiao et al., 2013). However, the influences of Br\(^{-}\) on BP-4 transformation were not involved. Negreira et al. (2012) preliminarily investigated the effects of Br\(^{-}\) on the transformation kinetics of BP-4 in chlorination system, and detected four brominated products (m/z: 384.9387, 400.9336, 478.8441, 434.8946). Theoretically, more brominated products would be formed, their molecular structures, and possible formation pathways in BP-4 chlorination system containing Br\(^{-}\) ions should be deeply explored. Therefore, in the present study, the brominated products were separated using gradient high performance liquid chromatography (or gas chromatography), and their structures were elucidated by mass spectrometry information. The possible formation pathways were proposed and verified by orthogonal experiments under different pH levels and FAC doses. Moreover, BP-4 chlorination experiments were conducted in ambient water matrices, to simulate its transformation characteristics in water treatment practices, and to confirm the formation of brominated products in bromide-containing chlorination disinfection system.

1. Materials and methods

1.1. Chemicals and solutions preparation

BP-4 (2-hydroxyl-4-methoxybenzophenone-5-sulfonic acid, purity \(>97\%\)) was purchased from Sigma-Aldrich (St. Louis, MO, USA). NaClO (6%) aqueous solution was obtained from Wako Co. (Tokyo, Japan). Methanol (for HPLC analysis) was purchased from Fisher Scientific (Fair Lawn, NJ, USA). Formic acid (for HPLC analysis) was purchased from Acros Organics (Belgium, WI, USA). Potassium bromide and all other chemicals were of reagent grade and used without further purification. Ultrapure water (Milli-Q water) generated from Millipore Purification System (Billerica, MA, USA) was used throughout the analytical experiments. All stock solutions were prepared and diluted with Milli-Q water without adding any organic co-solvent.

1.2. Chlorination procedures

The experiments were conducted in a 1000 mL of borosilicate glass conical flask which was placed in a water bath with a magnetic stirring apparatus to maintain the reaction temperature at 25 ± 0.5 °C. In order to have a comprehensive understanding of the reaction, experiments were carried out under three different pH values (pH 4.6, 7.5 and 11). And the relative distributions of FAC and bromine species are shown in Appendix A Fig. S1. Considering the buffer capacity and adverse effects of excessive salts on instrumental detection and toxicity tests, the concentrations of buffer solutions were optimized. The 0.1 mol/L of acetate buffer (pH = 4.6), 0.02 mol/L of phosphate buffer (pH = 7.5) and 0.02 mol/L of carbonate buffer (pH = 11.0) were used to maintain pH within 0.1 unit of variance during the reaction period.

In order to permit the isolation of sufficient amounts of products for characterization by HPLC/MS and GC/MS, the chlorination experiments were conducted with a relatively high concentration of BP-4 and FAC. Reactions were initiated by adding appropriate volumes of FAC solution (molar equivalent ratio of [FAC]:[BP-4] was set at 0.5:1, 1:1, 3:1, 5:1, 10:1 and 20:1) to 500 mL solutions containing 5 mmol/L of BP-4 and 5 mmol/L of KBr. Five milliliters of reaction mixture was subsequently taken at evenly-spaced time intervals and sodium sulfite solution was immediately added to quench residual FAC. The samples were then analyzed by ultra performance liquid chromatography and quadrupole-time of flight mass spectrometer (UPLC–QTOF–MS) or gas chromatography–mass spectrometer (GC–MS) to measure the loss of BP-4 and generation of transformation products.

For UPLC–QTOF–MS analysis, the quenched sample was directly injected after filtration through 0.22 μm glass fiber membrane. For GC–MS analysis, the sample is required to be anhydrous, so the aqueous reaction mixture after quenching was dehydrated. Specifically, 5 mL of aqueous sample was freeze-dried to remove solvent water, then 1 mL of methanol/acetone (1/1, V/V) solvents was added to extract transformation products. The extract was divided into two aliquots, one was for GC–MS analysis after filtrating through 0.22 μm glass fiber membrane, and the other was for acute toxicity test after a solvent conversion. The solvent methanol/acetone was dried with a gentle nitrogen gas stream (300 mL/min), and the solid was re-dissolved with 0.2 mL of DMSO. The DMSO was maintained at 0.1% in each exposing well.

1.3. Identification of transformation products

1.3.1. Ultra liquid chromatography–mass spectrometry method

To obtain MS² spectrum, an UPLC–QTOF–MS (Ultimate 3000, Dionex, Sunnyvale, CA, USA; micrOTOF QII, Bruker, Bremen,
Germany) was used. For UPLC conditions, an Agilent Zorbax Eclipse XDB-C18 column (4.6 × 150 mm, 5 μm, Santa Clara, CA, USA) was used to separate the products in reaction mixtures. Formic acid aqueous solution (A) (0.1%, V/V) and methanol (B) were used as mobile phases. The mobile phase flow was 0.4 mL/min and the following gradient was used: 0–3 min, 75% A; 4–10 min, 60% A; 11–14 min, 50% A; 15–22 min, 40% A; 23–25 min, 20% A; 27–36 min, 10% A; 40–50 min, 0% A. For QTOF-MS conditions, negative mode electrospray ionization (ESI) over a mass scan range of 50–500 m/z was used. Spray chamber temperature was 350 °C and drying gas flow was 10 mL/min. The same system was used to obtain MS² spectrum using target model with collision energy ramping from 15 to 25 eV.

1.3.2. Gas chromatography–mass spectrometry method

Determination of hydrophobic and semi-volatile transformation products was performed on an Agilent 7890A/5975C GC/MS (Santa Clara, CA, USA); the software used was an enhanced chemstation from Agilent Technologies (MSD ChemStation E.02.00.493, Santa Clara, CA, USA). The samples were injected using an Agilent 7693A auto injector including transfer turret for analysis. The separation of the analytes was performed with a capillary GC column of 30 m length and 25 μm internal diameter with a 0.25 μm film thickness of stationary phase of 5% phenyl methyl siloxane from HP. The carrier gas was helium with a flow rate of 1.0 mL/min. The injector temperature was at 280 °C and sample injection (1 μL) was in splitless mode. GC oven temperature was programmed from 70 °C, ramped at a rate of 20 °C/min to 250 °C for 2 min, then ramped at a rate of 20 °C/min to 300 °C and held for 5 min. For MS conditions, a full scan mode was chosen with a wide range from m/z 50 to 500. Electron ionization (EI) mode with 70 eV of electron energy was adopted. The ion source temperature was 230 °C. The GC–MS interface was kept at 280 °C. Quadrupole module temperature was set to 150 °C.

1.4. Acute toxicity test

A photobacterium bioassay was used to measure the acute toxicity formation during BP-4 chlorination in the presence of bromide ions. The freeze-dry powder of Photobacterium phosphoreum strain was provided by the Nanjing Institute of Soil Science, Chinese Academy of Science. Samples to be tested were added into 96-well microplate and diluted to 180 μL using 3% NaCl solution. Negative control, solvent control and positive control were 3% of NaCl solution, 0.1% DMSO and HgCl₂, respectively. The freeze-dried powder of P. phosphoreum was dissolved into 3% NaCl solution and pre-cultured for 30 min. Then, 20 μL of P. phosphoreum was added into each well. After a 15-min shaking and exposing at 20 ± 1 °C, Synergy TM2 Multi-Mode Microplate Reader (Biotek, Shoreline, WA, USA) was used to measure the bioluminescence intensity of each well. The inhibition ratio of bioluminescence (I, %) was calculated in accordance with Eq. (3):

\[ I = \frac{L_{\text{NC}} - L_{\text{Sample}}}{L_{\text{NC}}} \times 100\% \]  

(3)

where, \( L_{\text{sample}} \) represents luminescence intensity of test sample, and \( L_{\text{NC}} \) represents luminescence intensity of negative control.

2. Results and discussion

2.1. Identification of transformation products

Experiments were conducted under three pH values (pH 4.6, 7.5 and 11.0) with different doses of FAC. Samples were analyzed using UPLC-QTOF–MS. The total ion chromatogram (with full scan mode) of one BP-4 chlorination mixture (BP-4, 5 mmol/L; Br⁻, 5 mmol/L; NaClO, 25 mmol/L; reaction period, 1 hr; pH, 4.6) is shown in Appendix A Fig. S2a. Nine transformation products (abbreviated as P1 to P9) were detected. However, the peaks of P3, P4 and P5 were not significant in this chromatogram. Thus, the same sample was condensed for 5 times then analyzed by UPLC-MS. After subtracting interfering ion mass spectrum as background, the signals of P3, P4 and P5 were strong enough for qualitative analysis as shown in Appendix A Fig. S2b. The MS¹ and MS² spectra of the 9 detected products are shown in Appendix A Figs. S3 and S4. MS¹ spectra provide accurate mass and isotopic information of the parent ions for deducing the molecular structure of the transformation products, and MS² spectra provide more sufficient information of the fragment ions for defining the structure. Since UPLC–QTOF–MS with ESI mode has low responses to those compounds with low polarity, the same samples were also detected by GC–MS with EI mode. The products with low polarity (products P10–P12) had strong responses. Their structures are indentified based on the analyses of their parent ions and fragment ions (Appendix A Fig. S3). A total of 22 major products were identified, and 12 bromide-containing products are listed in Table 1.

Since three di-halogenated products (P8, P9 and di-chlorinated BP-4) had similar chromatographic retention characteristics, their MS¹ signals interfered with each other (as shown in Fig. 1). The reasons for attributing the three clusters of mass peaks (S1, S2, S3) to the three products were as below. Firstly, judging from the distribution of isotopic peaks, S1 corresponded to the ion containing two Br atoms (P9), S2 corresponded to the ion containing one Cl and one Br atoms (P8) and S3 corresponded to the ion containing two Cl atoms. Therefore, S3 and S2 couldn’t be the fragment peaks of S1. Secondly, ESI used to obtain the mass spectra was a kind of soft ionization mode, so the three peaks were more likely to be three quasi molecular ion peaks instead of fragment ion peaks. Thirdly, the formation of the three deduced products well complemented the transformation pathways and reasonably followed the reaction principles of organic chemistry.

2.2. Formation pathways of brominated products

Fig. 2 shows the time-dependent degradation of BP-4 and formation of brominated products P1–P9 at pH 4.6. It can be seen that about 80% of BP-4 rapidly degraded in the initial 5 sec, and its concentration had a very slow decrease during the followed 4 hr. Correspondingly, the product P7 (3-bromo-BP-4) immediately reached the maximum within 5 sec, and then rapidly decreased and kept the level stable during the followed 1 hr. Similarly, the products P5 (mono-brominated
ester) and its hydrolysis product P2 reached maximum within 5 sec, and then decreased slowly as well. A little later than the formation of P7, mono-brominated ester P1, bromo-chlorinated ester P6 and hydrolysis product P3 did not reach their maximum until 5 min. Much later than the formation of P7, the signals of di-halogenated products (P8, P9) increased gently and did not reach their peaks until 1 hr. The most lately formed product was five-member heterocyclic furan.

Table 1 – Major transformation products of BP-4 in the chlorination system in the presence of Br\(^{-}\) ions.

<table>
<thead>
<tr>
<th>No.</th>
<th>Structure</th>
<th>Formula</th>
<th>Exact mass</th>
<th>Mass-to-charge (m/z) of molecular ion</th>
<th>Difference a</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calculated</td>
<td>Measured</td>
<td>4.6</td>
<td>7.5</td>
</tr>
<tr>
<td>P1</td>
<td><img src="image" alt="Structure P1" /></td>
<td>C(<em>{14})H(</em>{11})BrO(_7)S</td>
<td>401.9409</td>
<td>400.9330</td>
<td>0.0017</td>
<td>√</td>
</tr>
<tr>
<td>P2</td>
<td><img src="image" alt="Structure P2" /></td>
<td>C(<em>{7})H(</em>{6})Br(_2)O(_5)S</td>
<td>359.8303</td>
<td>358.8224</td>
<td>358.8269</td>
<td>0.0045</td>
</tr>
<tr>
<td>P3</td>
<td><img src="image" alt="Structure P3" /></td>
<td>C(<em>{7})H(</em>{6})BrClO(_6)S</td>
<td>331.8757</td>
<td>330.8678</td>
<td>330.8704</td>
<td>0.0026</td>
</tr>
<tr>
<td>P4</td>
<td><img src="image" alt="Structure P4" /></td>
<td>C(<em>{8})H(</em>{6})BrClO(_5)S</td>
<td>291.8808</td>
<td>290.8729</td>
<td>290.8781</td>
<td>0.0052</td>
</tr>
<tr>
<td>P5</td>
<td><img src="image" alt="Structure P5" /></td>
<td>C(<em>{14})H(</em>{11})BrO(_7)S</td>
<td>401.9409</td>
<td>400.9330</td>
<td>400.9383</td>
<td>0.0053</td>
</tr>
<tr>
<td>P6</td>
<td><img src="image" alt="Structure P6" /></td>
<td>C(<em>{14})H(</em>{10})BrClO(_7)S</td>
<td>435.9019</td>
<td>434.8940</td>
<td>434.9000</td>
<td>0.0060</td>
</tr>
<tr>
<td>P7</td>
<td><img src="image" alt="Structure P7" /></td>
<td>C(<em>{14})H(</em>{11})BrO(_6)S</td>
<td>385.9460</td>
<td>384.9381</td>
<td>384.9426</td>
<td>0.0045</td>
</tr>
<tr>
<td>P8</td>
<td><img src="image" alt="Structure P8" /></td>
<td>C(<em>{14})H(</em>{10})BrClO(_6)</td>
<td>419.9070</td>
<td>418.8991</td>
<td>418.9063</td>
<td>0.0072</td>
</tr>
<tr>
<td>P9</td>
<td><img src="image" alt="Structure P9" /></td>
<td>C(<em>{14})H(</em>{10})Br(_2)O(_6)S</td>
<td>463.8565</td>
<td>462.8486</td>
<td>462.8539</td>
<td>0.0053</td>
</tr>
<tr>
<td>P10</td>
<td><img src="image" alt="Structure P10" /></td>
<td>C(<em>{14})H(</em>{11})BrO(_3)</td>
<td>307.1393</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>P11</td>
<td><img src="image" alt="Structure P11" /></td>
<td>C(<em>{14})H(</em>{10})BrClO(_3)</td>
<td>339.9502</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>P12</td>
<td><img src="image" alt="Structure P12" /></td>
<td>C(<em>{14})H(</em>{10})Br(_2)O(_3)</td>
<td>383.8997</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

a Differences between the calculated and measured mass. *P10, P11 and P12 were detected using GC/low-resolution MS. And their calculated mass, measured mass and differences of calculated and measured mass were not listed.
like product P4, which reached a maximum response at 2 hr, accompanying the decrease of its precursor P3. Therefore, it can be concluded that in BP-4 chlorination system containing Br\(^-\) ions, the first halogenation, oxidation and ester hydrolysis were set to be performed, while the secondary halogenation and oxidation were a little late and difficult to take place.

Considering the structures of transformation products and reaction principles of organic chemistry, the possible formation pathways of brominated products under acidic condition were proposed (Fig. 3a). Judging from the products detected under different pH conditions, the pH values had great effects on the transformation pathways (which will be discussed in the following section). Since all transformation products were found in the acidic system, the outcomes at pH 4.6 were taken as an example to disclose the possible formation pathways of brominated products. As shown in Fig. 3a, the first halogenation substitution readily occurred at the 3-C, the ortho-position of hydroxy group, to form 3-bromo-BP-4 (P7) (Deborde and Gunten, 2008). Subsequently, the secondary halogenation occurred at 6-C to form 3,6-di-halogenated-BP-4 (P9, P8) although it was a little difficult due to the large steric hindrance.

Halogenated products could be further oxidized by hypohalous acid (HOX) to form ester products. Gordon et al. (1993) named this kind of reaction as "a novel Baeyer–Villiger rearrangement reaction". In this reaction, HOX resembles peroxy acid in being both a weak acid and an oxidizing agent, and an oxygen atom could be inset into ketone molecule. Considering the migratory aptitude of two benzene rings of BP-4 and its chlorinated intermediates, the extraneous O atom would possibly bind with either 1-C or 1’-C, to form two corresponding ester products (P1, P5) (Fermin and Bruno, 1993). Subsequently, ester products underwent hydrolysis in the presence of strong nucleophilic agents such as, OX\(^-\) (Jencks and Carriuolo, 1960). Hydrolysis products of P5, e.g., benzoic acid derivatives, readily occurred decarboxylation and chlorination substitution under acidic conditions to form P3. For ester products P6, its phenolic hydrolysis product (P3) was detected within the acidic chlorination system as well. P3 could be further oxidized to form five-member heterocyclic furan-like product P4 due to the Baeyer–Villiger oxidation and subsequent condensation (Gordon et al., 1993). Additionally, desulfonation and electrophilic substitution occurred not only to BP-4, but also to its halogenated product P7, forming P10, P11 and P12 (Gilbert, 1965).

2.3. Verification and compliment of proposed pathways

Since the pH conditions and FAC doses would influence the transformation behaviors of BP-4 and formation pathways of brominated products, orthogonal experiments at various pH values and FAC doses were conducted to verify and complement the proposed formation pathways.
Firstly, pH value promoted the transformation of BP-4. It is well known that pH has a great influence on the distribution and reactivity of FAC and bromine (Appendix A Fig. S2) (Rook et al., 1978), transformation characteristics of BP-4 under three different pH conditions (4.6, 7.5 and 11.0) were investigated, respectively. The time-dependent degradation features of BP-4 (initial concentration: 5 mmol/L) in the FAC (initial concentration: 15 mmol/L) system are shown in Fig. 4. It can be seen that, at pH 4.6 and 7.5, BP-4 degraded 75% within the initial 5 sec and did not further decrease during the followed 10 min. The degradation of BP-4 at pH 11.0 was relatively slow, less than 50% of BP-4 was transformed in the initial 5 sec, thereafter, 100% of BP-4 eliminated within the followed 10 min. This phenomenon can be interpreted with the species
of FAC, bromine and their reactivity under various pH conditions (Appendix A Fig. S2). Under acidic and neutral condition (pH 4.6 and 7.5), HClO, HBrO, Br2 and Cl2 were the dominant species, which has high reactivity and readily react with not only BP-4 but also with its intermediates. Therefore, some intermediates with high reactivity would competitively react with FAC, resulting in the remainant of BP-4. Under alkaline condition (pH 11.0), there are two cases. On one hand, OCI− and OBr− were the predominant species, which have low reactivity. Reactions between OCI− (and/or OBr−) with intermediates were not ready, resulting in a higher BP-4 elimination. On the other hand, the phenolic hydroxy group in BP-4 would transform into phenoxylation anion under alkaline condition, which had higher reactivity than phenolic form. Therefore, BP-4 was completely transformed under alkaline condition than under acidic and neutral conditions.

Secondly, pH determined the transformation pathways of BP-4. Based on the detected brominated products, the formation pathways under three pH conditions were proposed as shown in Fig. 3. For the case under acidic condition, five kinds of chemical reactions (halogenations, oxidation, hydrolysis, de-carboxylation and desulfonation) were involved. Under pH 7.5 and 11.0, the secondary halogenations of 3-bromo-BP-4 (P7) to form di-halogenated BP-4 (P8, P9) were inhibited. Similarly, the secondary halogenations of mono-halogenated ester (P5) to form di-halogenated ester (P6) could occur at pH 7.5, while its subsequent hydrolysis and oxidation were inhibited. Under pH 11.0, even the formation of di-halogenated ester product (P6) was inhibited.

In addition, 9 products (P1 to P9) were detected using UPLC-QTOF-MS, while those hydrophobic and semi-volatile products (P10, P11, P12) had low responses. Therefore, GC-MS was used to monitor the generation of those hydrophobic products under three pH conditions. In acidic system, the desulfonation reaction could readily occur to form P10, P11, and P12, while it hardly occurs under neutral and alkaline conditions (Gilbert, 1965).

Thirdly, FAC dose promoted the formation of brominated products. The experiments were conducted with different equivalents of [FAC]0:[BP-4]0 under three pH conditions. Again, take the outcomes of the chlorination of BP-4 at pH 4.6 as example to explore the effects of FAC dose on the formation of brominated products, because all brominated products are involved in this case. The reactions of BP-4 with different doses of FAC (0.5-, 1-, 3-, 5-, 10-, and 20-equiv to BP-4) were performed for 24 hr, and the relative content of each major brominated product was measured. As shown in Fig. 5, with increasing FAC, BP-4 degraded rapidly, the brominated products increased to maximum generally and then decreased. At 0.5 equiv of FAC, mono-bromo-BP-4 (P7) and ester products (P5, P6) formed. When FAC dose increased to 1 equiv, di-bromo-BP-4 (P9) formed. And up to 3-equiv of FAC, the hydrolysis product (P3) and the further oxidation product (P4) formed. Therefore, it can be concluded that high dose of FAC could promote the elimination of BP-4 and the formation of brominated products.

2.4. Formation of brominated products in ambient water matrices

In order to investigate the formation characteristics of brominated products in the chlorination disinfection practices, a series of experiments simulating real environmental conditions and operational parameters in chlorination disinfection practices were conducted. The initial BP-4 concentration was set as 0.1 μg/mL, Br− concentration was 0.1 μg/mL, FAC dose was 2 μg/mL, and reaction time was 30 min. The experiments were respectively conducted in three real ambient water samples (secondary treatment effluent, swimming pool water, and lake water). BP-4 and bromide
ions were spiked into each test matrix, and respectively treated with FAC. Each sample was concentrated 20 times via rotary evaporation treatment, and analyzed by UPLC–QTOF–MS. Table 2 listed the brominated products detected within various matrices after chlorination disinfection treatment. The major brominated products (P7, P5, P6, P2) could still be formed in ambient water matrices just as those in ultrapure water matrix. The results implied that the proposed formation mechanisms of brominated products could be replayed in real chlorination disinfection process in water treatment plant. In addition, to estimate the potential hazards from the formation of brominated products, acute toxicity of the samples were tested using photobacterium assay as well. As shown in Table 3, even in ultrapure water matrix, chlorination disinfection of BP-4 in the presence of bromide ions would lead to toxicity increase. The most significant toxicity increase was observed in swimming pool water matrix, which exhibited a 71% inhibition ratio after chlorination disinfection. Considering the significant toxicity elevation in swimming pool water matrix, a further experiment was performed. It can be seen from Table 3 that chlorination disinfection treatment on swimming pool water containing BP-4 enhanced inhibition ratio from 32% to 58%, while the inhibition ratio increased from 58% to 71% due to the formation of brominated products. It is reported that the toxicities of chlorinated organic compounds derived from chlorination process were higher than their parent compounds, and brominated disinfection byproducts usually exhibited more significant toxicity than their chlorinated analogs (Hu et al., 2002, 2003, 2006; Kosaka et al., 2010; Richardson et al., 2007). In our reaction system, the great increase of acute toxicity might also be contributed by the formation of chlorinated and brominated products. However, due to the lack of standard substances of those transformation products and the difficulty to isolate adequate individual product from the reaction mixture, it’s hard to identify the specific products with high toxicity in this study.

3. Conclusions

This study discussed the formation of brominated products in FAC-promoted chlorination disinfection process of BP-4 in the presence of bromide ions. Using HPLC-QTOF–MS and GC–MS, 12 brominated products were identified and possible formation pathways were proposed. Specifically, BP-4 would rapidly undergo halogenation to form mono-halogenated products, followed by subsequent halogenation, oxidation, and hydrolysis, to form di-halogenated products, ester products, and hydrolyzed products. Phenolic catechol intermediates could go ring contraction to form furan-like products. The pH conditions greatly influenced the transformation process in two ways, one was the species distribution of FAC, and the other was the reaction types such as desulfonation, secondary halogenations, and further oxidation. With higher doses of FAC, more percentages of BP-4 were degraded, and more products with small molecular weight formed (with FAC doses above 3-equiv to BP-4). Experiments simulating the environmental conditions and chlorination disinfection practices were conducted in pure water, wastewater and swimming pool water. As expected, the major products were found in these matrices after the chlorination treatment. The acute toxicity tests showed that the chlorination disinfection treatment of these samples, in the presence of BP-4 and bromide ions, would enhance the acute toxicity of water sample. The specific contributions of brominated products to the higher toxicities, as well as SAR studies, need further clarification.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jes.2014.03.001.
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