Oxidation of sulfonamide antibiotics by chlorine dioxide in water: Kinetics and reaction pathways

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HIGHLIGHTS

- Sulfonamides (SAs) were effectively oxidized by ClO₂ following second-order kinetics.
- The reactivity of SAs with ClO₂ showed a strong dependence on pH and temperature.
- Breakage of S–N and C–S bonds and hydroxylation of aniline group induced SAs removal.
- Antibacterial functional moieties of SAs were disrupted by ClO₂.
- Effective removal of SAs can be expected under practical water treatment conditions.

GRAPHICAL ABSTRACT

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ABSTRACT

Sulfonamides (SAs), commonly used as human and veterinary antibiotics, are of great concerns because of their frequent detections in aquatic environment. This study investigated the oxidation of six SAs (i.e., sulfamethoxazole (SMX), sulfamethizole, sulfamethazine, sulfadimethoxine, sulfamerazine, and sulfathiazole) by chlorine dioxide (ClO₂). The results indicate that the reactions followed the second-order kinetic model, with rate constants ranging from 3.85×10^3 to $2.59 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ at pH 7.0 and 20 °C. For each SA, the rate constant increased by 1.6–2.2 orders of magnitude as the solution pH increased from 4.0 to 9.5. The activation energies of the selected SAs ranged from 31.6 to 39.8 kJ mol^{−1}. In addition, SMX was selected as a model compound to explore the degradation pathways during ClO₂ oxidation. The reactivity of SMX toward ClO₂ was strongly related to the ionization equilibrium of the amido-nitrogen in SMX molecule. The cleavage of S–N and C–S bonds and the hydroxylation of aniline moiety in the SMX molecule constituted the major degradation pathways. ClO₂ oxidation was likely to decrease the antibacterial activity of SMX solution because of the destruction of *p*-aminobenzenesulfonamide moiety. The obtained rate constants could well predict the fate of SAs during ClO₂ oxidation in a surface water, where an effective removal of SAs by ClO₂ can be expected under practical water treatment conditions.

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1. Introduction

Antibiotics in the environment have attracted intensive concerns due to the possibility of inducing the proliferation of resistant bacterial strains. Moreover, antibiotics may also pose other

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risks to ecosystems, such as causing toxic effects on aquatic species and affecting plant growth [1]. As an important antibiotic class, sulfonamides (SAs) are extensively used in human and animal medical practices. Because of their stable chemical property and high environmental mobility [2,3], SAs have been frequently detected in a variety of aqueous media, such as effluents of wastewater treatment plants, surface water and even drinking water [4–6].

In previous studies, various chemical and photo-catalytic oxidation processes have been applied to oxidize SAs in water, such as free chlorine, ozone, ferrate (Fe(VI)) and TiO₂ photocatalytic treatments [7–12], and fast reactions were generally observed. However, SAs can only be partly removed in practical ozonation and free chlorine disinfection units [6,13], while ferrate and photocatalytic oxidations have not been practically applied in water treatment plants. Hence, further studies on SAs removal by other water oxidants/disinfectants are still necessary.

Chlorine dioxide (ClO₂), a commonly-applied water disinfectant, shows a higher disinfection efficiency, less pH dependence, and less formation of disinfection byproducts than free chlorine. Many studies have been conducted on the reactions between ClO₂ and micro-pollutants in water, such as methiocarb [14], phenylurea herbicides [15], β -lactams [16], fluoroquinolones [17] and tetracyclines [18]. With regard to SAs, an appreciable reactivity of ClO₂ with sulfamethoxazole (SMX) has been reported in water treatment [19]. However, the reaction kinetics and degradation pathways of other SAs during ClO₂ oxidation still remain unclear.

Hence, in this study, the reaction kinetics of six SAs (i.e., SMX, sulfamethizole (SML), sulfamethazine (SMN), sulfadimethoxine (SDM), sulfamerazine (SMR), and sulfathiazole (STZ)) with ClO₂ were individually determined at different pHs and temperatures. Thereafter, SMX was selected as a model compound to clarify the degradation pathways. The reaction kinetics of two substructural compounds of SMX, namely, 3-amino-5-methylisoxazole (AMI) and 4-aminophenyl methyl sulfone (APMS), with ClO₂ were determined and the oxidation byproducts of SMX were identified. Finally, the applicability of obtained rate constants to surface water was assessed.

2. Materials and methods

2.1. Chemicals

The chemical structures of SAs, AMI and APMS are shown in Fig. S1, and their corresponding standards were purchased from Sigma-Aldrich (St. Louis, USA) with purities of >98%. Methanol, acetonitrile and formic acid of high performance liquid chromatography grade were obtained from Fisher Scientific (Pittsburgh, USA). The stock solutions of SAs, AMI and APMS were prepared individually in methanol at a concentration of 100 mg L⁻¹. To identify the oxidation byproducts of SMX, a stock solution of about 1000 mg L⁻¹ was purposely prepared in water by adding HCl. ClO₂ stock solution (350 mg L⁻¹) was prepared according to our previous work [14] and stored in brown bottles at 4 °C. All other reagents used (e.g., buffers, reductant sulfite, carboxylic acids, sulfate, nitrate) were of at least analytical grade quality. High purity Milli-Q water (resistivity of >18 M Ω ·cm) was used to prepare the aqueous solutions.

2.2. Experimental procedures

The reaction kinetics of SAs, AMI and APMS with ClO₂ were individually examined with at least 10-fold excess of ClO₂ (5–12.5 μ M), where the ClO₂ concentration could be considered as constant over the reaction course and the pseudo-first-order rate

constant of a target compound could be determined experimentally. The effect of pH on SAs degradation was investigated in a pH range of 4.0–9.5 with 10 mM acetate (pH 4.0–5.0), phosphate (pH 6.0–8.0) and borate buffer (pH > 8.0). The effect of temperature was tested from 5 to 34 °C. The reaction was initiated by adding a desired amount of ClO₂ stock solution into 20 mL of a buffered solution containing a target compound (0.5 μ M) under magnetic stirring. Water samples (1 mL each) were withdrawn at pre-selected time intervals and the residual oxidant was quenched immediately with excess sodium thiosulfate.

To identify the oxidation byproducts of SMX reacting with ClO₂, the initial molar ratios ([ClO₂]₀/[SMX]₀) of 1:1 and 4:1 were used and the SMX solution was prepared with an initial concentration of 40 μ M (i.e., about 1000 mg L⁻¹) at pH 7.5. After reaction for 1 h, water samples were taken for byproduct identification.

Degradation experiments of all selected SAs by ClO₂ were also carried out in a filtered surface water collected from Jingmi Trench in Beijing. The main characteristics of the filtered surface water were as follows: pH 7.8, dissolved organic carbon 4.8 mg L⁻¹, UV₂₅₄ 0.031 cm⁻¹, and alkalinity 1.8 mM. The filtered water was buffered with 5 mM phosphate and then spiked with each selected SA individually. The prepared reaction solutions were subject to ClO₂ oxidation with an initial dosage of 1.0 mg L⁻¹, which is typically applied for water disinfection. All kinetic experiments were conducted in triplicate.

2.3. Analytical methods

ClO₂ concentration was measured with Hach method 10126 at 530 nm on a DR 5000 UV-Vis spectrophotometer (Hach, Loveland, USA). The concentrations of SAs, AMI and APMS were analyzed by an ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS, Agilent 6240, USA) equipped with an Agilent SB-C18 column (2.1 $\times$ 150 mm, 1.8 μ m). The mobile phases consisted of an aqueous solution of formic acid (0.2%, v/v) and acetonitrile with a total flow rate of 0.3 mL min⁻¹, whose gradient ratio varied from 65:35 to 80:20 depending on different target compounds. The MS parameters were set as follows: capillary 4000 V, nebulizer 35 psi, drying gas 10 L min⁻¹, gas temperature 350 °C, and fragmentor 90–115 V. The limits of quantification for SMX, SML, SDM, SMN, SMR and STZ were determined to be 0.8, 1.7, 1.1, 1.0, 1.1 and 0.5 μ g L⁻¹, respectively.

Oxidation byproducts of SMX were identified by an ultra-performance liquid chromatography/hybrid quadrupole time-of-flight mass spectrometry (UPLC-Q/ToF-MS, AcQuity UPLC/Xevo G2 Q-ToF, Waters, USA) with an Eclipse plus C-18 column (2.1 $\times$ 150 mm, 3.5 μ m). Mobile phases A and B were formic acid aqueous solution (0.2%, v/v) and acetonitrile, respectively. The gradient program with a total flow rate of 0.3 mL min⁻¹ was set as follows (t (min), A (%)): (0–4, 5), (4–10, 75), and (10–14, 5). The MS parameters were as follows: capillary 3000 V, source temperature 100 °C, desolvation temperature 250 °C, cone gas 50 L h⁻¹, desolvation gas 600 L h⁻¹, cone voltage 40 V, and collision energy 6 V. The MS spectra were acquired over an *m/z* range of 50–400. Carboxylic acids, sulfate and nitrate were analyzed with an ion chromatograph (IC, ICS-2000, Dionex, USA) equipped with an IonPac AS19 column (4 $\times$ 250 mm).

3. Results and discussion

3.1. Determination of reaction order

For the reaction of ClO₂ with an organic pollutant, first-order kinetics was generally observed with respect to each reactant [14,20]. Fig. 1a shows a logarithmic representation of the kinetic

Fig. 1. Determination of the reaction order for SAs degradation by ClO_2 : (a) plot of $\ln(C_0/C)$ vs. reaction time; and (b) plot of k_{obs} vs. $[\text{ClO}_2]_0$. The reaction kinetics of STZ with ClO_2 is individually shown in the insets. Experimental conditions: $[\text{SA}]_0 = 0.5 - \mu\text{M}$, $\text{pH} = 7.0$, $T = 20^\circ\text{C}$. Error bars denote the standard deviation of triplicate experiments.

data, which exhibit a good linearity ($R^2 > 0.97$) indicating the validity of the pseudo-first-order kinetic model. Fig. 1b shows that the measured pseudo-first-order reaction rate constant of each SA (k_{obs}) increased linearly ($R^2 > 0.94$) with increasing ClO_2 concentration, implying that the reactions were also of first-order with respect to ClO_2 . Thus, the overall reaction followed the second-order kinetic model as follows:

$$\frac{d[\text{SA}]}{dt} = -k''[\text{SA}][\text{ClO}_2]_0 \quad (1)$$

$$k'' = \frac{k_{\text{obs}}}{[\text{ClO}_2]_0} \quad (2)$$

The second-order reaction rate constants (k'') of SAs with ClO_2 ranged from 3.85×10^3 (SML) to $2.59 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ (STZ) at $\text{pH} 7.0$ and

20°C (Table 1), which are generally higher than those with free chlorine (10^2 – $10^3 \text{ M}^{-1} \text{ s}^{-1}$) but lower than those with ozone (10^5 – $10^6 \text{ M}^{-1} \text{ s}^{-1}$) under comparable conditions [7,21]. Therefore, ClO_2 has an appreciable reactivity toward SAs considering its relatively lower standard oxidation-reduction potential (vs. normal hydrogen electrode) at $\text{pH} 7.0$ (ClO_2 , 0.935 V; free chlorine, 1.27 V; ozone, 1.67 V) [22,23].

3.2. Effect of pH

Fig. 2 shows that the reaction rate constants of SAs with ClO_2 strongly depended on the pH. The k'' values increased by approximately 1.6–2.2 orders of magnitude with increasing pH from 4.0 to 9.5 at 20°C , whose large variation with pH could be attributed to the varying reactivity of different SA acid-base species toward ClO_2 . The speciation of an SA in aqueous solution is shown as follows:

The concentration of each SA can be expressed by Eq. (4):

$$[\text{SA}]_{\text{tot}} = \alpha_{\text{cat}}[\text{SA}]_{\text{tot}} + \alpha_{\text{neu}}[\text{SA}]_{\text{tot}} + \alpha_{\text{ani}}[\text{SA}]_{\text{tot}} \quad (4)$$

where $[\text{SA}]_{\text{tot}}$ represents the total concentration of an SA; α_{cat} , α_{neu} and α_{ani} are the molar fractions of the cationic (SAH_2^+), neutral (SAH) and anionic (SA^-) species, respectively.

As ClO_2 does not change its form within the tested pH range, the degradation rate of SA can be expressed as follows:

$$\begin{aligned} \frac{d[\text{SA}]_{\text{tot}}}{dt} &= -k''[\text{SA}]_{\text{tot}}[\text{ClO}_2]_0 \\ &= -(k_{\text{cat}}\alpha_{\text{cat}}[\text{SA}]_{\text{tot}} + k_{\text{neu}}\alpha_{\text{neu}}[\text{SA}]_{\text{tot}} + k_{\text{ani}}\alpha_{\text{ani}}[\text{SA}]_{\text{tot}})[\text{ClO}_2]_0 \end{aligned} \quad (5)$$

Thus, one has

$$k'' = k_{\text{cat}}\alpha_{\text{cat}} + k_{\text{neu}}\alpha_{\text{neu}} + k_{\text{ani}}\alpha_{\text{ani}} \quad (6)$$

where k_{cat} , k_{neu} and k_{ani} represent the specific second-order rate constants for the reactions of ClO_2 with SAH_2^+ , SAH and SA^- , respectively.

The k_{neu} and k_{ani} values were calculated by the least-square regression of kinetic data with Eq. (6) and are summarized in Table 1. k_{cat} is not shown due to the negligible reaction between SAH_2^+ and ClO_2 . Kinetic modelling indicates that the contribution of SAH to the overall k'' was insignificant, while SA^- was the most reactive ($k_{\text{ani}} = 3.78 \times 10^3$ – $6.99 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$) toward ClO_2 . Hence, an increase of pH led to a larger fraction of SA^- , thus facilitating the reaction of an SA with ClO_2 . Similar trends were also observed for fluoroquinolones [17] and tetracyclines [18], indicating that the deprotonation of these antibiotics as pH increases considerably favors their oxidation by ClO_2 .

Besides the acid-base equilibria in aqueous solution, different substituent rings attached to the characteristic sulfinol group ($-\text{S}(=\text{O})_2-\text{NH}-$) of SAs could also influence their reactivity toward

Table 1
Dissociation constants (pK_a) of SAs and specific second-order rate constants of different SA species reacting with ClO_2 .

Compound	$\text{pK}_{a,1}^a$	$\text{pK}_{a,2}^a$	$k_{\text{neu}} (\text{M}^{-1} \text{s}^{-1})$	$k_{\text{ani}} (\text{M}^{-1} \text{s}^{-1})$	$k'' (\text{M}^{-1} \text{s}^{-1}) (\text{pH} = 7.0)$
SMX	1.85	5.60	$0.48 (\pm 0.07) \times 10^2$	$6.47 (\pm 0.15) \times 10^3$	$6.13 (\pm 0.12) \times 10^3$
SML	1.86	5.29	$0.90 (\pm 0.02) \times 10^2$	$3.78 (\pm 0.14) \times 10^3$	$3.85 (\pm 0.07) \times 10^3$
SDM	2.13	6.08	$0.35 (\pm 0.14) \times 10^2$	$5.33 (\pm 0.14) \times 10^3$	$4.36 (\pm 0.10) \times 10^3$
SMN	2.07	7.49	$9.45 (\pm 1.95) \times 10^2$	$1.18 (\pm 0.02) \times 10^4$	$4.13 (\pm 0.19) \times 10^3$
SMR	2.06	6.90	$9.39 (\pm 2.17) \times 10^2$	$8.88 (\pm 0.21) \times 10^3$	$5.61 (\pm 0.22) \times 10^3$
STZ	2.01	7.11	$9.86 (\pm 1.07) \times 10^2$	$6.99 (\pm 0.12) \times 10^4$	$2.59 (\pm 0.06) \times 10^4$

^a From Ref. [30].

^b Standard deviation of triplicate experiments.

Fig. 2. Effect of pH on the experimental and model-predicted second-order rate constants of SAs reacting with ClO_2 . Experimental conditions: $[\text{SA}]_0 = 0.5 \mu\text{M}$, $[\text{ClO}_2]_0 = 5\text{--}12.5 \mu\text{M}$, $T = 20^\circ\text{C}$. Error bars denote the standard deviation of triplicate experiments.

ClO_2 . A more electron-withdrawing substituent ring tended to lower the $\text{pK}_{\text{a},2}$ of an SA (as is the case for SMX, SML and SDM, with a maximum $\text{pK}_{\text{a},2}$ of 6.08), and at the same time made its oxidation by ClO_2 more difficult (a lower k_{neu}) than for other SAs (i.e., SMN, SMR and STZ) (Table 1). The k_{ani} was much higher than the k_{neu} for all SAs and not strongly dependent on the substituent ring except for STZ, which had by far the highest k_{ani} . A possible explanation is that besides the sulfonyl amido-nitrogen, the electron-rich thiazole ring might also be attacked by ClO_2 . Except for STZ, the k'' values fell in a relatively narrow range, which can be explained by the fact that the negative effect of an electron-withdrawing substituent on k_{neu} was compensated by a higher fraction of SA^- at pH 7.0.

3.3. Effect of temperature

The effect of temperature on the reaction rate constants of SAs with ClO_2 was examined over the range of $5\text{--}34^\circ\text{C}$ at pH 7.0. The dependence of k'' on the reaction temperature can be expressed by the Arrhenius equation:

$$\ln(k'') = \ln(A) - E_a/RT \quad (7)$$

Fig. 3. Effect of temperature on the second-order rate constants of SAs reacting with ClO_2 . Experimental conditions: $[\text{SA}]_0 = 0.5 \mu\text{M}$, $[\text{ClO}_2]_0 = 5\text{--}12.5 \mu\text{M}$, pH = 7.0. Error bars denote the standard deviation of triplicate experiments.

Fig. 4. Degradation of APMS and AMI by ClO_2 as a function of time. Experimental conditions: $[\text{AMI}]_0 = [\text{APMS}]_0 = 0.5 \mu\text{M}$, $[\text{ClO}_2]_0 = 12.5 \mu\text{M}$, $\text{pH} = 7.0$, $T = 20^\circ\text{C}$.

where A = frequency factor, E_a = activation energy, R = universal gas constant ($8.315 \text{ J K}^{-1} \text{ mol}^{-1}$), and T = absolute temperature (K).

Plotting $\ln(k'')$ vs. $1/T$ yielded linear curves as shown in Fig. 3. The E_a values were calculated to be 33.0, 31.6, 34.4, 38.1, 37.5 and 39.8 kJ mol^{-1} for SMX, SML, SDM, SMN, SMR and STZ at $\text{pH} 7.0$, respectively. A 10°C temperature increase would result in an increase of k'' by a factor of approximately 1.56–1.75 for the studied SAs. It is noted that an increase in temperature usually lowers

the pK_a of an ionizable compound [24], which causes a higher fraction of anionic species at a certain pH and thus enhances the reactivity toward ClO_2 . Hence, the temperature-dependence of pK_a may also affect the E_a values of the studied SAs.

3.4. Reaction sites of SMX

The reaction kinetics of two substructural compounds (i.e., AMI and APMS) of SMX with ClO_2 was examined at $\text{pH} 7.0$ and 20°C under the pseudo-first-order conditions ($[\text{ClO}_2]_0/[\text{substrate}]_0 = 25:1$). As shown in Fig. 4, AMI was degraded slowly, implying that the 5-methylisoxazole moiety of SMX was not a principal reaction site toward ClO_2 . By contrast, APMS showed a notably higher degradation rate by ClO_2 . On the one hand, the aniline amino-nitrogen of APMS could be directly attacked by ClO_2 , similar to the attacks by other oxidants such as free chlorine [8], ferrate [11] and ozone [25]. On the other hand, carboxylic acids (e.g., formic and oxalic acids), sulfate and nitrate anions were detected after the reaction of APMS with ClO_2 for 1 h, suggesting that APMS was disrupted by ClO_2 and the sulfonyl group ($-\text{S}(=\text{O})_2-$) was also involved in the reactions. However, the lower reactivity of APMS toward ClO_2 than SMX suggests that the sulfonyl amido-nitrogen of SMX could be a principal reaction site toward ClO_2 . Moreover, the pH dependence of the reaction rate constants of SAs with ClO_2 was directly linked to the deprotonation of sulfonyl amido-nitrogen, which also emphasizes the critical role of this moiety in ClO_2 oxidation. This reaction mechanism is similar to that of SMX with free chlorine [8].

Fig. 5. Proposed degradation pathways of SMX during ClO_2 oxidation.

3.5. Identification of degradation byproducts and reaction pathways of SMX

UPLC-Q/ToF-MS was applied to identify the degradation byproducts of SMX by ClO_2 at pH 7.5. The chromatograms and mass spectra of SMX and its degradation byproducts are shown in Figs. S2 and S3. The elemental composition of ion fragments was analyzed by a ToF analyzer with a high accuracy (<8 ppm error). The proposed structures of degradation byproducts based on the accurate mass measurements are detailed in Table S1.

Four degradation byproducts were identified and denoted as C1, C2, C3 and C4, according to the eluted sequence in the chromatograms. C1, with a molecular ion of m/z 179.0128, could arise

from the cleavage of the C–S bond in SMX. C2, with a molecular ion of m/z 99.0563, was identified to be AML, originating from the cleavage of the S–N bond in *p*-aminobenzenesulfonamide moiety. The molecular ion of C2 was also observed in the fragmentation patterns of C3, C4 and SMX, indicating that C3 and C4 had the same 5-methylisoxazole moiety as SMX. No alteration of the double bond equivalents (DBE) of C4 as compared to SMX implied that C4 largely kept the original molecular structure of SMX. The molecular ion of C4 was m/z 270.0566, showing a mass gain (+16) of this byproduct in comparison to SMX. Moreover, compared to the fragment ions of SMX, a mass gain of 16 commonly appeared in the C4 fragmentation ions (i.e., m/z values of 124.0402, 172.0074, 204.0782 and 270.0556). Hence, C4 could be

Fig. 6. Degradation kinetics of SAs by ClO_2 in a surface water at different pHs. Experimental conditions: $[\text{SA}]_0 = 0.1 \mu\text{M}$, $[\text{ClO}_2]_0 = 14.8 \mu\text{M}$ (equaling 1.0 mg L^{-1}), $T = 20^\circ\text{C}$. Symbols and lines represent measured data and model calculations, respectively. Error bars denote the standard deviation of triplicate experiments.

a hydroxylated (–OH) derivative of the aniline moiety of SMX. This byproduct was also identified from the SMX degradation by ozonation [25] and photo-Fenton oxidation [26].

The appearance of the fragment ion of m/z 99.0562, absence of fragment ions of m/z values of 108.0452 and 156.0120 (characteristic of the *p*-sulfoaniline ring), net mass gain of the molecular ion (+30) and DBE increase (+1) of C3 compared to SMX suggested that C3 contained the 5-mehtylisoxazole moiety and oxygenation forms of the aniline group of SMX referring to the addition of –OH and the formation of nitroso group (–N=O). It was also reported that the amino group could be transformed to the nitroso group when SMX was oxidized by ozone [25] and ferrate [16].

When the initial molar ratio of $[\text{ClO}_2]_0/[\text{SMX}]_0$ increased from 1:1 to 4:1, the signal of C4 disappeared while the abundance of C3 notably enhanced in the chromatogram (Fig. S2b). In addition, according to the evolution of degradation byproducts as a function of time (Fig. S4), the decay of the C4 signal was accompanied by the increase of the C3 signal during the reaction course. These results indicate that C4 could be further oxidized to C3 by excessive ClO_2 . The initial attack on the amino group of SMX probably occurred by single electron-transfer from the amino group to ClO_2 [16,27]. Then, the formed aminyl radical cation evolved into a radical by N–H deprotonation, which could couple with ClO_2 , oxygen or other reactive oxygen species to form hydroxylamine and hydroxylimine [16]. The hydroxylamine and hydroxylimine could be further oxidized to form the nitroso group.

Three carboxylic acids (i.e., formic, acetic and oxalic acids), and sulfate and nitrate anions were identified by IC, manifesting that the intermediates could be further oxidized. The similar observation in APMS degradation suggests that these degradation byproducts could arise from the disruption of the *p*-aminobenzenesulfonamide moiety.

Overall, the degradation pathways of SMX during ClO_2 oxidation were proposed based on the degradation byproducts identified above (Fig. 5), which included: (i) S–N bond cleavage to form C2 and sulfanilic acid; (ii) C–S bond cleavage to form C1 and aniline; and (iii) hydroxylation of the aniline moiety to form C4 and further oxidation of the amino group attached to benzene ring to form C3. According to the evolution of degradation byproducts as a function of time, under the initial molar ratio of $[\text{ClO}_2]_0/[\text{SMX}]_0$ of 4:1, C1 and C2 showed a rapid increase within the first 20 s and a continuous decrease thereafter, while C3 always showed a continuous increase (Fig. S4a). When the initial molar ratio of $[\text{ClO}_2]_0/[\text{SMX}]_0$ was increased to 10:1, C3 started to decrease after a reaction time of 10 min (Fig. S4b). Therefore, further disruption of C1, C2 and C3 could be expected by the oxidation of excessive ClO_2 , which led to the formation of carboxylic acids, and sulfate and nitrate anions. The proposed sulfanilic acid, aniline and hydroxyl-substituted C4 intermediates were not observed in the chromatograms, probably because these intermediates could be rapidly oxidized by ClO_2 once formed. Chlorine substitution, an important reaction mechanism of antibiotics with free chlorine [8,17,18], was not observed in any of the byproducts during the reaction of SMX with ClO_2 .

The antibacterial activity of SAs is derived from its antagonistic competition with *p*-aminobenzoic acid for the dihydropteroate synthase enzyme, which is necessary for bacterial folic acid synthesis [8,11]. Therefore, it is expected that the oxidation of the amino group, cleavage of the S–N bond, and disruption of the *p*-aminobenzenesulfonamide moiety will render SMX less of a mimic for the *p*-aminobenzoic acid, thus reducing its antibacterial activity. Based on the structural similarities of SAs, the antibacterial activities of other studied SAs are also expected to be reduced after reaction with ClO_2 . However, because of the different heterocyclic types, the degradation pathways of other studied SAs during ClO_2

oxidation are likely to be different from that of SMX, which requires further studies.

3.6. Degradation of SAs by ClO_2 in a surface water

The effect of water matrix on the reaction kinetics of the studied SAs toward ClO_2 was investigated. The SA concentrations could reach as high as $\mu\text{g L}^{-1}$ levels in surface water. For example, SDM, SMN and sulfapyridine were detected at concentrations of 15, 6.2 and $12 \mu\text{g L}^{-1}$, respectively, in surface water samples in U. S. and Spain [28,29]. Accordingly, surface water samples were spiked with $0.1 \mu\text{M}$ of SA and exposed to 1.0 mg L^{-1} of ClO_2 ($14.8 \mu\text{M}$, a typical dosage in water treatment) in this study. Oxidative degradation of SAs can be predicted using Eq. (8) along with the kinetic parameters for each target SA:

$$[\text{SA}] = [\text{SA}]_0 e^{-(k_{\text{cat}}\alpha_{\text{cat}} + k_{\text{neu}}\alpha_{\text{neu}} + k_{\text{ani}}\alpha_{\text{ani}}) \times CT} \quad (8)$$

where C is the ClO_2 concentration at time t , and T is the reaction time; so their product, CT , represents the integrated ClO_2 exposure during water treatment. The surface water samples exhibited a noticeable consumption of ClO_2 , with a 13.4% decrease of ClO_2 concentration after 1 min under the adopted experimental conditions (Fig. S5).

As shown in Fig. 6, the model predicted degradation curves of the studied SAs agreed quite well with the experimentally measured data in a surface water. The removal efficiencies of SAs reached 96–100% after a contact time of 1 min with 1.0 mg L^{-1} ClO_2 at pHs 7.5 and 9.0; while a decrease of pH to 6.1 retarded the removal of SAs to different degrees. Overall, a high removal of the studied SAs could be expected under typical water treatment conditions for ClO_2 oxidation.

4. Conclusions

The reactions between six studied SAs and ClO_2 in water followed the second-order kinetic model. The reaction rate constants ranged from 3.85×10^3 to $2.59 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ (at pH 7.0 and 20°C) and showed a strong pH dependence. The cleavage of S–N and C–S bonds and the hydroxylation of aniline moiety in the SMX molecule were the major degradation pathways. The degradation of SAs in a surface water could be well predicted by the kinetic parameters obtained in Milli-Q water. A high removal of SAs could be expected under typical water treatment conditions for ClO_2 oxidation.

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Appendix A. Supplementary material

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