Stable chlorine isotope analysis of triclosan using GC-qMS: Method development and applications

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ARTICLE INFO

ABSTRACT

Occurrence of triclosan (TCS) in water environment caused a serious concern due to TCS toxic properties as well as yield of toxic byproducts during natural attenuation. Here we developed an online approach for chlorine compound specific isotope analysis (CSIA) of TCS based on gas chromatography quadrupole mass spectrometry (GC-qMS). Specifically, the instrumental parameters including dwell time, ionization energy and split ratio values were tested and optimized. Moreover, the calculation scheme considering all the TCS molecular ions presented better precision compared with the method using the most abundant neighboring ion pairs. The optimized method was validated by applying it to differentiate various TCS manufacturers, and was used to resolve chlorine isotope fractionation occurring during TCS photodegradation induced by simulated solar radiation. Chlorine isotopic enrichment factor (ε_{Cl}) of -2.61 ± 0.37‰ and -0.72 ± 1.95‰ were obtained at pH values of 8.3 and 4.5, respectively. This indicates that preferential cleavage of C-Cl bonds occurred at a higher pH value. Thus, this study provides a robust and sensitive approach for chlorine CSIA of TCS, and could be readily applied to monitor chlorine isotope effects during TCS environmental transformations.

1. Introduction

Triclosan (TCS) is an antimicrobial agent often used in various personal care products, such as soap, toothpaste, cosmetics, and other household products (Lam et al., 2019). Due to the extensive consumption of TCS, it becomes frequently detected in surface water, wastewater effluents and sediment (Anger et al., 2013; Fernandes et al., 2011; Singer et al., 2003). In recent years, TCS in water has attracted dramatic attention due to its adverse effects on aquatic organisms and human health (Dann and Hontela, 2011; Dhillon et al., 2015). Understanding fate and transport of TCS in aquatic environment is crucial for environmental risk assessment of TCS.

Biotic and abiotic transformation of TCS often involve a complex reaction pathway, and forming a wide spectrum of reaction products. Yield of persistent and toxic substances have been noticed in several previous studies (Liu et al., 2020; Wang et al., 2018). However, identification of reaction byproducts often requires multiple mass spectrometric instrumentations, such as gas chromatography coupled with mass spectrometry (GC–MS), high resolution gas chromatography high

resolution mass spectrometry (HRGC-HRMS) and high-resolution accurate mass Q-Exactive Orbitrap mass spectrometry (HRAM-LC/MS) (Lam et al., 2019; Sanchez-Prado et al., 2006; Wu et al., 2019). Alternatively, compound-specific isotope analysis (CSIA) could determine isotopic compositions of a certain compound and might serve as a valuable tool for source identification of different chlorinated organic pollutants (Chen et al., 2017; Li et al., 2020; Zhou et al., 2020), as well as for characterization of their environmental transformation pathways (Knossow et al., 2020; Steinmetz et al., 2019; Wang et al., 2020). So far, carbon CSIA has been mostly applied in previous studies. Recently, an increasing number of studies have developed and applied chlorine CSIA as an emerging CSIA tool to investigate fate behavior of different chlorinated organic pollutants (Jendrzejewski et al., 2001; Ojeda et al., 2020; van Warmerdam et al., 1995; Zimmermann et al., 2019). Application of chlorine CSIA was promoted by development of the online chlorine CSIA approaches by using continuous flow isotope ratio mass spectrometry (CF-IRMS) (Shouakar-Stash et al., 2006). Sakaguchi-- Soeder et al. (2007) developed a simple and sensitive online approach for chlorine CSIA by using a widely available gas chromatography (GC)
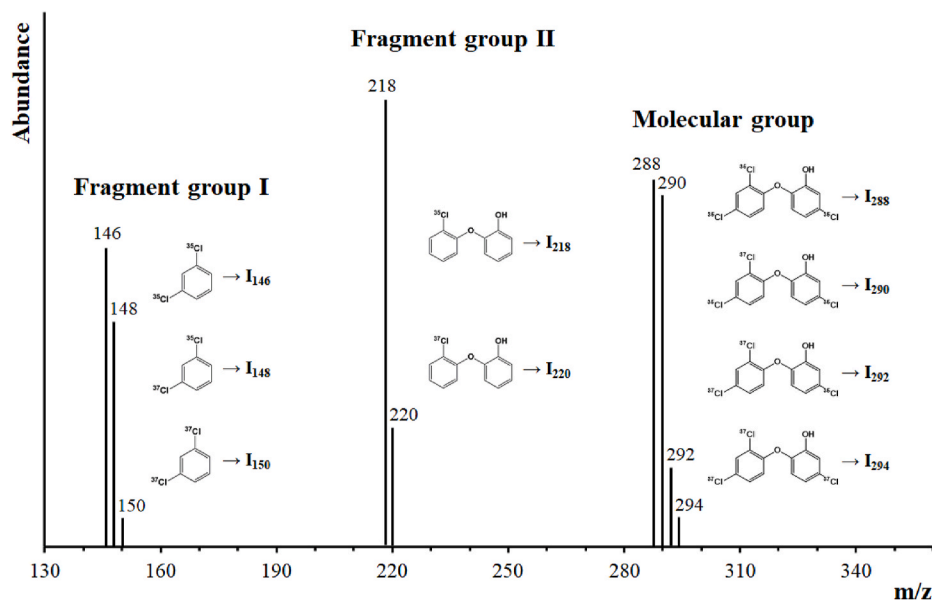

Fig. 1. Mass spectra and chlorine isotopologues of TCS obtained by GC-qMS.

coupled to a quadrupole mass spectrometry (qMS) (Sakaguchi-Söder et al., 2007). This method extracts the ion intensities of the selected molecular or fragment ions of target chlorinated compounds, and further derives chlorine isotope ratios based on different evaluation schemes (Jin et al., 2011). Recent studies have extended this method to determine chlorine isotope ratios of different chlorinated contaminants, including chlorinated methanes (Heckel et al., 2017), chlorinated benzenes (Aeppli et al., 2010), different chlorinated pesticides (Ponsin et al., 2019). Very recent studies even extended this approach to determine stable bromine isotopic ratios of brominated organic compounds (Jin et al., 2021; Zakon et al., 2016).

Environmental transformations of TCS such as direct photo-degradation and microbial reductive dechlorination, likely result in cleavage of carbon-chlorine bonds (Liu et al., 2020; Zhao et al., 2020). Cleavage of C-Cl bonds might also yield specific reaction products, among which some might be persistent and toxic (Liu et al., 2020). Thus, careful characterization of reaction mechanisms of TCS - is an essential task for understanding fate behavior of TCS. Chlorine CSIA has a great potential to provide a unique angle to elucidate chlorine-isotope sensitive steps during TCS transformation processes. However, to the best of our knowledge, chlorine CSIA approach focusing on TCS still remains unavailable.

The main goal of our study is to develop an online method for chlorine CSIA of TCS. To this end, we aim to i) develop a chlorine CSIA approach based on a GC-qMS; ii) to optimize evaluation schemes and instrumental parameters which might affect the precision and repro-ducibility of the method; iii) to evaluate the approach through different applications, including characterization of TCS from different manu-facturers using chlorine CSIA, and quantify chlorine isotope fraction-ation of TCS during direct photo transformation processes.

2. Experimental section

2.1. Chemicals

Neat TCS were purchased from Sigma-Aldrich (USA), Ryon (China) and Dr. Ehrenstorfer (Germany). Details about suppliers and purity are summarized in Table S1 (Supplementary Material). Hexamethylbenzene (HMB, purity > 99.8%) was obtained from Sigma-Aldrich (USA). Ethyl acetate (purity > 99.8%) and isooctane (purity > 99.8%) were provided by Macklin (China) and Aladdin (China), respectively. NaHCO$_3$ (purity

> 99.0%) and Na$_2$CO$_3$ (purity > 99.5%) were used to prepare pH buffer solutions, both supplied by CNW (China). Ultrapure water (18.2 MΩ cm^{-1}, Sartorius, Germany) was used for preparing all aqueous solutions. Standard stock solution of TCS was prepared in isooctane at 10 g/L and stored at 4 °C.

2.2. Chlorine isotope analysis using GC-qMS

The chlorine isotope ratios of TCS was measured using an Agilent (8890) gas chromatography coupled to an Agilent (5977B) quadrupole mass spectrometer (Agilent, Santa Clara, USA), equipped with electron ionization (EI) source. The compounds were separated using a DB-5ms capillary column (30 m × 0.25 mm × 0.25 μm; Agilent J&W, USA). One microliter of the sample was injected. Helium was used as carrier gas, at a flow rate of 1.2 ml min^{-1}. The inlet temperature was 280 °C and the ion source was at 230 °C. The oven temperature was programmed as follows: 80 °C (holding for 2 min) to 300 °C at a rate of 15 °C min^{-1}, holding for 5 min. The mass spectrometer (MS) was performed in the selected ion mode (SIM), targeting on the ions at m/z of 218, 220, 288, 290, 292 and 294, respectively. During the method optimization, important instrumental settings were tested.

2.3. Mathematical schemes for stable chlorine isotope ratio determination

Two calculation methods were applied and compared in order to derive chlorine isotope ratio of TCS based on mass spectral data (see Fig. 1). Specifically, chlorine isotope ratios are derived using the frag-ment ion intensities or the molecular ion intensities of TCS, respectively. Thus, the calculation schemes using the two different methods involve different ion groups, and the two methods are based on the abundance of the ions containing different number of chlorine atoms. Concerning the fragment ion method, chlorine isotope ratios are calculated using the most abundant adjacent fragment ion pairs containing single chlorine isotope (i.e. ions at 218 and 220 m/z, see Fig. 1). The chlorine isotope ratio of TCS is given as:

$$R_{TCS} = \frac{I_{220}}{I_{218}} \tag{1}$$

where I indicate the target ion intensities at different mass over charge ratios, and R is the chlorine isotope ratio of TCS.

The second approach considers all the molecular ions of TCS. The

chlorine isotope ratios are determined by counting total ^{37}Cl and ^{35}Cl isotopes in the TCS molecules (Jin et al., 2011):

$$R = \frac{Tot(^{37}Cl)}{Tot(^{35}Cl)} = \frac{\sum_{j=1}^{i} m_j \cdot I_j}{\sum_{j=1}^{i}(n - m_j) \cdot I_j} \quad (2)$$

where *Tot (^{37}Cl)* and *Tot (^{35}Cl)* are the total amount of ^{37}Cl and ^{35}Cl isotopes, i is the isotopologues of molecular or fragment ions; n is the total number of chlorine atoms in one chlorinated compound; m is the number of ^{37}Cl isotopes in a specific isotopologue j; I is the ion intensity of a certain isotopologue j. By substituting the corresponding TCS ions into eq (2), the equation could be expressed as:

$$R_{TCS} = \frac{I_{290} + 2 \cdot I_{292} + 3 \cdot I_{294}}{3 \cdot I_{288} + 2 \cdot I_{290} + I_{292}} \quad (3)$$

where I is the ion intensities of TCS isotopologues at different mass over charge ratios (m/z).

2.4. Correction for presence of dual ^{13}C isotopes

Due to the fact that presence of two ^{13}C isotopes might also generate two unit mass difference as the occurrence of one ^{37}Cl in TCS isotopologues. The ^{13}C-induced error might become significant with increasing number of carbon atom present in a certain molecule. For instance, the previous study pointed out that this error is neglectable for chlorinated ethylenes, but needs to be corrected for chlorinated benzenes which contain six carbon atoms (Jin et al., 2011). Given that TCS molecules contain twelve carbon atoms, a correction based on carbon isotopic compositions of the compound has to be adopted (Aeppli et al., 2010):

$$R_{Cl}^{corr} = R_{Cl} - \frac{1}{n_{Cl}} \cdot \frac{n_C(n_C - 1)}{2} R_C^2 \quad (4)$$

where n_C and n_{Cl} are the number of carbon atoms and chlorine atoms in TCS molecule, R_C and R_{Cl} are the carbon isotope ratio and the uncorrected chlorine isotope ratios of TCS, respectively. The detailed calculation procedures are available in the supplementary material (see Table S2).

2.5. TCS photodegradation experiment

TCS aqueous solution at 10 mg L^{-1} was filled into a double-wall glass reactor. During the experiment, a constant temperature (25 °C) was maintained by circulating water in the outer chamber of the reactor. A magnetic stirrer was placed to keep the solution well mixed. A high-voltage xenon lamp (500W, Precise Technology, China) was used as the light source, which is equipped with a filter to obtain environmentally relevant ultraviolet–visible (UV) radiation in the actinic wavelength region (300 nm < λ < 700 nm). The experiments were carried out for 8 hours, and every hour aliquots of 10 ml were sampled. Subsequently, samples were extracted using ethyl acetate and dissolved in isooctane for analysis. Detailed sample extraction procedures has been described in our previous study (Liu et al., 2020). The pH and chlorine isotope ratios of the samples were measured right after each experiment. The stable chlorine isotope fractionation of TCS photodegradation was evaluated using the isotope enrichment factor (ε_{Cl}) according to the Rayleigh equation:

$$\ln\left(\frac{R}{R_0}\right) = \varepsilon \ln\left(\frac{C}{C_0}\right) \quad (5)$$

where R and R_0 are the chlorine isotopic compositions ($^{37}Cl/^{35}Cl$ ratio) of TCS at a specific time and initial time, respectively. C and C_0 represent the concentration of TCS at a specific time and in start.
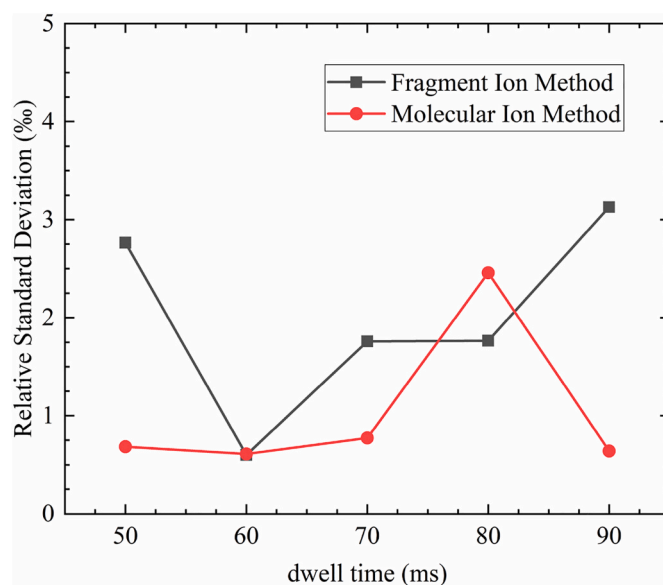

Fig. 2. Effects of the qMS instrument parameters, dwell time, on the precision of different evaluation schemes for determination of chlorine isotope ratios. The samples were prepared at 5 mg/L (i.e. 5 ng TCS on column), and were injected five times (i.e. n = 5) to obtain relative standard deviation. The MS was operated at a fixed EI energy (70 eV) and split ratios (1:1).
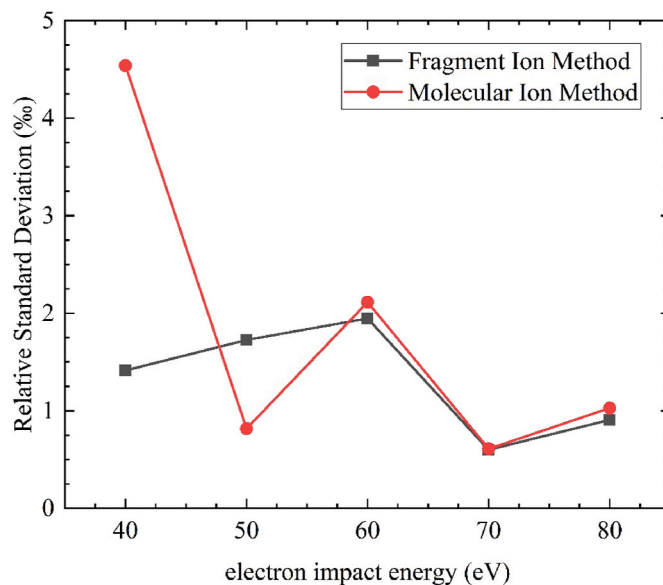

Fig. 3. Influence of electron impact energy strength on the precision of different evaluation schemes for determination of TCS chlorine isotope ratios. The samples were prepared at 5 mg/L (i.e. 5 ng TCS on column), and were injected five times to obtain relative standard deviation. The MS was operated at fixed dwell time (60 msecd) and split ratios (1:1).

3. Results and discussion

3.1. Optimization of instrumental parameters

Dwell time. Dwell time is an important parameter in mass spectrometry, since this parameter controls the frequency of mass spectral data acquisition, and thus influencing the precision and accuracy of the proposed method. In order to optimize this parameter, the parameter, dwell time, was set in five different levels, ranging from 50 ms to 90 ms. The precision of the method was tested at the different dwell time levels

Table 1
^{37}Cl/^{35}Cl ratios of TCS determined at different split ratios.

| spilt ratio	n	fragment ion method				molecular ion method		
		^{37}Cl/^{35}Cl ratio	STDEV (1σ)	RSD (‰)		^{37}Cl/^{35}Cl ratio	STDEV (1σ)	RSD (‰)
1:1	5	0.32414	0.00124	3.82067		0.32220	0.00023	0.71356
10:1	5	0.32373	0.00077	2.37708		0.32202	0.00015	0.45357
100:1	5	0.32361	0.00033	1.02104		0.32273	0.00020	0.61973
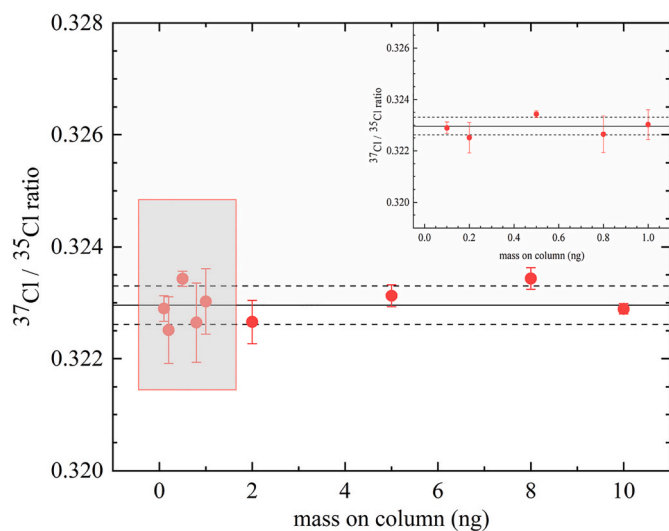
Fig. 4. The determined chlorine isotope ratios of TCS at different on-column mass (0.1 ng–10 ng). The solid and dashed lines represent the mean values and the standard deviation of the chlorine isotope ratios at different TCS concentrations, respectively (1σ, n = 5).

as shown in Fig. 2. The results indicate that the optimum precision was obtained at 60 ms, which corresponds to the lowest relative standard deviation at 0.6‰. In addition, the two calculation methods were also evaluated and compared. In general, the molecular ion method presents higher precision compared with the fragment ion method. The precision of the two methods might differ by 2.5‰ at most. The fragment ion method was more influenced by the dwell time values.

Electron impact energy. Intensity of electron impact (EI) energy of mass spectrometry controls ionization processes of analytes, and therefore influencing ion abundance of both fragment and molecular ions. Indeed, the two calculation schemes are based on ion intensities of the molecular ions or the fragment ions, respectively. In order to investigate impact of EI energy on precision of TCS chlorine isotope analysis, chlorine isotope ratios were determined at different EI energy levels (i.e. 40 eV–80 eV). As shown in Fig. 3, the highest precision was obtained at 70 eV for the both methods. Specifically, the fragment ion approach resulted in lower precision at lower EI levels, which corresponds to the maximum RSD value of 1.9‰. This might be due to the reduction of fragment ions intensities at the lower EI level. However, at a higher EI energy lowered the precision of the fragment ion approach, due to the excessive EI energy further decompose the target fragment ions. Concerning the molecular ion method, the RSD values varied from 0.6‰ to 4.5‰. The molecular ion method is more sensitive to the lower EI energy levels, where the RSD values even went up to 4.5‰ at 40 eV. This indicates lower EI energy might significantly reduce the molecular ions intensities, and thus lowers the precision of chlorine isotope measurements by using the molecular ion approach.

Split ratio. In order to investigate the potential effects of spilt ratio values on the chlorine isotope, five replicates of the standard TCS solutions at 0.1 mg/L, 1 mg/L, and 10 mg/L were prepared and analyzed at spilt ratios of 1, 10 and 100, respectively. The amount of TCS delivered to the GC column was kept the same for different injection conditions.
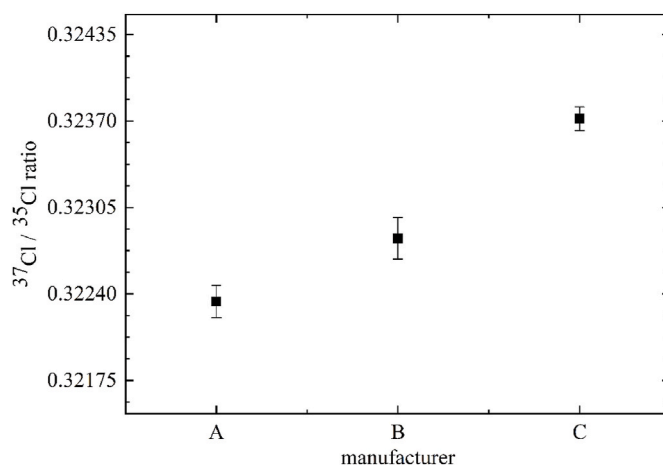
Fig. 5. Chlorine isotope ratios of neat TCS from three different manufacturers. Error bars represent the standard deviation values for the chlorine isotopic measurements for TCS. A, B and C represent different manufacturers (the detailed information is provided in Table S2).

The results were summarized in Table 1. In general, the molecular ion method showed much higher precision comparing with the results using the fragment ion method, where the RSD values varied from 0.45‰ to 0.71‰. Also, less deviation of the chlorine isotopic ratios were observed by using the molecular ion method. This indicates the standard ionization in qMS produces higher-quality mass spectral data for the molecular ions, rather than the fragment ions which undergo more complex fragmentation processes.

3.2. Evaluation of the method

Concentration effects. In order to evaluate the approach at different TCS concentrations, five replicate samples at each concentration were prepared, and the chlorine isotope ratios of TCS were determined by using the above mentioned optimal method (i.e. molecular ion method). On column mass of TCS, ranging between 0.1 ng and 10 ng, were delivered into the column. As shown in Fig. 4, more injected TCS mass resulted in higher precision, where the RSD values varied from 0.6‰ to 1.9‰ (see Fig. S1). Also, the chlorine isotope ratios of TCS deviated from 0.3218 ($\pm 6 \times 10^{-4}$) to 0.3227 ($\pm 2 \times 10^{-4}$). Thus, minimal sufficient mass of TCS (i.e. 1 ng) need to be delivered into the GC column, since injected amount could influence both precision and reproducibility of the approach.

Source identification. In order to validate our approach, 5 mg L^{-1} TCS standard solutions were prepared by using neat TCS purchased from three different manufacturers (The supplier and purity of TCS are provided in Table S1). The three TCS manufacturers were differentiated by their chlorine isotope ratios (see Fig. 5). Specifically, the TCS from different manufacturers were carrying distinct chlorine isotopic compositions. This might result from different synthetic protocols and/or raw materials (Deconinck et al., 2008). Our approach was applied to determine the chlorine isotopic signatures of the three TCS sources, and successfully identified the three TCS manufacturers based on their chlorine isotopic signatures.
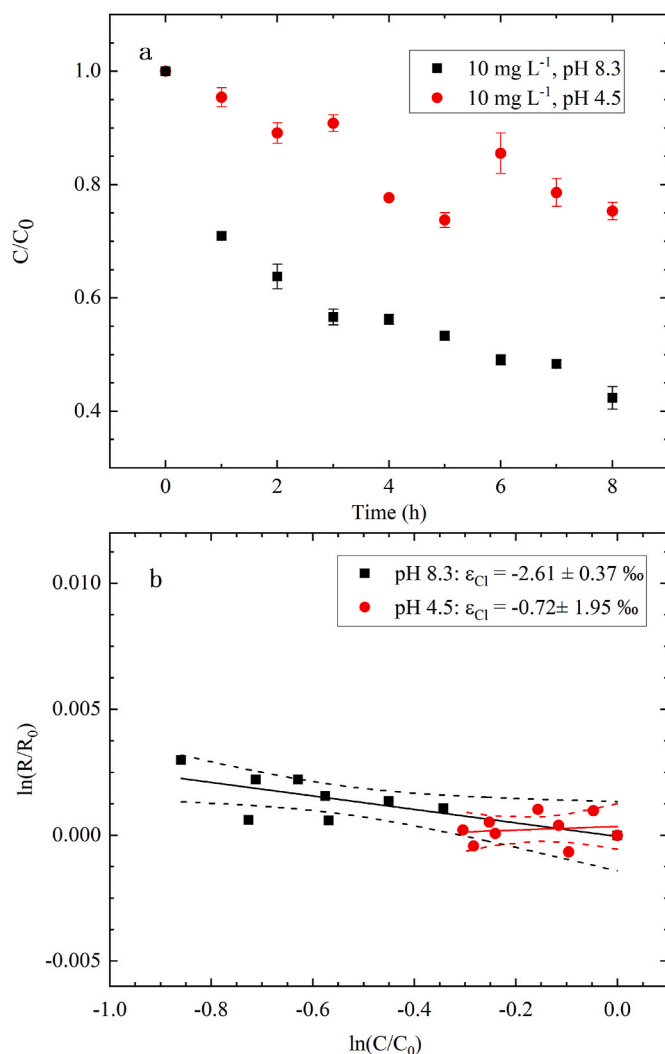
Fig. 6. Concentration profile (panel a) and Rayleigh plots (panel b) for chlorine isotope fractionation observed during TCS photodegradation. The solid and dashed lines represent the linear fitting curve and the associated 95% confidence bands, respectively (n = 5).

TCS Photodegradation. Direct photodegradation is an important process to eliminate TCS in water environment, and pH value was found crucial for reaction kinetics as well as for formation of certain reaction intermediates (Kliegman et al., 2013; Liu et al., 2020; Sanchez-Prado et al., 2006). In order to further explore the applicability of our method, the chlorine isotope ratios of TCS were resolved during TCS photodegradation under a simulated sunlight condition. The experiment was conducted at pH 8.3 and pH 4.5 in order to investigate chlorine isotopic effects of TCS at phenolic and neutral form, respectively. After 8 hours of irradiation, the results showed that at pH 8.3 about 60% of TCS were degraded, but much less TCS (20%) were degraded at pH 4.5, which corresponds to a ε_{Cl} value of $-2.61‰$ (apparent kinetic isotope effect, AKIE = 1.0079, details for the calculation are available in supplementary material) and $-0.72‰$ (AKIE = 1.0022), respectively (see Fig. 6). We speculate that higher chlorine isotope enrichment factor of TCS is due to the fact that a higher pH might favor C-Cl bond cleavage, and similar findings were reported in the previous study, where the observed carbon isotope effects at a higher pH value were closer to the theoretical values of $AKIE_{carbon}$ for C-Cl bond cleavage (Liu et al., 2020). Our results indicated that chlorine CSIA of TCS might serve as an emerging tool to characterize bond-cleavage reaction pathways of TCS, in particular, in the cases involving C-Cl bond cleavage.

4. Conclusion

Recently, there is an increasing number of chlorine CSIA applications on different chlorinated organic contaminants (Heckel et al., 2019; Lihl et al., 2019, 2020; Rosell et al., 2019), providing a unique angle to elucidate the compounds underlying transformation processes. Our study developed an online chlorine CSIA method for TCS based on a common GC-qMS. The study indicated that instrumental parameters, including dwell time, ionization energy and split ratio values, are influential for performance of the proposed approach. Also, calculation schemes considering all the molecular ions of TCS presented a higher precision for determination of the chlorine isotope ratios.

Increasingly more studies have been focusing on characterization of environmental transformation pathways of TCS, since more persistent and toxic reaction products might yield and enter water environment. Degradation of TCS often involves cleavage of C-Cl bonds, resulting in less chlorinated reaction products. For instance, our study demonstrated that pH values could influence extent of TCS chlorine isotope fractionation, indicating variation of TCS photodegradation mechanisms. Chlorine CSIA of TCS might offer a unique tool to elucidate and even to quantify different dechlorination transformation processes, based on observed stable chlorine isotope effects. Concerning further development of the current approach, compound-specific TCS chlorine isotopic standards with known $\delta^{37}Cl$ signatures would be beneficial to test the calibrated accuracy of the developed GC-qMS method. Moreover, a combined carbon-chlorine dual isotope approach could be further developed, and therefore providing even a more powerful tool for identification and quantification of (bio)geochemical processes during TCS natural attenuation. To end, the validated chlorine CSIA approach developed in this study is simple and robust, and thus provides a valuable tool to track fate and transport of TCS in water environments.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apgeochem.2021.104961.

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