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Compound-Specific Chlorine Isotope Analysis of Tetrachloromethane and Trichloromethane by Gas Chromatography-Isotope Ratio Mass Spectrometry vs Gas Chromatography-Quadrupole Mass Spectrometry: Method Development and Evaluation of Precision and Trueness

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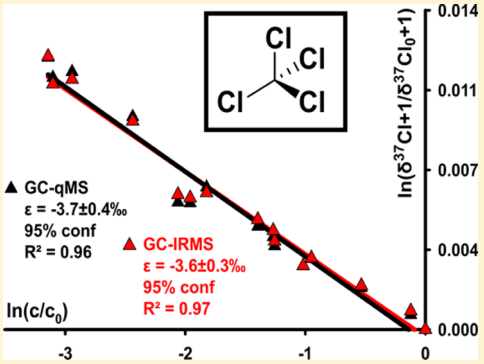
Supporting Information

ABSTRACT: Compound-specific chlorine isotope analysis of tetrachloromethane (CCl_4) and trichloromethane ($CHCl_3$) was explored by both, gas chromatography-isotope ratio mass spectrometry (GC-IRMS) and GC-quadrupole MS (GC-qMS), where GC-qMS was validated in an interlaboratory comparison between Munich and Neuchâtel with the same type of commercial GC-qMS instrument. GC-IRMS measurements analyzed CCl isotopologue ions, whereas GC-qMS analyzed the isotopologue ions CCl_3, CCl_2, CCl (of CCl_4) and $CHCl_3$, $CHCl_2$, CHCl (of $CHCl_3$), respectively. Lowest amount dependence (good linearity) was obtained (i) in H-containing fragment ions where interference of ^{35}Cl- to ^{37}Cl-containing ions was avoided; (ii) with tuning parameters favoring one predominant rather than multiple fragment ions in the mass spectra. Optimized GC-qMS parameters (dwell time 70 ms, 2 most abundant ions) resulted in standard deviations of 0.2‰ ($CHCl_3$) and 0.4‰ (CCl_4), which are only about twice as large as 0.1‰ and 0.2‰ for GC-IRMS. To compare also the trueness of both methods and laboratories, samples from CCl_4 and $CHCl_3$ degradation experiments were analyzed and calibrated against isotopically different reference standards for both CCl_4 and $CHCl_3$ (two of each). Excellent agreement confirms that true results can be obtained by both methods provided that a consistent set of isotopically characterized reference materials is used.



Chlorinated methanes such as trichloromethane ($CHCl_3$) and tetrachloromethane (CCl_4) have been used as dry cleaning agents, solvents and for the production of chlorofluorocarbons. As a consequence of accidents and inadvertent handling, spills of these chemicals have led to groundwater and soil contaminations. Because of their potential to cause cancer and chronic diseases, both compounds have received attention as notorious legacy chemicals at contaminated sites.[1,2]

To characterize on-site contamination and to explore best remediation strategies, compound-specific isotope analysis (CSIA) offers the possibility to distinguish chemically identical contamination sources by their isotope values and to quantify transformation of chlorinated solvents by the observation of degradation-induced changes in these isotope ratios.[3,4] While the ability to derive both lines of evidence is limited if isotope ratios of only one element are measured, the possibilities of CSIA are magnified when analyzing isotopic information from several elements.[5−8] Specifically, as shown for chlorinated ethylenes, analysis of carbon and chlorine isotopes makes it possible to create dual element isotope plots offering the opportunity to distinguish sources more confidently, to detect degradation, and importantly to investigate different transformation mechanisms.[9−16] For CCl_4 and $CHCl_3$ this perspective became achievable by the introduction of viable approaches for compound-specific chlorine isotope analysis of organic compounds.[17−19] Traditionally, the analysis of chlorine isotopes does not only require dedicated instrumentation but also time-demanding offline preparation, such as analyte conversion to CH_3Cl.[20,21] Subsequently, CH_3Cl can be measured on a dual-inlet gas isotope ratio mass spectrometer (DI-IRMS). This so-called offline method for chlorine isotope

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analysis was established by Holt et al.[22] Another possibility is the conversion to cesium chloride for thermal ion mass spectrometry analysis[23] or the atomization of compounds in an inductively coupled plasma followed by multicollector MS.[24,25] A breakthrough for compound-specific chlorine isotope analysis by continuous flow ("online") measurements without laborious offline preparation was accomplished by Shouakar Stash et al.[21] and Sakaguchi-Soder et al.[26] Chlorine isotope analysis was performed on original target analyte molecules of tetrachloroethylene (PCE) and trichloroethylene (TCE) eluting from the gas chromatographic separation. Measurements rely on molecular ions, or fragment ions, generated in the ion source of an IRMS[21] or qMS.[26] In 2010, Aeppli et al.[27] obtained chlorine isotope ratios for PCE, PCP, and DDT using this GC-qMS approach. To improve the qMS measurements of PCE and TCE, Jin et al.[28] optimized the method and compared different evaluation schemes. Palau et al. investigated for the first time 1,2-dichloroethane[11] and 1,1,1-trichloroethane.[29] Chlorine isotope measurements for $CHCl_3$ were reported but not yet systematically validated by Breider and Hunkeler.[30] Hitzfeld et al.[31] and Renpenning et al.[32] introduced yet an alternative and potentially improved strategy to measure chlorine, bromine, and sulfide isotopes. In their studies, GC separation was followed by H_2-induced high temperature conversion (HTC) to HCl, HBr, or H_2S, respectively, and subsequent qMS[31] or IRMS[32] analysis. While this approach represents a universal strategy irrespective of target compound structure, memory effects, and short reactor lifetimes are presently reported to limit HTC applications.[32] Consequently, analyses of unconverted target analytes by GC-IRMS[21] or GC-qMS[26] are the current methods of choice. They represent an emerging opportunity for field studies and mechanistic investigations that is far from being explored. Specifically, current applications are restricted for several reasons. On the one hand, parameters for GC-qMS and GC-IRMS analyses must be carefully validated for each new target compound[33] and the choice of adequate analyte/fragment ions to achieve optimum performance (sensitivity, linearity) in isotope analysis is still an open question.[28] On the other hand, interlaboratory comparisons show that the use of two isotopically distinct isotopic reference materials of each target compound are necessary to ensure comparable results in different laboratories.[11,33,34] Comparisons between the performance of GC-qMS and GC-IRMS using the same reference materials are highly desirable yet limited to a few comparative studies.[11,33]

In this study we, therefore, optimized and carefully evaluated compound-specific chlorine isotope analysis for two new important target compounds, $CHCl_3$ and CCl_4, by both GC-IRMS and GC-qMS, with a particular focus on the comparison of precision and trueness for both approaches. Also, we focused on the question whether rules of thumb can be derived to choose the best analyte/fragment ions for optimum performance (sensitivity, linearity) of isotope analysis. We evaluated the performance using reference material with independently determined isotope ratios as well as with samples from degradation experiments to investigate if measured shifts in isotope ratios and enrichment factors are consistent among methods. In addition, GC-qMS methods were validated in an interlaboratory comparison between Munich and Neuchâtel.

EXPERIMENTAL SECTION

Chemicals. All chemicals in this study were used as received: $CHCl_3$ (Fluka), CCl_4 (Panreac), sodium formate (HCOONa, Merck), cast iron (92% Gotthart Maier Metallpulver GmbH), dibasic anhydrous sodium phosphate (Na_2HPO_4, Panreac AppliChem), sodium hydroxide (NaOH, Baker), hydrochloric acid (HCl, 32 wt %, Sigma-Aldrich).

Abiotic Degradation of CCl_4 with Sodium Formate. A volume of 10 μL of CCl_4 was dissolved in 35 mL of degassed ultrapure water by vigorous stirring for 24 h in a 40 mL vial. The reaction was started inside an anoxic chamber with the addition of 1 g of sodium formate. The vial was closed with a mininert valve (Supelco) and constantly stirred with a magnetic stir plate. Seven samples were taken over a time course of 7 h. For each time point, 0.5 mL was removed from the reaction mixture and diluted in 7 mL of hydrogen peroxide solution (1%), and 1 mL of subsamples were immediately taken from this solution to analyze concentrations and chlorine isotope values. One experimental replicate was performed with 2 g instead of 1 g of sodium formate and was analyzed in the same way.

Abiotic Degradation of $CHCl_3$ with Cast Iron at pH 12. The cast iron was washed with 0.1 M HCl for an hour, rinsed, and dried overnight to activate the surface.[35] The surface of the activated iron was determined by the BET (Brunauer–Emmett–Teller) method as 1.624 ± 0.007 m^2 g^{-1}. The 42 mL vials (20 reaction vials, 12 blank vials) were wrapped in aluminum foil to inhibit photoreaction and 2 g of cast iron were added to each vial. Subsequently, a buffer solution of pH 12 was added until nearly no headspace was left. To start the reaction, pure $CHCl_3$ was added to reach a concentration of 100 mg/L. During the whole reaction vials were placed on a horizontal shaker (IKA KS 260 BASIC, Stanfen, Germany). Samples were taken over 9 days, and for each time point one vial was sacrificed. To stop the reaction, 0.2 μm filtration and subsequent neutralization by acetic acid was done. Samples were frozen[36] in 10 mL vials until analyses for concentrations, carbon and chlorine isotope ratios.

Stable Carbon Isotope Analysis by GC-C-IRMS. Carbon isotope analyses of $CHCl_3$ were performed in the Centres Científics i Tecnològics at the Universitat de Barcelona (CCiTUB) according to the method described elsewhere[37] by using a Thermo Finnigan Trace GC Ultra instrument coupled via a GC-Isolink interface to a Delta V Advantage isotope ratio mass spectrometer (Thermo Scientific GmbH, Bremen, Germany). The GC was equipped with a Supelco SPB-624 column (60 m × 0.32 mm × 1.8 μm, Bellefonte, PA). The GC program started at 60 °C for 5 min, the GC was heated to 165 °C at a rate of 8 °C/min, then heated to 220 °C at 25 °C/min, and finally held at 220 °C for 1 min. A split ratio of 1:5 was used at an injector temperature of 250 °C. Helium (5.0) served as a carrier gas (2.2 mL min^{-1}). The chlorinated methanes were extracted from aqueous samples by automated headspace solid-phase microextraction (HS-SPME) using a 75 μm Carboxen-PDMS fiber (Supelco, Bellefonte, PA) and a TriPlus autosampler equipped with a SPME holder (Thermo Fisher Scientific, Waltham). Samples were extracted at a constant agitation rate (600 rpm) for 20 min at 40 °C. After extraction, the SPME fibers were desorbed at 250 °C for 5 min in the GC injector. The analytical uncertainty (2σ) of carbon isotopic measurements never exceeded ±0.5‰. A pulse of CO_2 as monitoring gas was introduced at the beginning and at the end of each run. For carbon, the monitoring gas had been calibrated beforehand so that values are stated relative to the international reference material Vienna Pee Dee Belemnite (VPDB) on the international per mille scale. Moreover, several

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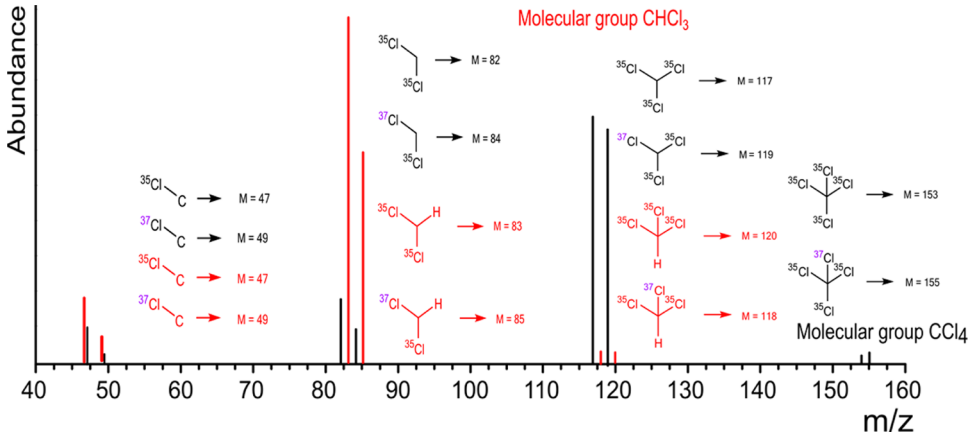

Figure 1. Mass spectra of the isotopologue ion peaks of CCl_4 (in black) and $CHCl_3$ (in red) in analysis by GC-qMS.

$CHCl_3$ aqueous control standards were prepared daily at the same concentration range than the samples from a pure in-house standard of known carbon isotopic composition ($\delta^{13}C$) and analyzed on the same days as the samples to ensure accuracy of the isotopic measurements and to correct slight carbon isotopic fractionation induced by the HS-SPME preconcentration technique.[38] The $\delta^{13}C$ of this pure $CHCl_3$ standard (−48.96 ± 0.04‰) was determined previously using a Flash EA1112 (Carlo-Erba, Milano, Italy) elemental analyzer (EA) coupled to a Delta C IRMS (Thermo Fisher Scientific, Bremen, Germany) through a Conflo III interface (Thermo Finnigan, Bremen, Germany) using six international reference materials (NBS 19, IAEA-CH-6, USGS40, IAEA-600, IAEA-CH-7, L-SVEC) with respect to the VPDB standard, according to Coplen et al.[39] All the controls injected together with the present samples had an average $CHCl_3$-$\delta^{13}C$ value of −50.0 ± 0.3‰ (n = 15).

Stable Chlorine Isotope Analysis by GC-IRMS in Munich. GC-IRMS analysis of CCl_4 and $CHCl_3$ was conducted by recording the masses m/z = 47 and 49 (CCl fragment), which correspond to half of the masses for which the IRMS instrument is specifically configured (98, dichloroethene molecular ion; 94, double dechlorinated tetrachloroethene fragment ion). The GC-IRMS system (Thermo Scientific) consisted of a Trace GC that was connected via a transfer line to a MAT 253 IRMS equipped with a dual inlet system. The gas chromatograph was operated with He carrier gas (5.0) at 1.4 mL/min and contained a 30 m VOCOL column (Supelco) with 0.25 mm inner diameter and a film thickness of 1.5 μm. The GC program started at 60 °C for 2 min, followed by a temperature ramp of 8 °C/min to 165 °C and of 25 °C/min to 220 °C (held for 1 min). The 1 mL gas phase was injected from 10 mL headspace vials that contained 1 mL of aqueous sample and that had previously been equilibrated for 5 min at 40 °C. Injection was performed in split mode (1:10 split ratio) at 220 °C through a split/splitless injector. No difference was observed in isotope values obtained with a split ratio of 1:10 compared to 1:20 (data not shown).

To provide an anchor between individual measurements, pulses of a monitoring gas of CCl_4 and $CHCl_3$ were introduced via the dual inlet system at the beginning and the end of each measurement. Monitoring gas was never adjusted to sample concentration, but instead the amount dependency ("linearity") of isotope measurements was carefully investigated using external standards (see below). In addition, to convert delta values relative to the international reference Standard Mean Ocean Chloride (SMOC), a two point calibration was performed with external standards of CCl_4 and $CHCl_3$. These external standards were placed into daily measurement sequences in the following way. At the beginning of a sequence, 10 injections of the first standard and four injections of the second standard were performed with different headspace volumes. This resulted in a series of amplitudes that allowed evaluating the linearity of the method and, if necessary, performing an amplitude correction. After that, duplicate measurements of both standards were introduced after every 10 sample injections to enable a drift correction accounting for slow outgassing of the CCl_4 monitoring gas from the reference bellow of the IRMS. The measurement sequence was, finally, concluded by quadruplicate measurements of both standards with the same concentration and headspace volumes. Values of the external standards (after amplitude and drift correction) were plotted against their values on the SMOC scale and sample measurements were evaluated using the intercept and the slope of this regression (again, after amplitude and drift correction). The chlorine isotope signatures ($\delta^{37}Cl$) of the external CCl_4 standards were +1.98 ± 0.1‰ (n = 2) and −4.11 ± 0.07‰ (n = 2), as characterized at the University of Delaware (Newark, DE) and those of the external $CHCl_3$ standards were −3.02 ± 0.17‰ (n = 17) and −5.4 ± 0.3‰ (n = 8), as characterized in Waterloo (Isotope Tracer Technologies Inc., Waterloo, Canada), in both cases by IRMS after conversion to CH_3Cl.[22]

Concentration and Stable Chlorine Isotope Measurements with GC-qMS. GC-qMS measurements for analysis of CCl_4 and $CHCl_3$ concentrations and chlorine isotope values were performed in Munich (GC-qMS-1) and Neuchâtel (GC-qMS-2). A summary of instrument parameters in the GC-qMS-1 and GC-qMS-2 setups can be found in the Supporting Information (Table S1). The isotope data from both qMS were also corrected by a two-point calibration with the external standards mentioned above. For each run, four samples of both standards with the same concentration were measured at the beginning, two after every 10 measurements and again four at the end to enable a drift correction. In contrast to GC-IRMS, an amplitude ("linearity") correction was not necessary, because we did not observe an amount-dependency (for further discussion see the Results section below). The data acquisition frequency was chosen such that 15−25 data points are obtained across the chromatographic peaks (Agilent GC/

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MSD ChemStation and Instrument Operation, Course Number H4043A Volume I, page 100). This requires around 3 measurement cycles/s corresponding to a total scan time for each cycle of around 300 ms. A suitable dwell time is then obtained by dividing this time interval by the number of ions (n) analyzed. Reasonable dwell times were calculated in milliseconds.

$$\text{dwell time} = \frac{300}{n+1} \tag{1}$$

In this study, the dwell time was varied around this typical value.

Evaluation of Chlorine Isotope Data. Instrument isotope values for chlorine and carbon measurements by IRMS were in a first step derived from the instrument's software, where samples were evaluated relative to a monitoring gas in each run. For the calculation of chlorine isotope values eq 2 was used:

$$\delta^{37}\text{Cl}_{\text{compound}} = \frac{(^{37}\text{Cl}/^{35}\text{Cl})_{\text{compound}} - (^{37}\text{Cl}/^{35}\text{Cl})_{\text{ref}}}{(^{37}\text{Cl}/^{35}\text{Cl})_{\text{ref}}} = \frac{R_{\text{t}}}{R_{\text{ref}}} - 1 \tag{2}$$

where values are given in per mille For example, a value of 10 ‰ indicates that a substance contained 10 per mille (or one percent) more $^{37}\text{Cl}/^{35}\text{Cl}$ than the compound to which it was compared. An analogous equation applies with $^{13}\text{C}/^{12}\text{C}$ for carbon.

For chlorine isotope measurements by GC-qMS-1, we tested settings with different numbers of ion pairs and different dwell times (i.e., 2, 4, and 6 ions and dwell times between 40 and 100). The molecular ion peaks and fragment ion peaks of CCl_4 and $CHCl_3$ are shown in Figure 1. The masses 119/117, 84/82, and 49/47 were chosen for CCl_4 and 120/118, 85/83, and 49/47 for $CHCl_3$. For the evaluation of selected-ion monitoring (SIM) measurements relying on only two ions we chose the peak intensities of the two most abundant fragment ions (m/z 83 and 85) for $CHCl_3$ and (m/z 117, 119) for CCl_4. These ion couples correspond to the isotopologue pairs ($[^{35}Cl_2{}^{12}CH]^+$ and $[^{35}Cl^{37}Cl^{12}CH]^+$) and ($[^{35}Cl_3{}^{12}C]^+$ and $[^{35}Cl_2{}^{37}Cl^{12}C]^+$), respectively.[27] The isotope ratio was obtained from the ratio of these isotopologues according to eqs 3 and 4.[40]

For the fragment ions m/z 83 and 85 of $CHCl_3$ the equation applies

$$R = \frac{^{37}\text{Cl}}{^{35}\text{Cl}} = \frac{^{37}p}{^{35}p} = \frac{k}{(n-k+1)} \frac{^{35}\text{Cl}_{(k)}{}^{35}\text{Cl}_{(n-k)}}{^{37}\text{Cl}_{(k-1)}{}^{35}\text{Cl}_{(n-k+1)}} = \frac{1}{2}\frac{^{85}I}{^{83}I} \tag{3}$$

where ^{37}p and ^{35}p are the probabilities of encountering ^{37}Cl and ^{35}Cl, n is the number of Cl atoms in the fragment (here, 2), k is the number of ^{37}Cl isotopes in the "heavy" isotopologue (here, 1), $^{37}\text{Cl}_{(k)}{}^{35}\text{Cl}_{(n-k)}$ and $^{37}\text{Cl}_{(k-1)}{}^{35}\text{Cl}_{(n-k+1)}$ represent the isotopologues containing k and $(k-1)$ heavy isotopes (here, $[^{35}Cl^{37}Cl^{12}CH]^+$ and $[^{35}Cl_2{}^{12}CH]^+$), respectively, and I indicates the ion peak intensities. An analogous equation applies to the fragment ions m/z 117 and 119 ($[^{35}Cl_2{}^{37}Cl^{12}C]^+$ and $[^{35}Cl_3{}^{12}C]^+$ of CCl_4, respectively):

$$R = \frac{^{37}\text{Cl}}{^{35}\text{Cl}} = \frac{^{37}p}{^{35}p} = \frac{k}{(n-k+1)} \frac{^{35}\text{Cl}_{(k)}{}^{35}\text{Cl}_{(n-k)}}{^{35}\text{Cl}_{(k-1)}{}^{35}\text{Cl}_{(n-k+1)}} = \frac{1}{3}\frac{^{119}I}{^{117}I} \tag{4}$$

with $n = 3$ and $k = 1$. Values calculated this way were subjected to a calibration with the external standards as described above (measured values of standards were plotted against their values on the SMOC scale, sample measurements were subsequently evaluated using the intercept and the slope of this regression). Resultant values were reported in the δ-notation in parts per thousand relative to the international Standard Mean Ocean Chloride (SMOC) standard.

In contrast, for evaluation of the 4 and 6 ion settings for CCl_4 and $CHCl_3$, the modified multiple ion method was used.[28] Equations 5 and 6 show the corresponding expressions for $CHCl_3$.

Four ions:

$$R_{\text{CHCl}_3} = aR_{\text{F1}}^{\text{CHCl}_3} + bR_{\text{F2}}^{\text{CHCl}_3}$$
$$a = \frac{I_{85} + I_{83}}{(I_{85} + I_{83}) + (I_{49} + I_{47})}$$
$$b = \frac{I_{49} + I_{47}}{(I_{85} + I_{83}) + (I_{49} + I_{47})} \tag{5}$$

Six ions:

$$R_{\text{CHCl}_3} = aR_{\text{M}}^{\text{CHCl}_3} + bR_{\text{F1}}^{\text{CHCl}_3} + cR_{\text{F2}}^{\text{CHCl}_3}$$
$$a = \frac{I_{120} + I_{118}}{(I_{120} + I_{118}) + (I_{85} + I_{83}) + (I_{49} + I_{47})}$$
$$b = \frac{I_{85} + I_{83}}{(I_{120} + I_{118}) + (I_{85} + I_{83}) + (I_{49} + I_{47})}$$
$$c = \frac{I_{49} + I_{47}}{(I_{120} + I_{118}) + (I_{85} + I_{83}) + (I_{49} + I_{47})} \tag{6}$$

where R_{M} is the isotope ratio of the molecular group, R_{F1} of fragment 85/83 and R_{F2} of the fragment 49/47 (eq 3). For a quantitative evaluation of degradation experiments, isotopic enrichment factors (ε) were determined according to the Rayleigh equation[41,42]

$$\ln\left(\frac{\delta^{37}\text{Cl} + 1}{\delta^{35}\text{Cl}_0 + 1}\right) = \varepsilon \ln f \tag{7}$$

where $\delta^{37}\text{Cl}_0$ is the chlorine isotope value at time zero, δ^{37}Cl is the chlorine isotope value at time t, and f is the residual fraction of the substrate (i.e., the concentration at time t divided through the concentration at time zero). The isotopic enrichment factor expresses the difference in reaction rates of molecules containing light and heavy isotopes, respectively, where a value of, e.g., −3.5‰ indicates that heavy isotopologues reacted by 3.5‰ more slowly than light isotopologues.

RESULTS AND DISCUSSION

Acquisition Parameters for GC-qMS Analysis. A crucial parameter for chlorine isotope measurements on a GC-qMS is the optimum configuration in SIM mode. On the one hand,

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instrument fluctuations and also "isotope swings" (i.e., changing isotope values over a chromatographic peak) are better accounted for when measurements jump quickly back and forth between masses. On the other hand, each mass is analyzed more precisely when recorded over a longer time. Finally, different masses can be selected to derive isotope values (see Figure 1). In a first step it was, therefore, our aim to find the optimal choice of ions and dwell times. As described in detail above, we evaluated the most abundant ions method (eqs 3 and 4) plus dwell times of 100, 70, or 50 ms, on the one hand, and the multiple ion method (eqs 5 and 6) for 4 and 6 ions with dwell times of 60 and 40 ms, respectively, on the other hand. For each configuration, 25 identical aqueous samples with concentrations of 1−5 mg/L were measured and the resultant standard deviations were plotted in Figure 2A (after

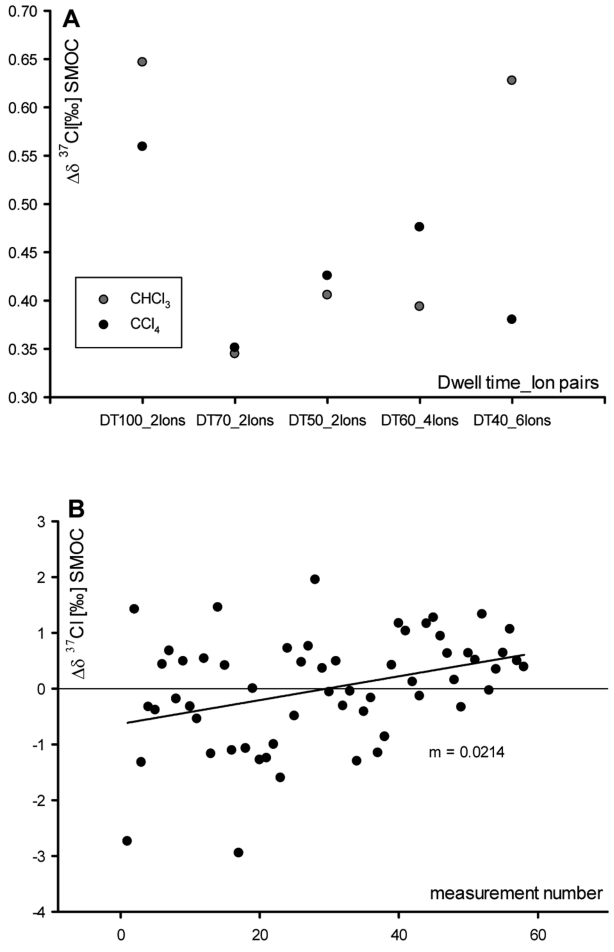

Figure 2. (A) Standard deviation (n = 25) of δ^{37}Cl of CCl_4 and $CHCl_3$ with different ion pair/dwell time settings measured on GC-qMS-1. Delta values (in per mille) are calibrated against SMOC. (B) $\delta^{37}Cl_{CCl4}$ measurements with dwell times of 70 ms and 2 ions in per mil and calibrated against SMOC, indicating a small drift over time for CCl_4 in GC-qMS-1.

two-point calibration against the international standard SMOC to convert instrument readings into per mille units of the δ-scale). This plot of precision versus instrument configuration showed that the recording of 2 ions with a dwell time of 70 ms gave the most precise results for both CCl_4 and $CHCl_3$, with a low standard deviation of around 0.35 per mille. Consequently, we used this setting for all subsequent evaluations in GC-qMS-1. In Neuchâtel (GC-qMS-2), the method already established for $CHCl_3$ by Breider and Hunkeler,[27] using the two most abundant ions and 50 ms as dwell time, was followed.

Figure 2B gives an example of CCl_4 standard measurements over time (60 measurements in a range of 1−25 mg/L) showing a small drift, which occurs with increasing measurement number. We observed such a shift in nearly all measurements and a corresponding drift correction was applied, both in GC-qMS-1 as well as in GC-IRMS measurements. To this end, a linear regression similar to Figure 2B was performed from external standards analyzed along the sequence. Subsequently, the regression parameters were used to correct isotope values of samples.

Amount Dependency ("Linearity") of Chlorine Isotope Analysis of CCl_4 by GC-qMS and GC-IRMS. To determine the precision of CCl_4 measurements on the GC-IRMS instrument, we analyzed 70 standards in a range of 0.03−2.6 mg/L. Even at the lowest amplitude (100 mV), CCl_4 measurements had a standard deviation of only ±0.6‰ (n = 10) and at signals greater than 1 V a very small standard deviation of ±0.1‰ (n = 60) was accomplished (Figure 3A). No amount dependency of the trueness (i.e., the target value) was detected, which is consistent with results obtained previously with chlorinated ethylenes on the GC-IRMS system.[33] Figure 3B shows the precision of CCl_4 measurements by GC-qMS.

For signals of small areas below 10 million TIC (total ion count), chlorine isotope values of GC-qMS-1 measurements showed a rather low precision (±3‰). Above an area of 30 million, in contrast, standard deviations of ±0.6 to 0.4‰ (n = 13) were obtained, which represent an excellent precision for a GC-qMS.[33] In support of these data, an interlaboratory comparison using the same type of GC-qMS gave identical results in Neuchâtel for the GC-qMS-2 (Figure 3B). Therefore, even though standard deviations (i.e., the precision) were clearly affected by the injected amount, the target value (i.e., the trueness) appeared to be hardly amount-dependent in both laboratories. This is in remarkable contrast to previous TCE measurements with GC-qMS,[33] where the concentrations of external standards had to be adjusted to sample concentrations for accurate chlorine isotope analysis by GC-qMS. To compare the precision of GC-IRMS and GC-qMS, the same standard and concentration range (on-column amounts) was measured on the three instruments (Figure 3C). Here, the x axis displays the amount of analyte that, after accounting for the split flow in the injector, reaches the chromatographic column and is measured at the ion source. This amount is also reflected in the signal amplitudes of Figure 3A,B.

Amount Dependency ("Linearity") of Chlorine Isotope Analysis of $CHCl_3$ by GC-IRMS. Chlorine isotope measurements of $CHCl_3$ by GC-IRMS were conducted identically, meaning that, like for CCl_4, also the fragment masses 49 and 47 were recorded on the GC-IRMS (corresponding to $[^{12}C^{37}Cl]^+$ and $[^{12}C^{35}Cl]^+$ in both cases). Figure 4A shows that, in contrast to CCl_4, for $CHCl_3$ a strong amount-dependency of isotope values was observed, which could be taken into account by an amplitude correction. We attribute this observation to the fact that, besides the fragment $[^{12}C^{37}Cl]^+$, also the fragment $[^{13}C^{1}H^{35}Cl]^+$ fell on the detector cup that analyzed the mass 49 (Figure 4B). Therefore, as the number of ions increased, also the probability of collisions increased so that more H atoms were stripped from the $[^{13}C^{1}H^{35}Cl]^+$ fragment and were transferred to other ions (which were not analyzed) and therefore the interference by

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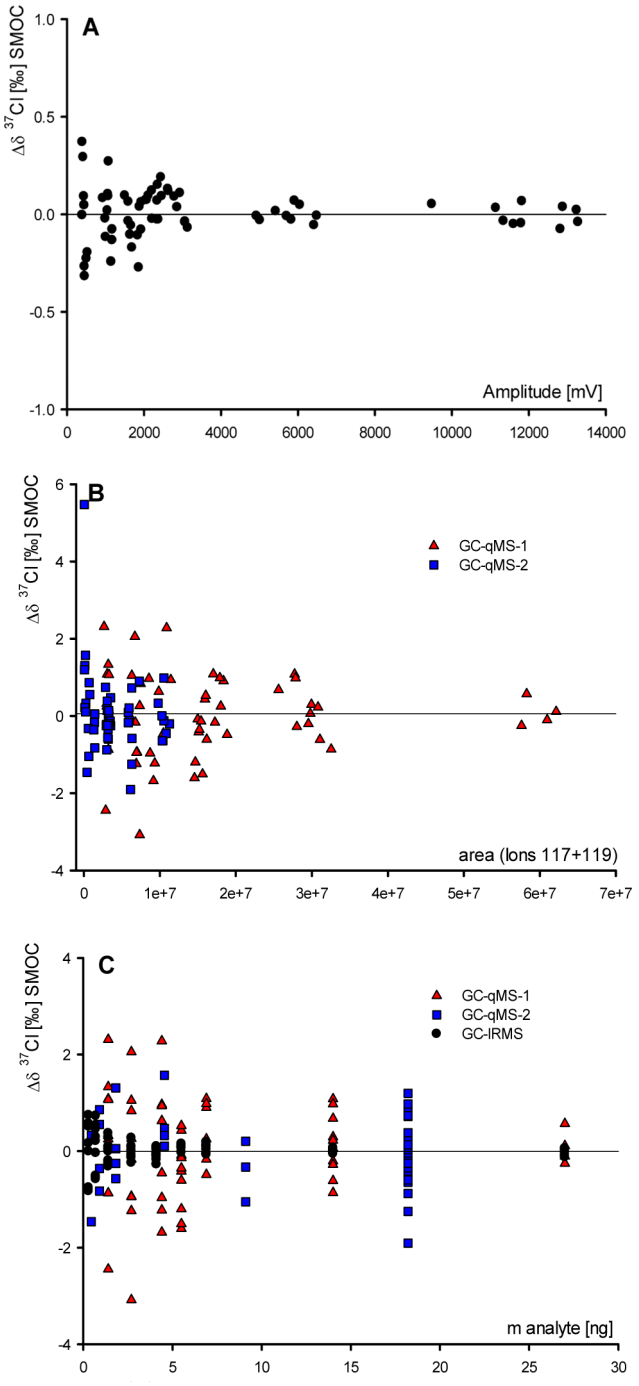

Figure 3. (A) Precision of chlorine isotope measurements vs signal amplitude of CCl_4 measured by GC-IRMS (70 data points). (B) Precision of chlorine isotope measurements of CCl_4 on GC-qMS-1 and GC-qMS-2 in dependence on signal intensity, where $\delta^{37}Cl_{CCl4}$ (calibrated to SMOC scale) of the two most abundant ions are plotted against area (from 119 + 117 ions; GC-qMS-1: 58 data points; GC-qMS-2: 50 data points). (C) Comparison of the precision of chlorine isotope analysis by GC-IRMS vs GC-qMS-1 and GC-qMS-2 in dependence on the mass of analyte (CCl_4) on column.

$[^{13}C^1H^{35}Cl]^+$ decreased. The phenomenon is well-known from H-measurements where hydrogen atoms are transferred to H_2 molecules creating ions of the mass H_3^+ that are detected together with $[^2H^1H]^+$. In both cases the probability of H transfer increases with the amount of analyte molecules in the ion source. However, while in the case of hydrogen, more

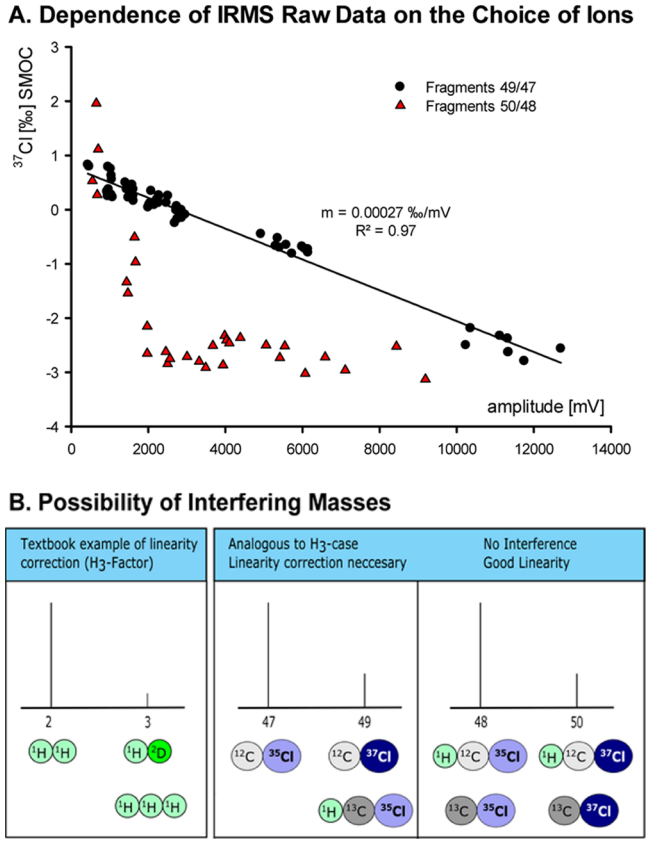

Figure 4. (A) Chlorine isotope values of $CHCl_3$ in dependence on increasing amplitudes on the GC-IRMS (fragments 49/47, 60 data points; fragments 50/48, 30 data points). (B) "Crossover interference" where ions containing a light isotope (^{35}Cl or ^1H) contribute to the mass of a heavy isotope (^{37}Cl or ^2H). This interference is dependent on intermolecular proton transfer in the ion source of the GC-IRMS and, hence, amount-dependent. Such interference is possible for the masses m/z = 3 ($^1H_3^+$ vs $^1H^2H$, left) and m/z = 49 ($^{37}Cl^{12}C$ vs $^{35}Cl^{13}C^1H$, center) but not for mass 50 (right).

collisions create more H_3^+ ions and, hence, increase the interference, in the case of $CHCl_3$ more collisions decreased the number of $[^{13}C^1H^{35}Cl]^+$ ions so that the interference became smaller. For hydrogen isotope measurements, the problem is circumvented by a linear correction of the amount-dependency, i.e., determination of a (positive) H_3-factor. Following an analogous strategy, we introduced an amplitude correction with a negative factor to take into account the amount-dependency of the interference by $[^{13}C^1H^{35}Cl]^+$. This amplitude correction did not require additional analytical effort because external standards needed to be measured anyways, and an injection of different amounts of headspace from the same standard was sufficient to calibrate for the amount-dependency according to Figure 4A (see the Experimental Section above).

Our hypothesis of this "crossover interference" (where ions containing a light isotope (^{35}Cl) contributed to the mass of a heavy isotope (^{37}Cl)) is confirmed by analysis of the fragment masses 50 and 48 of $CHCl_3$, which did *not* show a mass dependency between 2000 to 12000 mV. Figure 4B illustrates the underlying reason: unlike in the case of mass 49 and 47, there is no possibility for ions containing ^{35}Cl to contribute to the mass recorded for ions containing heavy isotopes, $^{37}Cl^{12}CH$ (note that ^2H is of too low abundance for $^{35}Cl^{13}C^2H$ to make a difference). Since in the case of chloroform, the sensitivity of

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measurements of the masses 50 and 48 was 2.5 times lower and standard deviation was worse compared to masses 49 and 47, we nevertheless decided against measurements of the masses 50 and 48 and rather performed an amplitude correction on the masses 49 and 47. Figure 5B illustrates the resulting linearity demonstrating that, after correction, excellent accuracy could be obtained.

Amount Dependency ("Linearity") of Chlorine Isotope Analysis of $CHCl_3$ by GC-qMS. To accomplish a similar method comparison of GC-IRMS and GC-qMS as for CCl_4, $CHCl_3$ standards were measured again by both GC-qMS instruments in Munich and Neuchâtel (Figure 5A). As in the case of CCl_4, standard deviations were amount-dependent ranging from ±1.0‰ (low concentrations of 0.24−0.36 mg/L, n = 20) to ±0.4‰ (higher concentrations of 1.2−2.4 mg/L, n = 15). On the one hand, the low standard deviations for GC-qMS are remarkable. On the other hand, however, Figure 5B illustrates that GC-IRMS still showed better precision, especially when on-column amounts of samples became smaller.

In contrast to the amount-dependency of precision, no amount-dependency was observed for the trueness of chlorine isotope values of CCl_4 and $CHCl_3$ on both GC-qMS (Figure 3B and 5A). This can partly be explained by the fact that masses of fragment ions of the type $CHCl_x^+$ were analyzed, where "crossover interferences" as in Figure 4B can be avoided. However, amount dependencies of mean values did occur on some instruments in previous analysis of TCE[43] despite the fact that also there, only the fragments with hydrogen atoms were measured (e.g., TCE mass 97/95 "$C_2HCl_2^+$") and not those without (e.g., TCE mass 96/94 "$C_2Cl_2^+$"). It is important to understand the reasons for this poor linearity. Since "crossover interferences" are not a possible explanation, Figure 5C explores an additional factor.

Expected isotope fractionation trends in Figure 5C predict that the isotope ratios of molecular and fragment ions should be more stable if the respective ion pair is the predominant one in a given mass spectrum, i.e., to the very left of the reactant (molecular ion) curve or to the very right of the product (fragment ion) curve. The reason is that these are the locations where the slope of the isotope fractionation graph is shallowest (i.e., least sensitive to changes in the extent of fragmentation). Indeed, we found that the relative peak intensities in mass spectra differed significantly between chlorinated methanes and TCE (Figure 5C). Measuring all three compounds with the same ion source settings showed for each chlorinated methane mainly one fragment but three fragments of similar intensity for TCE. Hence, the "lesson learned" from this observation is that instruments should be tuned for either soft ion source settings which preserve mainly the original molecule or for strong ion source fragmentation which ideally leads to one predominant fragment.

Trueness of Chlorine Isotope Analysis of CCl_4 and $CHCl_3$ by GC-qMS and GC-IRMS. While Figures 3, 4, and 5 illustrate the methods' performances in terms of precision, the trueness requirements of both methods can only be tested with samples that include a range of isotope values. Therefore, for each substance one degradation experiment was conducted. CCl_4 was reduced with sodium formate and $CHCl_3$ with zerovalent iron. Both reactions gave rise to pronounced chlorine isotope fractionation, which is a necessary precondition for reliable investigations of trueness over a representative range of δ values. Figure 6A shows changes in isotope values

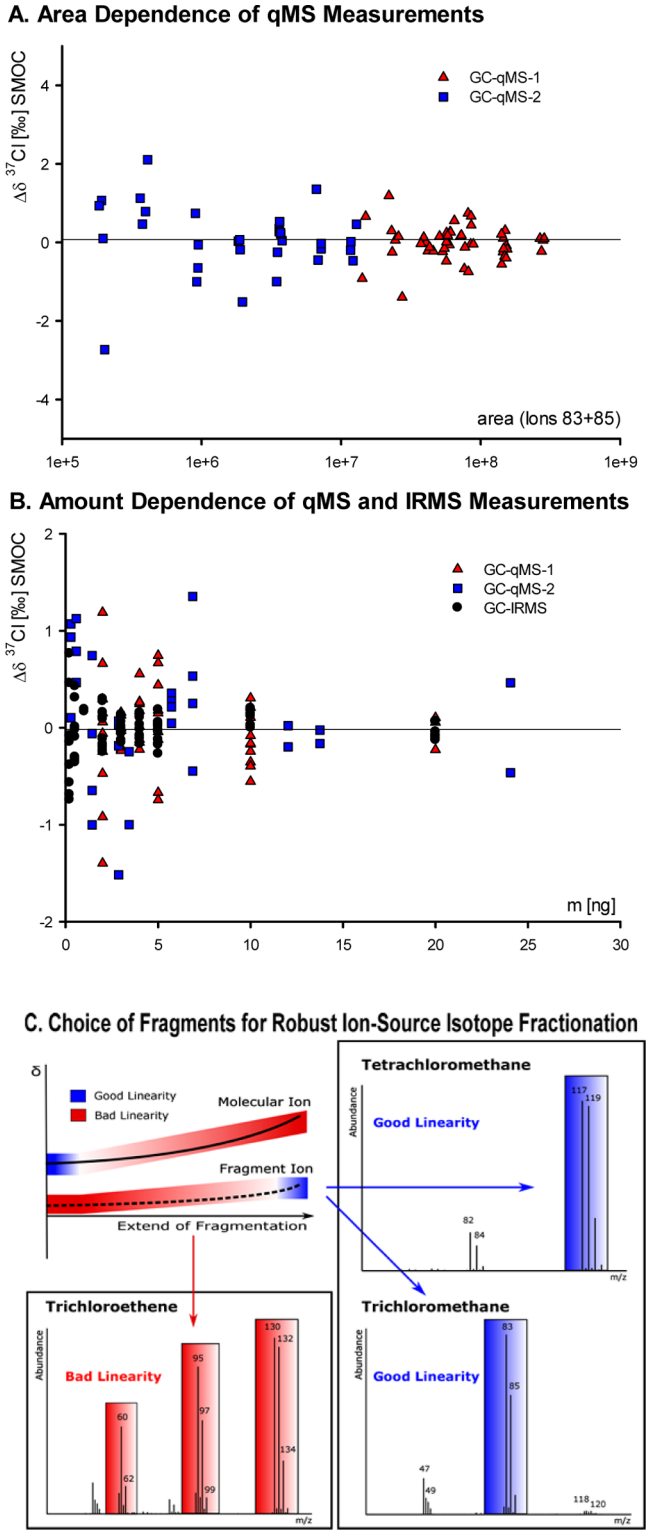

Figure 5. (A) Interlaboratory comparison of $CHCl_3$ measurements on GC-qMS-1 and GC-qMS-2, where the $\delta^{37}Cl_{CHCl3}$ (calibrated to SMOC scale) of the two most abundant ions are plotted against area (from 83 + 85 ions) readings (GC-qMS-1, 51 data points; GC-qMS-2, 32 data points). (B) Comparison of the precision of chlorine isotope analysis by GC-IRMS (after amplitude correction) vs both GC-qMS in dependence on the mass of analyte ($CHCl_3$) on column (IRMS, 60 data points). (C) Expected isotope fractionation trends of molecular and product ions (see, e.g., ref 44) predict that isotope values are not amount dependent if one kind of ion predominates (either parent or product). Mass spectra of $CHCl_3$ and CCl_4 illustrate that, indeed, CCl_4

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Figure 5. continued

gives almost exclusively rise to the fragment of mass m/z = 117/119/121 and $CHCl_3$ almost exclusively to that of m/z = 83/85. This contrasts with ionization of TCE, where several fragments of similar intensity are formed under identical tune settings.

during the degradation of CCl_4 with sodium formate determined by GC-qMS-1. The figure illustrates the importance of a two-point standard calibration. On the one hand, without an external standard that projects instrument values on the international SMOC scale, the start isotope value would be wrong by 5‰ precluding comparisons between laboratories. On the other hand, however, the data show that a two-point calibration is important to quantify changes in isotope values relative to this starting value, as demonstrated by a difference of 0.5‰ in the enrichment factor ε (Figure 6A). The underlying reason for this is illustrated in Figure 6B which shows isotope data obtained from degradation experiments for CCl_4 and $CHCl_3$. In this figure, uncorrected "instrument" chlorine isotope values determined by GC-qMS are plotted against corrected ones by a two-point calibration relative to SMOC. The deviation of the slopes from unity and the differences between compounds and laboratories strongly emphasize the need of calibration by two characterized compound-specific isotope standards for chlorine isotope measurements. The effect is particularly pronounced for $CHCl_3$, where the isotope values would be strongly overestimated without a standard correction (m(Munich) = 1.6 and m(Neuchâtel) = 1.9). These slopes show even small variations between measurement days (or sequence number, Figure 6C) over a period of half a year for CCl_4 and 2 years for $CHCl_3$. For CCl_4, the average slopes were 0.91 ± 0.03 in Munich and 1.06 ± 0.02 in Neuchâtel, whereas for $CHCl_3$ average slopes were 1.6 ± 0.2 and 1.8 ± 0.2, respectively. With a two-point calibration, in turn, reliable results were obtained by GC-qMS for CCl_4, as evidenced by the strong agreement of GC-qMS-1 versus GC-IRMS results shown in Figure 7A, indicating that excellent trueness can be achieved by both methods. Good agreement was also accomplished for $CHCl_3$ degradation with iron, as shown in Figure 7 where results of chlorine isotope values measured on both instruments were combined with carbon isotope values analyzed by GC-C-IRMS in a dual element isotope plot. Very good agreement of linear regressions performed on GC-qMS vs GC-IRMS, both regarding the slope and 95% confidence intervals, confirms that both methods are able to deliver precise and true results.

CONCLUSION

With its enabling role for dual element isotope studies, compound-specific chlorine isotope analysis can greatly increase the identification of groundwater contamination sources and the elucidation of pollutant transformation pathways, and the dual element approach may be a game changer in the assessment of contaminated sites. However, chlorine CSIA has been validated for only a handful of compounds, and systematic method comparisons have been rare. This study contributes to closing this gap by validating, on the one hand, the method for $CHCl_3$ and CCl_4 as important environmental contaminants. On a more fundamental (and general) level, it highlights factors that may lead to strong amount dependence (poor linearity) of chlorine isotope values: (i) protonation of ions containing ^{13}C and ^{35}Cl that may contribute to the mass off ^{37}Cl ions; and (ii) deviation from "ideal" fragmentation conditions where multiple fragment ions rather than one predominant ion are formed. This insight will

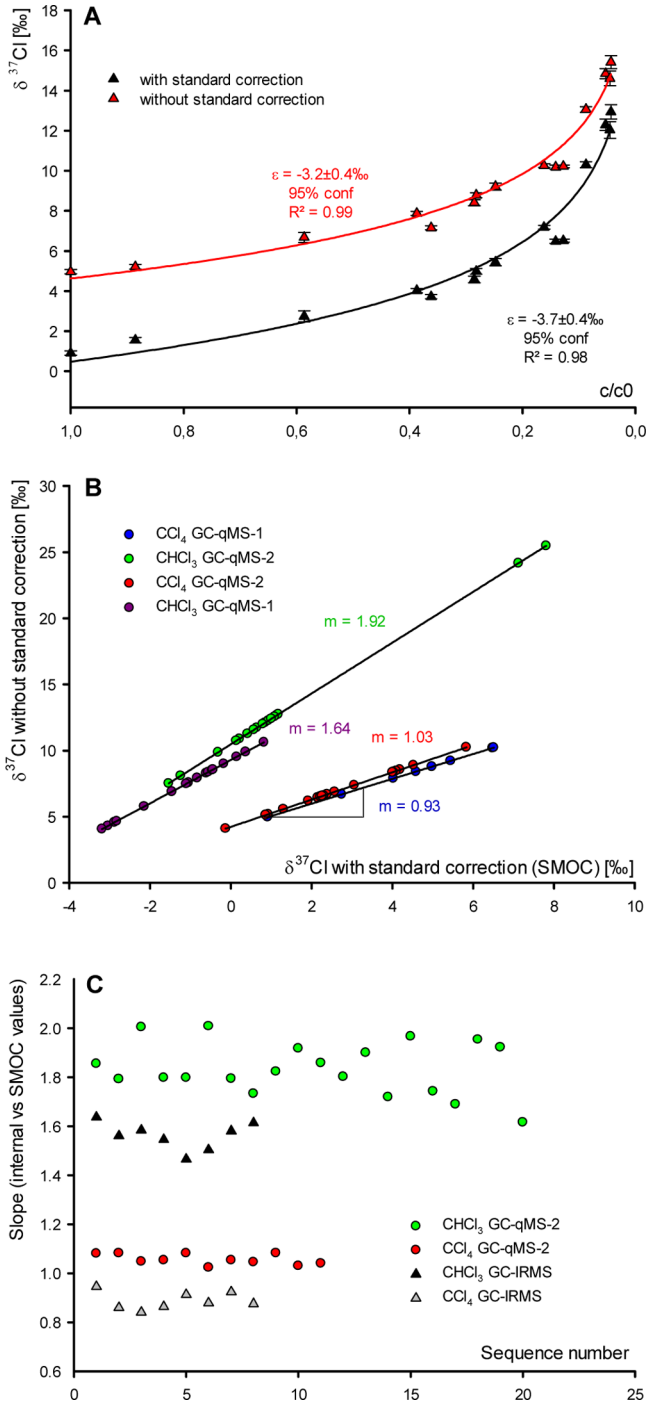

Figure 6. (A) CCl_4 degradation with sodium formate measured at the GC-qMS-1. (Four measurements were conducted for each data point.) Calibration of isotope values by external standards is not only necessary to fix the start chlorine isotope value to the SMOC scale but also to obtain true enrichment factors. (B) Comparison of chlorine isotope values of $CHCl_3$ and CCl_4 from degradation experiments determined with and without correction in two different sequences from GC-qMS-2 and GC-qMS-1. (C) Plot of slope vs sequence number for CCl_4 and $CHCl_3$ from Munich and Neuchâtel shows small variations for different measurement days over longer time periods.

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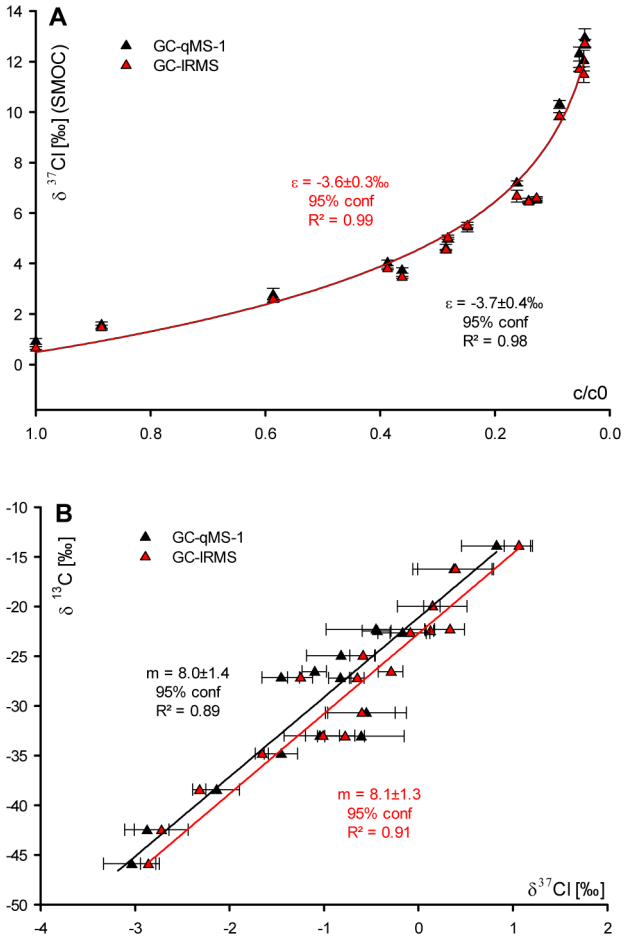

Figure 7. (A) Comparison of $\delta^{37}Cl_{CCl4}$ results against remaining fraction in sodium formate experiments from GC-IRMS and GC-qMS-1 after two-point calibration. (Four measurements were conducted for each data point) (B) Dual element isotope plot of $CHCl_3$ degradation with metallic iron at pH 12 and comparison of regressions from GC-qMS-1 and GC-IRMS chlorine isotope measurements. (Four measurements were conducted for each data point).

be valuable to guide future method developments also for other target compounds.

On the other hand, our study systematically addresses the question of trueness: whether accurate results are obtained by different methods (GC-qMS vs GC-IRMS) in different laboratories. Our results show indeed that measurements of $CHCl_3$ and CCl_4 on a GC-qMS are a very promising alternative if no GC-IRMS is available. Especially at higher concentrations (1.2−2.4 mg/L) isotope measurements with a low standard deviation and a high trueness can be obtained ($\Delta\delta^{37}Cl$ = 0.2−0.6‰). In turn, the possibility to measure chlorine isotope values of $CHCl_3$ and CCl_4 on a GC-IRMS can provide the extra precision that may be critical to distinguish different sources of groundwater contaminations and to detect the onset of degradation in field samples. Finally, our results stress the importance of a two-point calibration with compound-specific chlorine isotope standards bracketing a range of different chlorine isotope values. For true results, the need must, therefore, be addressed for standards with large differences in chlorine isotope values.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.analchem.6b04129.

Overview of the setup of GC-qMS-1 (Munich) and GC-qMS-2 (Neuchâtel) instruments (PDF)

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

The authors declare no competing financial interest.

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