A novel method for determination of inorganic oxyanions by electrospray ionization mass spectrometry using dehydration reactions

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Novel methods for the determination of inorganic oxyanions by electrospray (ES) ionization mass spectrometry have been developed using dehydration reactions between oxyanions and carboxylic acids at the ES interface. Twelve oxyanions (VO$_3^-$, CrO$_4^{2-}$, MoO$_4^{2-}$, WO$_4^{2-}$, BO$_4^{3-}$, SiO$_4^{4-}$, AsO$_4^{3-}$, AsO$_5^{3-}$, SeO$_4^{2-}$ and NO$_2^-$), out of 16 tested, reacted with at least one of fouraminopolycarboxylic acids, i.e. iminodiacetic acid (IDA), nitrilotriacetic acid (NTA), trans-1,2-diaminocyclohexane-$N,N,N'$,N'-tetraacetic acid and triethylenetetramine-$N,N,N'$,N'-hexaacetic acid, at the ES interface to produce the dehydration products that gave intense mass ion responses, sufficient for trace analysis. As examples, trace determinations of CrVI and silica in water samples were achieved after online ion exchange chromatography, where the dehydration product of CrO$_4^{2-}$ and NTA (m/z 290) and that of SiO$_4^{4-}$ and IDA (m/z 192) were measured. The limits of detection of the respective methods were 17 nM (0.83 ng Cr/ml) for CrVI and 0.17 μM (4.8 ng Si/ml) for SiO$_4^{4-}$. Copyright © 2016 John Wiley & Sons, Ltd.

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Introduction

The determination of inorganic ions remains one of the oldest research themes in analytical chemistry. The current state of the art for such analyses is based on inductively coupled plasma (ICP) emission and mass spectrometry (MS) for metal ions and ion chromatography for anions. Although these techniques deliver impressive analytical performance, researchers in this field continue to seek improvements in sensitivity, selectivity and convenience. For instance, electrospray ionization MS (ESIMS) has attracted a wide interest as testified in a number of recent studies. [1-13]

Electrospray ionization MS is one of the most powerful analytical techniques for identification and quantitation of inorganic and organic species in various fields because of attractive features such as direct sampling of solution samples, soft ionization, high sensitivity and selectivity. A key disadvantage, however, is the susceptibility to sample matrix effects, which impacts adversely on quantitative analysis. For the determination of inorganic ions, therefore, ESIMS has often been combined with a pre-separation step, whereby the analytes are first separated from the sample matrix using liquid chromatography (LC) and/or extraction techniques. The ion chromatography (IC)-ESIMS system has been applied to determine various inorganic ions by a number of researchers as summarized in recent reviews. [1-3] The use of ESIMS and complexation–extraction techniques for sample pretreatments has been extensively developed by Minakata et al. for trace analysis. [4-12]

For trace determination of metal ions using ESIMS, a number of studies have been reported since the pioneering experiments of Horlick’s group in the 1990s. [13,14] However, few studies, until recently, have been applied to real samples, probably reflecting the issue of sample matrix effects. Minakata et al. used diethylthiocarbamate (DDC) and pyrrolidine dithiocarbamate (PDC) to ligate metal and metalloid ions and to extract the complexes into the organic phase. Methods were described for determinations of cobalt, [15] platinum, [16] molybdenum, [17] hexavalent chromium, [18] copper, silver and gold [19] based on DDC and for determinations of arsenic(III) and arsenic(V) [20] in clinical samples using PDC. A novel method was also proposed for trace metal analyses based on negative ion mode ESIMS, where metal–aminopolycarboxylate (metal–APC) complexes, particularly those of trans-1,2-diaminocyclohexane-$N,N,N'$,N'-tetraacetic acid (CyDTA), were measured after online separation of the complexes from sample matrices with a size exclusion column. This approach was used for determination of heavy metals in environmental samples. [15-17]

The group of Armstrong has devised more sensitive analytical methods for trace analysis using positive ion mode ESIMS (or ESIMS/MS) where the ion-pair formation of negatively charged...
metal–APC complexes and dicatonic ion-pairing reagents were utilized. These approaches realized sensitivities for some metal ions that were comparable with ICP-MS.\textsuperscript{[18,19]}

In the case of anions, methods for the determination of perchlorate and perbromate ions in environmental samples by IC-ESIMS, as reported by Dasgupta and co-workers, are noteworthy because of their importance in environmental chemistry. A key feature of these methods is the formation of ion pairs of organic dications and perchlorate ion (or other inorganic anions), which are measured.\textsuperscript{[20–22]} Minakata et al. described the formation of gold(II) complexes followed by ion-pair extraction into an organic phase for determination of cyanide,\textsuperscript{[10]} thiocyanate\textsuperscript{[11]} and iodide\textsuperscript{[12]} in clinical samples. The concept of ternary complex formation for determination of halide and cyanide ions has been proposed by the authors, whereby the ternary complexes of group (III) elements with nitrolitriacetic acid (NTA) and halides and that of copper(lii), 4-(2-pyridylazo)-resorcinol and cyanide permitted determinations of halides and cyanide, respectively.\textsuperscript{[15,17,23]} In particular, ultra-trace amounts of fluoride were determined using [AlF(NTA)]\textsuperscript{−}.\textsuperscript{[15]}

For differential measurement of Cr species, HCrO\textsubscript{4} (m/z 117) was directly monitored by ESIMS for Cr\textsuperscript{VI}, while Cr\textsuperscript{III} was detected as the Cr\textsuperscript{III}–CyDTA complex.\textsuperscript{[24]} The limits of detection (LODs) were ~13 nmol/dm\textsuperscript{3} for Cr\textsuperscript{VI} and 56 nmol/dm\textsuperscript{3} for Cr\textsuperscript{III}. The proposed methods, applied to the measurement of chromate and trivalent chromium in conversion coatings on steel samples, gave results that were consistent with those by the diphenylcarbazide spectrophotometric method for Cr\textsuperscript{VI} and ICP-atomic emission spectroscopy (AES) for total Cr. During this study, it was noted that chromate ions reacted with various APCs at the electrospray (ES) interface to produce dehydrated products, which gave prominent MS signals. Also, the MS response was found to be linear with the Cr\textsuperscript{VI} concentration. The oxyanions, molybdate and orthosilicate were then tested, and it was noted that they also underwent dehydration reaction with APCs. Thus, the idea to use this dehydration reaction as a general reaction scheme for determination of oxyanions by ESIMS was conceived.

O’Haire’s group has observed dehydration reactions at the ESIMS interface, where group VI oxyanions ([MO\textsubscript{3}(OH)]\textsuperscript{−} and [M\textsubscript{2}O\textsubscript{6}(OH)]\textsuperscript{−}, M = Mo, W) acted as catalysts for a two-step gas-phase catalytic cycle for the dehydration of acetic acid to ketene, where at the initial step, the condensation product of acetic acid, [MO\textsubscript{3}(OCOCH\textsubscript{3})]\textsuperscript{−} or [M\textsubscript{2}O\textsubscript{6}(OCOCH\textsubscript{3})]\textsuperscript{−} was formed at the ES interface.\textsuperscript{[25,26]} The aforementioned workers also reported gas-phase reactions of group VI oxyanions and [VO\textsubscript{4}(OH)]\textsuperscript{2−} and [V\textsubscript{2}O\textsubscript{5}(OH)]\textsuperscript{−} with methanol.\textsuperscript{[27,28]} However, their interest in these studies appears to be limited to elucidation of reaction pathways and mechanisms of the gas-phase reactions and not the exploitation of the reactions for analytical purposes.

In this paper, we have tested the reactions of 16 oxyanions with four APCs and found that 12 oxyanions gave prominent MS signals. Next, the potential for trace measurement of these oxyanions was evaluated. The selective determination of trace amounts of inorganic oxyanions is generally difficult, and ESIMS is a good candidate for such a purpose. However, its application has been limited to specific oxyanions such as halogen species\textsuperscript{[20–22]} and phosphate.\textsuperscript{[29]}

Also, it was found that a previous approach for measurement of Cr\textsuperscript{VI} was not appropriate for some oxyanions that have a low acidity.\textsuperscript{[24]}

Moreover, this latter approach was unique in applying the gas-phase reaction at the ES interface to derivatize the oxyanions, which then makes it possible to perform trace analysis. Finally, methods for the determination of chromate and orthosilicate in waters based on the combination of IC and ESIMS were demonstrated.

**Materials and methods**

**Reagents and chemicals**

Each oxyanion standard solution was prepared by dissolving the pure compound in high-purity water as shown in Table S1. The oxyanion standards were purchased from Wako Pure Chemicals, Japan (analytical grade). Some of the standard solutions such as metasilicate (SiO\textsubscript{2}\textsuperscript{2−}) and orthosilicate (SiO\textsubscript{2}\textsuperscript{4−}) were cross-checked by ICP-AES using commercial elemental standard solutions. Inomiodiacetic acid (IDA), NTA, CyDTA and triethylenetetramine-N, N,N′,N″,N‴-hexaacetic acid, supplied by Dijindo, Japan (analytical grade), were used as chelating agents. Acetic acid and halogenaotic acids as well as some organic acids were also from Wako Pure Chemicals, Japan (analytical grade). Water was purified by a Millipore Milli-Q system (Millipore Corp., USA). The potassium salt of Co\textsuperscript{III}–EDTA complex, synthesized according to a published procedure,\textsuperscript{[30]} was added to sample solutions to evaluate the condition of the instrument, when indicated in the text.\textsuperscript{[15]} This addition did not show any observable effects on the signal intensities of the dehydration products.

**Apparatus**

An LC-ESI-quadrupole MS system, LCMS-2010 (Shimadzu Co., Japan), was used in flow injection mode. The schematic diagram of the instrument was shown in Fig. S1. The negative ion mode was used throughout. Unless stated otherwise, the instrumental conditions were as follows: ES voltage, −5.0 kV; Q-array voltage, 0 V; nebulizer gas (N\textsubscript{2}) pressure, 0.1 MPa; the curve desolvation line (CDL) temperature, 300 °C; and block heater temperature, 300 °C. The CDL and the heater block are parts of the interface following the ES where desolvation of ions occurs. Sample solutions, introduced with a six-way loop injector whose sample loop volume was 5 μl, were propelled with an LC pump (LC-10AD, Shimadzu Co. Japan). Pure water was used as a carrier solution (flow rate, 0.2 ml/min), unless otherwise stated. The ICP-AES instrument was a Spectroblue unit from Spectro (Kleve, Germany).

**Results and discussion**

**Dehydration reaction of chromate and/or dichromate with carboxylic acids**

In the context of method development and for direct measurement of HCrO\textsubscript{4} (m/z 117) by ESIMS, it was found that chromate ion reacted with various APCs as well as some organic acids at the ES interface to produce dehydrated products, giving prominent MS signals (Table 1). As shown in the table, chromate and all the carboxylic acids tested gave intense signals due to the 1:1 dehydration products (−H\textsubscript{2}O), although the signal for HCrO\textsubscript{4} (m/z 117) was always observed, showing that chromate did not react completely with the carboxylic acids. The ratio of the signal of the dehydration product with NTA to that of HCrO\textsubscript{4} (m/z 117) was highest, suggesting that the reaction efficiency of NTA with chromate was the highest for the combinations of chromate and carboxylic acids tested. Figure 1 shows the mass spectrum of a solution containing 100 μM of K\textsubscript{2}Cr\textsubscript{2}O\textsubscript{7}, 500 μM of NTA and 40 μM of Co\textsuperscript{III}–EDTA, where the signal for the dehydration product was observed at m/z 290. A possible reaction scheme for NTA with chromate is shown in Scheme 1. As mentioned in the introduction, O’Haire’s group observed similar reactions at the interface, where group VI oxyanions...
(\[\text{MO}_3\text{OH}\]) \text{and [M}_2\text{O}_6\text{(OH)}\] \text{, M = Mo, W)} acted as catalysts in a two-step gas-phase catalytic cycle for the dehydration of acetic acid to ketene, although they reported that chromate hardly reacted with acetic acid.[26] Our observations were clearly different from that of O’Hair et al. Moreover, other organic acids, i.e. citric acid, malic acid and oxalic acid, were also found to react with chromate as shown in Table 1, although signal intensities were lower than those of the APCs. To study the effect of the acidity of the carboxylic acid on the efficiency of the dehydration reaction, acetic acid and five halogenoacetic acids were examined. First, a solution containing 25 μM of chromate and 200 μM of acetic acid (pK<sub>a</sub> 4.75), monochloroacetic acid (MCA) (pK<sub>a</sub> 2.88), dichloroacetic acid (DCA) (pK<sub>a</sub> 1.48) or trichloroacetic acid (TCA) (pK<sub>a</sub> 0.7) was tested. The order for the intensities of the signals for the dehydration products was acetic acid < MCA < DCA < TCA. Moreover, when a solution containing the three halogenoacetic acids (200 μM each) and chromate (25 μM) was tested, only the dehydration product of TCA gave a strong MS signal (m/z 261). Thus, it seemed that the higher the acidity of the carboxylic acid, the more reactive the acid was. This result was consistent with that of O’Hair’s group; i.e. the order of the reactivity with [\text{Mo}_2\text{O}_6\text{(OH)}]\text{–} was acetic acid > CF<sub>3</sub>–CH<sub>2</sub>OH > CH<sub>3</sub>OH, depending on their acidities.[25] They also proposed the mechanism of the dehydration reaction of [\text{V}_2\text{O}_5\text{(OH)}]\text{–} and methanol based on their theoretical calculation study, which said that the reaction begins by the formation of an ion–molecule complex between [\text{V}_2\text{O}_5\text{(OH)}]\text{–} and methanol; then, it is followed by the formation of a bridging oxo ligand deprotonating methanol with concomitant opening of the VO<sub>2</sub>V ring (transition state).[28] That is, the deprotonation process is one of the most important ones; thus, the acidities of carboxylic acids may affect their reactivities greatly. In contrast, different results were obtained with trifluoroacetic acid (pK<sub>a</sub> 0.3), TCA and tribromoacetic acid (TBA) (pK<sub>a</sub> 0.8) where almost the same intensities were noted for the three acids. Moreover, when a solution containing all three halogenoacetic acids (200 μM each) and chromate (25 μM) was tested, only the dehydration product of TBA gave a strong MS signal (m/z 395). These findings suggested that there was an optimum acidity of the carboxylic acid for this reaction, which should be quite low, probably around a pK<sub>a</sub> value of 0.8. Table 1. Dehydration reactions of chromate ion with various carboxylic acids

| Carboxylic acid | Iminodiacetic acid | Nitrilotriacetic acid | EDTA-OH | EDTA | Trans-1,2-diaminocyclohexane-N,N,N′,N′-tetraacetic acid | Malic acid | Citric acid | Oxalic acid |
|----------------|--------------------|----------------------|---------|------|------------------------------------------------------|-----------|------------|------------|
| m/z of dehydration product (−H<sub>2</sub>O) | 232 | 290 | 377 | 391 | 445 | 233 | 291 | 189 |
| Signal intensity (A) of HCrO<sub>4</sub>\text{−} (m/z 117) (×10<sup>5</sup> counts) | 1.3 | 0.3 | 0.8 | 0.8 | 1.0 | 0.4 | 0.3 | 0.5 |
| Signal intensity (B) of dehydration product (×10<sup>5</sup> counts) | 1.9 | 3.3 | 4.6 | 3.1 | 3.9 | 0.8 | 1.3 | 0.3 |
| B/A | 1.5 | 11 | 5.8 | 4.1 | 3.9 | 1.9 | 4.2 | 0.6 |

A solution containing 10 μM of K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, 500 μM of each carboxylic acid, 1 mM of ammonium acetate and 40 μM of Co<sup>II</sup>–EDTA was tested.

**Figure 1.** Mass spectrum for a solution containing 100 μM of K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, 500 μM of nitrilotriacetic acid (NTA) and 40 μM of Co<sup>III</sup>–EDTA.

**Scheme 1.** Possible dehydration reaction of chromic acid and nitrilotriacetic acid.
of 1; the exact reason for this is not yet known. Although the gas-phase acidities of these acids might have some effects, we were not able to evaluate them because of lack of data on them. This may be one of the reasons why APCs gave higher intensities than other organic acids that did not contain a N atom.

**Dehydration reaction of various oxyanions with APCs**

As the dehydration reaction seemed not to be limited to chromat ion, dehydration reactions of 16 oxyanions with several APCs, i.e. IDA, NTA, CyDTA and triethylenetetramine-N,N,N′,N″,N″',N″'-hexacetic acid, were next investigated. The test solutions contained 0–100 μM of each oxyanion, 500 μM of each APC and 40 μM of Co(III)-EDTA as an internal standard. The internal standard did not affect the formation of dehydration products and was effective in compensating for the daily changes in instrument sensitivity. As for the pH of the test solutions, the pH values for solutions containing IDA were ~4, and the others were ~9. Table 2 summarizes the occurrences of the dehydration reaction for each test solution and specifies the LOD for the oxyanion (3σ of blank sample) when the reaction was used for the determination of the oxyanion. Moreover, the chemical forms of the supposed dehydration products of some oxyanions with IDA are shown in Fig. 2 as examples. It should be noted that the optimization of the measurement conditions for each combination was not performed; thus, the LOD would be improved, if reaction conditions were optimized. In fact, some of the combinations, i.e. chromate and NTA, orthosilicate and IDA, and molybdate and NTA, gave very high sensitivities. It is possible to classify the 16 oxyanions into three groups, i.e. group 1, metal elements; group 2, metalloid elements; and group 3, non-metal elements as follows:

**Group 1** VO$_2^+$, CrO$_4^{2-}$, MO$_4^{2-}$ and WO$_4^{2-}$. All of the oxyanions in this group gave prominent MS signals for the dehydration products for all of the APCs tested. In particular, MO$_4^{2-}$ and WO$_4^{2-}$ formed dehydration products that had lost two water molecules. Although O’Hair’s group reported that CrO$_4^{2-}$ did not react with acetic acid, this was not the case in this study, the dehydration product giving a strong MS signal as mentioned earlier. Moreover, although O’Hair’s group reported the formation of the dehydration products with binuclear oxyanions ([M$_2$O$_6$(OH)$_2$]$^-$, M = Mo, W, and [V$_2$O$_6$(OH)$_2$]$^-$), we did not observe such products, probably because of differences in the respective measurement conditions. The MS signals of the dehydration products were sufficiently intense to be suitable for trace analyses. In this work, the dehydration product of NTA and CrO$_4^{2-}$ was used for trace determination of Cr(VI) in water samples (see below).

**Group 2** BO$_3^{−}$, SiO$_3^{2-}$, SiO$_4^{4-}$, AsO$_3^{−}$, AsO$_4^{−}$, SeO$_4^{−}$ and SeO$_3^{3−}$. Although oxyanions of this group still formed dehydration products that may be useful for trace determinations, their reactivities seemed to be lower than those of group 1. Some of the APCs did not form dehydration products with some oxyanions, e.g. those of BO$_3^{−}$, AsO$_3^{−}$, AsO$_4^{−}$, SeO$_4^{−}$ and SeO$_3^{3−}$. It is speculated that complex formation involving the oxyanion and APC in the gas phase may occur prior to the dehydration reaction, and this step may be responsible for differences between the APCs. As shown in Table 2, direct measurement of some oxyanions of group 2 such as BO$_3^{−}$, SiO$_3^{2-}$, SiO$_4^{4-}$ and AsO$_3^{−}$ was not possible because of low acidity; nevertheless, the dehydration products did give high sensitivities. Thus, the use of these dehydration reactions for trace analysis may be important given that there are few alternative methods. There are two forms of oxyanions for Si, i.e. metasilicate (SiO$_2^{3−}$) and orthosilicate (SiO$_4^{4−}$). The dehydration product of metasilicate from which one water molecule is lost has the same m/z as that of orthosilicate from which two water molecules are lost, as shown in Table 2 and in Si-1 and Si-2 of Fig. 2. Thus, there was difficulty in differentiating between the two forms, which seemed to show only slight differences in sensitivities. In careful experiments using an ion-exclusion chromatography (IEC)-ESIMS system (see below), however, metasilicate and orthosilicate gave the same sensitivity where IDA was used as a carboxylic acid. This suggests that both silicates gave the same dehydration product, i.e. Si-1 or Si-2 in Fig. 2. Given that the main chemical form of silica in natural water is monomeric orthosilicate, the dehydration product of orthosilicate has mainly been studied in this paper, and an analytical method for silica in natural waters was developed as outlined later. In the case of the oxyanions of As and Se, there are two predominant species for each element, where the valencies of the central atoms are different from each other, i.e. AsO$_3^{3−}$ and AsO$_4^{−}$, and SeO$_3^{3−}$ and SeO$_4^{−}$. In these cases, the dehydration products give different m/z values; thus, we can distinguish them from each other, as shown in Table 2 and Fig. 2 (As-1 to As-4 and Se-1 and Se-2, respectively). In both cases, the oxyanions of the lower-valency species, i.e. arsenite (AsO$_3^{3−}$) and selenite (SeO$_3^{3−}$), gave much higher sensitivities than those with higher valency, i.e. arsenate (AsO$_4^{−}$) and selenate (SeO$_4^{−}$), respectively. The higher valency of the central atom of the oxyanion species may cause a higher acidity (Table S2), in other words, a lower gas-phase basicity, therefore resulting in lower ability to accept proton from carboxylic acids (see above). Nevertheless, the dehydration products of arsenite (AsO$_3^{3−}$) and arsenate (AsO$_4^{−}$) with IDA gave high sensitivities; particularly, the 1:2 product of arsenite and IDA (m/z 337) from which two water molecules were lost (As-2 in Fig. 2) resulted in a very low LOD of 0.69 nM (0.052 ng As/mL) (Table 2). Accordingly, the development of speciation methods for arsenite and arsenate is planned.

**Group 3** NO$_3^{−}$, NO$_2^{−}$, PO$_3^{4−}$, SO$_4^{2−}$ and ClO$_4^{−}$. Oxyanions of this group did not react with APCs except for the combination of NO$_2^{−}$ and IDA. Thus, the dehydration reaction may not be useful for the trace determination of these oxyanions except in the case of NO$_2^{−}$. These results may be due to the higher valencies of the central atom (M), which results in too low gas-phase basicity for reaction with carboxylic acids as discussed earlier for group 2 species. Although PO$_3^{4−}$ did react with CyDTA at the highest temperature conditions of CDL, the MS signal was very weak. Thus, other measurement strategies such as direct measurement of the oxyanions or the application of ion-pair formation may be more effective for trace analysis. The possibility does, however, remain to exploit the dehydration reaction for trace determination of NO$_2^{−}$.
Table 2. Dehydration reactions of various oxyanions with iminopolycarboxylates (APCs)\(^a\)

| Oxyanion | Direct\(^b\) | Imidodiacetic acid | Nitritodiacetic acid | Trans-1,2-diaminocyclohexane-N,N',N''-hexaacetate | Triethylenetetramine-N,N',N''-hexaacetic acid |
|----------|--------------|-------------------|---------------------|-------------------------------------------------|-----------------------------------------------|
| VO\(_4^{2-}\) | LOD (µM) 1.0 | 0.84              | 2.9                 | 0.72                                            | 0.37                                          |
| m/z (−H\(_2\)O) | 99 (VO\(_3^−\)) | 214              | 272                 | 427                                             | 575                                          |
| CrO\(_4^{2-}\) | LOD (µM) 0.013 \(^b\) | 0.84              | 0.016               | 0.16                                            | 0.67                                          |
| m/z (−H\(_2\)O) | 117 (HCrO\(_4^-\)) | 232              | 290                 | 445                                             | 593                                          |
| MoO\(_4^{2-}\) | LOD (µM) 3.9 | 0.31              | n.d.                | n.d.                                            | n.d.                                          |
| m/z (−H\(_2\)O) | 163 (HMnO\(_4^-\)) | 278              | 336                 | 491                                             | 639                                          |
| LOD (µM) | 0.31 | 0.060             | 1.23                | 2.3                                             |                                               |
| m/z (−2H\(_2\)O) | 260 | 318               | 473                 | 621                                           |                                               |
| WO\(_4^{2-}\) | LOD (µM) 1.0 | 0.88              | n.d.                | n.d.                                            | n.d.                                          |
| m/z (−H\(_2\)O) | 249 (HWO\(_4^-\)) | 364              | 422                 | 577                                             | 725                                          |
| LOD (µM) | 1.6 | 5.4               | 1.9                 | 1.6                                             |                                               |
| m/z (−2H\(_2\)O) | 346 | 404               | 559                 | 707                                           |                                               |
| BO\(_3^{3-}\) | LOD (µM) n.d. | n.d.              | n.d.                | n.d.                                            | 0.69                                          |
| m/z (−2H\(_2\)O) | 61 (H\(_2\)BO\(_3^-\)) | 158              | 216                 | 371                                             | 519                                          |
| SiO\(_3^{2-}\) | LOD (µM) 0.014 | 3.4              | 1.1                 | 3.7                                             |                                               |
| m/z (−H\(_2\)O) | 77 (HSiO\(_3^-\)) | 192              | 250                 | 405                                             | 553                                          |
| LOD (µM) | 0.011 | n.d.               | 10                  | 2.1                                             |                                               |
| m/z (−2H\(_2\)O) | 192 | 250               | 405                 | 553                                           |                                               |
| AsO\(_3^{3-}\) | LOD (µM) 0.95 | n.d.              | n.d.                | 1.5                                             | 1.0                                          |
| m/z (−H\(_2\)O) | 141 (H\(_2\)AsO\(_3^-\)) | 256              | 314                 | 469                                             | 617                                          |
| LOD (µM) | 0.035 | n.d.               | n.d.                | n.d.                                            |                                               |
| m/z (−2H\(_2\)O) | 238 | 296               | 451                 | 599                                           |                                               |
| LOD (µM) | 0.11 | n.d.               | n.d.                | n.d.                                            |                                               |
| m/z (−3H\(_2\)O) | 353 \(^d\) | —                 | —                   | —                                               |                                               |
| AsO\(_2^-\) | LOD (µM) n.d. | 0.034             | 0.27                | n.d.                                            | n.d.                                          |
| m/z (−H\(_2\)O) | 107 (AsO\(_2^-\)) | 222              | 280                 | 435                                             | 583                                          |
| LOD (µM) | 0.00069 | n.d.               | n.d.                | n.d.                                            |                                               |
| m/z (−2H\(_2\)O) | 337 \(^d\) | n.d.               | n.d.                | n.d.                                            |                                               |
| SeO\(_3^{2-}\) | LOD (µM) 0.065 | 13               | n.d.                | n.d.                                            | n.d.                                          |
| m/z (−H\(_2\)O) | 145 (HSeO\(_3^-\)) | 260              | n.d.                | n.d.                                            |                                               |
| SeO\(_3^{2-}\) | LOD (µM) 1.2 | 0.16              | n.d.                | n.d.                                            |                                               |
| m/z (−2H\(_2\)O) | 129 (HSeO\(_3^-\)) | 226              | n.d.                | n.d.                                            |                                               |
| NO\(_3^-\) | LOD (µM) 113 | n.d.              | n.d.                | n.d.                                            | n.d.                                          |
| m/z (−H\(_2\)O) | 62 (NO\(_3^-\)) | 177              | 235                 | 390                                             | 538                                          |
| NO\(_2^-\) | LOD (µM) 0.49 | n.d.              | n.d.                | n.d.                                            |                                               |
| m/z (−H\(_2\)O) | 46 (NO\(_2^-\)) | 161              | 219                 | 374                                             | 522                                          |
| PO\(_4^{3-}\) | LOD (µM) 1.2 | n.d.              | n.d.                | n.d.                                            |                                               |
| m/z (−H\(_2\)O) | 97 (H\(_2\)PO\(_4^-\)) | 212              | 270                 | 425                                             | 573                                          |
| SO\(_4^{2-}\) | LOD (µM) 0.37 | n.d.              | n.d.                | n.d.                                            |                                               |
| m/z (−H\(_2\)O) | 97 (H\(_2\)SO\(_4^-\)) | 212              | 270                 | 425                                             | 573                                          |
| ClO\(_4^-\) | LOD (µM) n.d. | n.d.              | n.d.                | n.d.                                            |                                               |
| m/z (−H\(_2\)O) | 99 (ClO\(_4^-\)) | 214              | 272                 | 427                                             | 575                                          |

LOD, limit of detection; n.d., not detected.

\(^a\) A solution containing 0–100 µM of each oxyanion, 500 µM of each APC and 40 µM of Co\(^{II}\)-EDTA was tested. A 1:1 product (oxyanion:APC) was measured, unless otherwise stated.

\(^b\) A solution containing 0–100 µM of each oxyanion and 40 µM of Co\(^{II}\)-EDTA was tested. Each oxynion itself was measured.

\(^c\) A 1:2 product (AsO\(_3^{3-}\) :IDA) from which three waters were removed was observed.

\(^d\) A 1:2 product (AsO\(_2^-\) :IDA) from which two waters were removed was observed.
Determination of CrVI by post-column IC-ESIMS using dehydration reaction of chromate with NTA

A post-column IC-ESIMS system, which exploited the dehydration reaction of chromate ion with NTA, was used for the trace determination of CrVI, as shown in Fig. 3. For the post-column reaction, the optimized concentration of 500 μM NTA solution (flow rate, 0.3 ml/min) was added to the eluate (35 mM NH₄HCO₃ solution), and the dehydration product was monitored at m/z 290 in selected ion monitoring (SIM) mode. An anion exchange column (AG4A-SC Dionex) was used to separate chromate ion from other anion and cation species. An example of a river water analysis is shown in Fig. 4, where sulfate was separated from chromate ion. Linear calibration for chromate was maintained up to 10 μM. At higher concentrations, the graph deviated slightly from linearity (Fig. S2). The LOD for chromate was 17 nM, whereas it was 62 nM when HCrO₄ (m/z 117) was measured directly. The method was used for analysis of river samples (Kiryu River near the university), and although CrVI was not detected in the samples, analyte recoveries were 97 ± 3.5% and 98 ± 3.9% for spike additions of 5 and 10 μM of CrVI, respectively. These results demonstrated the potential of the present method for trace determinations of CrVI in real samples.

Determination of silica in water samples by ESIMS using the dehydration reaction of silica with IDA

As shown in Table 2 and Fig. 5, orthosilicate ion and IDA formed the dehydration product (m/z 192), from which two water molecules were lost, to give very high sensitivity for orthosilicate ion. Thus, this reaction was utilized to determine silica in water samples. Moreover, the dehydration product of the dimer of orthosilicate (H₆Si₂O₇) and IDA (m/z 270), from which two water molecules were lost, was also observed as shown in Fig. 5. This dimer probably does not exist in sample solutions but may form at the CDL, because the signal became very weak compared with the monomer product (m/z 192) when the CDL temperature was lower. Moreover, the monomer and the dimer gave the same retention time in IEC (see below).

The measurement conditions were as follows: a water methanol (v/v) ratio of 3:7 was found to be most suitable (Fig. 6a); the CDL temperature was the most important instrumental parameter, and the signal intensity increased with an increase in temperature (Fig. 6b). This result suggested that the dehydration reaction occurred mainly at the CDL, although the dissociation processes may also occur in the heater block region. A linear calibration curve for orthosilicate was obtained up to 1 μM; at higher concentrations, the graph showed a curvature. The LOD for orthosilicate was 11 nM (0.31 ng Si/ml). Direct analyses of bottled mineral water samples were attempted, but we were not able to obtain reproducible results presumably because of the presence of matrix effects. Thus, the method could not be applied to bottled water samples.

Figure 2. Possible chemical structures of some dehydration products.

Figure 3. Schematic of ion chromatography electrospray ionization mass spectrometry (ESIMS) instrument. Experimental conditions for CrVI determination: eluate, 35 mM NH₄HCO₃ aqueous solution; post-column reagent, 500 μM nitrilotriacetic acid aqueous solution; column, anion exchange column (Dionex, AG4A-SC, 2.0-mm inner diameter (ID) × 50 mm). Experimental conditions for silica determination: eluate, pure water; post-column reagent, 100 μM iminodiacetic acid methanol–water (80:20 w/w) mixed solution; column, cation-exchange column (Tosoh TSKgel SuperIC-A/C (6.0-mm ID×15 cm)) with a guard column (TSKgel guard column SuperIC-A/C, 4.6-mm ID×2 cm).

Figure 4. Chromatogram of chromate and sulfate ions in river water sample containing 5 μM of CrVI as spike. The dehydration product of chromate ion and nitrilotriacetic acid (m/z 290) was monitored in SIM mode. HSO₄⁻ (m/z 97) was also monitored.
IEC was used to separate silica from the sample matrix constituents, according to the procedure of Ikedo et al. The instrumental setup was basically the same as that of Fig. 3. The separation column was a polymethacrylate-based weakly acidic cation-exchange resin in the H⁺ form, Tosoh TSKgel SuperIC-A/C (6.0-mm inner diameter × 15 cm) with a guard column (TSKgel guard column SuperIC-A/C, 4.6-mm inner diameter × 2 cm). The eluate was pure water (flow rate, 0.3 ml/min). A methanol–water (80:20 w/w) solution containing the optimized concentration of 100 μM IDA (flow rate, 0.3 ml/min) was used as a post-column solution. The dehydration product of silicate and IDA was monitored at m/z 192 in SIM mode. Figure S3 shows the chromatogram of orthosilicate (m/z 192) and sulfate (HSO₄⁻/CO₃⁻) in SIM mode, where a model sample containing 5 mM NaCl, 2 mM MgCl₂, 3 mM MgSO₄, 1 mM KCl, 1 mM CaCl₂ and 5 μM Na₄SiO₄ was used to represent a typical sample matrix. The model sample gave a signal intensity of 97.1 ± 5.7% compared with that of 2.0 × 10³ for 5 μM Na₄SiO₄ standard solution. On this basis, the IEC system was

Figure 5. Mass spectrum of a solution containing 50 μM Na₄SiO₄, 500 μM iminodiacetic acid and 40 μM Co²⁺–EDTA.

Figure 6. Optimization of measurement conditions of electrospray ionization mass spectrometry for the detection of dehydration product of orthosilicate ion and iminodiacetic acid (m/z 192). (a) Effect of solvent constituents of sample solutions. Instrumental conditions; electrospray voltage, −5.0 kV; Q-array voltage, 0 V; nebulizer gas (N₂) pressure, 0.1 MPa; the curve desolvation line (CDL) temperature, 300 °C; block heater temperature, 300 °C. (b) Effect of CDL temperature. Instrumental conditions; the same as above (except for CDL temperature).

IEC was used to separate silica from the sample matrix constituents, according to the procedure of Ikedo et al. The instrumental setup was basically the same as that of Fig. 3. The separation column was a polymethacrylate-based weakly acidic cation-exchange resin in the H⁺ form, Tosoh TSKgel SuperIC-A/C (6.0-mm inner diameter × 15 cm) with a guard column

Table 3. Determination of silica in water samples

| Sample          | Si/μM | Inductively coupled plasma–atomic emission spectroscopy | Molybdenum yellow method | Hardness b (mg/l) |
|-----------------|-------|--------------------------------------------------------|--------------------------|-------------------|
| Mineral water   | 372 ± 14 | 382                                                  | 410                      | 27                |
| sample #1      |       |                                                       |                          |                   |
| Mineral water   | 206 ± 20 | 204                                                  | 221                      | 281               |
| sample #2      |       |                                                       |                          |                   |
| Mineral water   | 113 ± 10 | 121                                                  | 134                      | 1200              |
| sample #3      |       |                                                       |                          |                   |
| River water     | 204 ± 14 | 175                                                  | 206                      | 28                |
| sample f       |       |                                                       |                          |                   |

aAverage of three determinations.

bHardness of samples was obtained by determining Mg and Ca by inductively coupled plasma–atomic emission spectroscopy.

* Dilution of 77 times.

* Dilution of 45 times.

* Dilution of 35 times. The sample was obtained from Kiryu River.
effective in removing the matrix interferences present in the sample. The LOD was 0.17 µM for orthosilicate (4.8 ng Si/ml), and the calibration curve was linear up to 10 µM. This LOD was slightly higher than that of the literature (1.0 ng Si/ml) where a molybdenum blue method was used for post-column detection. However, the sensitivity of the present method should be high enough to determine silica in natural waters except for seawater samples. To analyze seawater samples, desalination may be necessary, and the development of such a system is now in progress. The present method was applied to the analysis of bottled mineral water samples and a river water sample, and, as shown in Table 3, the results were in good agreement with those of ICP-AES and the molybdenum yellow method.

To confirm that the dehydration reactions occur not only in the present instrument (Shimadzu LCMS2010) but also in other ESIMS systems, the dehydration reaction between orthosilicate and IDA was examined (any other system was not examined) using three further ESIMS systems, i.e. Nano Frontier from Hitachi High-Technologies Co., Japan; Model 6120 from Agilent Technologies, USA; and QTRAP 3200 from AB Sciex, USA. Although instrument optimizations were not attempted, prominent MS signals for the dehydration product (m/z 192) were realized in the three instruments. Thus, the proposed methods have generic potential, and trace measurement of oxyanions may be undertaken on various ESIMS platforms.

Conclusions

The oxyanions, VO$_4^{3-}$, CrO$_4^{2-}$, MoO$_4^{2-}$, WO$_4^{2-}$, BO$_3^{3-}$, SiO$_3^{3-}$, SiO$_4^{4-}$, AsO$_3^{3-}$, AsO$_4^{3-}$, SeO$_3^{2-}$, SeO$_4^{2-}$ and NO$_2^-$, reacted with four APCs at the ES interface to produce dehydration products that gave intense ion responses. We assume that these dehydration reactions should take place in the gas phase, considering the works of O’Hare’s group. However, it should be noted that we do not have any evidence to eliminate the possibility that the dehydration reactions take place in the liquid phase, and further studies should be necessary to clarify the mechanism of these reactions. Signal strength was sufficient to permit trace measurement of the oxyanions. In particular, the measurement of species that have relatively high pK$_a$ values such as BO$_3^{3-}$, SiO$_3^{3-}$, AsO$_3^{3-}$ and NO$_2^-$ would be significant given that direct measurement of these oxyanions by ESIMS is not possible. Moreover, simultaneous determination of several oxyanions should be possible by this method, as IDA, for example, reacts with various oxyanions as mentioned earlier. Methods for the determination of Cr$^{6+}$ and silica in water samples were developed in combination with IC where the dehydration products of CrO$_4^{2-}$ and NTA (m/z 290) and SiO$_4^{4-}$ and IDA (m/z 192) were measured, respectively. The LODs were 17 nM for Cr$^{6+}$ and 0.17 µM for SiO$_4^{4-}$. There remain two outstanding problems with the present methodology. First, there is a need to improve method sensitivity. The optimization of chelating agent chemistry as well as the use of state-of-the-art instrumentation may result in sensitivity enhancement. Also, there is a need to improve the performance of the online matrix removal system. In this respect, we are developing an online electrodialysis system, which may make it possible to realize a more efficient and higher-throughput system compared with the present IC-based system.

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