Fortuitous Ion–Molecule Reaction Enables Enumeration of Metal–Hydrogen Bonds Present in Gaseous Ions

Zhaoyu Zheng, Julius Pavlov, and Athula B. Attygalle*©

Center for Mass Spectrometry, Department of Chemistry and Chemical Biology, Stevens Institute of Technology, Hoboken, New Jersey 07030, United States

Supporting Information

ABSTRACT: Upon mass selection and ion activation under mass spectrometric conditions, gaseous formate adducts of many metal formates undergo decarboxylation and form product ions that bear metal–hydrogen bonds. Fortuitously, we noted that negative-ion spectra of several such formate adducts showed many peaks that could not be rationalized by the conventional fragmentation pathways attributed to the precursor ion. Subsequent experimentation proved that these enigmatic peaks are due to an ion–molecule reaction that takes place between traces of adventitious water vapor in the collision gas and the in situ formed product anions bearing metal–hydrogen bonds, generated by the fragmentation of the formate adducts. Results show that metal–hydrogen bonds of the group 2 elements are particularly susceptible to this reaction. For example, in the product-ion spectrum of [Sr(η^2-O2CH)3]−, the peak at m/z 91 for SrH2− was accompanied by three peaks at higher m/z ratios. These peaks, at m/z 107, 123, and 139, represented SrH2(OH)−, SrH3(OH)2−, and Sr(OH)3−, respectively. These satellite peaks, which were separated by 16 m/z units, were attributed to adducts formed due to the high affinity of gas-phase anions bearing metal–hydrogen bonds to water. Although undesired, these peaks are diagnostically useful to determine the number of metal–hydrogen bonds present in a precursor ion. Even though the peaks were less pronounced, analogous reactions were noted from the adducts of the group 1 elements as well. Moreover, Gibbs free energy values computed for the interaction of [H-Mg(η^2-O2CH)3]− with water to form [HO-Mg(η^2-O2COH)2]^− and H2 indicated that this is an exergonic reaction.

INTRODUCTION

Unwarranted ion–molecule reactions that occur under tandem mass-spectrometric conditions are often a nuisance because they complicate spectral interpretations. Occasionally, such reactions take place in the ion source under electrospray ionization (ESI) conditions. Ion–molecule reactions are more common in mass spectrometric investigations conducted in tandem-in-time devices, such as ion traps, because the ions are stored in a confined space for a relatively longer period of time prior to ion activation. Although less common, ion-neutral adduct peaks have also been observed in the spectra recorded on tandem-in-space instruments when reactants such as water, methanol, ethanol, nitrogen, oxygen, and carbon dioxide are either present as impurities, or added intentionally as reagents to the collision gas.

Once comprehended, these ion–molecule reactions can become a powerful tool for structural elucidations. For example, such reactions have been employed to differentiate among different types of isomers. However, the presence of unexpected adduct peaks makes the interpretation of mass spectrometry (MS)/MS data, or quantitation by targeted scan modes, more complicated. There is a strong inclination to rely on artificial intelligence computer programs for positive compound identification. However, unwarranted ion–molecule reactions could easily lead to false-positive dubious results.

Among ion–molecule reactions, the addition of water is the most commonly encountered transformation. Water adds not only to positively charged reaction centers but also to anions. Recently, we published a paper on periodic trends in the fragmentation patterns of formate adducts of metal formate anions generated from groups 1 to 2 and groups 13 to 15 metals of the periodic table. Upon collision-induced dissociation (CID), the formate adducts of metal formates undergo decarboxylation to form ionic products that bear metal–hydrogen bonds. The spectra reported previously showed several peaks that could not be attributed to ions originating from direct dissociation of mass-selected precursor ions. Herein, we present details of an extensive study to demonstrate that the enigmatic peaks originate from an ion–molecule reaction between product ions that bear M–H bonds and traces of water present in the collision gas.
RESULTS AND DISCUSSION

Under negative-ion-generating electrospray ionization conditions, ion pairs of metal formates generate gaseous adducts with formate anions. Such formate adducts, upon mass selection and ion activation under mass spectrometric conditions, typically dissociate by losing either a molecule of the metal formate to form the formate ion or by ejecting a molecule of CO₂ (decarboxylation) to form an anion bearing a metal–hydrogen bond.³⁰ Acetate adducts of alkaline-earth metal acetates [Metal(O₂CCH₃)₃]⁻ are known to fragment analogously, and form the organometallate anions [CH₃Metal-(O₂CCH₃)₂]⁻ by ejecting CO₂.³¹

For the adducts of alkali formates (group 1 elements), the ejection of a neutral metal formate molecule to generate the formate ion is the more favorable mechanism. In contrast, the decarboxylation process is the preferred fragmentation pathway for the adducts of groups 2, 13, 14, and 15 metal formates.³⁰ However, in addition to the peaks expected for the products of the two predicted pathways, the MS² spectra recorded from the formate adducts of metal formates showed several additional peaks. At first blush, these peaks appeared to be enigmatic. For example, an ESI product-ion mass spectrum recorded from m/z 97 as the precursor ion generated from an aqueous solution of lithium formate showed peaks at m/z 45.

Figure 1. Product-ion spectrum of the mass-selected m/z 97 ion for [Li(η²-O₂CH)₂]⁻ generated by electrospraying an aqueous solution of lithium formate. The spectrum was recorded on a Synapt G2 instrument at a transfer collision energy setting of 5.5 eV and a resolving power of 10 000 at m/z 97.

Figure 2. Product-ion spectrum of m/z 159 for [Mg(η²-O₂CH)₃]⁻ (recorded at a transfer collision energy setting of 5.5 eV and a resolving power of 9000 at m/z 157) (A). Product-ion spectrum of m/z 175 for [Ca(η²-O₂CH)₃]⁻ (recorded at a transfer collision energy setting of 10.0 eV and a resolving power of 9000 at m/z 175) (B). Product-ion spectrum of m/z 223 for [Sr(η²-O₂CH)₃]⁻ (recorded at a transfer collision energy setting of 25.0 eV and a resolving power of 11 000 at m/z 223) (C). Product-ion spectrum of m/z 273 for [Ba(η²-O₂CH)₃]⁻ (recorded at a transfer collision energy setting of 30.0 eV and a resolving power of 10 000 at m/z 273) (D). All spectra were recorded on a Synapt G2 instrument under negative-ion-generating ESI conditions.
and 53, representing the formate anion and the decarboxylated precursor ion ([H-Li-O2CH]−), respectively (Figure 1). Albeit small, a peak was also noted at m/z 69 (Supporting Information Figure S1). The nominal m/z value of this ion was 28 Da smaller than that of the precursor ion (m/z 97) and 16 Da higher than that of the m/z 53 ion formed from decarboxylation. Arguably, the m/z 69 ion could be attributed to a loss of either a carbon monoxide molecule from the precursor ion (m/z 97) or the formation of a mono-oxygen adduct from the m/z 53 ion.

A similar, but a more pronounced set of enigmatic peaks were observed in the spectra recorded from group 2 metal formates (Figure 2). To start with, the formate adducts of magnesium and calcium formates can undergo two consecutive CO2 losses (decarboxylation steps):

\[ \text{m/z } 223 \rightarrow \text{m/z } 159 \rightarrow \text{m/z } 115 \]

\[ \text{m/z } 175 \rightarrow \text{m/z } 151 \rightarrow \text{m/z } 131 \rightarrow \text{m/z } 87 \]

In the spectrum recorded for magnesium formate, there was an unaccounted additional peak at m/z 131 (Figure 2A). Likewise, an analogous peak appeared at m/z 147 in the calcium-formate spectrum (Figure 2B). Moreover, between the peaks for the first and the second decarboxylation steps, there was an unaccounted additional peak at m/z 87 ([H-Mg(OH)(η2-O2CH)]−) in the magnesium-formate spectrum (Figure 2A). Likewise, an analogous peak appeared at m/z 147 in the calcium-formate spectrum (Figure 2B). Because the nominal masses of m/z 103 and 119 ion were 16 and 32 Da higher than that of the m/z 87 ion ([H2-Ca(η2-O2CH)]−), respectively, these ions appeared to be...
formed by the addition of one or two oxygen atoms to the m/z 87 ion (Figure 2B).

As previously reported, the formate adduct of strontium can undergo three consecutive CO2 losses under high collision energy conditions: m/z 223 [Sr(O2CH)3]− → m/z 179 [H-Sr(O2CH)2]− → m/z 135 [H2-Sr(O2CH)]− → m/z 91 [SrH3]− (Scheme 1). Along with these expected peaks, representing the fragment ions formed from the first, second, and third decarboxylation processes, there were one (m/z 195, marked red in Figure 2C), two (m/z 103 and 119, marked in blue), and three (m/z 107, 123, and 139, marked in green) additional peak sets that could not be rationalized by the main fragmentation mechanisms (Figure 2C). For example, the ions detected at m/z 107, 123, and 139 as shown in the spectrum depicted in Figure 2C appeared to be associated with the m/z 91 ion that originated from a triple decarboxylation of the precursor m/z 223 ion. The nominal masses of the ions corresponding to the m/z 107, 123, and 139 peaks were 16, 32, or 48 Da higher than that of the m/z 91 ion. At first look, these enigmatic ions appeared to represent the consecutive addition of a 16 Da “oxygen atoms” to the m/z 91 ion. To gain insights into the origin of these intriguing sets of ions, the m/z 135 ion was generated by collision-induced dissociation in the ion source by increasing the cone-voltage conditions. The m/z 135 ion, which originated from two consecutive CO2 losses from the precursor ion [Sr(\eta^2-O2CH)3]− (Scheme 1), was mass-selected and passed through the transfer collision cell under very mild fragmentation conditions. Interestingly, in the product-ion spectrum recorded, there were peaks at m/z ratios higher than that of the mass-selected precursor ion (Figure 3). Evidently, ions such as m/z 139, 151, and 167 were products of a neutral-gain process that took place by ion–molecule reactions in the collision cell.

To verify the origin of the atom(s) added during the formation of these enigmatic ions, first we determined the accurate masses (Supporting Information Table S1). The results agreed with the values predicted for increases due to the addition of one or more oxygen atoms. To confirm the prediction, a sample of Sr(\eta^2-O2CH)1 was synthesized and its CID spectrum was recorded. The product-ion spectrum of the m/z 235 ion for [Sr(\eta^2-O2CH)3]− showed an intense peak at m/z 187 for a 48 Da C18O2 loss, which was accompanied by a peak at m/z 203 (Figure 4B). This result proved that the additional oxygen atom required for the formation of the m/z 203 ion does not originate from any of the oxygen atoms of the precursor ion. In other words, an extraneous oxygen atom is added to the product ion(s) that originate from decarboxylation(s) (Figure 4B). Since a direct addition of an oxygen atom by itself is unlikely, we envisaged that the fragment ion is reacting with traces of water in a manner similar to the known behavior of metal hydrides in aqueous solutions. Metal–hydrogen bonds are known to be highly susceptible to moisture, forming products with metal–hydroxide bonds. If this indeed were the case, the hydrogen atom in the OH groups of the enigmatic ions should also be from an external source, and not from the original hydrogens in the M–H bonds. To verify this, a sample of Sr(O2CD)2 was synthesized. The CID spectrum of m/z 226 ion for [Sr(\eta^2-O2CD)3]− showed a peak at m/z 197, depicting a 15 Da separation from the m/z 182 ion: this proved that the deuteride, initially attached to the strontium atom, was replaced by an extraneous hydroxyl group during the ion–molecule reaction (Figure 4C). Thus, it was clear that ions with metal–hydrogen bonds react with minute traces of moisture present in the collision gas [although 4.8 grade is claimed to be “dry” by the suppliers, its purity is 99.998% and it could contain up to 3 ppm (v/v) H2O] and produce an M–OH bond. In other words, the interaction of water with a metal–hydrogen bond leads to the formation of a metal–OH bond by the elimination a molecule of dihydroxide (Scheme 1). Thus, the peaks at m/z 151 and 167 in Figures 2C and 3 can be attributed to the products formed by the interaction of water with the m/z 135 ion (Figures 2 and 3). Analogously, the m/z 195 ion originated from the reaction with the m/z 179 ion (Figures 2C and 4A).

Evidently, the H2 elimination reaction follows an explicit pathway because a product-ion spectrum of the m/z 138 ion for [D2-Sr(\eta^2-O2CD)3]− showed peaks at m/z 109, 124, and 139. These ions originated from the interaction of H2O with the SrD3− ion (m/z 94) (Figure 5). For the formation of the m/z 109 ion, the m/z 94 ion interacts with H2O and eliminates specifically a molecule of HD. In this way, the dubious 15 Da increases from the m/z 94 could be rationalized (Scheme 2).

Although less reactive to water than the Ca–H and Sr–H bonds, the Ba–H bond formed by CID decarboxylation of [Ba(\eta^2-O2CH)3]− is also susceptible to traces of water in the collision gas. For example, the peaks at m/z 201 and 217 in the product-ion spectrum (Figure 2D) are due to [H-Ba(OH)(\eta^2-O2CH)]− and [Ba(OH)2(\eta^2-O2CH)]−, respectively.

To support the reaction mechanisms proposed for the water interaction, we conducted a computational study on the following system (Scheme 3). The calculated Gibbs free energies of reactants and products predicted that the water interaction, [H-Mg(\eta^2-O2CH)3]− + H2O → [HO-Mg(\eta^2-O2CH)2]− + H2 (Scheme 3), is an exergonic reaction. This is not a surprise because the higher affinity of group 2 elements for oxygen is well known.

Moreover, computations also indicated that as a water molecule approaches the [H-Mg(\eta^2-O2CH)3]− ion, one of its formate moieties opens up and becomes monodentate when the reactant complex (2) is formed (Figure 6 and Supporting Information Table S4). Upon activation of the reaction complex (2), the monodentate formate moiety pivots back and becomes bidentate again as it reaches the transition state (3), where the Mg–H bond is more elongated. As the reaction...
proceeds to form the product complex (4), the Mg−OH and H−H bonds become shorter (Figure 6 and Supporting Information Table S6). Finally, the two entities in the product complex (4) are separated to give \([\text{H-Mg(}\eta^2-\text{O}_2\text{CH})_2]^-\) as the final product.

Generally, ion−molecule reactions taking place in the collision cell are considered a nuisance because they may obscure the true identity of the precursor ions. However, peaks attributed to water interactions observed in the present study are in fact diagnostically useful because the number of so-called “oxygen-adduct” peaks that accompany the specific precursor-ion peak enable the enumeration the metal−hydrogen bonds present in the precursor ion. For example, in Figure 3, the peaks at \(m/z\) 151 (135 + 16) and 167 (135 + 32) indicate the presence of two Sr−H bonds in the \(m/z\) 135 precursor. Analogously, the peaks at \(m/z\) 107 (91 + 16), 123 (91 + 32), and 139 (91 + 48) show the presence of three Sr−H bonds in \(m/z\) 91. Apparently, the H₂ elimination reported here is analogous to the CH₄ loss reported in the formation of metal−hydrogen bonds from organometallic ions such as \([(\text{CH}_3\text{M-}(\text{O}_2\text{CCH}_3))_n]^-\) upon interaction with water. Moreover, an analogous water addition reaction followed by a subsequent H₂ loss has been observed previously by Osburn et al. during their studies under positive-ion-generating conditions with mixed-metal complexes containing silver, calcium, and deprotonated glycine. Interestingly, when silver was the only metal present, then only the addition of water took place without the loss of H₂. Analogously, tandem mass spectra of certain mass-selected product ions bearing metal−hydrogen bonds generated by the collision-induced dissociation of anionic uranyl complexes \([\text{UO}_2(\text{O}_2\text{C-H})_3]^-\) have been observed to show a peak at 16 mass units greater than that of the precursor ion. Our results are congruent with the conclusions made by Perez et al. that these ions are formed by a process that involves H₂O addition and H₂ elimination.

**CONCLUSIONS**

We have demonstrated the utility of adventitious traces of water in the argon collision gas to enumerate the metal−hydrogen bonds present in gas-phase anions generated during the fragmentation of formate adducts of various metal ions.
formates. However "dry" the collision gas may be labeled, there is sufficient water vapor present in ppm concentrations for it to cause the emergence of MS peaks, spaced at 16 Da at higher m/z values than those of the corresponding precursor ions bearing metal−hydrogen bonds. The number of those peaks
chloride, cesium carbonate, and formic acid-hydroxide, potassium hydroxide, sodium formate, rubidium hydroxide, and calcium oxide were obtained from Fisher AAPER (Brookfield, CT). Formic acid (88%), barium hydroxide, and calcium oxide were obtained from Fisher Scientific (Fair Lawn, NJ). Metal magnesium turnings, lithium and products are associated with all positive vibrational state on the potential energy surface. In other words, reactants and products are associated with all positive vibrational frequencies, whereas transition states (TS) are associated with only one imaginary frequency, for which the normal vibrational mode corresponds to the expected bond formation/breaking movements in a specific reaction pathway. Gibbs free energies calculations were conducted for species at ambient pressure (1 atm) and room temperature (298.15 K).

**EXPERIMENTAL SECTION**

**Mass Spectrometry.** A Synapt G2 HDMS (Waters, U.K.) mass spectrometer equipped with an ESI source was used for high-resolution and accurate-mass collision-induced dissociation (CID) experiments. Using a syringe pump, sample solutions were infused to the ion source at a rate of 20 µL/min. Typically, the capillary voltage was set to 2.5 kV. Nitrogen was used as the nebulizer gas. The desolvation gas (N2) flow rate was 500 L/h. High-purity argon (Grade 4.8, 99.998%, Praxair, Inc., Danbury, CT) was used as the collision gas of Trap and Transfer collision cells at a pressure setting of 8 × 10⁻⁶ bar (however, the pressure of the transfer collision cell was slightly higher than that in the Trap collision cell). For CID experiments, the trap collision energy was kept at 4 eV, and the transfer collision energy was varied between 2 and 30 eV. The source and desolvation gas temperatures were held at 100 and 150 °C, respectively. Mass calibration (m/z 20–1200) was performed using a 100 ppm sodium formate solution in 50% isopropanol: 50% water (v/v). The instrument was operated at a resolving power of 10 000 measured at m/z 97.

**Chemicals.** Millipore water was obtained from Milli-Q water system. Acetonitrile was purchased from PHARMCO-AAPER (Brookfield, CT). Formic acid (88%), barium hydroxide, and calcium oxide were obtained from Fisher Scientific (Fair Lawn, NJ). Metal magnesium turnings, lithium hydroxide, potassium hydroxide, sodium formate, rubidium chloride, cesium carbonate, and formic acid-d₅ (95 wt % in D₂O, 98 atom % D) were obtained from Sigma-Aldrich (Saint Louis, MO). Strontium carbonate was obtained from J. T. Baker (Avantor, Center Valley, PA). H₂¹⁸O was purchased from Cambridge Isotope Laboratories (Cambridge, MA). All chemicals were used without further purification.

**Metal Formates.** All formates that were not commercially available were prepared as described previously. To prepare 18O-substituted strontium formate, formic acid (96%, 10.00 µL) was dissolved in H₂¹⁸O (25 µL). After 12 h, the HC¹⁸OH prepared in this way was added to SrCO₃ (0.0105 g, 0.07 mmol) and the mixture was diluted with Millipore water. Analogously, deuterium-substituted strontium formate was synthesized by adding formic acid-d₅ (95 wt % in D₂O, 98 atom % D) to SrCO₃.

**Sample Preparation.** Samples for MS analyses were prepared in water as 100 ppm solutions. Using a syringe pump, all solutions were infused at a flow rate of 20 µL/min.

**Computational Methods.** All DFT calculations were carried out using the Gaussian 09W program. Proposed structures were fully optimized by using the B3LYP 34,35 hybrid density functional method with a large 6-311++g(2d,2p) basis set. Complete geometry optimizations were conducted at the same level for all species to verify the nature of each stationary state on the potential energy surface. In other words, reactants and products are associated with all positive vibrational frequencies, whereas transition states (TS) are associated with only one imaginary frequency, for which the normal vibrational mode corresponds to the expected bond formation/breaking movements in a specific reaction pathway. Gibbs free energies calculations were conducted for species at ambient pressure (1 atm) and room temperature (298.15 K).

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