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Gas-Phase Structures of Pb²⁺-Cationized Phenylalanine and Glutamic Acid Determined by Infrared Multiple Photon Dissociation Spectroscopy and Computational Chemistry

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Ⓢ *Supporting Information*

ABSTRACT: Infrared multiple photon dissociation (IRMPD) spectroscopy in the 3200−3800 cm⁻¹ region was used to determine the gas-phase structures of bare and monohydrated [Pb(Phe-H)]⁺ and [Pb(Glu-H)]⁺. These experiments were supported by infrared spectra calculated at the B3LYP/6-31+G(d,p) level of theory as well as 298 K enthalpies and Gibbs energies determined using the MP2(full)/6-311++G-(2d,2p)//B3LYP/6-31+G(d,p) method. The gas-phase structure of [Pb(Phe-H)]⁺ has Pb²⁺ bound in a tridentate fashion between Phe's amine nitrogen, one oxygen of the deprotonated carboxyl group, and the aromatic ring. The IRMPD spectrum of [Pb(Glu-H)]⁺ can be assigned to a structure where the side chain carboxyl group is deprotonated. The structure of [Pb(Phe-H)H₂O]⁺ is simply the hydrated analogue of [Pb(Phe-H)]⁺ where water attaches to Pb²⁺ in the same hemisphere as the ligated amino acid. The spectrum of [Pb(Glu-H)H₂O]⁺ could not be assigned a unique structure. The IRMPD spectrum shows features attributed to symmetric and antisymmetric O−H stretching of water and a broad band characteristic of a hydrogen bonded O−H stretching vibration. These features can only be explained by the presence of at least two isomers and agree with the computational results that predict the four lowest energy structures to be within 6 kJ mol⁻¹ of one another.
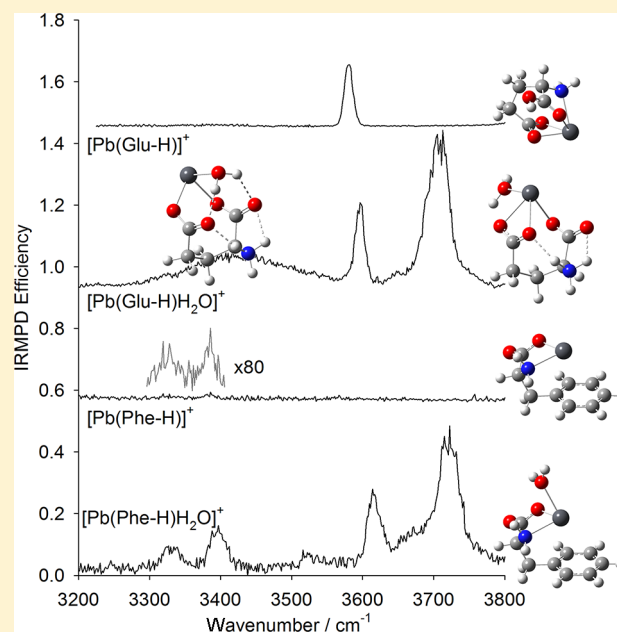
1. INTRODUCTION

Gas-phase amino acids primarily exist as their canonical forms, but zwitterionic tautomers can often be stabilized through metal chelation.[1−21] The extent to which a metal cation alters the structure of an amino acid is dictated by its size and valency.[6,20,22−28] Most of the research into the structures of metal-cationized amino acids has focused on complexes of the form [M(Aa)]⁺/²⁺.[4−10,15−31] These experiments have revealed that, in general, amino acids with nonpolar side chains are more sensitive to the polarizability of the metal cation, whereas those with more functionalized side chains are dependent on the effective shielding of the cation due to the greater degree of charge solvation. This means that increasing the size of the metal cation will have opposite effects on aliphatic and functionalized amino acids. For example, when arginine (Arg) is complexed with the alkali metals, Li⁺ forms a charge-solvated complex, [Na(Arg)]⁺ exists as a mixture of both conformers, and [K(Arg)]⁺, [Cs(Arg)]⁺, and [Rb(Arg)]⁺ are zwitterionic.[32] A similar trend exists for serine (Ser); Li⁺, Na⁺, K⁺, and Rb⁺ each produce three-coordinate charge-solvated structures where the metal is bound between the amine nitrogen, carbonyl oxygen, and side chain hydroxyl group. Starting with K⁺, a bidentate charge-solvated structure begins to contribute to the gas-phase population as the cation size increases, and [Cs(Ser)]⁺ is partly zwitterionic.[6] In contrast, proline (Pro) and N-methylalanine both form salt bridges with Li⁺ and Na⁺, and their charge-solvated isomers become increasingly stable as the cation size increases through K⁺, Cs⁺, and Rb⁺.[20]

Recently, we have focused on using IRMPD spectroscopy[33−37,52] to characterize bare and hydrated Pb²⁺ complexes with amino acids.[1,3] Lead is unique among p-block metals in that it chelates with every amino acid, and the resulting complexes are deprotonated and of the form [Pb(Aa-H)]⁺. Lead chelation also plays an important role in biochemical processes ranging from heme synthesis to hypertension and anemia, making the characterization of these complexes
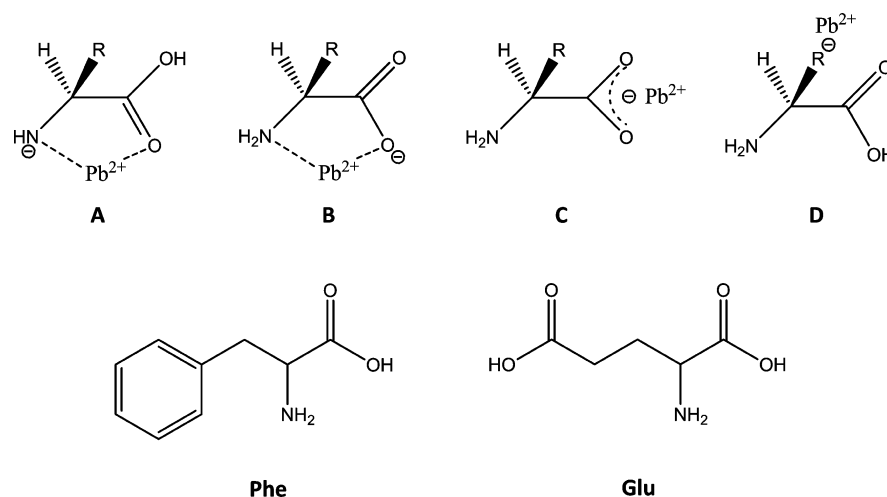
Figure 1. Four principle isomers of Pb^{2+}/amino acid complexes. Skeletal drawings of phenylalanine and glutamic acid are also shown.

physiologically relevant.[38] Previous work with glycine (Gly), alanine (Ala), valine (Val), leucine (Leu), isoleucine (Ile), proline (Pro), and lysine (Lys) demonstrated that [Pb(Aa-H)]$^+$ complexes adopt one of three structures shown in Figure 1: an A-type conformer, which has a charge-solvated Pb^{2+} cation bound between the amine nitrogen and carbonyl oxygen of an N-deprotonated amino acid; a B-type conformer, which is similar to the A-type complex but is O-deprotonated instead, and a C-type complex, where Pb^{2+} forms a salt bridge with an O-deprotonated amino acid. Each of the [Pb(Aa-H)]$^+$ ions involving nonpolar amino acids are A-type complexes, whereas [Pb(Lys-H)]$^+$ adopts the C-type tautomer. These differences in structure were easily determined spectroscopically, the A-type complexes contain a characteristic COO−H stretch around 3560 cm^{-1} that is absent in the spectra of the O-deprotonated B- and C-type ions. The difference between [Pb(Lys-H)]$^+$ and the nonpolar amino acids was attributed to Lys's basic side chain. The ε-amine group presents an additional binding site which preferentially stabilizes the C-type isomer of [Pb(Lys-H)]$^+$.

IRMPD experiments were also carried out on monohydrated [Pb(Aa-H)]$^+$ ions, as solvation plays a critical role in stabilizing zwitterionic amino acids in the condensed phases.[1,3]

The [Pb(Aa-H)H$_2$O]$^+$ ions were generally determined to be the hydrated analogues of the bare complexes where water directly attaches to Pb^{2+}; the attached water remains intact in the B- and C-type ions but donates a proton to the deprotonated amine group in the A-type complexes. Stepwise microsolvation, however, was seen to stabilize higher-energy tautomers different from those observed for the bare complexes.[39−44] For example, hydration causes A-type [Pb-(Pro-H)]$^+$ and C-type [Pb(Lys-H)]$^+$ to isomerize to the C- and B-type [Pb(Aa-H)H$_2$O]$^+$ complexes, respectively. [Pb(Lys-H)H$_2$O]$^+$ is also stabilized by an interaction with Lys's side chain, as is the case for the bare complex.

To better understand the role additional binding sites play in complexes between Pb^{2+} and the conjugate bases of amino acids, this work uses IRMPD spectroscopy to determine the bare and monohydrated gas-phase structures of Pb^{2+} complexes with two amino acids containing functionalized side chains: phenylalanine (Phe), which has a nonpolar side chain containing an aromatic ring and is often considered as the archetypical system for cation−π interactions;[30,31] and glutamic

acid (Glu), whose side chain is polar and contains an acidic γ-carboxyl group capable of binding metal cations.[21]

2. METHODS

2.1. IRMPD Spectroscopy. Gas-phase [Pb(Phe-H)]$^+$ and [Pb(Glu-H)]$^+$ were prepared from 50/50 solutions of methanol (99.8%, ACP Chemicals) and 18.2 MΩ water (Millipore) containing 0.1 mM Pb(NO$_3$)$_2$ (>99%, Fluka Chemika) and either 0.1 mM Phe or Glu (Nutritional Biochemicals). Each solution was electrosprayed using the Apollo II ion source of a Bruker Apex Qe 7 T Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer at a rate of 100 μL/h and allowed to accumulate between 10^{-3} and 1 s; the voltage across the source exit capillary was 294 V. The ions were then selected by a quadrupole mass filter and stored in a hexapole collision cell for 1.0−2.0 s before being accelerated through electrostatic optics and isolated in the ICR cell. The hydrated complexes, [Pb(Phe-H)H$_2$O]$^+$ and [Pb(Glu-H)H$_2$O]$^+$, were produced in the hexapole by minimizing the collision gas (Ar) flow and introducing a modest pressure (10^{-2} mbar) of water vapor through a microvalve separating the cell from a degassed water reservoir.[45]

Once trapped in the ICR cell, the isolated complexes were irradiated by a tunable potassium titanyl phosphate optical parametric oscillator (KTP OPO) pumped collinearly using a Brilliant B Nd:YAG laser (Big Sky Laser) as described previously.[1] The ions were irradiated for 1−2 s at 1.5 cm^{-1} steps between 3200 and 3800 cm^{-1}, and four mass spectra were averaged per interval. The tunable radiation emitted by the OPO is directed toward the ion packet in the ICR cell through a path purged of CO$_2$ and H$_2$O vapor.[1] The cell itself is surrounded by a homemade heating jacket that can be thermalized between 25 and 100 °C. The higher temperatures facilitate dissociation of the complexes and can yield better spectra. The IRMPD spectra were then prepared by plotting the IRMPD yield, which is the base 10 logarithm of the normalized precursor ion intensity, against the wavenumber of the output of the OPO. The reported intensities were not adjusted to account for wavelength-dependent variations in the efficiency of the output pulse.

2.2. Calculations. The minimum energy structures of the [Pb(Aa-H)]$^+$ and [Pb(Aa-H)H$_2$O]$^+$ complexes were determined using the Gaussian 09 software package.[46] A total of 38−

110 unique structures were created for each complex by altering the sites of deprotonation and lead chelation in an attempt to fully explore the stabilization of lead by the amino acid functional groups. Bond and torsional angles were also adjusted to vary the amount of hydrogen bonding or to relieve molecular strain. Geometry optimizations and harmonic frequency calculations were performed on each conformer using B3LYP density functional theory. The LANL2DZ basis set with relativistic core potential were applied to lead;[47] however, 6-31+G(d,p) was used for all other atoms. This method is abbreviated here as B3LYP/6-31+G(d,p) for simplicity, although it should be noted that LANL2DZ is always used for lead. The extracted vibrational modes were scaled by 0.955 to better compare computed infrared spectra with the experimental IRMPD data.[1,3,48] Single point energy calculations were performed on each B3LYP/6-31+G(d,p) optimized conformer using the MP2(full)/6-311++G(2d,2p) method (LANL2DZ was still used for lead). The 298 K enthalpies and Gibbs energies determined by this method are reported as MP2(full)/6-311++G(2d,2p)//B3LYP/6-31+G(d,p). This approach is a popular method for determining the relative stabilities of candidate structures and has been shown to be reasonably accurate for similar complexes.[6,7]

3. RESULTS AND DISCUSSION

3.1. IRMPD Spectroscopy of [Pb(Aa-H)]⁺ and [Pb(Aa-H)H₂O]⁺.

3.1. IRMPD Spectroscopy of $[Pb(Aa-H)]^+$ and $[Pb(Aa-H)H_2O]^+$. The IRMPD spectra of $[Pb(Phe-H)]^+$, $[Pb(Glu-H)]^+$, and their hydrated analogues are shown in Figure 2
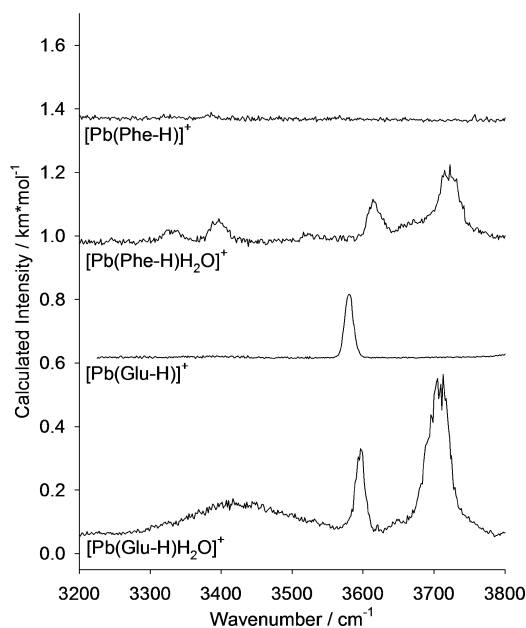

Figure 2. IRMPD spectra of $[Pb(Phe-H)]^+$, $[Pb(Phe-H)H_2O]^+$, $[Pb(Glu-H)]^+$, and $[Pb(Glu-H)H_2O]^+$ in the 3200−3800 cm^{-1} region.

between 3200 and 3800 cm^{-1}. Each complex loses H$_2$O when activated by IRMPD using the KTP OPO. This is similar to previous IRMPD experiments performed on $[Pb(Aa-H)]^+$ complexes containing nonpolar amino acids[1,3] and agrees with recent CID work that establishes H$_2$O loss as the most likely dissociation channel.[49] The hydrated complexes were also seen to have a secondary loss of H$_2$O, attributed to the dissociation of $[Pb(Phe-H)]^+$ and $[Pb(Glu-H)]^+$; this amounts to 50−80% of the first water loss over the O−H stretch region

of $[Pb(Glu-H)H_2O]^+$, and 5% of the first water loss for $[Pb(Phe-H)H_2O]^+$.

The IRMPD spectrum of $[Pb(Glu-H)]^+$ contains a strong absorbance (3580 cm^{-1}) in the O−H stretch region that must be a carboxylic acid O−H stretch. The existence or absence of this band has previously been used to assess whether or not other $[Pb(Aa-H)]^+$ complexes are carboxyl- or amine-deprotonated.[1] However, glutamic acid contains two carboxylic acid moieties so the lone O−H stretch likely means that $[Pb(Glu-H)]^+$ is carboxyl deprotonated at either the terminal or side-chain functional group. Because this carboxylic acid O−H stretch is ∼20 cm^{-1} higher in energy than similar bands observed in the IRMPD spectra of other $[Pb(Aa-H)]^+$ (Aa = Pro, Ala, Val, Leu, and Ile) complexes, it could suggest that the terminal carboxylic acid is deprotonated instead of the γ-carboxyl group. In contrast to $[Pb(Glu-H)]^+$, the IRMPD spectrum of $[Pb(Phe-H)]^+$ contains no bands in the O−H stretch region but has two N−H stretches barely visible at 3386 and 3320 cm^{-1}. Although the N−H bands are very weak, the KTP OPO was observed to be capable of causing $[Pb(Phe-H)]^+$ to dissociate in the ICR cell; hence the lack of a strong O−H stretch means that $[Pb(Phe-H)]^+$ is carboxyl-deprotonated with an intact amine group.

The hydrated complexes have slightly more complex IRMPD spectra. The spectrum of $[Pb(Phe-H)H_2O]^+$ has two absorptions in the O−H stretching region at 3615 and 3720 cm^{-1} as well as two pronounced N−H stretches at 3330 and 3395 cm^{-1}. The IRMPD spectrum of $[Pb(Glu-H)H_2O]^+$ also exhibits two O−H stretches at 3597 and 3710 cm^{-1} and contains a broad band centered around 3415 cm^{-1}. The broad band masks any potential N−H stretches that might be observed.

The O−H stretching bands of both $[Pb(Phe-H)H_2O]^+$ and $[Pb(Glu-H)H_2O]^+$ appear at higher wavenumber positions relative to two strong bands observed in the same region for the $[Pb(Aa-H)H_2O]^+$ ions with nonpolar amino acid side chains (Ala, Val, Leu, Ile).[1,3] It was concluded that for the nonpolar amino acids the addition of water to N-deprotonated $[Pb(Aa-H)]^+$ leads to an observed structure where a proton was transferred from the water to the deprotonated amine group. In the O−H stretch region this resulted in a carboxylic acid O−H stretch observed at 3570−3580 cm^{-1}, and a PbO−H stretch observed at 3680−3690 cm^{-1}. The intensity of the carboxylic acid O−H stretch was also observed to be equal to the intensity of the PbO−H stretch, whereas for $[Pb(Phe-H)H_2O]^+$ and $[Pb(Glu-H)H_2O]^+$ the higher energy band is significantly more intense. Figure S1 (Supporting Information) clearly shows significant differences in position and intensity for the two bands observed in the O−H stretch region in the IRMPD spectra for $[Pb(Ala-H)H_2O]^+$, compared to when the amino acid is either Phe or Glu.

3.2. $[Pb(Phe-H)]^+$ and $[Pb(Phe-H)H_2O]^+$. Four representative lowest-energy computed structures for $[Pb(Phe-H)]^+$ are shown in Figure 3 (additional structures can be found in Figure S2 of the Supporting Information). The most thermodynamically stable structure, Phe-Bi, is a B-type ion where Pb^{2+} is ligated to the NH$_2$ group, a carboxylate oxygen and the phenyl group. This π-interaction significantly stabilizes Phe-Bi. The most favorable B-type ion without the Pb^{2+}-phenyl π-interaction (Phe-Bii) is 58.4 kJ mol^{-1} higher in Gibbs energy at the MP2 level of theory. In general, the conformers that have a Pb^{2+}-phenyl π-interaction (Phe-Ai, -Bi, and -Ci) are significantly more stable than those without it (Phe-Aii, -Bii,
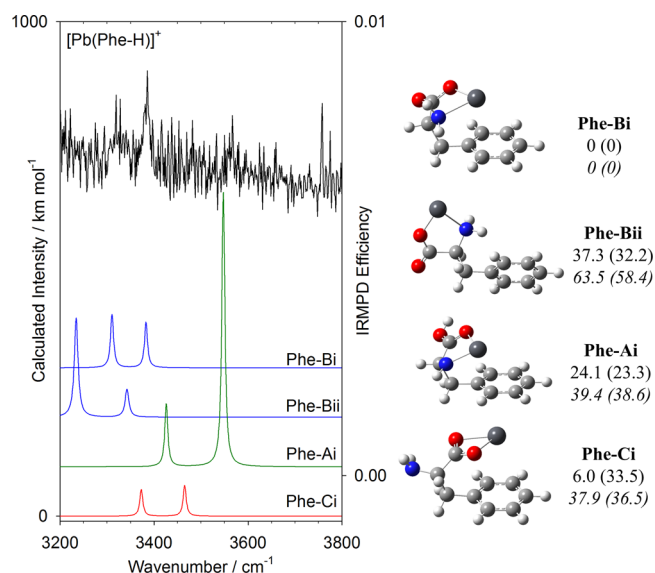
Figure 3. IRMPD spectrum of $[Pb(Phe-H)]^+$ (black) compared with four computed IR spectra. The computed spectra are from the B3LYP/6-31+G(d,p) optimized structures of Phe-Ai, -Bi, -Bii, and -Ci. The 298 K relative enthalpies and Gibbs energies (in parentheses) are provided at the B3LYP/6-31+G(d,p) (top) and MP2(full)/6-311++G(2d,2p) (bottom and italicized) level of theories. In both cases, the LANL2DZ basis set and effective core potential were applied to Pb^{2+}.

and -Cii). It is interesting to note that when the Pb^{2+}-phenyl π-interaction is absent from the structure of $[Pb(Phe-H)]^+$ the energy ordering of the A-, B-, and C-type conformers is similar to that of the other nonpolar $[Pb(Aa-H)]^+$ ions (Aa = Gly, Ala, Val, Leu, and Ile).[1] The stabilizing influence of Phe's side chain can be further demonstrated by comparing the thermochemistries of both the N- and O-deprotonated complexes for $[Pb(Ala-H)]^+$ and $[Pb(Phe-H)]^+$. N-deprotonation of $[Pb(Ala)]^{2+}$ is 7.9 kJ mol^{-1} lower in Gibbs energy than O-deprotonation[1] but is only 0.8 kJ mol^{-1} more favorable for the $[Pb(Phe)]^{2+}$ structure without the Pb^{2+}−phenyl π-interaction. However, the additional stabilization of Pb^{2+} by the side chain in the $[Pb(Phe)]^{2+}$ structure that includes the π-interaction makes O-deprotonation 38.6 kJ mol^{-1} more stable than N-deprotonation. It is also worth noting that the MP2 calculations more strongly favor the π-interaction than the B3LYP calculations. For example, at the B3LYP level of theory, Phe-Bi is 37 kJ mol^{-1} lower in enthalpy than Phe-Bii but at the MP2 level Phe-Bi is further by another ~26 kJ mol^{-1} compared to Phe-Bii. Similar stabilization at the MP2 level of theory of the A and C structures by the Pb^{2+}−π interaction are computed.

In Figure 3 the computed IR spectra of the $[Pb(Phe-H)]^+$ isomers are also compared with the experimental IRMPD spectrum of $[Pb(Phe-H)]^+$. $[Pb(Phe-H)]^+$ must be O-deprotonated because the IRMPD spectrum does not contain a strong O−H stretch band. Instead, two very weak N−H stretches at 3386 and 3320 cm^{-1} are observed, which suggests an intact amine group. This spectroscopically rules out the N-deprotonated conformers, Phe-Ai and Phe-Aii, because both have a COO−H stretch expected at about 3560 cm^{-1}. Phe-Bi is by far the most thermodynamically favorable structure and is supported by the IRMPD spectrum. Phe-Bii, -Ci, and -Cii are 36.5−98.5 kJ mol^{-1} higher in Gibbs energy than Phe-Bi and could be ruled out on energetic grounds alone; however, calculated spectra for these isomers also predict N−H stretches at higher or lower wavenumber positions than the two that

were observed. Gas-phase $[Pb(Phe-H)]^+$ is, therefore, most probably a B-type ion where Pb^{2+} is stabilized by the aromatic ring on the side chain.

Three $[Pb(Phe-H)H_2O]^+$ isomers are shown in Figure 4. With water binding directly to Pb^{2+} in each structure, it is clear
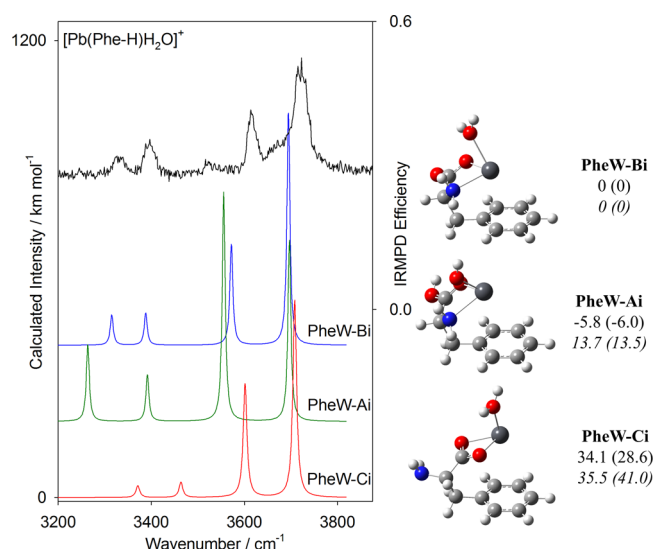

Figure 4. IRMPD spectrum of $[Pb(Phe-H)H_2O]^+$ (black) compared with three computed IR spectra. The computed spectra are from the B3LYP/6-31+G(d,p) optimized structures of PheW-Ai, -Bi, and -Ci. The 298 K relative enthalpies and Gibbs energies (in parentheses) are provided at the B3LYP/6-31+G(d,p) (top) and MP2(full)/6-311++G(2d,2p) (bottom and italicized) level of theories. In both cases, the LANL2DZ basis set and effective core potential were applied to Pb^{2+}.

that lead displays a four-coordinate, hemidirected geometry due to the lone pair of electrons which are in orbitals with p-type character.[50] The B- and C- type ions are simply the hydrated analogues of the $[Pb(Phe-H)]^+$ structures; however, like the other nonpolar amino acids, the lowest energy A-type ion is the result of a subsequent proton transfer from the attached water to the amine group. The Pb^{2+}−π interaction with the side chain of Phe significantly stabilizes the $[Pb(Phe-H)H_2O]^+$ complex by between 24.2 and 52.8 kJ mol^{-1} (Figures 4 and S2, Supporting Information), similar to the bare complexes. The most thermochemically stable structure is the B-type ion, which is ~13 kJ mol^{-1} more stable than the A-type structure at the MP2 level of theory. However, the B3LYP calculations actually favor the A-type structure by about 6 kJ mol^{-1}. The C-type complex, PheW-Ci, is calculated to be significantly less stable than PheW-Bi and PheW-Ai at both levels of theory.

The computed IR spectra of each $[Pb(Phe-H)H_2O]^+$ isomer are also compared with the IRMPD spectrum of $[Pb(Phe-H)H_2O]^+$ in Figure 4. The experimental spectrum contains two features at 3330 and 3395 cm^{-1}, which are due to the symmetric and asymmetric NH_2 stretches. The positions of the N−H stretching bands are well reproduced by the calculated spectrum of PheW-Bi; the predicted spectrum for PheW-Ai shows a significantly larger separation of the NH_2 symmetric and antisymmetric stretches.

The experimental spectrum also has two strong features at 3615 and 3720 cm^{-1}, which are assigned to O−H stretching vibrations. As was discussed above, and as can be seen in Figure S1 (Supporting Information), the shape and positions of the O−H stretching bands in this region are significantly different

for [Pb(Phe-H)H$_2$O]$^+$ (and [Pb(Glu-H)H$_2$O]$^+$) than for the complexes of other amino acids with nonpolar side chains.[1] For [Pb(Ala-H)H$_2$O]$^+$, the bands at 3569 and 3688 cm^{-1} were assigned to the carboxylic acid O—H stretch and the PbO—H stretch, respectively. Furthermore, the two bands were observed to have equal intensity, in agreement with the computed spectrum. The bands for [Pb(Phe-H)H$_2$O]$^+$ are significantly to the blue of those for [Pb(Ala-H)H$_2$O]$^+$, and the 3615 cm^{-1} band is much weaker than the 3720 cm^{-1} band. The observed intensity ratio is also in agreement with the predicted spectrum for PheW-Bi. The complexes that are not stabilized by a Pb^{2+}—phenyl π-interaction are too high in energy to have a significant population in the gas phase, and the same is true for PheW-Ci, which is also eliminated spectroscopically on the basis of its higher energy N—H stretches. [Pb(Phe-H)H$_2$O]$^+$ is best described as a B-type complex in the gas phase, with water directly bound to Pb^{2+} and the 3615 and 3720 cm^{-1} bands are assigned to the symmetric and asymmetric stretching vibrations, respectively, of the water ligand.

3.3. [Pb(Glu-H)]$^+$ and [Pb(Glu-H)H$_2$O]$^+$. Six [Pb(Glu-H)]$^+$ isomers are shown in Figure 5 and an additional ten

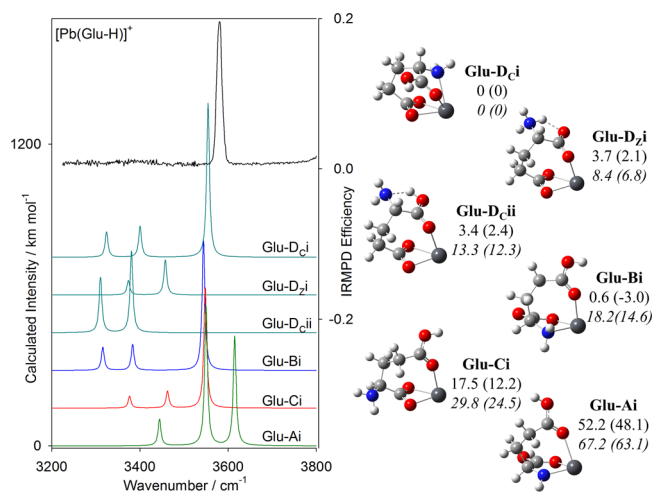**Figure 5.** IRMPD spectrum of [Pb(Glu-H)]$^+$ (black) compared with six computed IR spectra. The computed spectra are from the B3LYP/6-31+G(d,p) optimized structures of Glu-Ai, -Bi, -Ci, -D$_Z$i, -D$_C$i, and -D$_C$ii. The 298 K relative enthalpies and Gibbs energies (in parentheses) are provided at the B3LYP/6-31+G(d,p) (top) and MP2(full)/6-311++G(2d,2p) (bottom and italicized) level of theories. Note that the LANL2DZ basis set and effective core potential were applied to Pb^{2+} for both levels of calculation.

structures are included in Figure S4 of the Supporting Information. The most stable A-, B-, and C-type complexes exhibit an additional interaction between Pb^{2+} and the γ-carboxyl side chain. This Pb^{2+}—side chain interaction in Glu-Ai, -Bi, and -Ci stabilizes these complexes by between 29 and 86 kJ mol^{-1} with respect to the structures where the side chain has no intramolecular noncovalent interaction (Glu-Aiv, -Bii, and -Cii). Furthermore, the relative stabilities of the three complexes are similar to those seen for [Pb(Phe-H)]$^+$; Glu-Bi is more stable than Glu-Ci and Glu-Ai by 9.8 and 48.5 kJ mol^{-1} in Gibbs energy, respectively. However, unlike [Pb(Phe-H)]$^+$, [Pb(Glu-H)]$^+$ is also capable of producing a D-type complex where Pb^{2+} forms a salt bridge with the deprotonated γ-carboxyl group of the side chain. Pb^{2+} can be further stabilized by the terminal amine and/or carboxyl groups, which will either be zwitterionic

(D$_Z$) or canonical (D$_C$). The lowest energy D-type structure, and the lowest energy structure overall at the MP2 level of theory, is Glu-D$_C$i, which is coordinated to both side chain carboxylate oxygens as well as the carbonyl oxygen of the carboxyl group as well as the amine group. Two other low-energy D-type structures are also shown in Figure 5.

The computed IR spectra for six [Pb(Glu-H)]$^+$ structures are also compared with the IRMPD spectrum of [Pb(Glu-H)]$^+$ in Figure 5. The experimental spectrum contains one absorbance at 3580 cm^{-1} designated as a COO—H stretch, but no N—H stretches were observed. The lack of N—H stretches may be due to the presence of an intramolecular hydrogen bond but could also imply that the absorbances are too weak to see, as was previously observed in the case of [Pb(Gly-H)]$^+$.[3] The predicted spectrum for the lowest energy structure, Glu-D$_C$i, is consistent with the observed strong COO—H stretch. Glu-Ai is predicted to have two COO—H stretches and therefore can be ruled out spectroscopically. Both Glu-D$_Z$i and -D$_C$ii do not have a strong COO—H stretch because there is no carboxyl group in Glu-D$_Z$i and the —OH is hydrogen bonded to the amino group in Glu-D$_C$ii. Neither of these structures can be ruled out spectroscopically; however, they cannot account for the strong COO—H stretching absorption. There are three other D-type structures, DCiii, DCiv, and DCv (Figure S4, Supporting Information) that cannot be ruled out spectroscopically (Figure S5, Supporting Information), but which are all more than 20 kJ mol^{-1} higher in energy. Glu-Bi and Glu-Ci are calculated to be 14.6 and 24.5 kJ mol^{-1}, respectively, higher in energy than the lowest energy structure. Though neither can be ruled out spectroscopically, on the basis of the calculated thermochemistry, they are not expected to be major contributors to the spectrum.

Eight isomers of [Pb(Glu-H)H$_2$O]$^+$ are collected in Figure 6 (ten more are in Figure S6, Supporting Information). As has

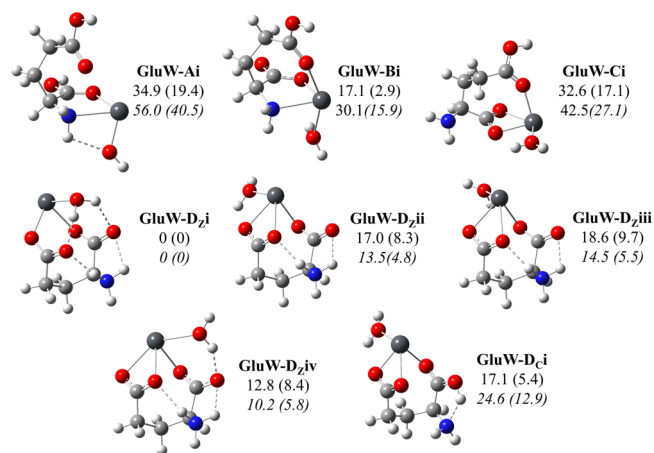**Figure 6.** B3LYP/6-31+G(d,p) optimized structures of [Pb(Glu-H)H$_2$O]$^+$. The 298 K relative enthalpies and Gibbs energies (in parentheses) are provided at the B3LYP/6-31+G(d,p) (top) and MP2(full)/6-311++G(2d,2p) (bottom and italicized) level of theories. Note that the LANL2DZ basis set and effective core potential were applied to Pb^{2+} for both levels of calculation.

been observed in previous works, the most stable hydrated [Pb(Aa-H)]$^+$ complexes have water attached directly to Pb^{2+}. GluW-Bi and GluW-Ci are simply the hydrated analogues of Glu-Bi and Glu-Ci and can be ruled out as contributing to the experimental IRMPD spectrum because three bands in the

IRMPD spectrum are expected, a COO−H stretch and two water O−H stretching absorptions (Figure S7, Supporting Information). They are also 16 and 27 kJ mol^{-1} higher in energy than the lowest energy structure. Glu-Ai is 41 kJ mol^{-1} higher in Gibbs energy than the lowest energy structure and is also not expected to be a contributor to the IRMPD spectrum. As was discussed in section 3.1, the observed bands in the IRMPD spectrum of $[Pb(Glu-H)H_2O]^+$ are higher in energy and not of the same intensity as those observed previously for other hydrated A-type structures.[1,3] Furthermore, because the predicted spectrum (Figure S7, Supporting Information) has three bands in the O−H stretch region, two COO−H and one PbO−H, it is unlikely that the ion(s) responsible for the present IRMPD spectrum have A-type structures.

The four lowest energy D-type structures are all zwitterionic and separated by less than 6 kJ mol^{-1}. Like $[Pb(Phe-H)H_2O]^+$ these structures are hemidirected; the lone pair on Pb^{2+} repels the ligands. The lowest energy structure, GluW-D$_Z$i, has lead bound to one oxygen on each carboxylate and to water. In this structure water also forms two hydrogen bonds, one with a carbonyl on each of the carboxylate groups. The hydrogen bond strengths are quite different, as is evidenced by the bond lengths, one is 1.770 Å, and the other is 2.099 Å. There are also two hydrogen bonds with the same carbonyl oxygens, but with two N−H bonds acting as donors. The two N−H--O hydrogen bonds have similarly different strengths. The predicted IR spectrum for this structure is compared with the experimental spectrum in Figure 7. Due to hydrogen bonding, it has no free
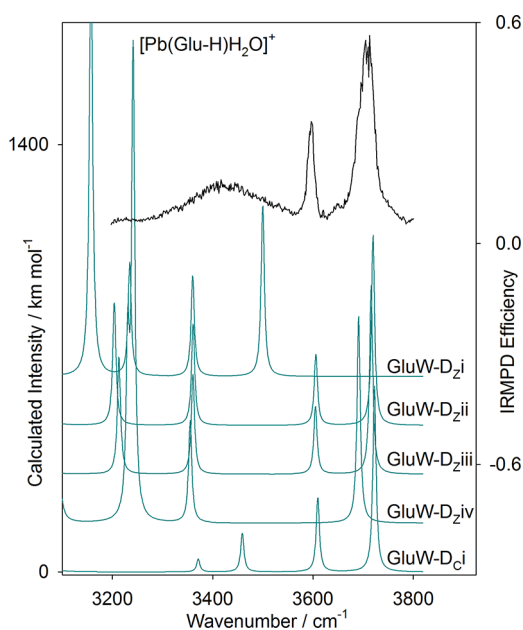

Figure 7. IRMPD spectrum of $[Pb(Glu-H)H_2O]^+$ (black) compared with five computed IR spectra. The computed spectra are from the B3LYP/6-31+G(d,p) optimized structures of GluW-D$_Z$i, -D$_Z$ii, -D$_Z$iii, -D$_Z$iv, and -D$_C$i shown in Figure 6.

O−H stretching vibrations and therefore cannot account for the two higher energy bands. However, the broad band below 3600 cm^{-1} is similar to other hydrogen bonded features observed previously.[19,48,51] The weaker O−H--O stretch is the strong band expected at 3500 cm^{-1}. The stronger O−H--O stretch is predicted to be at 3157 cm^{-1} whereas the N−H--O stretches are predicted to occur at 3234 and 2940 cm^{-1}. Based

on the inability of these harmonic calculations to accurately predict positions of hydrogen bonded stretching vibrations of this type, it is impossible to say which one(s) are being observed in this spectrum. This broad feature is, however, consistent with what is expected for the lowest-energy structure, GluW-D$_Z$i.

The next two lowest energy D$_Z$-type ions each have water forming only one very weak intramolecular hydrogen bond and have O−H--O hydrogen bond lengths greater than 2.45 Å. These structures are only about 5 kJ mol^{-1} higher in Gibbs energy at the MP2 level of theory than the lowest energy structure. The positions of the symmetric and asymmetric O−H stretches of the water ligand are predicted to occur in the same position as those observed, and with a similar intensity ratio. The fourth D$_Z$-type structure, GluW-D$_Z$iv, is similar in energy to GluW-D$_Z$iii and -D$_Z$ii. In this structure, the water molecule has a strong hydrogen bond with the carboxylate oxygen that does not complex with Pb, and the O−H--O distance is 1.746 Å. This structure cannot be ruled out, but due to the absence of the symmetric O−H stretch due to the hydrogen bond in the O−H stretch region, it cannot alone account for the experimental spectrum.

The lowest energy D$_C$-type structure is predicted to be about 13 kJ mol^{-1} higher in energy than the global minimum structure and has the carboxylate O−H strongly hydrogen bonded to the amine group; the O−H--N bond is 1.805 Å. This higher energy structure can also account for the two bands in the N−H stretching region. The computed IR spectra for other higher-energy structures are compared with the experimental spectrum in Figure S7 (Supporting Information). Some cannot be ruled out spectroscopically, but their higher relative energies indicate that they will be minor contributors in the gas phase. One final note, the lowest-energy D-type ions, deprotonated at the side chain, were determined to account for the single O−H stretch observed in the IRMPD spectrum of $[Pb(Glu-H)]^+$. The IRMPD spectrum of $[Pb(Glu-H)H_2O]^+$ is also accounted for by D-type ions, but for the hydrated ion, more than one structure is necessary to account for the experimental spectrum and the structures identified are all within 6 kJ mol^{-1} of the lowest-energy structure.

4. CONCLUSIONS

IRMPD spectroscopy and electronic structure calculations were used to determine the structures of bare and hydrated $[Pb(Phe-H)]^+$ and $[Pb(Glu-H)]^+$. The IRMPD spectrum of $[Pb(Phe-H)]^+$ is consistent with that of a B-type ion where Pb^{2+} is chelated between the amine nitrogen and deprotonated carboxyl group, and where there is an additional interaction between Pb^{2+} and the aromatic ring on Phe's side chain. $[Pb(Phe-H)H_2O]^+$ is simply the hydrated version of $[Pb(Phe-H)]^+$ where water binds directly to Pb^{2+}.

The IRMPD spectrum for $[Pb(Glu-H)]^+$ is consistent with the lowest-energy canonical D-type structure in which the side chain carboxyl group is deprotonated. The lowest-energy zwitterionic D-type structure, where Pb^{2+} forms a salt bridge with the deprotonated γ-carboxyl group and is further stabilized by Glu's terminal carbonyl oxygen, is only 6.8 kJ mol^{-1} higher in Gibbs energy and cannot be ruled out. $[Pb(Glu-H)H_2O]^+$ exists as at least two, but probably four different low-energy zwitterionic D-type isomers. The lowest-energy structure, where the water participates as a hydrogen bond donor to two different carbonlyl oxygens, accounts for the broad feature below 3600 cm^{-1} in the IRMPD spectrum. The three other

structures account for the two observed symmetric and antisymmetric O−H stretches, which arise from the ligated water molecule.

The amino acid side chain clearly plays a role in stabilizing higher energy tautomers. When the side-chain interaction is removed, calculations predict that $[Pb(Phe-H)]^+$ and $[Pb(Glu-H)]^+$ should be A-type ions. This is similar to the IRMPD-determined structures of several $[Pb(Aa-H)]^+$ and $[Pb(Aa-H)H_2O]^+$ complexes with nonpolar side chains, which generally adopt A-type structures.[1,3] The structures of lead-cationized amino acids are therefore extremely sensitive to the functionalization of the amino acid, as might be expected. Furthermore, the calculations show that the hydrating water in $[Pb(Phe-H)H_2O]^+$ and $[Pb(Glu-H)H_2O]^+$ is bound in the same hemisphere of Pb^{2+} as the deprotonated amino acid. The structure around Pb is found to be hemidirected in that all four ligands are bound to one hemisphere of the complex due to the p character of the orbital containing the lone pair of electrons.[50]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Additional computed structures and IR spectra for the bare and hydrated Phe and Glu complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

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