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# Infrared Multiple Photon Dissociation Spectroscopy of Potassiated Proline

**Miriam K. Drayss,[†] Dirk Blunk,[†] Jos Oomens,[‡] and Mathias Schäfer*,[†]**

*Institute for Organic Chemistry, University Cologne, Greinstraße 4, 50939 Köln, Germany, and*
*FOM-Institute for Plasmaphysics, Rijnhuizen, Edisonbaan 14, NL-3439 MN Nieuwegein, The Netherlands*

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The structure of proline in [proline + K]$^+$ has been investigated in the gas phase using high level DFT and MP2 calculations and infrared photo dissociation spectroscopy with a free electron laser (FELIX). The respective FELIX spectrum of [proline + K]$^+$ matches convincingly the calculated spectra of two structurally closely related and nearly iso-energetic zwitterionic salt bridge (SB) structures. An additional unresolved band at ~1725 cm$^{-1}$ matching with the characteristic CO stretching mode of charge solvation (CS) structures points toward the presence of a minor population of these conformers of proline in [proline + K]$^+$. However, theory predicts a significant energy gap of 18.9 kJmol$^{-1}$ (B3LYP/6-311++G(2d,2p)) or 15.6 kJ mol$^{-1}$ (MP2) between the lowest CS conformer of proline and the clearly favored SB structure.

All natural amino acids, among which proline plays a special role due to its cyclic structure, form zwitterions, when dissolved in polar media, e.g., water. In contrast, molecular ions of amino acids in the gas phase are lacking the stabilization of the solvation shell. Hence, conservation of zwitterionic structures in the gas phase is limited to amino acids with a pronounced gas-phase basicity, e.g., arginine, lysine, and proline, and large polarizable metal ions, e.g., K$^+$, Rb$^+$, and Cs$^+$, that strongly stabilize the formation of an internal salt bridge (SB).[1−4] It should be noted that SB structures of amino acid molecules can also be stabilized by the presence of neutral polar molecules ($H_2O$)[5,6] or the formation of oligomer cluster ions, e.g., the serine octamer.[7]

For the structure elucidation of gas-phase molecular ions of proline with alkali metal ions collision induced dissociation[4,8−11] and infrared photo dissociation spectroscopy with a wavelength tunable free electron laser (FEL)[12] have been successfully applied. Structure assignments are in all cases achieved by correlation to ion structures identified by high level of theory DFT or ab initio calculations.[13,14]

Extensive studies of alkali metal cationized arginine, lysine, serine, and threonine with photo dissociation spectroscopy provided ample evidence that zwitterionic structures of the amino acids are explicitly favored with increasing size of the alkali metal ion.[2,3,15,16] It turned out that, depending on the amino acid, the transition from CS to SB structures was observed for arginine with sodium, for *N*-methyl lysine with potassium, and for Ser and Thr with rubidium in the respective [amino acid + alkali metal]$^+$ molecular ion.[2,3,15,16] However, the photo dissociation spectrum of sodiated proline presented by Kapota et al. matched the calculated spectrum of the most stable proline SB structure (B3LYP with the 6-31G* basis set), when a scaling factor of 0.98 was applied.[12]

**TABLE 1: Relative Energies (ΔH) Including ZPE Corrections of the Gas-Phase Conformers Relevant for [proline + K]$^+$**

| conformer | B3LYP [kJ mol$^{-1}$] | MP2 [kJ mol$^{-1}$] |
|---|---|---|
| SB1 | 0 | 5.5 |
| SB1a | 4.3 | 0 |
| CS1 | 18.9 | 15.6 |
| CS1a | 20.5 | 17.6 |
| CS2 | 26.0 | 22.3 |

In the present work, the molecular ion of proline with potassium has been investigated using infrared multiple photon dissociation (IRMPD) spectroscopy and theoretical calculations.[17] A wavelength tunable free electron laser was used as the source of infrared radiation for these experiments.[2,3] Arbitrary CS and SB structures of [proline + K]$^+$ were chosen as input structures for a mixed low mode/Monte Carlo multiple minimum conformation search using MacroModel 8.1 (Schroedinger Inc., Portland, OR). 5000 LCMM steps were performed, each followed by minimization using the Merck Molecular Force Field (MMFF94s). Candidate structures with low MMFF energy were selected for subsequent higher level calculations. These were performed on the DFT and MP2 level of theory as implemented in Gaussian 03 applying the 6-311++G(2d,2p) basis set on all atoms.[18] Harmonic frequency calculations verified that all structures corresponded to local minima on the potential energy surface. Optimized energies including zero point energy (ZPE) corrections of the B3LYP and MP2 calculations are given in Table 1. As shown by Russo et al.[13] each isomer exists as a conformer pair differing by the puckering of the five-membered ring. Both the DFT and MP2 calculations predict a SB structure to be the energetic minimum. Figure 1 shows the most stable structures of [proline + K]$^+$. The energetically favored SB1 structure exhibits a nearly linear salt bridge, which obviously provides optimum stabilization of the charges (Figure 1).[8,11] A complete list of all [proline + K]$^+$ structures identified with their corresponding energies are given in Figure 1S and Table S1 in the Supporting Information.

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* To whom correspondence should be addressed. E-mail: mathias.schaefer@uni-koeln.de.
[†] University of Cologne.
[‡] FOM Institute for Plasma Physics "Rijnhuizen".

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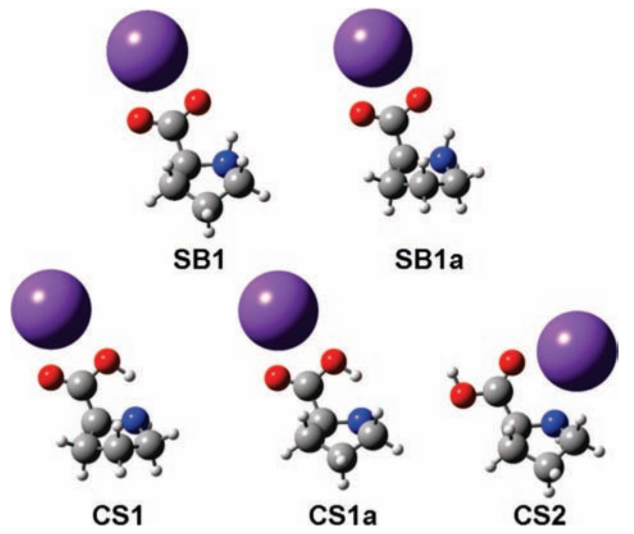

**Figure 1.** Most stable structures of [proline + K]$^+$ complexes calculated at the B3LYP/6-311++G(2d,2p) level of theory. Van der Waals radii are considered for the presentation of the structures (sodium: purple, oxygen: red, nitrogen: blue; carbon: gray, hydrogen: light gray).

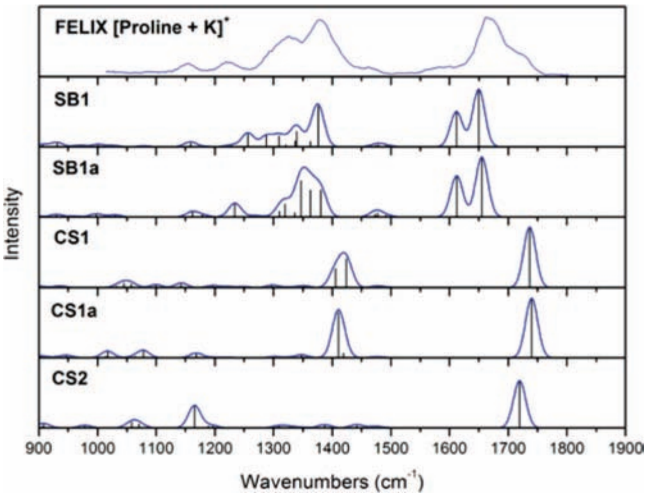

**Figure 2.** FELIX spectrum of [proline + K$^+$] and calculated spectra of the five most stable isomers (SB1, SB1a, CS1, CS1a, and CS2).

Frequencies are scaled by a uniform factor of 0.98 found to be best suited for the level of theory applied.[19] For comparison to experiment, calculated vibration frequencies are broadened using a 20 cm$^{-1}$ full width at half-maximum Gaussian line shape.

The FELIX-spectrum was recorded over the wavelength range 1000−1900 cm$^{-1}$. The characteristic CO stretching mode which is very indicative for the presence of either SB or CS structures is expected to be located in the examined IR region.[20,21] For SB structures, this vibration is located in the region of around 1650−1700 cm$^{-1}$, for CS structures between 1700 and 1800 cm$^{-1}$. Figure 2 shows the experimental FELIX-spectrum of [proline + K]$^+$ and the calculated spectra of five low-energy conformers.

The FELIX spectrum exhibits a broad band around 1670 cm$^{-1}$, which correlates very well with the expected position of the characteristic CO stretching mode of the calculated SB structures. The conformers SB1 and SB1a are structurally closely related, only differing in the folding of the five-membered pyrrolidine ring. Hence, both IR-spectra are almost identical and can not be distinguished experimentally. B3LYP calculations predict SB1 to be slightly more stable than the respective SB1a structure, whereas MP2 calculations predict an inverted ordering (Table 1).

The less intense band around 1590 cm$^{-1}$, corresponding to the $NH_2$ scissoring mode, calculated at 1620 cm$^{-1}$, also supports our assignment. Obviously, the signal intensities of the recorded FELIX spectrum differ from the intensities predicted by theory. Such discrepancies were experienced before and different reasons are noted to explain the significant deviations.[20,22,23] Despite its relatively low intensity the band at 1475 cm$^{-1}$ matches well to that calculated at 1470 cm$^{-1}$ for the SB conformers. The wavenumber region 1250−1420 cm$^{-1}$ exhibits a clear similarity between the recorded and the calculated spectra for the SB structures, including the intense band at 1380 cm$^{-1}$. The measured spectrum exhibits a low-intensity band in the region of the characteristic CO stretches at ~1725 cm$^{-1}$ which is not predicted for the SB structures of proline. The calculated spectra of the lowest energy CS conformer CS1 and its bended ring isomer CS1a show a band at 1735 cm$^{-1}$. This overlap hints toward the presence of CS conformers of potassiated proline, despite the significant energy gap (≥16 kJ mol$^{-1}$) predicted by both DFT and MP2 calculations (see Table 1). No other bands characteristic for the CS conformers can be identified selectively, since these vibrations coincide with multiple absorption bands of zwitterionic SB structures.

In summary, the FELIX spectrum of [proline + K]$^+$ correlates convincingly with the calculated spectrum of the zwitterionic structure identified to be the most stable conformer (SB1) of proline. However, the unresolved band found at ~1725 cm$^{-1}$ which is observed in both photo dissociation spectra of either sodiated[12] or potassiated proline lead to different structure assignments. In the latter case we propose the presence of a mixture of SB and CS structures of proline conformers in [proline + K]$^+$, whereas Kapota et al. exclusively postulate a SB conformer for proline in [proline + Na]$^+$.[12] Obviously, a proper scaling of the experimental data is crucial for correct structure assignments. A conclusive answer to this question awaits either the complete examination of all alkali metal complex ions of proline with photo dissociation spectroscopy or other experimental strategies, e.g., by ion mobility-MS.

The results presented in this communication are integral part of a systematic and multidimensional study of gas-phase ion structures of a series of synthetic amino acid derivatives, which is currently conducted.

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**Supporting Information Available:** Figure 1S and Table 1S. This material is available free of charge via the Internet at http://pubs.acs.org.

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