

# Zwitterionization of Glycine at Outer Space Conditions due to Microhydration by Six Water Molecules

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**ABSTRACT:** We investigate glycine microsolvation with water molecules, mimicking astrophysical conditions in our laboratory by embedding these clusters in helium nanodroplets at 0.37 K. We recorded mass selective infrared spectra in the frequency range 1500-1800  $\text{cm}^{-1}$  where two bands centered at 1630 and 1724  $\text{cm}^{-1}$  were observed. By comparison with the extensive accompanying calculations, the band at 1630  $\text{cm}^{-1}$  was assigned to the  $\text{COO}^-$  asymmetric stretching mode of the zwitterion and the band at 1724  $\text{cm}^{-1}$  was assigned to red-shifted C=O stretch within neutral clusters. We show that zwitterion formation of amino acids readily occurs with only few water molecules available even under extreme conditions.

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The three-dimensional structure, function and dynamics of peptides and proteins are almost exclusively governed by non-covalent interactions [1-4]. Despite the importance of amino acids as the building blocks of life, the question of whether the smallest amino acid glycine was formed on primitive Earth or was delivered to our home planet remains to date intriguing, yet unanswered [5-8]. Detection of amino acids in meteorites and comets supports the hypothesis that impact of these extra-terrestrial bodies on infant earth could have brought in prebiotic building blocks, including amino acids that ignited primordial evolution [9-16]. Although glycine precursors, such as  $\text{CH}_3\text{NH}_2$ ,  $\text{NH}_2\text{CHO}$ , and  $\text{CH}_3\text{CN}$ , have been detected in the interstellar medium (ISM), the presence of glycine in ISM remains inconclusive and thus controversial [17-20]. Glycine exists in vacuum in its non-ionic (or neutral) form,  $\text{NH}_2\text{CH}_2\text{COOH}$ , but its hydrophilic amino and carboxyl groups can strongly interact with water via hydrogen bonding. In aqueous solutions at ambient conditions, this leads to proton transfer and, thus, to its well-known zwitterionic form,  $^+\text{NH}_3\text{CH}_2\text{COO}^-$ . The addition of a single water molecule to glycine was found to be not sufficient to observe charge separation in helium nanodroplets [21].

At such ultra-cold conditions, a distinctive feature of chemical reactions is their aggregation-induced character due to growing the cluster in a stepwise manner by adding the molecules one-by-one [22,23]. The corresponding mechanism leading to proton transfer, e.g. for HCl, greatly

differs from that of the very same reaction at high temperatures due to thermal activation at constant cluster size [24,25]. Thus, not only the reaction pathway but also the required number of water molecules may be different at ultra-low compared to ambient temperatures [22-25]. Moreover, in case of glycine-water clusters, the energy differences between non-ionic and zwitterionic species are very small in the relevant cluster size regime [26], which hampers computational predictions. For decades the nagging but open question was how many water molecules are required to invoke zwitterionization, proposals ranging from only three up to nine water molecules [26,27,28].

The spectroscopic fingerprints of glycine [29] are expected to differ significantly depending on its dissociation state. Therefore, unfolding the chemistry of glycine in the abundant interstellar cold ( $\sim 10\text{-}20\text{ K}$ ) water ices holds the key for its detection in ISM. Prior to searches in space, however, laboratory measurements need to answer the question of whether glycine is bound to remain neutral, or if it can zwitterionize at the extreme conditions of the chemical habitats as provided by icy comets or extra-terrestrial meteorites [30,31].

Previous studies suggested that the interaction with photons (UV, X,  $\gamma$ , or cosmic rays) or impinging particles (e.g. ions and protons) followed by thermalization at these very low temperatures triggers the formation of complex organic molecules and amino acids on astrophysical ice surfaces found in dense cold

molecular clouds, meteorites or cometary bodies [32,33]. Experiments mimicking the conditions of icy mantles revealed that glycine itself can form on ices containing CO<sub>2</sub>, NH<sub>3</sub>, CH<sub>3</sub>OH, H<sub>2</sub>O, CO, and HCN [34,35]. Yet, the molecular mechanism and even the form in which glycine molecules exists in space (i.e. non-ionic or zwitterionic) is still under debate [36,37] since detection in the gas-phase interstellar medium has been unsuccessful till date [18,20].

In our present study we put a spotlight on the question of whether glycine – once it is formed under extreme astrophysical conditions – will be present in non-ionic or zwitterionic forms, or both. To mimic such very low temperatures in the realm of laboratory spectroscopy, we used superfluid helium nanodroplets at 0.37 K as ultracold nanotraps to embed non-ionic glycine, which was sublimed by heating in an oven. Subsequently, single water molecules were added to the helium nanodroplets in a second pickup chamber under controlled water vapor pressure to adjust the water content at the molecular level.

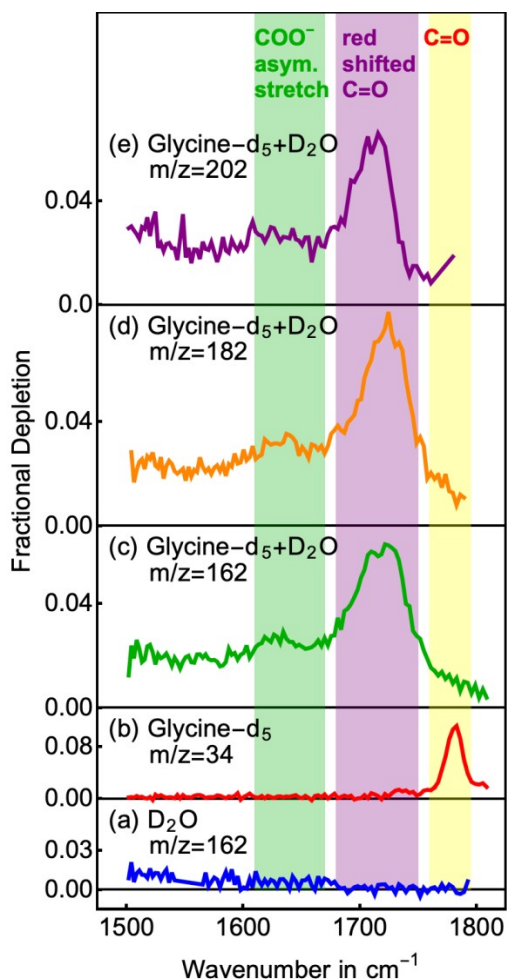
Using such a cryolab approach, we report in what follows an infrared spectroscopic study of glycine-water systems isolated in helium droplets. The details of the experiments are described in SI Section 1 as well as in preceding literature [38]. Our previous study [21] of glycine monomer and glycine-H<sub>2</sub>O covered the frequency range 1000–1450 cm<sup>-1</sup>. We are now using the ultrabright FELIX radiation source [39], allowing us to record depletion spectra in the frequency range between 1500–1800 cm<sup>-1</sup>. Importantly, this frequency range covers both, the COO<sup>-</sup> asymmetric stretching mode, which serves us as the unambiguous fingerprint of the onset of zwitterion formation, as well as the C=O stretch of the neutral COOH state [40,41]. To avoid a possible overlap with the well-known bending mode of water clusters (at 1600–1650 cm<sup>-1</sup>) as well as with the NH bending resonance (~1600 cm<sup>-1</sup>) of the NH<sub>3</sub><sup>+</sup> group, we switched to fully deuterated (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters [42–44]. This provides us a clean spectroscopic window to unambiguously probe the existence of zwitterions under outer space conditions.

First, we recorded the individual depletion IR spectra of the pure components, D<sub>2</sub>O and glycine-d<sub>5</sub>. The partial pressure of D<sub>2</sub>O was set to 2 × 10<sup>-5</sup> mbar, corresponding to preferred pickup of more than six water molecules (see SI). Under these conditions, the IR spectrum shows no absorption in the 1500–1800 cm<sup>-1</sup> frequency region, taken at a mass channel attributed to (D<sub>2</sub>O)<sub>n≥9</sub> cluster fragments (m/z = 162, (D<sub>2</sub>O)<sub>8</sub>D<sup>+</sup>) and also for smaller water clusters, no absorption is expected in this frequency range (Figure 1a). For glycine-d<sub>5</sub>, the temperature of the sublimation oven was optimized to 95°C. At this temperature droplets preferentially pickup single glycine molecules, as was confirmed by a systematic variation of pick-up

pressure via temperature changes in the oven (see SI). In this way, a spectrum of pure glycine-d<sub>5</sub> was recorded at mass channel m/z = 34, corresponding to the CD<sub>2</sub>ND<sub>2</sub><sup>+</sup> mass fragment. The spectrum features a single band at 1782 cm<sup>-1</sup>, which is assigned to the C=O stretch of the carboxylic group (COOH) of monomeric non-ionic glycine-d<sub>5</sub> (Figure 1b).

To prepare micro-hydrated (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters, helium droplets were subsequently doped with glycine-d<sub>5</sub> and D<sub>2</sub>O at a partial pressure of 2 × 10<sup>-5</sup> mbar. The IR spectrum was recorded at the mass channels m/z = 162, 182 and 202, which are expected to have major contributions from clusters of glycine with five, six and seven water molecules, yielding the fragments (glycine-d<sub>5</sub>)(D<sub>2</sub>O)<sub>4</sub>D<sup>+</sup>, (glycine-d<sub>5</sub>)(D<sub>2</sub>O)<sub>5</sub>D<sup>+</sup> and (glycine-d<sub>5</sub>)(D<sub>2</sub>O)<sub>6</sub>D<sup>+</sup> upon ionization, respectively. However, as fragmentation upon ionization leads to loss of water molecules, every mass channel and hence the depletion spectrum will always in addition contain contributions from clusters with a larger number of water molecules (see SI Section 2). Therefore, mass selective measurements provide information on the minimum number of water involved. However, for an unambiguous determination of cluster size pressure dependent intensity measurements, pick-up depletion curves are mandatory.

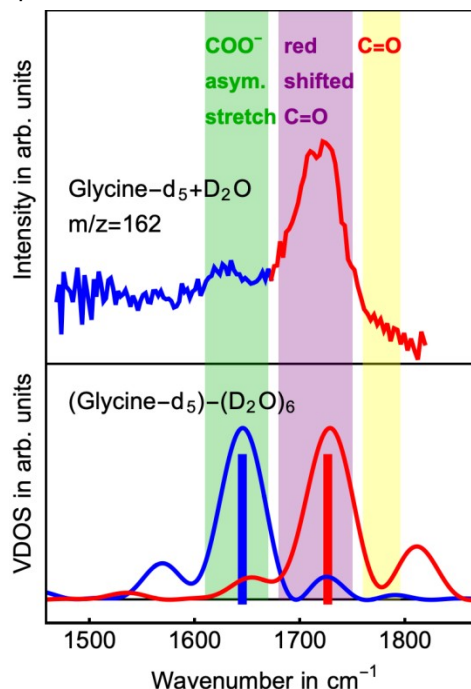
We want to note that the spectra of all three recorded mass channels contain two bands centered at 1630 and 1724 cm<sup>-1</sup> (Figure 1c-e). As these features are not observed in either the D<sub>2</sub>O or the glycine-d<sub>5</sub> spectrum, we assign the bands to micro-hydrated (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters. Further assignment is made based on a comparison of the experimental spectra to predicted vibrational resonances of (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters, which include anharmonic shifts and mode couplings on top of the harmonic estimates as obtained from divide-and-conquer semiclassical dynamics simulations [45,46] that have been focused on these key vibrational modes (see SI Section 6). Experimentally, a band at 1743.3 cm<sup>-1</sup>, observed in the Ar matrix was assigned to the glycine-water complex [47].



**Figure 1.** IR depletion spectra obtained for helium droplets doped with D<sub>2</sub>O clusters, glycine-d<sub>5</sub> monomer and a combination of glycine-d<sub>5</sub> and D<sub>2</sub>O, measured at different mass channels in the frequency range between 1500 and 1800 cm<sup>-1</sup>. a) IR spectrum of pure D<sub>2</sub>O clusters at mass channel m/z = 162, yielding no band in the investigated frequency range b) IR spectrum of pure glycine-d<sub>5</sub> at mass channel m/z = 34. c-e) IR spectra of (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters at mass channels m/z = 162, 182 and 202 recorded at a pressure of 2 mPa. The yellow, purple and green shaded regions indicate the bands assigned to the C=O stretch of glycine-d<sub>5</sub> monomer (1782 cm<sup>-1</sup>), the red-shifted C=O stretch of non-ionic (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters (1724 cm<sup>-1</sup>) and the asymmetric stretch of the COO<sup>-</sup> group in zwitterionic (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters (1630 cm<sup>-1</sup>), respectively. Note that m/z=202 corresponds to a micro-solvated glycine-d<sub>5</sub>-cluster containing at least 7 water molecules. The signal-to-noise ratio is reduced compared to the measurements at lower mass channels, because only fewer measurements were carried out and averaged.

Based on these computations we assign the absorption band centered at 1630 cm<sup>-1</sup> to the asymmetric carboxylate anion COO<sup>-</sup> stretch of zwitterionic (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> and the band at 1724 cm<sup>-1</sup>

to the red-shifted C=O stretch of the COOD group of glycine-d<sub>5</sub> in corresponding non-ionic clusters (Figure 2 and Figure S9). The intensities of the bands at 1630 and 1724 cm<sup>-1</sup> suggest that, compared to the zwitterionic cluster, a larger amount of non-ionic (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters is formed in the helium droplets, taking into account the predicted intensities. This is attributed to the unique stepwise aggregation process in helium nanodroplets, involving rapid cooling of the embedded molecules. Therefore, addition of a water molecule to a (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> might result in geometries in which this process of zwitter-ionization is not facilitated, or even possible, despite being energetically favourable. Similarly, as observed for other clusters, in helium droplets, local minima next to the global minimum of the potential energy surface can be populated even at 0.37 K [23].



**Figure 2.** Comparison of the IR spectrum of (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>n</sub> clusters recorded at mass channel m/z = 162 (top panel) with the vibrational density of states of (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>6</sub> according to on-the-fly semiclassical dynamics (bottom panel). The harmonic frequencies of the C=O stretch of non-ionic (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>6</sub> clusters and the asymmetric stretch of the COO<sup>-</sup> group within zwitterionic (glycine-d<sub>5</sub>)-(D<sub>2</sub>O)<sub>6</sub> clusters are shown by red and blue sticks, respectively. The anharmonic spectra (solid lines) have been obtained from divide-and-conquer semiclassical simulations of these modes. Frequency scaling w.r.t. the C=O stretch of pure glycine-d<sub>5</sub> serving as an intrinsic reference is applied (see SI Section 6). Please note, that e.g. dissociated clusters with n=10 is predicted to be red-shifted bands (see SI, Figure S9). Thus higher clusters might contribute to the broad absorbance below 1630 cm<sup>-1</sup>.

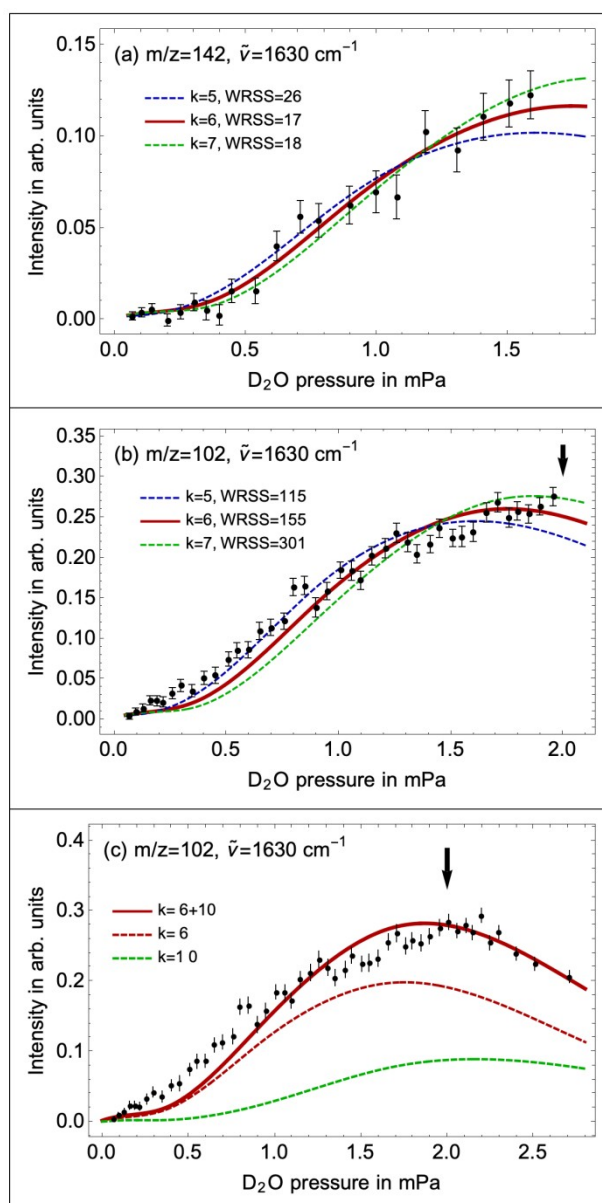
Is there finally a chance to pinpoint the minimum number of water molecules required to zwitterionize glycine at these ultra-low temperatures? While we cannot discriminate the number of water molecules based on the mass-selected IR spectra alone, the cluster size can be determined by pressure-dependent intensity measurements, so-called pickup curves. In helium droplets, the pickup probability of solutes as a function of partial pressure follows approximately a Poisson distribution, which can be utilized to identify the number of molecules contributing to a given signal (see SI for details) [48].

The pick-up curve recorded at a resonant frequency of  $1724\text{ cm}^{-1}$ , i.e. the center frequency of the band assigned to neutral  $(\text{glycine-d}_5)\text{-(D}_2\text{O)}_n$  yields a minimum number of two water molecules (see Figure S9). This is in accordance with the assignment of the  $1724\text{ cm}^{-1}$  band to non-ionic  $(\text{glycine-d}_5)\text{-(D}_2\text{O)}_n$  clusters, which are predicted to exist even for smaller cluster sizes.

In Figure 3 top we show the pick-up curve of the band at  $1630\text{ cm}^{-1}$  at a mass channel of  $m/z = 142$ , corresponding to all glycine-clusters with at least four water. As this band is assigned to the stretching vibration of  $\text{COO}^-$  of the zwitterionic cluster, only cluster with the necessary number of water molecules required for zwitterionization will contribute to this signal. The depletion curve shows an increase up to a  $\text{D}_2\text{O}$  partial pressure of  $2.0\text{ mPa}$ , for higher pressures the signal intensity is found to decrease again. While we expect an overlap of several cluster sizes to contribute to the measured pick-up curve, the maximum of the Poisson distribution will be shifted to higher pressures with increasing cluster size. Thus, we expect a contribution also of higher cluster sizes and therefore a broad plateau at higher pressures. Thus, information on the minimum number of water molecules can be extracted from the fit to rising edge of the pick-up curve, which is dominated by the cluster of smallest size. Including the data points in the medium pressure range of the pick-up curve, we find best agreement for  $k=6$  and  $7$  molecules of water for  $m/z=142$  and  $k=5$  and  $6$  water molecules for  $m/z=102$ , as shown in Figure 3 middle. Therefore, we find overall best agreement for  $k=6$  molecules of water, while fits restricted to  $k=5$  or  $k=7$  give poorer agreement for  $m/z=142$  or  $m/z=102$ , respectively. A global fit to pickup curves recorded at several mass channels yields the same result, which shows the robustness of our approach (Figure S8). This means that clusters with *at least* six water molecules contribute to this signal, while contributions from larger clusters are expected to dominate the curve at higher water pressures. If we fit the pick-up curve up to a water pressure of  $2.5\text{ mPa}$ , which includes these contributions from larger clusters, we find that even cluster with ten

water molecules contribute to the signal (Figure 3 bottom).

The assignment of the  $1630\text{ cm}^{-1}$  band to the smallest zwitterionic cluster  $(\text{glycine-d}_5)\text{-(D}_2\text{O)}_6$  and the  $1724\text{ cm}^{-1}$  band to non-ionic  $(\text{glycine-d}_5)\text{-(D}_2\text{O)}_n$  cluster is furthermore supported by comparison of the experimental spectra to simulated anharmonic spectra of the non-ionic and zwitterionic clusters. Specifically, the red shifted  $\text{C=O}$  stretching resonance of the  $\text{COO}^-$  group and the asymmetric stretching band of the  $\text{COO}^-$  group of glycine- $\text{d}_5$  have been computed within the divide-and-conquer approach to the multiple coherent states semiclassical initial value representation for several water clusters (see SI Section 6, Figure S9) [45,46]. By comparison, we find an excellent agreement to the experimental data when considering six water molecules as the minimum number for which the zwitterionic form is present in experiment, see Figure 2.





**Figure 3.** Fit of the pick-up curve at  $1630\text{ cm}^{-1}$  of the zwitterionic (glycine- $d_5$ )-(D<sub>2</sub>O)<sub>6</sub> clusters. a) Depletion signal as a function of D<sub>2</sub>O partial pressure at mass channel  $m/z = 142$  (black dots) in comparison with reference pick-up curves for  $k=5, 6,$  and  $7$ . The quality of the fit is evaluated based on the weighted residual sum of squares (WRSS). The best fit (smallest WRSS) is obtained for  $k=6$  and  $k=7$ . b) Depletion signal as a function of D<sub>2</sub>O partial pressure at mass channel  $m/z = 102$  (black dots). The best fit (smallest WRSS) is obtained for  $k=5$  and  $k=6$ . c) Fits of the pick-up curve for a combination of clusters with six to ten water molecules (red line), showing the individual contribution of six (dashed red line) and ten (dashed green line) clusters.

Based on a combination of experimental and theoretical investigations of perdeuterated glycine-water clusters, we discovered that zwitter-ionization of the simplest amino acid at very low temperature mimicking outer space conditions is already possible if six water molecules are available. Therefore, we propose that on icy objects in the interstellar medium, not only the non-ionic neutral species should be present, but in particular zwitterionic amino acids should be highly abundant. Based on a direct comparison of the measured infrared spectra with computed anharmonic spectra, we assigned the bands at  $1630$  and  $1724\text{ cm}^{-1}$  to the COO<sup>-</sup> asymmetric stretch of zwitterionic glycine in water clusters and to the strongly red-shifted C=O stretch of non-ionic microhydrated glycine- $d_5$ , respectively. Thus, given the ubiquitous presence of extra-terrestrial water ices, infrared spectroscopic surveys aiming at detecting amino acids in outer space should focus on both species.

Funded by the Deutsche Forschungsgemeinschaft (DFG; German Research Foundation) under Germany's Excellence Strategy—EXC 2033—Projekt-nummer 390677874. D.M. thanks DFG for partial support via his grant MA 1547/11-2. F.G., R.C. and M.C. acknowledge financial support from the European Research Council (Grant Agreement No. 647107 - SEMICOMPLEX-ERC-2014-CoG) under the European Union's Horizon 2020 research and innovation program, and from the Italian Ministry of Education, University, and Research (MIUR: FARE program Grant No. R16KN7XBRBproject QURE). Computational resources have been provided by HPC@ZEMOS, HPC-RESOLV, and BoViLab@RUB. FELIX is supported by the Stichting voor Fundamenteel Onderzoek der Materie (FOM) and LASERLAB-EUROPE grant 654148. We thank Stefan Henkel for carefully reading the manuscript and helpful discussions.

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