THE JOURNAL OF
PHYSICAL CHEMISTRY
LETTERS
A JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

pubs.acs.org/JPCL
Letter

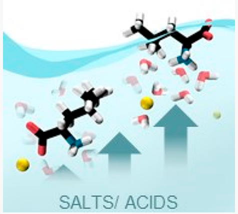
Amino Acids Are Driven to the Interface by Salts and Acidic Environments

Kyle J. Angle, Christopher M. Nowak, Aakash Davasam, Abigail C. Dommer, Nicholas A. Wauer, Rommie E. Amaro, and Vicki H. Grassian*

Cite This: J. Phys. Chem. Lett. 2022, 13, 2824−2829

Read Online

ABSTRACT: Amino acids (AAs), the building blocks of proteins, are enriched by several orders of magnitude in sea spray aerosols compared to ocean waters. This suggests that AAs may reside at the air−water interface and be highly surface active. Using surface tension measurements, infrared reflection−absorption spectroscopy, and molecular dynamics simulations, we show that AAs are surface active and that salts and low-pH environments are drivers of surface activity. At typical sea spray salt concentrations and pH values, we determine that the surface coverage of hydrophobic AAs increases by approximately 1 order of magnitude. Additionally, divalent cations such as Ca^{2+} and Mg^{2+} can further increase AA surface propensity, particularly at neutral pH. Overall, these results indicate that AAs are likely to be found at increased concentrations at the surface of sea spray aerosols, where they can impact the cloud activation properties of the aerosol and enhance peptide formation under certain conditions.



Amino acids (AAs) are the building blocks of proteins and thus critical to life. In ocean waters, dissolved free AAs are an important source of nitrogen and carbon for marine life, particularly bacteria.[1] Despite being present in concentrations of only 1−3000 nM, AAs can be transferred efficiently across the air−water interface from ocean waters into aerosols.[1−4] Most notably, Triesch et al. recently demonstrated that AAs are enriched in sea spray aerosols (SSA) by up to 7 orders of magnitude, with greater enrichment identified for smaller aerosols.[5] While the selective transfer of longer chain fatty acids across the ocean−air interface has been well-established, AAs are relatively understudied in marine aerosol chemistry.[6] Their presence in SSA is important, as it has been shown that AAs impact the hygroscopicity and phase state of aerosols.[7] In addition, AAs can contribute to the formation of new particles in the atmosphere.[8]

The chemical environment within SSA is complex. Within minutes of emission from the ocean, SSA can be rapidly acidified from slightly alkaline ocean levels to acidic pH values from 2 to 4 and can further drop to below pH 0 with atmospheric aging.[9,10] Additionally, the ionic strengths of SSA are much higher than that of the ocean (∼0.7 m), containing up to 5 m sodium chloride.[11] It has also been shown that calcium can be greatly enriched in SSA.[6,12,13] Magnesium, the other main divalent cation in seawater, is enriched relative to sodium in SSA, as well.[13]

These low-pH, high-salt, and high-divalent cation conditions could have an important impact on the behavior of AAs within SSA. In near neutral aqueous solutions, many AAs are zwitterions, containing cationic amine and anionic carboxylate groups. At highly acidic pH levels, the carboxylate ion becomes protonated and the AA becomes cationic. This can impact the solubility of the AA and whether it dissolves more readily in the core of the SSA or at the air−water interface. In fact, Herboth et al. used molecular dynamics simulations to show that phenylalanine (Phe) and valine (Val) have greater affinity for the interface at low pH, while glycine (Gly) did not.[14] It has also been shown that salts can drive proteins to or away from the air−water interface.[15−17] Determining whether AAs reside at SSA interfaces is important because the surface of an aerosol impacts its properties of water uptake, morphology, and heterogeneous chemical transformations.[18−20] It is also essential to determine the behavior of AAs and peptides in aerosols as they are used in food and medicine, including trileucine as a medicinal aerosol dispersibility enhancer.[21]

To quantify the surface propensity of AAs in SSA-like environments, we applied surface tension measurements and infrared reflection−absorption spectroscopy (IRRAS) for six different AAs (structures in Table S1). Leucine (Leu) and isoleucine (Ile) were chosen as they are the most hydrophobic AAs at the low pH of SSA.[22] Phe, Val, and Gly were chosen to expand on the simulation work by Herboth et al.[14] Finally, methionine (Met) was chosen because its side chain contains a sulfur atom that displays strong reactivity with atmospherically relevant species such as hypochlorous acid.[23] To further gain insight into the interfacial orientation and energetics of AAs, we applied potential of mean force (PMF) calculations to Leu, one of the most hydrophobic AAs. The overall goal was to

Received: January 24, 2022
Accepted: March 8, 2022

https://doi.org/10.1021/acs.jpclett.2c00231
J. Phys. Chem. Lett. 2022, 13, 2824−2829

quantify the enhancement of the surface concentration of AAs due to the low-pH and high-ionic strength conditions typical of SSA to better understand how these key biological building blocks behave in the marine atmosphere.

To determine the impact of ions on the surface propensity of AAs, the surface pressure of AA solutions as a function of bulk concentration was first determined for each pH condition (Figure S1). The surface pressure, π, was calculated by eq 1

$$\pi = \gamma_0 - \gamma \tag{1}$$

where γ_0 is the surface tension of a solution at a given pH and salt concentration and γ is the surface tension of the same solution with the added AA. For the hydrophobic AAs studied here, π increases with AA concentration, because the surface activity of the AAs decreases the surface tension of water. A linear regression was performed on each data set, and the resulting slope was used to calculate the surface excess concentration, Γ, as defined by the Gibbs adsorption equation (eq 2).[24]

$$\Gamma = -\frac{C}{RT}\left(\frac{\partial \pi}{\partial C}\right)_T \tag{2}$$

where C is the AA concentration, R is the gas constant, and T is the temperature. At a bulk concentration of 65 millimolal (see the Experimental Methods in the Supporting Information), the Γ values for the hydrophobic amino acids we studied ranged from 0.1 to 0.8 μmol/m^2. This is below the Γ values typical of fatty acids and comparable to high mole fractions of methanol, which makes sense given that AAs, on their own, are only weakly surface active.[25,26]

Next, the impact of each salt on π was determined by measuring a series of solutions in which only the salt concentration changed. Measurements were made across the range of solubility for NaCl, $MgCl_2$, and $CaCl_2$, and the resulting data were typically linear (Figure S1).[27] Note that the non-zero intercepts obtained by linear regression of these data are expected, because the AA solutions exhibit π even in the absence of added salts. From these data, it is clear that these 65 millimolal AA solutions in the presence of high salt concentrations exhibit π comparable to that of pure AA solutions of significantly higher concentrations. For example, in the case of Phe, the π values at high concentrations correspond to monolayers of Phe with packing densities of >15 Å^2/molecule.[28] To quantify the salt-driven π enhancement, we defined a surface enhancement factor, SEF (eq 3).

$$\mathrm{SEF} = \frac{\pi_s}{\left(\frac{\partial \pi}{\partial C}\right)_T C_s} \tag{3}$$

where π_s and C_s are the surface pressure and AA concentrations at the salt concentration of interest, respectively, which we chose to be 5 m, a concentration observed for NaCl in SSA.[11] A comparison of SEF values for various AA, salt, and pH conditions is given in Figure 1. These SEF values represent the minimum surface enhancement expected for AAs under the given conditions (for further details, see the Discussion in the Supporting Information).

The data show that surface enhancement at pH 1 is consistently either greater than or equal to that at pH 6 within the margin of error. This is consistent with recent data showing that the cationic form of surface active AAs has the greatest affinity for the air−water interface.[14] The effect is particularly apparent for $CaCl_2$ solutions with the branched chain AAs along with Met. The exception is Phe, which shows no statistically significant difference for pH 1 and 6 $CaCl_2$ solutions. This may be due to π-stacking effects making side chain interactions more dominant than interactions between the carboxylic acid or carboxylate group and salts.[29] Regardless of the cause, the data are also consistent with the findings of Griffith and Vaida, who found the equilibrium surface pressures of Phe solutions at low and neutral pH levels to be identical within experimental error.[30] We also obtained data for solutions with the cationic and zwitterionic forms of the AA present at pH 3 (Figure S2), where the average surface pressure results are between the pH 1 and 6 surface pressures.

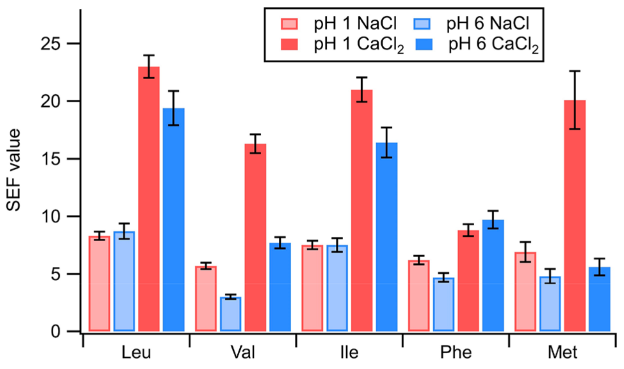


Figure 1. Comparison of SEF values for various aqueous phase conditions of pH and different salts. Data show the average of replicate experiments, and error bars reflect one standard deviation.

In addition, the data in Figure 1 show the enhancement in π in the presence of $CaCl_2$ to be greater than that of NaCl. For pH 6, we attribute this to the greater affinity of Ca^{2+} for binding with the COO- group compared to the Na^+ cation. For pH 1, this is likely due to the increased concentrations of Cl^- that can screen positive charges at the interface to allow more efficient surface packing.[31] This is supported when the π data for both NaCl and $CaCl_2$ are plotted together as a function of Cl^- concentration (Figure S3). The relationship between surface pressure and $[Cl^-]$ is nearly identical for NaCl and $CaCl_2$ at pH 1, whereas there is a noticeable distinction for the two salts at pH 6. This indicates the identity of the cation is more important at pH 6 while the amount of anion is more important at pH 1.

To probe the impact of the identity of the cation on AA surface pressure, we compared measurements of samples in $CaCl_2$ and $MgCl_2$ solutions (Figure S4). We observed that, at pH 1, there was no statistically significant difference between the π measurements. This corroborates our hypothesis that the salt-driven surface activity is dominated by the anion in acidic solutions. At pH 6, by contrast, the π values from $CaCl_2$ solutions are consistently higher than those of $MgCl_2$ solutions for the branched chain AAs. Because the side chains of these AAs are hydrophobic, it is likely that they are "sticking up" into the air at the interface, leaving the zwitterionic groups in the water. The strong ability of Ca^{2+} to screen these adjacent charges may contribute to stabilization at the interface.[32] We note again that Phe is the exception, possibly due to the aromatic side chains causing a different orientation at the interface.[29]

For a point of contrast, we also measured the π of Gly solutions at pH 1 and 6 in the presence of NaCl and $CaCl_2$. As the smallest AA and one that is substantially more soluble than the other AAs measured here, we expected Gly to exhibit less

https://doi.org/10.1021/acs.jpclett.2c00231
J. Phys. Chem. Lett. 2022, 13, 2824−2829

surface activity. The results are given in Figure S5, where negative π values indicate Gly behaves more like a solute than a surfactant in the presence of NaCl. Interestingly, as the concentration of $CaCl_2$ increases, π gradually undergoes a transition from negative to positive, indicating that highly concentrated calcium solutions can change the role of Gly from a solute to a surfactant. This is noteworthy, because Gly is expected to always reside in the bulk solution away from the interface due to its solubility.[33] However, these new data presented here indicate that under certain conditions this may not be the case, although we emphasize the effect is small.

To confirm our hypothesis that salts increase the surface propensity of AAs, we used IRRAS to measure AA solutions with and without salts present. A representative result is given in Figure 2 where several (negative) peaks show greater intensity in the presence of 3 versus 0 m $CaCl_2$. It has been demonstrated that IRRAS band intensities are not expected to increase linearly with surface concentration due to exciton delocalization and the loss of many small bands in the IRRAS baseline.[34] As a result, and due to the potential impact of different cations on the interfacial structure of water, we have not attempted to use IRRAS in a quantitative way to compare the efficacy of different salts in driving AAs to the surface. Nevertheless, our data corroborate our π measurements by showing that AA peaks are enhanced in the presence of salts. Additional spectra of other amino acids are given in Figures S6 and S7.

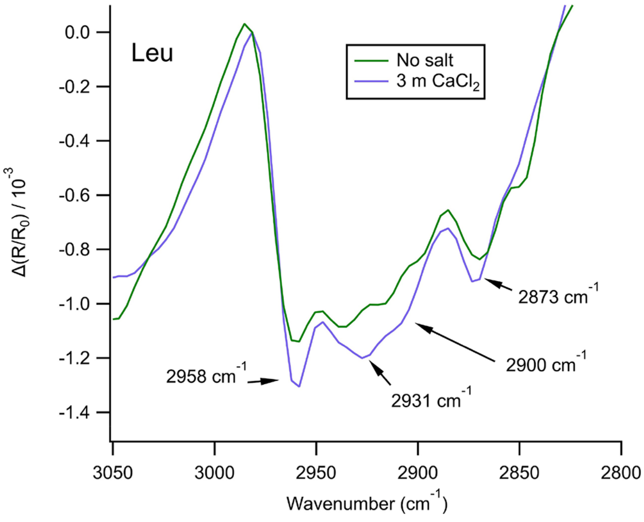


Figure 2. Representative IRRAS spectra for Leu pH 1 solutions with 0 and 3 m $CaCl_2$ concentrations. Enhancements in C−H stretches are apparent (note peaks are negative).

To aid in the explanation of these experimental data and to better understand the behavior of AAs at the air−water interface, we turned to molecular dynamics (MD) pulling simulations combined with umbrella sampling. These were performed as described by Herboth et al.[14] From these simulations, we were able to calculate the potential of mean force of pulling Leu from a salt solution into the gas phase. Representative results for Leu are given in Figure 3 (top), and an image of a Leu cation at the air−water interface is also shown. The energy minimum corresponds to the air−water interface and is seen to be 8 ± 2 kJ/mol lower for the cation than for the zwitterion. Additionally, while we observed that the COOH group of the Leu cation occasionally faced the gas phase at the air−water interface, the COO^- group of the zwitterion rarely did so (Figure S8). This is consistent with our experimental determination that the identity of the salt cation is less important for highly acidic solutions, where interfacial carboxylic groups may be less likely to interact with aqueous ions. Additional details of computations and further data are given in the Experimental Methods in the Supporting Information and Figure S9.

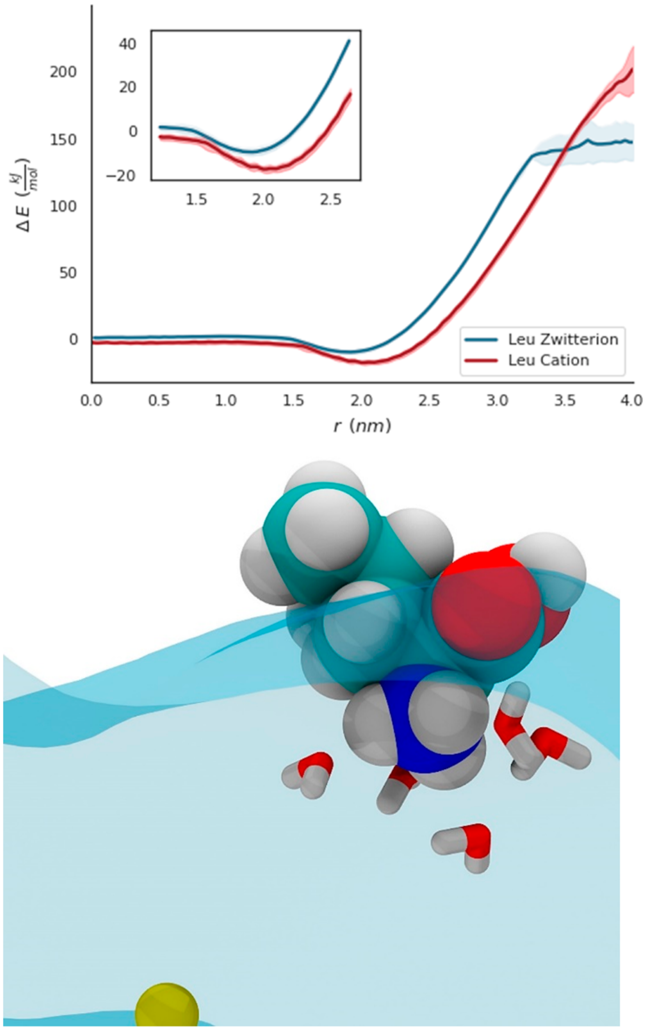


Figure 3. Potential of mean force profile and energy well comparison for a Leu zwitterion and cation (top). The inset shows an expanded view of the energy minimum. Representative image of the Leu cation at the air−water interface (bottom).

The surface propensities of AAs at the air−water interface are shown to be increased under high-salt and low-pH conditions as well as in the presence of divalent cations. These conditions are highly relevant to SSA as it has been shown that these aerosols undergo rapid acidification after emission from the ocean.[9] In addition, water loss after emission causes concentration of existing components such as NaCl and $CaCl_2$. Therefore, while AAs may have low surface activity under most conditions and be most energetically stable in the bulk solution, the combination of acidification and increased concentrations of salts and AAs will drive them to the aerosol−air interface. At the interface, they can more readily undergo chemical reactions, including peptide formation under certain conditions, which is of interest from an origin of life perspective.[35] AAs can be a factor in aerosol hygroscopicity and cloud formation.[36] For example, Marsh et al. found that AAs are more hygroscopic than predicted by models, likely because their zwitterionic form makes them behave more like salts than other organics.[37] Therefore, for investigation of water uptake or even aerosol morphology with the assumption that the aerosol is coated with organics, it is important to consider whether AAs driven to the surface as part of this coating behave more like salts or disrupt the structure of existing monolayers.[38] In terms of heterogeneous chemistry, in addition to the aforementioned reaction of Met with HOCl,[23] there are likely a wide range of interfacial reactions possible with AAs, including acid−base chemistry, given the diversity of their side chains and the presence of both amine and carboxylate groups. Combined with the recent demonstration of the 10^3−10^7-fold enrichment of AAs from the ocean into sea spray aerosols,[5] our data showing that AAs are driven to the surface by salts and low-pH conditions indicate that AAs may be more important components of marine aerosol interfacial chemistry than has been previously realized. These results can also provide insights into the behavior of free AAs in different environments where air−water interfaces are present.

EXPERIMENTAL METHODS

Details of the experimental and computational methods used in this study are given in the Supporting Information. Briefly, we note that in this report "pH 1" and "pH 6" are used to succinctly refer to highly acidic (pH 0.55) solutions and unadjusted solutions at the isoelectric point of the AA (pH ∼5.8−6.1), respectively. These pH values were chosen to isolate different protonation states of the AAs. The pH 1 solutions caused >97% of the AAs to be in the cationic form (with lower-pH solutions not being possible due to equipment corrosion), and the pH 6 solutions caused >99% of the AAs to be in the zwitterionic form (see Table 1).

Table 1. Amino Acid Speciation Data and Aerosol Enrichment Factors

AA	aerosol enrichment factor[a]	pK_{a1}[39]	cation fraction present at "pH 1"	zwitterion fraction present at "pH 6"
Leu	6.6×10^{2} to 1.3×10^{6}	2.32	0.983	1.000
Ile	9.7×10^{3} to 1.8×10^{6}	2.26	0.981	1.000
Val	5.1×10^{3} to 7.4×10^{6}	2.27	0.981	1.000
Phe	4.1×10^{3} to 3.4×10^{6}	2.18	0.977	0.999
Met	[b]	2.16	0.976	0.999
Gly	4.2×10^{4} to 3.5×10^{7}	2.34	0.984	1.000

[a] Aerosol enrichment factors are taken from the range of size-separated values measured by Triesch et al.[5] [b] Data analysis in ref 5 did not include Met.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jpclett.2c00231.

Materials and Methods, discussion of SEF values as minima, representative linear fits for surface pressure measurements, intermediate pH surface pressure measurements, surface pressure data plotted against chloride concentration, comparison of $CaCl_2$ and $MgCl_2$ solutions, glycine measurement results, additional IRRAS spectra, comparison of interfacial carboxylate orientations, umbrella histograms, structures of amino acids studied, surface pressure data collected at higher concentrations, and comparison of IRRAS peak frequencies (PDF)

AUTHOR INFORMATION

Corresponding Author

Vicki H. Grassian − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States;* orcid.org/0000-0001-5052-0045; Email: vhgrassian@ucsd.edu

Authors

Kyle J. Angle − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*

Christopher M. Nowak − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*

Aakash Davasam − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*

Abigail C. Dommer − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*

Nicholas A. Wauer − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States*

Rommie E. Amaro − *Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States;* orcid.org/0000-0002-9275-9553

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.jpclett.2c00231

Notes

The authors declare no competing financial interest.

Numerical data used for all figures, a representative pulling simulation video, and additional computational files are available in the data package.[40]

ACKNOWLEDGMENTS

This work was supported by the National Science Foundation (Grant CHE-1801971). The authors thank Dr. Mark Young for assistance with IRRAS measurements. The authors thank Dr. Andy Goetz for assistance in developing PMFs. The authors thank Dr. Malin Wohlert and Radost Herboth for assistance in applying a flat bottom potential and Dr. Justin Lemkul for providing a user-friendly umbrella sampling tutorial. This work used the PSC Bridges-2 supercomputer through Extreme Science and Engineering Discovery Environment (XSEDE) allocation TG-CHE060073 provided to R.E.A., which is supported by National Science Foundation Grant ACI-1548562.

REFERENCES

(1) Fuhrman, J. A.; Ferguson, R. L. Nanomolar Concentrations and Rapid Turnover of Dissolved Free Amino Acids in Seawater: Agreement between Chemical and Microbiological Measurements. *Mar. Ecol. Ser.* **1986**, *33*, 237−242.

(2) Hubberten, U.; Lara, R. J.; Kattner, G. Amino Acid Composition of Seawater and Dissolved Humic Substances in the Greenland Sea. *Mar. Chem.* **1994**, *45* (1−2), 121−128.

(3) Barbaro, E.; Zangrando, R.; Moret, I.; Barbante, C.; Cescon, P.; Gambaro, A. Free Amino Acids in Atmospheric Particulate Matter of Venice, Italy. *Atmos. Environ.* **2011**, *45* (28), 5050−5057.

(4) Triesch, N.; Van Pinxteren, M.; Engel, A.; Herrmann, H. Concerted Measurements of Free Amino Acids at the Cabo Verde Islands: High Enrichments in Submicron Sea Spray Aerosol Particles and Cloud Droplets. *Atmos. Chem. Phys.* **2021**, *21* (1), 163−181.

(5) Triesch, N.; Van Pinxteren, M.; Salter, M.; Stolle, C.; Pereira, R.; Zieger, P.; Herrmann, H. Sea Spray Aerosol Chamber Study on Selective Transfer and Enrichment of Free and Combined Amino Acids. *ACS Earth Sp. Chem.* **2021**, *5* (6), 1564−1574.

(6) Cochran, R. E.; Jayarathne, T.; Stone, E. A.; Grassian, V. H. Selectivity across the Interface: A Test of Surface Activity in the Composition of Organic-Enriched Aerosols from Bubble Bursting. *J. Phys. Chem. Lett.* **2016**, *7* (9), 1692−1696.

(7) Luo, Q.; Hong, J.; Xu, H.; Han, S.; Tan, H.; Wang, Q.; Tao, J.; Ma, N.; Cheng, Y.; Su, H. Hygroscopicity of Amino Acids and Their Effect on the Water Uptake of Ammonium Sulfate in the Mixed Aerosol Particles. *Sci. Total Environ.* **2020**, *734*, 139318−139327.

(8) Liu, J.; Liu, L.; Rong, H.; Zhang, X. The Potential Mechanism of Atmospheric New Particle Formation Involving Amino Acids with Multiple Functional Groups. *Phys. Chem. Chem. Phys.* **2021**, *23* (17), 10184−10195.

(9) Angle, K. J.; Crocker, D. R.; Simpson, R. M. C.; Mayer, K. J.; Garofalo, L. A.; Moore, A. N.; Mora Garcia, S. L.; Or, V. W.; Srinivasan, S.; Farhan, M.; Sauer, J. S.; Lee, C.; Pothier, M. A.; Farmer, D. K.; Martz, T. R.; Bertram, T. H.; Cappa, C. D.; Prather, K. A.; Grassian, V. H. Acidity across the Interface from the Ocean Surface to Sea Spray Aerosol. *Proc. Natl. Acad. Sci. U. S. A.* **2021**, *118* (2), No. e2018397118.

(10) Keene, W. C.; Pszenny, A. A. P.; Maben, J. R.; Sander, R. Variation of Marine Aerosol Acidity with Particle Size. *Geophys. Res. Lett.* **2002**, *29* (7), 5.1−5.4.

(11) Bertram, T. H.; Cochran, R. E.; Grassian, V. H.; Stone, E. A. Sea Spray Aerosol Chemical Composition: Elemental and Molecular Mimics for Laboratory Studies of Heterogeneous and Multiphase Reactions. *Chem. Soc. Rev.* **2018**, *47* (7), 2374−2400.

(12) Salter, M. E.; Hamacher-Barth, E.; Leck, C.; Werner, J.; Johnson, C. M.; Riipinen, I.; Nilsson, E. D.; Zieger, P. Calcium Enrichment in Sea Spray Aerosol Particles. *Geophys. Res. Lett.* **2016**, *43* (15), 8277−8285.

(13) Jayarathne, T.; Sultana, C. M.; Lee, C.; Malfatti, F.; Cox, J. L.; Pendergraft, M. A.; Moore, K. A.; Azam, F.; Tivanski, A. V.; Cappa, C. D.; Bertram, T. H.; Grassian, V. H.; Prather, K. A.; Stone, E. A. Enrichment of Saccharides and Divalent Cations in Sea Spray Aerosol During Two Phytoplankton Blooms. *Environ. Sci. Technol.* **2016**, *50* (21), 11511−11520.

(14) Herboth, R.; Gopakumar, G.; Caleman, C.; Wohlert, M. Charge State Dependence of Amino Acid Propensity at Water Surface: Mechanisms Elucidated by Molecular Dynamics Simulations. *J. Phys. Chem. A* **2021**, *125* (22), 4705−4714.

(15) Li, Y.; Shrestha, M.; Luo, M.; Sit, I.; Song, M.; Grassian, V. H.; Xiong, W. Salting Up of Proteins at the Air/Water Interface. *Langmuir* **2019**, *35* (43), 13815−13820.

(16) Lindman, S.; Xue, W. F.; Szczepankiewicz, O.; Bauer, M. C.; Nilsson, H.; Linse, S. Salting the Charged Surface: pH and Salt Dependence of Protein G B1 Stability. *Biophys. J.* **2006**, *90* (8), 2911−2921.

(17) Yuan, G.; Kienzle, P. A.; Satija, S. K. Salting Up and Salting Down of Bovine Serum Albumin Layers at the Air−Water Interface. *Langmuir* **2020**, *36* (50), 15240−15246.

(18) Nguyen, Q. T.; Kjær, K. H.; Kling, K. I.; Boesen, T.; Bilde, M. Impact of Fatty Acid Coating on the CCN Activity of Sea Salt Particles. *Tellus B Chem. Phys. Meteorol.* **2017**, *69* (1), 1304064−1304078.

(19) Ovadnevaite, J.; Zuend, A.; Laaksonen, A.; Sanchez, K. J.; Roberts, G.; Ceburnis, D.; Decesari, S.; Rinaldi, M.; Hodas, N.; Facchini, M. C.; Seinfeld, J. H.; O' Dowd, C. Surface Tension Prevails over Solute Effect in Organic-Influenced Cloud Droplet Activation. *Nature* **2017**, *546* (7660), 637−641.

(20) Zhang, C.; Bu, L.; Fan, F.; Ma, N.; Wang, Y.; Yang, Y.; Größ, J.; Yan, J.; Wiedensohler, A. Surfactant Effect on the Hygroscopicity of Aerosol Particles at Relative Humidity Ranging from 80% to 99.5%: Internally Mixed Adipic Acid-Ammonium Sulfate Particles. *Atmos. Environ.* **2021**, *266*, 118725−118736.

(21) Ordoubadi, M.; Gregson, F. K. A.; Wang, H.; Carrigy, N. B.; Nicholas, M.; Gracin, S.; Lechuga-Ballesteros, D.; Reid, J. P.; Finlay, W. H.; Vehring, R. Trileucine as a Dispersibility Enhancer of Spray-Dried Inhalable Microparticles. *J. Controlled Release* **2021**, *336*, 522−536.

(22) Sereda, T. J.; Mant, C. T.; Sönnichsen, F. D.; Hodges, R. S. Reversed-Phase Chromatography of Synthetic Amphipathic Alpha-Helical Peptides as a Model for Ligand/Receptor Interactions. Effect of Changing Hydrophobic Environment on the Relative Hydrophilicity/Hydrophobicity of Amino Acid Side-Chains. *J. Chromatogr. A* **1994**, *676* (1), 139−153.

(23) Armesto, X. L.; Canle L, M.; Fernández, M. I.; García, M. V.; Santaballa, J. A. First Steps in the Oxidation of Sulfur-Containing Amino Acids by Hypohalogenation: Very Fast Generation of Intermediate Sulfenyl Halides and Halosulfonium Cations. *Tetrahedron* **2000**, *56* (8), 1103−1109.

(24) Costanza, J.; Arshadi, M.; Abriola, L. M.; Pennell, K. D. Accumulation of PFOA and PFOS at the Air−Water Interface. *Environ. Sci. Technol. Lett.* **2019**, *6*, 487−491.

(25) Luo, M.; Wauer, N. A.; Angle, K. J.; Dommer, A. C.; Song, M.; Nowak, C. M.; Amaro, R. E.; Grassian, V. H. Insights into the Behavior of Nonanoic Acid and Its Conjugate Base at the Air/Water Interface through a Combined Experimental and Theoretical Approach. *Chem. Sci.* **2020**, *11* (39), 10647−10656.

(26) Chodzińska, A.; Zdziennicka, A.; Jańczuk, B. Volumetric and Surface Properties of Short Chain Alcohols in Aqueous Solution−Air Systems at 293 K. *J. Solution Chem.* **2012**, *41* (12), 2226−2245.

(27) Bretti, C.; Giuffrè, O.; Lando, G.; Sammartano, S. Modeling Solubility and Acid−Base Properties of Some Amino Acids in Aqueous NaCl and (CH3)4NCl Aqueous Solutions at Different Ionic Strengths and Temperatures. *SpringerPlus* **2016**, *5* (1), 1−21.

(28) Petelska, A. D.; Naumowicz, M.; Figaszewski, Z. A. The Equilibrium of Phosphatidylcholine−Amino Acid System in Monolayer at the Air/Water Interface. *Cell Biochem. Biophys.* **2011**, *60* (3), 155−160.

(29) Perkins, R. J.; Kukharchuk, A.; Delcroix, P.; Shoemaker, R. K.; Roeselová, M.; Cwiklik, L.; Vaida, V. The Partitioning of Small Aromatic Molecules to Air−Water and Phospholipid Interfaces Mediated by Non-Hydrophobic Interactions. *J. Phys. Chem. B* **2016**, *120* (30), 7408−7422.

(30) Griffith, E. C.; Vaida, V. Ionization State of L-Phenylalanine at the Air−Water Interface. *J. Am. Chem. Soc.* **2013**, *135* (2), 710−716.

(31) Qazi, M. J.; Schlegel, S. J.; Backus, E. H. G.; Bonn, M.; Bonn, D.; Shahidzadeh, N. Dynamic Surface Tension of Surfactants in the Presence of High Salt Concentrations. *Langmuir* **2020**, *36* (27), 7956−7964.

(32) Tang, N.; Skibsted, L. H. Calcium Binding to Amino Acids and Small Glycine Peptides in Aqueous Solution: Toward Peptide Design for Better Calcium Bioavailability. *J. Agric. Food Chem.* **2016**, *64* (21), 4376−4389.

(33) Mocellin, A.; Gomes, A. H. de A.; Araúјo, O. C.; de Brito, A. N.; Björneholm, O. Surface Propensity of Atmospherically Relevant Amino Acids Studied by XPS. *J. Phys. Chem. B* **2017**, *121* (16), 4220−4225.

(34) Carter-Fenk, K. A.; Carter-Fenk, K.; Fiamingo, M. E.; Allen, H. C.; Herbert, J. M. Vibrational Exciton Delocalization Precludes the Use of Infrared Intensities as Proxies for Surfactant Accumulation on Aqueous Surfaces. *Chem. Sci.* **2021**, *12* (24), 8320−8332.

(35) Danger, G. G.; Plasson, R.; Pascal, R. Pathways for the Formation and Evolution of Peptides in Prebiotic Environments. *Chem. Soc. Rev.* **2012**, *41* (16), 5416−5429.

(36) Griffith, E. C.; Vaida, V. In Situ Observation of Peptide Bond Formation at the Water-Air Interface. *Proc. Natl. Acad. Sci. U. S. A.* **2012**, *109* (39), 15697−15701.

(37) Marsh, A.; Miles, R. E. H.; Rovelli, G.; Cowling, A. G.; Nandy, L.; Dutcher, C. S.; Reid, J. P. Influence of Organic Compound Functionality on Aerosol Hygroscopicity: Dicarboxylic Acids, Alkyl-Substituents, Sugars and Amino Acids. *Atmos. Chem. Phys.* **2017**, *17* (9), 5583−5599.

(38) Saha, A.; SenGupta, S.; Kumar, A.; Naik, P. D. Interaction of L-Phenylalanine with Lipid Monolayers at Air−Water Interface at Different pHs: Sum-Frequency Generation Spectroscopy and Surface Pressure Studies. *J. Phys. Chem. C* **2018**, *122* (7), 3875−3884.

(39) Rumble, J. R., Ed. Properties of Amino Acids. In *CRC Handbook of Chemistry and Physics*; Taylor and Francis Ltd.: Boca Raton, FL, 2021.

(40) Data from: Angle, K. J.; Nowak, C. M.; Davasam, A.; Dommer, A. C.; Wauer, N. A.; Amaro, R. E.; Grassian, V. H. Amino Acids are Driven to the Interface by Salts and Acidic Environments. Center for Aerosol Impacts on Chemistry of the Environment (CAICE), UC San Diego Library Digital Collections, 2022.