ACS OMEGA

Article

Cite This: ACS Omega 2019, 4, 22426−22430

http://pubs.acs.org/journal/acsodf

Combination of Thin-Layer Chromatography and Mass Spectrometry Using Cluster-Induced Desorption/Ionization

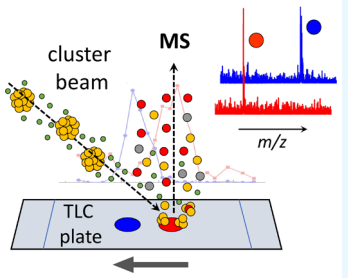
Julian Heep,[†] Paul H. K. Tuchecker,[†] Christoph R. Gebhardt,[§] and Michael Dürr*[,†]

[†]Institut für Angewandte Physik and Zentrum für Materialforschung, Justus-Liebig-Universität Giessen, Heinrich-Buff-Ring 16, D-35392 Giessen, Germany

[§]Bruker Daltonik GmbH, Fahrenheitstr. 4, D-28359 Bremen, Germany

Supporting Information

ABSTRACT: Desorption/ionization induced by neutral clusters (DINeC) was employed for mass spectrometry (MS) of oligopeptides and lipids after separation by means of thin-layer chromatography (TLC). Clear and fragmentation-free spectra were obtained from the TLC plates without any further sample treatment. Mass-resolved chromatograms were deduced when scanning the TLC plates with the cluster beam along the direction of solvent movement. Using vancomycin and noncovalently bound complexes, the soft nature of DINeC was demonstrated also when used in combination with TLC. As a test application, TLC and DINeC−MS were employed to separate and detect different phospholipids obtained from egg yolk.



INTRODUCTION

Given its simplicity in terms of sample preparation and application, thin-layer chromatography (TLC) is a wide-spread method to separate and identify complex mixtures in solution.[1,2] However, in the case of unknown compounds, additional spectroscopic information is required for their identification. Thus, TLC has been combined with additional analytical methods, such as absorption or fluorescence spectroscopy. Alternatively, mass spectrometry (MS) as one of the most powerful techniques in analytical chemistry and biochemistry was successfully coupled to TLC.[3−6] Different ionization techniques for MS have been applied; among the most common are, for example, electrospray ionization (ESI) and matrix-assisted laser desorption and ionization (MALDI).[4−7] For solution-based techniques such as ESI, the separated compounds first have to be redissolved from the TLC plate in order to acquire the mass spectrum of the mixture at a given spot on the TLC plate;[8] the use of MALDI typically requires the application of the respective matrix when using standard TLC plates.[4,6,9] As a matrix-free, desorption-based ionization method, secondary ion MS (SIMS) was combined with TLC;[10] however, SIMS leads to substantial fragmentation when sputtering organic molecules, even when large Ar clusters are used as primary ions.[11] Alternative approaches to directly couple TLC with matrix-free desorption/ionization techniques are thus further explored.[12]

Desorption/ionization induced by neutral SO_2 clusters (DINeC) is a soft desorption-based ionization method for MS which does not require any special sample preparation; it has been applied for a multitude of different substances such as peptides, proteins, lipids, and dyes.[13−19] The SO_2 clusters used in this method both provide the energy required for desorption as well as they serve as a transient matrix in which the analyte molecules are dissolved during cluster surface impact.[20] As a consequence, desorption/ionization induced by neutral SO_2 clusters proceeds at low cluster energies and the desorbed molecules are effectively cooled by evaporation of SO_2 molecules from the cluster fragment in which the desorbed molecule is dissolved.[13] Thus, DINeC features an in general very soft desorption process leading to fragmentation-free spectra of the analyzed compounds.[13,17,21,22]

In this work, we show that TLC−MS can be performed by means of DINeC as desorption/ionization source. For mixtures of oligopeptides, we obtained clear and fragmentation-free mass spectra of the biomolecules directly from the TLC plates. Mass-resolved chromatograms along the TLC plate were recorded by scanning the cluster beam with respect to the plate (Figure 1). The advantage of the soft nature of DINeC was demonstrated, among others, with the help of noncovalently bound adducts to angiotensin II which were detected in samples directly prepared from the original solution but which were removed after application of TLC. TLC + DINeC−MS is thus a combination of TLC and MS with minimum effort in sample preparation which is in particular suited when matrix-free and soft desorption/ionization is required.

EXPERIMENTAL SECTION

TLC was performed using commercial TLC plates (TLC silica gel 60 F_{254}, thickness approx. 200 μm, Merck Millipore, Darmstadt, Germany). The plates were developed in a twin trough chamber (CAMAG, Muttenz, Switzerland) using a

Received: September 18, 2019
Accepted: November 26, 2019
Published: December 20, 2019

DOI: 10.1021/acsomega.9b03060
ACS Omega 2019, 4, 22426−22430

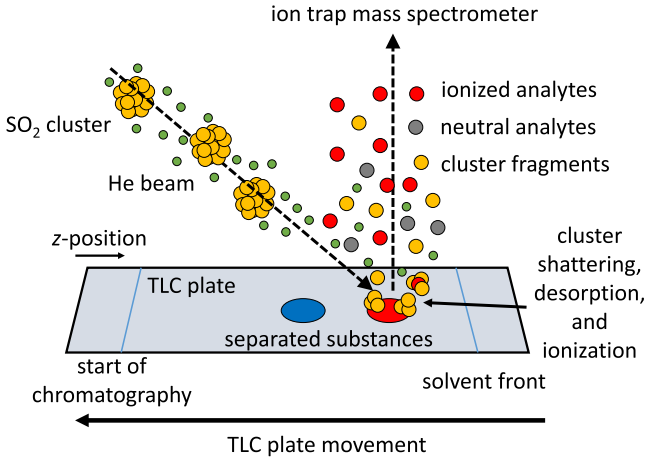


Figure 1. Schematics of the combination of TLC and DINeC-MS. The TLC plate is moved in *z*-direction in small steps with the position of the SO_2 cluster beam fixed. The clusters impact on the sample and a small fraction of the analyte molecules is desorbed and ionized. The ionized analyte molecules are then transferred into the ion trap mass spectrometer.

mobile phase appropriate for the respective analytes (details see below). Photographic images were taken from the developed plates under irradiation with UV-light. Either suppression of the plates' green fluorescence (excitation at λ = 254 nm) by analyte molecules or the blue fluorescence of fluorescamine (excitation at λ = 366 nm), which was sprayed onto the plates, was used to localize the compounds on the TLC plate. For DINeC−MS, the TLC plates were mounted on a sample holder and transferred into the vacuum chamber.

The ions generated by means of cluster-induced desorption/ionization were analyzed in a commercial ion trap mass spectrometer (*amaZon speed*, Bruker Daltonics, Bremen, Germany) equipped with a custom-made DINeC source.[17] In brief, for generating the cluster beam, a gas mixture containing 3% SO_2 and 97% He was expanded from 15 bar into high vacuum ($p \approx 1 \times 10^{-6}$ mbar) using a pulsed supersonic nozzle. The resulting SO_2 clusters exhibit a mean size of 10^3 to 10^4 molecules; the cluster source is separated from the sample chamber by a skimmer (2 mm in diameter) which determines the beam diameter on the sample. In the current setup, the beam profile on the sample can be approximated by a Gaussian profile of approx. 5 mm in diameter [full width at half-maximum (fwhm)]; it can be significantly reduced (to <1.5 mm) in order to resolve closer spots on the TLC plate when using a skimmer with a smaller orifice. Cluster surface impact leads to desorption and ionization of analyte molecules which are transferred into a quadrupole ion trap. Position-dependent mass spectra were acquired by moving the TLC plate in steps of 1 mm, measuring a mass spectrum at each position. The experimental setup is summarized in Figure 1.

The oligopeptides angiotensin II and vancomycin were dissolved in water; a mixture of 2-butanol, water, pyridine, and ammonia solution served as mobile phase.[23] The method of Bligh and Dyer[24] was used to extract phospholipids from the yolk of a chicken egg bought at a local supermarket. For the lipids, a mixture of chloroform, triethylamine, ethanol, and water with a volume ratio of 1:1:1:0.2 was used as the mobile phase.

RESULTS AND DISCUSSION

Figure 2a shows an image of the TLC plate after separation of a mixture of angiotensin II and vancomycin. The image is a

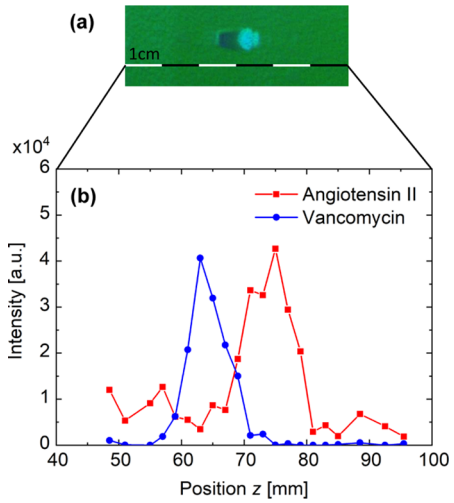


Figure 2. (a) Photographic image of the TLC plate and (b) MS-chromatograms after TLC of a mixture of angiotensin II and vancomycin. The image of the TLC plate in (a) is a superposition of photographs taken under illumination with UV-light at λ = 254 nm and λ = 366 nm, indicating spatial separation of the two compounds. The chromatograms in (b) show the intensities of the monoisotopic masses $[M + H]^+$ taken from positive ion mass spectra acquired in small steps from the TLC plate by means of DINeC−MS. The investigated m/z values were 1448.4 (vancomycin) and 1046.6 (angiotensin II).

superposition of photographs taken at both excitation wavelengths, 254 and 366 nm. It features two different spots with a distance of approx. 8−9 mm between the spot centers. In Figure 2b, an MS-chromatogram, that is, intensity of a given m/z value as a function of position on the TLC plate, is shown for each peptide. The maximum of the curve of the monoisotopic mass of vancomycin (m/z = 1448.4) is at position z = 63 mm and it is around 7 mm in width (fwhm). This position matches the dark blue spot in the photograph. The graph of the monoisotopic mass of angiotensin II (m/z = 1046.6) shows a maximum at position z = 75 mm. Thus, the distance between the two respective intensity maxima is approx. 1 cm, in good agreement with the visual inspection of the TLC plate. In case of the m/z = 1448.4 signal, the background intensity is approximately zero, in case of the m/z = 1046.6 signal, a slightly higher background is observed, in particular toward lower z-values. The latter correlates with the fluorescence signal of the plate indicating traces of angiotensin II which have not been spatially separated from vancomycin by means of TLC. The width of the peaks observed in the MS-chromatogram are given by a convolution of the cluster beam profile and the spot size on the sample. For increased spatial resolution, the diameter of the cluster beam can be significantly reduced when using a skimmer with reduced orifice diameter.

The mass spectra obtained at the positions z = 63 mm and z = 75 mm are shown in Figure 3. At position z = 75 mm, the only peak detectable is attributed to angiotensin II (m/z = 1046.6); at position z = 63 mm (bottom), the signal of vancomycin (m/z = 1448.4) is predominant. The insets in Figure 3 show the measured isotopic patterns for angiotensin II (red) and vancomycin (blue) and, for comparison, the

DOI: 10.1021/acsomega.9b03060
ACS Omega 2019, 4, 22426−22430

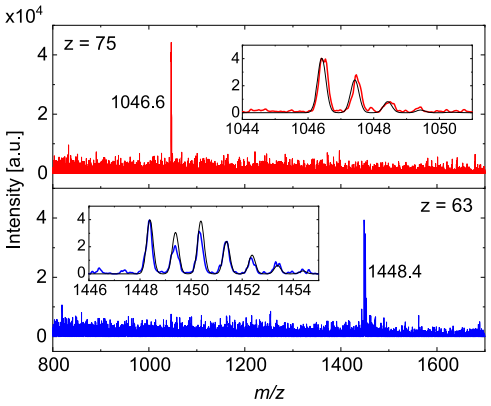


Figure 3. Positive ion mass spectra measured at the positions of the two intensity maxima shown in Figure 2. Top: z = 75 mm, maximum of angiotensin II intensity; bottom: z = 63 mm, maximum of vancomycin intensity. The molecular peaks are labeled with the respective m/z value. Insets: Measured (red/blue) isotopic pattern as obtained by averaging the spectra measured close to the respective maximum. In comparison, the simulated isotopic patterns of the respective analytes, angiotensin II (top) and vancomycin (bottom), are shown in black.

respective simulated isotopic patterns (black). The good agreement between the measured and simulated peak patterns strongly backs the peak assignment as discussed so far.

We used vancomycin as one of our test compounds as glycopeptides are prone to fragmentation during desorption/ionization. In our spectra, we find the $[M + H]^+$ peak to be predominant, thus indicating the soft nature of the cluster-induced desorption/ionization process. Further evidence for the soft nature of DINeC and its advantage for applications in TLC–MS is shown in Figure 4, where the mass spectra as obtained from a batch of contaminated angiotensin II are shown. Figure 4a shows a positive ion mass spectrum of a

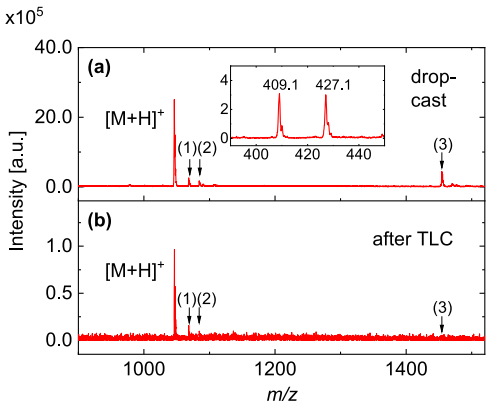


Figure 4. Positive ion mass spectra from a contaminated angiotensin II sample as obtained by means of DINeC. (a) DINeC–MS from a dropcast sample on silicon oxide which predominantly features the bare, singly charged ion $[M + H]^+$, as well as three peaks indicating the analyte ion with different adducts, A1 to A3. The m/z values are m/z = 1068.4, 1085.4, and 1454.4 for the three peaks labeled (1), (2), and (3), respectively. The inset shows a range of lower m/z values where signals at m/z = 409 and m/z = 427 are detected, corresponding to $[A3 + H]^+$ and $[A3 + H_2O + H]^+$, respectively, with m/z = 408 for A3. (b) Cationic DINeC mass spectrum after TLC of the identical solution as used for preparation of the sample used for the spectrum in (a).

sample prepared by dropcasting angiotensin II of this particular batch. It features a peak of the molecular ion of angiotensin II, $[M + H]^+$, as well as a prominent peak with an m/z value which is 408 higher than the $[M + H]^+$ peak. This peak is attributed to angiotensin II carrying an adduct A3, $[M + A3 + H]^+$, as we also observe a peak at m/z = 409 which is then attributed to $[A3 + H]^+$. Furthermore, when we apply MS/MS to the m/z = 1454.4 peak, major fragment peaks occur at m/z = 1046.6 and m/z = 409. After TLC of the same solution used for Figure 4a, the mass spectrum predominantly features a peak at m/z = 1046.6 but no peak at m/z = 1454.4. As DINeC is soft enough to desorb the (M+A3)-complex, we can safely conclude that the adduct was separated from angiotensin II in the TLC run. Both in Figure 4a,b, additional minor adduct peaks are detected at m/z = 1068.4 and m/z = 1084.4 which correspond to $[M + Na]^+$ and $[M + K]^+$, respectively.[25] They are attributed to some additional salt contamination of the original solution.

Figure 5 shows the results of the analysis of lipids extracted from egg yolk. (a) and (b) show two clearly different mass spectra obtained at the positions labeled with the respective color in the photographic image of the TLC plate shown in (b). The spectrum (a) contains peaks between m/z = 700 and m/z = 730 which can be assigned to SPH, the peaks between

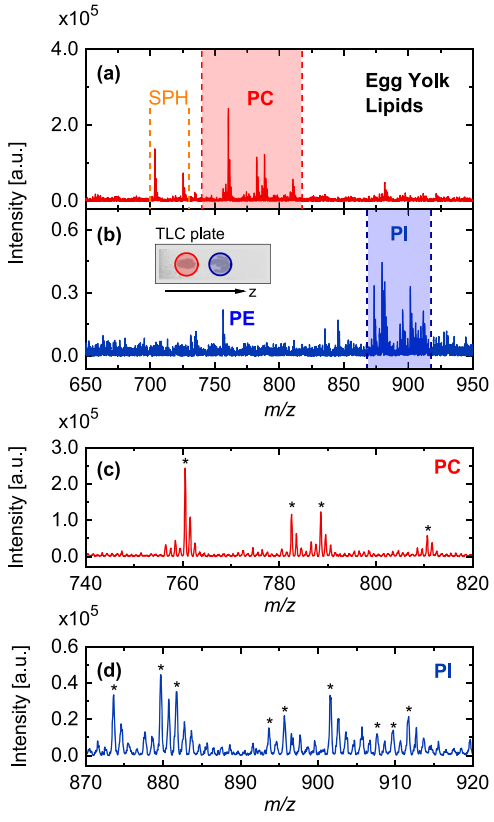


Figure 5. DINeC mass spectra (cations) of lipids extracted from egg yolk after TLC. A photograph of the TLC plate is shown as the inset in (b). (a) Spectrum at the position labeled with a red circle. The detected peaks can be assigned to sphingomyelin (SPH) and phosphatidylcholine (PC). (b) Spectrum at the position labeled with a blue circle. Most of the observed peaks can be assigned to phosphatidylinositol (PI) and phosphatidylethanolamine (PE). (c,d) PC and PI spectra [as indicated in (a,b)] in detail; assigned peaks are labeled with a star (compare the Supporting Information,[6,26–28]).

DOI: 10.1021/acsomega.9b03060
ACS Omega 2019, 4, 22426–22430

m/z = 750 and m/z = 820 were assigned to PC.[6,26−28] In contrast, the spectrum in (b) has its main peaks between m/z = 860 and m/z = 920 which were assigned to PI;[6,26−28] additionally, the peak at m/z = 756.5 was assigned to PE.[26] For the assignment of the SPH, PC, PI, and PE peaks, protonated species as well as lipids with sodium or potassium adducts were taken into account (for details please refer to the Supporting Information); good agreement with literature was obtained.[6,26−28] We note a relatively low abundance of PE in our spectra which might be attributed to differences in the ionization probability.[26,28]

In the following, we compare the combination of TLC and DINeC with established combinations of mass spectrometric analysis methods and TLC, in particular TLC + ESI and TLC + MALDI. TLC + ESI is well established and a high degree of automation allows simple handling of the TLC plates after the chromatography step when the separated compounds of the analyte have to be redissolved in order to spray them into the ESI−MS system. Typical limits of detection (LOD) are in the nanogram range. For MALDI, progress has been reported recently in preparing TLC layers which do not need additional matrices.[29,30] Standard method, however, is still to apply a matrix adjusted to the compounds to be analyzed. In that case, an additional process step is necessary between the TLC run and MS. Furthermore, matrix molecules can lead to additional peaks in the lower mass range m/z < 300.

In contrast, the TLC plate can be directly mounted into the DINeC apparatus after the TLC run has been completed. The spectra are clean and fragmentation free, as the method is extremely soft and no additional matrix has to be applied. For an estimation of the LOD, we assume that the analyte homogeneously covers the surface of the porous TLC material, whereas the SO_2 beam of DINeC−MS probes only the surface of the uppermost particles of the TLC plate. If we furthermore take into account typical values for thickness (d = 0.2 mm) and specific surface area of the porous material (500 m^2/g), as well as the detection limit of DINeC as determined on flat samples (femtomol regime),[13] an LOD in the nanomol range can be estimated for the TLC experiments. It can be further reduced when using TLC plates with lower thickness.[31] Still, TLC + ESI, which makes full use of all analyte molecules in the TLC, is of advantage with respect to LOD.

In comparison to desorption ESI, which is also a soft, desorption-based ionization method which can be directly coupled to TLC,[12] DINeC has been shown to give quantitative information;[19] it does not exhibit a significant matrix effect[32] and can be also applied to nonpolar analytes.[33]

CONCLUSIONS

In conclusion, TLC was successfully combined with MS based on desorption/ionization induced by neutral clusters. The extremely soft desorption process was shown to be also applicable for sample material distributed in the porous TLC plates; clear and fragmentation-free spectra were obtained from the plates after the respective TLC runs. Between TLC run and DINeC−MS measurement, no additional sample treatment has to be applied thus making this combination an easy-to-use method for TLC-MS as demonstrated for the analysis of lipids extracted from egg yolk. The soft nature of DINeC allows for clear identification of weakly bound complexes and fragile molecules.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.9b03060.

Detailed assignment of peaks in the mass spectra from egg yolk lipids (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: michael.duerr@ap.physik.uni-giessen.de. Phone +0049 (0)641 9933490.

ORCID

Michael Dürr: 0000-0002-4676-8715

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Funding by BMBF through grants 1712X09 and 05K19RG1 is acknowledged.

REFERENCES

(1) Jupille, T. H.; Perry, J. A. High-Performance Thin-Layer Chromatography: A Review of Principles, Practice, and Potential. *CRC Crit. Rev. Anal. Chem.* **1977**, *6*, 325−359.

(2) Gocan, S. Stationary Phases for Thin-Layer Chromatography. *J. Chromatogr. Sci.* **2002**, *40*, 538−549.

(3) Fuchs, B.; Süß, R.; Nimptsch, A.; Schiller, J. MALDI-TOF-MS Directly Combined with TLC: A Review of the Current State. *Chromatographia* **2008**, *69*, 95−105.

(4) Morlock, G.; Schwack, W. Coupling of planar chromatography to mass spectrometry. *Trends Anal. Chem.* **2010**, *29*, 1157−1171.

(5) Cheng, S.-C.; Huang, M.-Z.; Shiea, J. Thin layer chromatography/mass spectrometry. *J. Chromatogr. A* **2011**, *1218*, 2700−2711.

(6) Fuchs, B.; Schiller, J.; Süß, R.; Schürenberg, M.; Suckau, D. A direct and simple method of coupling matrix-assisted laser desorption and ionization time-of-flight mass spectrometry (MALDI-TOF MS) to thin-layer chromatography (TLC) for the analysis of phospholipids from egg yolk. *Anal. Bioanal. Chem.* **2007**, *389*, 827−834.

(7) Poole, C. F. Thin-layer chromatography: challenges and opportunities. *J. Chromatogr. A* **2003**, *1000*, 963−984.

(8) Van Berkel, G. J.; Sanchez, A. D.; Quirke, J. M. E. Thin-Layer Chromatography and Electrospray Mass Spectrometry Coupled Using a Surface Sampling Probe. *Anal. Chem.* **2002**, *74*, 6216−6223.

(9) El-Aneed, A.; Cohen, A.; Banoub, J. Mass Spectrometry, Review of the Basics: Electrospray, MALDI, and Commonly Used Mass Analyzers. *Appl. Spectrosc. Rev.* **2009**, *44*, 210−230.

(10) Banno, K.; Matsuoka, M.; Takahashi, R. Quantitative analysis by thin-layer chromatography with secondary ion mass spectrometry. *Chromatographia* **1991**, *32*, 179−181.

(11) Yokoyama, Y.; Aoyagi, S.; Fujii, M.; Matsuo, J.; Fletcher, J. S.; Lockyer, N. P.; Vickerman, J. C.; Passarelli, M. K.; Havelund, R.; Seah, M. P. Peptide Fragmentation and Surface Structural Analysis by Means of ToF-SIMS Using Large Cluster Ion Sources. *Anal. Chem.* **2016**, *88*, 3592−3597.

(12) Paglia, G.; Ifa, D. R.; Wu, C.; Corso, G.; Cooks, R. G. Desorption Electrospray Ionization Mass Spectrometry Analysis of Lipids after Two-Dimensional High-Performance Thin-Layer Chromatography Partial Separation. *Anal. Chem.* **2010**, *82*, 1744−1750.

(13) Gebhardt, C. R.; Tomsic, A.; Schröder, H.; Dürr, M.; Kompa, K. L. Matrix-Free Formation of Gas-Phase Biomolecular Ions by Soft Cluster-Induced Desorption. *Angew. Chem., Int. Ed.* **2009**, *48*, 4162−4165.

(14) Baur, M.; Lee, B.-J.; Gebhardt, C. R.; Dürr, M. Soft cluster-induced desorption and ionization of biomolecules-Influence of

DOI: 10.1021/acsomega.9b03060
ACS Omega 2019, 4, 22426−22430

surface load and morphology on desorption efficiency. *Appl. Phys. Lett.* **2011**, *99*, 234103.
(15) Lee, B.-J.; Gebhardt, C. R.; Schröder, H.; Kompa, K. L.; Dürr, M. Observation of ionic desorption channels in cluster-induced desorption of alkali halides—Influence of surface electronic properties and surface configuration. *Chem. Phys. Lett.* **2013**, *556*, 77−81.
(16) Lee, B.-J.; Baur, M.; Gebhardt, C. R.; Dürr, M. Quantification of the ionization probability during desorption/ionization of oligopeptides induced by neutral cluster impact. *Rapid Commun. Mass Spectrom.* **2013**, *27*, 1090.
(17) Baur, M.; Gebhardt, C. R.; Dürr, M. Desorption/ionization induced by neutral cluster impact as a soft and efficient ionization source for ion trap mass spectrometry of biomolecules. *Rapid Commun. Mass Spectrom.* **2014**, *28*, 290−296.
(18) Portz, A.; Gebhardt, C. R.; Dürr, M. Real-Time Investigation of the H/D Exchange Kinetics of Porphyrins and Oligopeptides by Means of Neutral Cluster-Induced Desorption/Ionization Mass Spectrometry. *J. Phys. Chem. B* **2017**, *121*, 11031−11036.
(19) Portz, A.; Baur, M.; Rinke, G.; Abb, S.; Rauschenbach, S.; Kern, K.; Dürr, M. Chemical Analysis of Complex Surface-Adsorbed Molecules and Their Reactions by Means of Cluster-Induced Desorption/Ionization Mass Spectrometry. *Anal. Chem.* **2018**, *90*, 3328−3334.
(20) Portz, A.; Baur, M.; Gebhardt, C. R.; Frank, A. J.; Neuderth, P.; Eickhoff, M.; Dürr, M. Influence of the cluster constituents' reactivity on the desorption/ionization process induced by neutral SO_2 clusters. *J. Chem. Phys.* **2017**, *146*, 134705.
(21) Kley, C. S.; Dette, C.; Rinke, G.; Patrick, C. E.; Čechal, J.; Jung, S. J.; Baur, M.; Dürr, M.; Rauschenbach, S.; Giustino, F.; Stepanow, S.; Kern, K. Atomic-Scale Observation of Multiconformational Binding and Energy Level Alignment of Ruthenium-Based Photosensitizers on TiO_2 Anatase. *Nano Lett.* **2014**, *14*, 563−569.
(22) Rauschenbach, S.; Rinke, G.; Gutzler, R.; Abb, S.; Albarghash, A.; Le, D.; Rahman, T. S.; Dürr, M.; Harnau, L.; Kern, K. Two-Dimensional Folding of Polypeptides into Molecular Nanostructures at Surfaces. *ACS Nano* **2017**, *11*, 2420−2427.
(23) *Separation and identification of Peptides on HPTLC Silica gel 60 F_{254} MS-grade for MALDI; HPTLC Application number 408*; Merck Millipore: Darmstadt, Germany, 2013.
(24) Bligh, E. G.; Dyer, W. J. A rapid Method of total Lipid Extraction and Purification. *Can. J. Biochem. Physiol.* **1959**, *37*, 911−917.
(25) Portz, A.; Baur, M.; Gebhardt, C. R.; Dürr, M. Mass spectrometry of oligopeptides in the presence of large amounts of alkali halides using desorption/ionization induced by neutral cluster impact. *Biointerphases* **2016**, *11*, 02A316.
(26) Pacetti, D.; Boselli, E.; Hulan, H. W.; Frega, N. G. High performance liquid chromatography-tandem mass spectrometry of phospholipid molecular species in eggs from hens fed diets enriched in seal blubber oil. *J. Chromatogr. A* **2005**, *1097*, 66−73.
(27) Zhou, L.; Zhao, M.; Ennahar, S.; Bindler, F.; Marchioni, E. Determination of phosphatidylethanolamine molecular species in various food matrices by liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS2). *Anal. Bioanal. Chem.* **2012**, *403*, 291−300.
(28) Shinn, S.; Liyanage, R.; Lay, J.; Proctor, A. Improved Fatty Acid Analysis of Conjugated Linoleic Acid Rich Egg Yolk Triacylglycerols and Phospholipid Species. *J. Agric. Food Chem.* **2014**, *62*, 6608−6615.
(29) Esparza, C.; Borisov, R. S.; Varlamov, A. V.; Zaikin, V. G. Composite glycerol/graphite/aromatic acid matrices for thin-layer chromatography/matrix-assisted laser desorption/ionization mass spectrometry of heterocyclic compounds. *J. Chromatogr. A* **2016**, *1470*, 118−122.
(30) Kucherenko, E.; Kanateva, A.; Kurganov, A.; Borisov, R.; Pirogov, A. Monolithic thin-layer chromatography plates with covalently bonded matrix for hyphenation with matrix-assisted laser desorption/ionization. *J. Sep. Sci.* **2018**, *41*, 4387−4393.
(31) Griesinger, H.; Fuchs, B.; Süß, R.; Matheis, K.; Schulz, M.; Schiller, J. Stationary phase thickness determines the quality of thin-layer chromatography/matrix-assisted laser desorption and ionization mass spectra of lipids. *Anal. Biochem.* **2014**, *451*, 45−47.
(32) Portz, A.; Aoyagi, S.; Dürr, M. Soft depth-profiling of mixed peptide/lipid samples by means of cluster induced desorption/ionization mass spectrometry-High depth resolution and low matrix effect. *Biointerphases* **2018**, *13*, 03B405.
(33) Schneider, P.; Dürr, M. Cluster-induced desorption investigated by means of molecular dynamics simulations-Microsolvation in clusters of polar and non-polar constituents. *J. Chem. Phys.* **2019**, *150*, 214301.

DOI: 10.1021/acsomega.9b03060
ACS Omega 2019, 4, 22426−22430