Nanosolvation by acetonitrile and 18-Crown-6 ether induce strongly different effects on the Electron-Capture Induced Dissociation of aromatic tripeptide cations in the gas phase

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Electron-Capture Dissociation (ECD) is a powerful technique that allows, when coupled to mass spectrometry, top-down protein sequencing, indirectly probing their three-dimensional structure, as well as detecting their post-translational modifications. This is also a way to investigate the intrinsic damage done by electrons to biologically-relevant molecular systems. Since they are surrounded by other molecules in a cell, we are particularly interested by the effect of nanosolvation on the fragmentation of these systems.

In this study, we focus on the influence of non-covalent binding of two different molecules, acetonitrile and 18-crown-6 ether (CE), to tripeptide cations on the relative probabilities of their main fragmentation channels (H loss, NH_3 loss and N-C_α bond cleavage) after electron capture from sodium atoms. Experimental gas-phase Electron Capture-Induced Dissociation (ECID, a technique mimicking ECD) coupled to mass spectrometry has been performed on the doubly-protonated tripeptides Lys-Trp-Lys (KWK) and Lys-Tyr-Lys (KYK). First, we recorded the spectra of bare peptide ions, and found that N-C_α bond cleavage leads to fragments containing the aromatic amino acid. The structures and energies of the low-lying conformers of the tripeptide dications and radical monocations obtained from our DFT and MP2 calculations are in line with this observation. Second, the ECID spectra of KWK and KYK dications nanosolvated by one and two molecules show that acetonitrile evaporation is almost complete a few microseconds after electron capture, whereas fragments nanosolvated by CE are abundant. This is consistent with the binding energy of these molecules to lysine-containing peptides, which is much higher for CE than for acetonitrile. One or two acetonitrile molecules have also been found to induce little effect on the fragmentation patterns of the charge-reduced peptide ions. By contrast, one or two CE decreases the NH3-loss probability, which is accounted for by the inhibition of this channel upon CE binding to the N-terminal ammonium group. Besides, this experimental result is consistent with our DFT calculations, which suggest a lower abundance of N terminally-protonated $[KWK+2H]^{2+}(CE)_2$ compared to bare tripeptide cations. Extracting the H-loss contribution from ECID data had never been done for tripeptides nanosolvated by CE. This allowed us to observe the enhancement of H loss from KWK and KYK nanosolvated by two CE, but surprisingly, not by one. This peculiar behavior might be due to H transfer from the reduced radical NH_3 group to CE, followed by loss of the $[CE+H]^{\bullet}$ radical.