CHEM 6003: PhD Departmental Seminar

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Thursday, November 28, 2024, at 1:00 PM (via Webex)

Title: Exploration of Protonated and Metalated Amino Acid and Radiosensitizer Complexes with Methylated Nucleobases Through Experimental and Computational Methods

Abstract:

The presence of protons and metal ions in a biological system can significantly impact the expected non-covalent interactions of nucleobases with other molecules. In binding to significant sites, this can result in substantially different complexes than the neutral interaction would produce. These complexes can be isolated and studied in the gas-phase to determine their structures and thermodynamic properties.

This seminar examines the presence and influence of protonation and alkali metal ions in the complexation of 1-methyluracil (1-mUra) with glycine, serine and cysteine using infrared multiphoton dissociation (IRMPD) spectroscopy and density functional theory (DFT) computational methods. The structure for each complex changes to accommodate the different sizes of alkali metal cation. In each case, there is evidence of a shift in the lowest-energy isomers between the sodiated and potassiated structures, in agreement with literature regarding lone metalated amino acids.[1–3]

The complexation of glycine with uracil and alkaline earth/transition metal dications has also been studied, of the form $[(Gly)(Ura)-H]M^+$. Sustained off-resonance irradiation collision-induced dissociation (SORI-CID) presents different fragmentation pathways relating to the size of the metal ion, with Ca^{2+} and larger alkaline earth metal ions dissociating whole glycine or uracil from the complex, whereas Mg^{2+} and transition metal complexes show fragmentation of the glycine by loss of H_2O, CO_2 and formic acid, among others, losses noted by previous group literature on metalated amino acid dimers.[4,5]

Work regarding protonated complexes of methylated nucleobases with 5-nitroimidazole radiosensitizers will also be discussed. Spurred by previous literature regarding favored nucleobases to bind to radiosensitizers,[6] complexes of 25 different combinations were investigated with DFT calculations and six complexes were studied using IRMPD spectroscopy. This talk will summarize these results and indicate favored bonding interactions among the nucleobases.

References:

1. Armentrout, P. B., Stevenson, B. C., Ghiassee, M., Boles, G. C., Berden, G. & Oomens, J. Infrared multiple-photon dissociation spectroscopy of cationized glycine: effects of alkali metal cation size on gas-phase conformation. *Phys. Chem. Chem. Phys.* **24**, 22950–22959 (2022).

2. Armentrout, P. B., Rodgers, M. T., Oomens, J. & Steill, J. D. Infrared multiphoton dissociation spectroscopy of cationized serine: Effects of alkali-metal cation size on gas-phase conformation. *J. Phys. Chem. A* **112**, 2248–2257 (2008).

3. Citir, M., Stennett, E. M. S., Oomens, J., Steill, J. D., Rodgers, M. T. & Armentrout, P. B. Infrared multiple photon dissociation spectroscopy of cationized cysteine: Effects of metal cation size on gas-phase conformation. *Int. J. Mass Spectrom.* **297**, 9–17 (2010).

4. Gholami, A. & Fridgen, T. D. The unimolecular chemistry of [Zn(amino acid)2-H]+ in the gas phase: H2 elimination when the amino acid is a secondary amine. *Phys. Chem. Chem. Phys.* **16**, 3134–3143 (2014).

5. Jami-Alahmadi, Y. & Fridgen, T. D. Structures and unimolecular chemistry of M(Pro2-H)+ (M = Mg, Ca, Sr, Ba, Mn, Fe, Co, Ni, Cu, Zn) by IRMPD spectroscopy, SORI-CID, and theoretical studies. *Phys. Chem. Chem. Phys.* **18**, 2023–2033 (2016).

6. Pandeti, S., Feketeová, L., Reddy, T. J., Abdoul-Carime, H., Farizon, B., Farizon, M. & Märk, T. D. Binding preference of nitroimidazolic radiosensitizers to nucleobases and nucleosides probed by electrospray ionization mass spectrometry and density functional theory. *J. Chem. Phys.* **150**, 014302 (2019).