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Young Scientist Feature

Protonation of methyluracils in the gas phase: The particular case of 3-methyluracil

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Dedicated to Terrance B. McMahon on the occasion of his 70th birthday.

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ABSTRACT

The gas-phase structure of the protonated isomeric methyl uracils (1-Me-, 3-Me- and 6-Me-) was examined using mid-infrared multiple photon dissociation (IRMPD) spectroscopy performed at CLIO, the Orsay (France) free electron laser facility. Experimental infrared spectra were recorded for protonated species generated by electrospray ionization, isolated and irradiated in a quadrupole ion trap, and compared to calculated infrared absorption spectra of the different low-lying isomers computed at the B3LYP/6-31 + + G(d,p) level of theory. For both protonated 1-Me-uracil and 6-Me-uracil, the global energy minima correspond to enolic tautomers, whose infrared absorption spectra were found to match very well with the experimental IRMPD spectra. A small fraction of another low energy lying keto tautomer is also present under electrospray conditions. Protonation of 3-Me-uracil by electrospray results exclusively in the formation of a keto form. 3-Me-uracil therefore constitutes a particular case in the series of pyrimidine nucleobases studied so far. Methylation of the N3 position of uracil prevents the interconversion between the keto and enol forms, as encountered for uracil and uracil methylated on N1, C5, or C6. These data also give new insights about the unimolecular reactivity of protonated uracils.

1. Introduction

Within DNA, the strong hydrogen bonds (HBs) between the canonical forms of purine and pyrimidine nucleobases ensure the structural integrity of the biopolymer and subsequently the encoding and expression of the genetic information. Thymine, for instance, is found in its canonical structure, a dioxo tautomer, in the Watson-Crick base-pair made with adenine. Besides the formation of canonical AT and GC base pairs, other recognition patterns are possible. Through internal proton transfers, which are correlated to the intrinsic acid-base properties of their electronegative centers, different tautomeric forms of the nucleobases can be formed, leading to the establishment of non-canonical hydrogen bonds. The role of tautomerization in genetic expression has therefore been extensively studied. Some of these studies have determined that the production of these tautomers can lead to mispairs and eventual mutations during nucleic acid replication [1–4].

Because of the probable relationship between the occurrence of these rare tautomeric forms and point mutations, the evaluation of the tautomeric behaviour of nucleobases and the characterization of their acid-base properties is of fundamental importance. To address these questions, working in the gas phase is particularly appropriate because it allows one to obtain information on their intrinsic properties by eliminating any influence from solvent and conformational averaging effects. Furthermore, such studies allow for a direct comparison between experimental and theoretical data. Professor Terrance B McMahon has followed this strategy all along his extraordinary career dedicated to the study of the reactivity of gaseous ions, and recently provided new insights about the proton transport within protonated nucleobases, notably catalyzed by ammonia [5].

Over the past decade, mass spectrometry has been increasingly useful in gas-phase studies of nucleobases, thanks to the combination of two technical developments that have occurred during the last thirty years. The first one is the advent of electrospray ionization [6], which allows for facile formation of ions in the gas phase from non-volatile compounds and greatly simplifies the study of nucleic acid building blocks (from nucleobases to double strands) by mass spectrometry. The second one is the development of structure-sensitive activation techniques, which enables one to obtain direct structural information on

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Scheme 1. Most stable calculated neutral tautomers of 1-Me, 3-Me and 6-Me uracil.

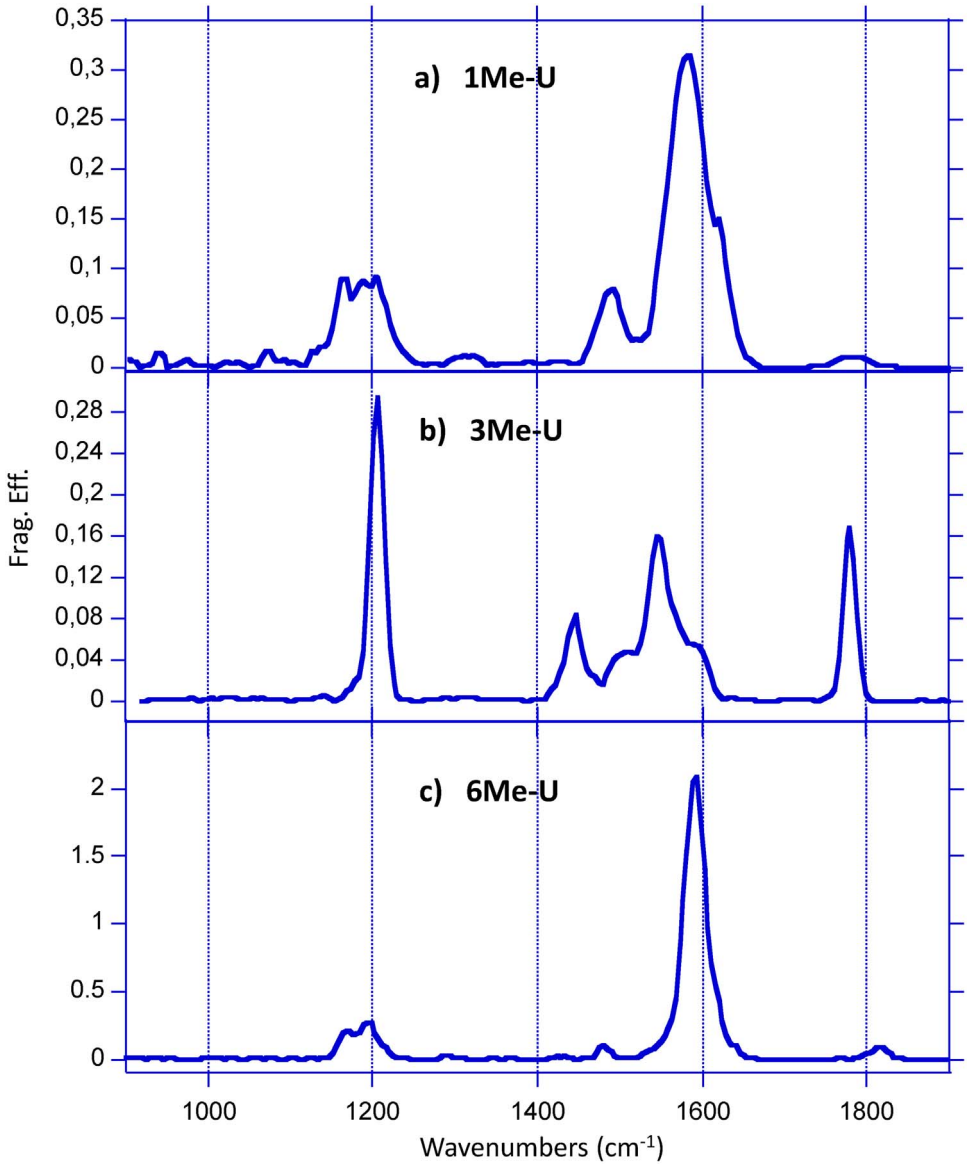

Fig. 1. Experimental IRMPD spectra recorded for protonated (a) 1-Methyluracil, (b) 3-Methyluracil and (c) 6-Methyluracil.

gaseous ions. Among those, infrared multiple photon dissociation spectroscopy (IRMPD) of mass-selected ions, is now established as a very powerful approach to probe the structure of gaseous ions of moderate size [7–10], and different groups have used IRMPD spectroscopy to study the structure and tautomerization of protonated DNA and RNA building blocks generated by electrospray [11–24]. In our continuing effort to study the structure and unimolecular reactivity of gaseous nucleobases, either protonated [11–13,25,26] or complexed to metals [27–32], the present paper reports the IRMPD study in the fingerprint region between 900 and 1900 cm^{-1} of three protonated methyluracils, namely 1-Me, 3-Me and 6-Me-uracil (Scheme 1), generated by electrospray ionization and trapped in a quadrupole ion trap. The study is complemented by DFT and *ab-initio* electronic structure calculations that provide information regarding the relative stability of the different conformers and their vibrational modes. Several recent theoretical studies have been dedicated to the effect of methylation on