ABSTRACT

The aggregation and conformations of sodiated dinucleotides were examined by mass spectrometry, ion mobility and molecular modeling methods. Single-strand, duplex and triplex ions of the form \([M + nNa - (n-1)H]^+\) with \(n=1-10\) were observed in the MALDI-TOF mass spectra. Deprotonation sites were determined to be on the phosphates and the thymine and guanine bases. Collision cross-sections of each sodiated complex were measured using ion mobility methods and compared to calculated cross-sections of theoretical structures generated by molecular dynamics (AMBER). Three distinct single-strand conformers are observed: one with the nucleobases stacked, one with the bases perpendicular to each other and one with the bases coplanar. As more \(Na^+\) ions attach to the single-strands, the dinucleotides tend to favor the stacked form. The duplexes and triplexes are held together via \(Na^+\) bridging between the deprotonated phosphates, eventually forming a \(Na^+-O\) ring. Additional \(Na^+\) ions that cannot fit in the ring bind to various places on the bases. Dinucleotides with guanine bases do not form triplexes, presumably because the guanines stack in such a way that the phosphates cannot be bridged together with \(Na^+\) ions.

METHODS

A molecule of interest is dried on a stainless steel rod. The rod is inserted into the source chamber and a nitrogen laser is used to desorb and ionize the molecule. The MALDI-TOF 1-meter flight tube allows the accelerated ions to mass separate. A reflectron is used to redirect the ion packet in order to obtain high-resolution mass spectra. High resolution mass spectra are detected and recorded on a computer. The 20-cm long cylindrical glass drift cell filled with ~1.5 torr of helium gas under the influence of a weak uniform electric field. The cell temperature can be varied from 90 K to 500 K. Ions exiting the drift cell are mass selected to eliminate any fragmentation that might occur through collisions with the buffer gas and are detected.

EQUATIONS

The reduced mobility, \(K_o\), is obtained from ATDs using the equation above where \(l\) is the length of the cell, \(T\) is the temperature in Kelvin, \(p\) is the pressure of the He gas (in torr), \(V\) is the strength of the electric field, \(t_o\) is the ion arrival time taken from the center of the ATD peak, and \(t_a\) is the amount of time the ion spends outside the drift cell before reaching the detector. The ion’s collision cross-section, \(\sigma\), is calculated using the equation above where \(q\) is the charge of the ion, \(N_o\) is the number density of He at STP, \(\mu\) is Boltzmann’s constant, and \(m\) is the ion-He reduced mass.

DATA ANALYSIS

Experimental Method  

\[\text{ARRIVAL TIME DISTRIBUTIONS (ATDs)} \rightarrow \text{MOBILITIES} \rightarrow \text{COLLISION CROSS-SECTIONS}\]

Theoretical Method  

\[\text{MOLECULAR MECHANICS/DYNAMICS} \rightarrow \text{STRUCTURES} \rightarrow \text{COLLISION CROSS-SECTIONS}\]
Sodiated Single-Strands

Na⁺ Dinucleotide Mass Spectra Analysis

Sodiated Duplexes

Sodiated dGG Duplex Theoretical Structures

Dinucleotides form duplexes and triplexes in the gas phase upon addition of Na⁺.

In all cases, the maximum number of Na⁺ ions attached equals the number of acidic hydrogens plus one. T and G are the only bases that deprotonate in the presence of Na⁺ ions.

3 structural families are observed for the single-strand systems: bases stacked, bases perpendicular or bases planar. The addition of Na⁺ ions cause the single-strand to favor the formation of the stacked conformer.

The duplexes and triplexes are held together by Na⁻O bridging between the phosphate groups.

G helps triplex formation, presumably due to its strong inclination for base stacking.