

HYDROIODIC ACID (HI) ATTACHMENT TO PEPTIDES AND PROTEINS IN THE GAS-PHASE

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We have recently noted that hydroiodic acid (HI) has a tendency to attach to peptides and proteins in the gas-phase under typical ion storage conditions in a quadrupole ion trap¹. A strong correlation has been observed between the number of basic sites in the peptide/protein (i.e., arginine, lysine, histidine and N-terminus) and the sum of the charge state plus the number of HI molecules that will attach to an ion². Evidence has been presented that supports the hypothesis that HI attaches to neutral basic sites in the molecule, rather than at charge sites¹. In this regard, HI attachment is an unusual ion/molecule reaction because it is not directly mediated by ion/induced dipole interactions. It is therefore possible that HI attachment measurements can serve as a unique structural probe for gaseous peptide and protein ions that complements other probes such as ion mobility/cross-section measurements, hydrogen/deuterium exchange rate measurements, and proton transfer rate measurements.

While there is a strong tendency to attach a maximum number of HI molecules, based on charge state and number of basic sites, the kinetics of the reactions and final product distributions for ions that can attach multiple HI molecules can vary remarkably. From the relatively large set of observations made to date, a number of general observations can be drawn regarding the structural factors that affect HI attachment chemistry. These factors can affect either the kinetics of the reactions, the thermodynamics of the reactions (thereby affecting the position of equilibrium), or both. They include composition (i.e. numbers and identities of basic sites), three-dimensional structure, local interactions (i.e., intramolecular proton binding, salt bridging), and size. Size is most important for relatively small peptides because it plays an important role in determining the lifetime of the incipient ion/HI complex. The general trend observed thus far shows that the binding strength for HI attachment to the candidate reaction sites goes as: arginine > lysine > N-terminus > histidine. In comparisons with isomeric ions (of the same charge state) known to differ in three-dimensional structure, HI attachment kinetics show clear differences. HI chemistry is therefore clearly sensitive to higher order structure. In fact, several cases have been noted recently that clearly show mixtures of isomeric structures in ion populations that have not been noted heretofore.

1. J.L. Stephenson, Jr. and S.A. McLuckey *J. Am. Chem. Soc.*, **119** (1997) 1688-1696.
2. J.L. Stephenson, Jr. and S.A. McLuckey *Anal. Chem.*, **69**, (1997) 281-285