Sugars in the Gas Phase – Novel Techniques to Unravel the Glycocode

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Currently, the vast majority of glycans are characterized using mass spectrometry-based techniques (MS). Measuring the molecular weight of a sugar, however, immediately poses a fundamental problem: entire classes of monosaccharide building blocks exhibit an identical atomic composition and, consequently, an identical mass. Therefore, glycan MS data can be highly ambiguous and often it is not possible to clearly assign a particular structure.

A promising approach to overcome this limitation is to implement an additional gas-phase separation step using ion mobility-mass spectrometry (IM-MS). Here, ions travel through a gas-filled cell aided by an electric field and are separated according to their collision cross section (CCS). Proof of principle experiments showed that linkage- and stereoisomers, which are difficult to distinguish using established techniques, can be separated and unambiguously identified on basis of their CCS.[1] Further analyses revealed that also glycopeptides, which merely differ in the regiochemistry of the attached glycan can be distinguished using fragmentation and subsequent IM-MS analysis.[2]

Furthermore, we recently assessed the potential of cold-ion IR spectroscopy for oligosaccharide analysis.[3] Gas-phase IR spectra of a series of synthetically derived mono-, di- and trisaccharide standards were recorded. For each of these oligosaccharides, unique and highly diagnostic absorption patterns with a variety of well-resolved bands was obtained. This unprecedented resolution reveals remarkable differences in the overall IR signatures and allows a simple, fingerprint-based discrimination between isomers, even if they merely differ in the stereochemistry of a single OH group.

Encouraged by these results, we used cold-ion IR spectroscopy to study reactive glycosyl cation intermediates that occur during glycosidic bond formation.[4] These intermediates often determine the stereochemical outcome of the reaction, however, due to their transient and short-lived nature their exact structure remained elusive to date. Our results show that glycosyl cations with participating C2 protective groups form a covalent bond with the anomeric carbon that leads to C1-bridged acetoxonium-type structures. The resulting bicyclic structure strongly distorts the ring, which leads to a unique conformation for each individual monosaccharide. This novel level of mechanistic understanding fundamentally impacts glycosynthesis and allows tailoring building blocks and reaction conditions.

References

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