

Both structural diversity and conformational flexibility renders carbohydrates a promising and green material in future design of nanomaterials. However, complex assembly rules renders carbohydrates a challenging target for chemical synthesis. Multiple strategies have been designed to control reaction regio- and stereoselectivity. The most common approach to couple two carbohydrates selectively employs installation of protecting group at the glycosyl donor. However, understanding the influence of protecting groups on the reaction outcome remains limited because traditional condensed phased techniques, such as NMR, cannot resolve the short-lived and reactive glycosyl ion intermediate. Lack of such understanding hinders rational design and non-empirical reaction optimizations which

Here, we characterize the intermediates of the glycosylation reaction, so-called glycosyl cation, by combination of gas-phase IR spectroscopy in helium nanodroplets and first principles methods. The analyzed intermediate structures, encoded in the mid-IR fingerprint region, include a series of 2-acetylated glycosides as well as galactose with acetyl participating group at C4, C6 or both C4 and C6. We show that the intermediate involved in the trans-glycosylation adopts dioxolenium type of structure with a covalent bond formed between anomeric carbon and acetyl oxygen. In effect, this 1,2-cis-fused bicyclic motif distorts the low-energy chair conformation of each glycosyl cation in unique fashion which impacts the reaction energy profile. The remote group participation at C4 as well as both C4 and C6 shows similar behavior, with a formation of the bicyclic dioxolenium type of ion. In case of C6 participation, we observe significant oxocarbenium ion population in which the anomeric carbon interacts only weakly with the protecting groups.

The structural characterization of the ion provides fundamental understanding of the reaction required to further improve the reaction conditions and building blocks in the future. Future in-depth ab initio molecular dynamics investigations of the glycosylation reaction in solution are discussed.