ELUCIDATING REACTIVE SUGAR-INTERMEDIATES BY CRYOGENIC INFRARED SPECTROSCOPY

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Carbohydrates are ubiquitous in nature. The stereochemistry (α/β configuration) of glycosidic bonds plays a crucial role in glycan function within biological systems. However, it remains a long-standing challenge to precisely control glycosidic bond formation. Particularly in carbohydrate chemistry, it relies on a centenary reaction: glycosylation. During this reaction, glycosyl cations act as key intermediates. These intermediate structures directly influence the stereochemical outcomes of the glycosylation reaction. Despite their importance, the role of glycosyl cations is still not fully understood. This, in turn, makes it difficult to fully control the stereoselectivity of glycosidic bonds in the synthesis of complex glycans.

Studying the structure of the glycosyl cation is particularly challenging. The glycosyl cation is a cationic S_N1-type intermediate. It has an extremely short lifetime, making it inaccessible to traditional analytical techniques. Here, we report the first high-resolution structure of a glycosyl cation (Figure 1). Technically, this is achieved by isolating the intermediates in the gas phase of a mass spectrometer. Using cryogenic infrared spectroscopy, we probe the vibrational patterns of glycosyl cations. The high-resolution IR spectra enable the reconstruction of their three-dimensional structure using computational calculation.

Gas-phase research provides a snapshot of the S_N1-glycosylation reaction. The intermediate structure in the gas-phase holds great potential to disclose the origins of the stereoselective outcome in this reaction. Besides, it provides evidence for many key concepts in organic synthesis, including neighbouring group effect [1], remote participation [2], and benzylidene- directed glycosylation [3]. Consequently, these discoveries establish a platform for designing building blocks and optimizing reaction conditions.

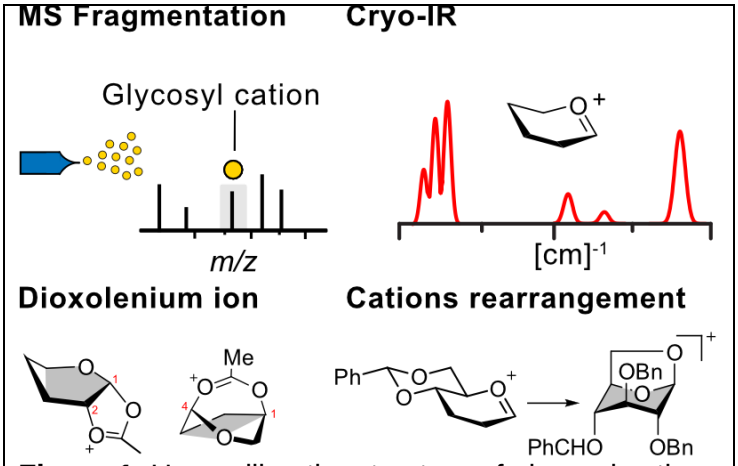

Figure 1. Unravelling the structure of glycosyl cations through gas-phase and synthetic approaches.

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