INVESTIGATING CURTIN-HAMMETT SCENARIOS IN GLYCOSYLATION REACTIONS: THE HIGH IMPACT OF LOW-ABUNDANCE REACTION INTERMEDIATES

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The stereoselective introduction of glycosidic bonds (glycosylation) is one of the main challenges in the chemical synthesis of carbohydrates. Glycosylation reactions can be difficult to control because in many cases the exact reactive species driving product formation cannot be detected and the product outcome cannot be explained by the primary reaction intermediate observed. In these cases, reactions are expected to take place *via* other, low-abundance, reaction intermediates that are in rapid equilibrium with the primary reaction intermediate according to a Curtin-Hammett scenario. Despite this principle being well-known in organic synthesis, mechanistic studies investigating this model in glycosylation reactions are complicated by the challenge of detecting the extremely short-lived reactive species responsible for product formation. I will discuss the utilization of the chemical equilibrium between low abundance reaction intermediates and the stable, readily observed, axial-glycosyl triflate intermediate to infer the structure of the former species by employing various forms of exchange NMR. Using these techniques, we enabled the detection of elusive reaction intermediates such as equatorial-glycosyl triflates and glycosyl dioxanium ions [1-4]. This demonstrates the power of exchange NMR to unravel reaction mechanisms and to build a catalogue of kinetic parameters allowing for the understanding and the eventual prediction of glycosylation reactions that are under Curtin-Hammett control.

References:

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