WEAVING NONCOVALENT INTERACTIONS INTO CARBOHYDRATE SYNTHESIS: AN EMERGING FRONTIER IN GLYCOSYLATION STEREOCONTROL

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The exploitation of unconventional noncovalent interactions (NCIs) has emerged as a powerful strategy to access difficult-to-synthesize glycosides [1,2]. In my talk, I will describe our group's efforts in developing mild and robust *σ*-hole based noncovalent catalyzed methods for selective carbohydrate synthesis – an approach our laboratory now defines as the "*σ-hole glycosylation strategy*". These methods have facilitated the access of elusive glycosidic chemical space (Figure 1), with selectivity and scope that was not possible with alternative means.

I will offer an overview of our early discovery efforts in the development of exclusively halogen bonding (XB) catalyzed strain-release glycosylation [3] and 2-deoxyglycosylation [4]. These strategies had unraveled unique advantages, such as the elevation of anomeric selectivity as well as expanded substrate tolerance compared to classical catalytic methods.

Next, I will introduce an emerging concept from my laboratory, which is the use of the highly modular phosphonochalcogenide (PCH) catalyst [5] for chalcogen bonding (ChB) catalyzed glycosylations and glycomimetic synthesis. We recently demonstrated in a series of studies that the ChB activation imparted by PCH catalyst performed exceptionally on glycosyl substrates. As a consequence, we developed versatile strategies that enabled access into biologically relevant 7-membered ring sugars known as septanosides [6,7], β-indolyl glycosides [8] as well as the underexplored iminoglycosides [9]. I will also touch on recent efforts to exploit NCIs for carbohydrate stereocontrol in the context of asymmetric transition metal catalysis [10].

Benefiting from insights gained through experiment and theory, we discovered that a blend of unconventional NCIs is synergistically dictating the stereoselectivity determining steps in many glycosylations. By bridging supramolecular chemistry, physical organic chemistry, catalytic method development and carbohydrate chemistry, we are optimistic that innovative solutions into highly desired glycosidic chemical space will be discovered at the interface of these fields.

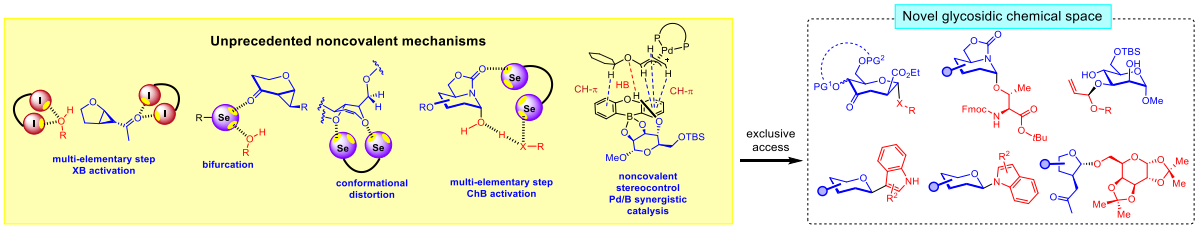

Figure 1. Emerging noncovalent strategy in stereoselective carbohydrate synthesis

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