TAILORED IMINOSUGARS TO TACKLE COMPLEX DISEASES

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Iminosugars are a fascinating class of glycomimetics and are more and more investigated as potential new drugs, as they offer the opportunity to mimic the biological action of carbohydrates, often with a higher activity than sugar themselves, while circumventing their inherent drawbacks. Their synthesis is highly challenging due to the presence of several chirality centers, which in turn give the synthetic organic chemists the opportunity to investigate new stereoselective reactions, with the chiral pool approach from carbohydrates being certainly the most straightforward route. Precision-engineered modifications and decoration of iminosugars with task-specific moieties can not only enhance affinity and selectivity towards the biological target, but also improve their drug-like properties, which are important for their biologic applications.
Widely known as inhibitors of glycosidases and glycosyl transferases, iminosugars have recently gained attention in the treatment of complex and multisystemic diseases, such as lysosomal storage disorders (e.g. Gaucher disease) and neurodegenerative diseases (e.g. Parkinson’s disease).
In this Keynote lecture, I will illustrate our recent synthetic efforts to access new task-specific iminosugars based on a trihydroxypiperidine *core* derived from D-mannose. The decoration of the iminosugar *core* with specific moieties allowed not only to selectively bind a specific lysosomal enzyme, but also to impart additional features such as antioxidant properties, important in multisystemic neuronopathic diseases, or the capacity to bind intrinsically disordered proteins, whose aggregation is responsible for neurodegenerative diseases (i.e. α-synuclein in Parkinson’s disease) [1,2].

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