A new stereoselective approach to polyhydroxylated azepanes

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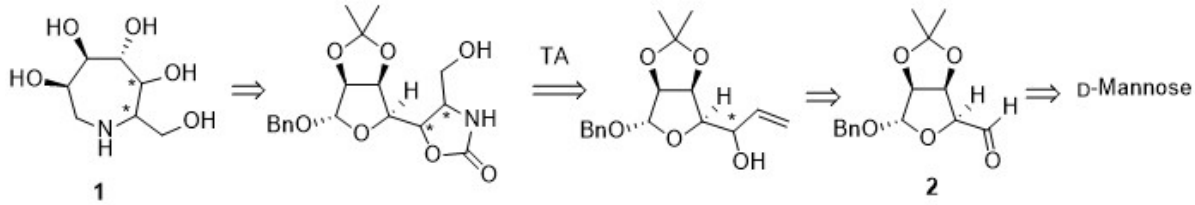
Iminosugars represent the most important class of glycomimetics, as they mimic the biological action of carbohydrates while circumventing their drawbacks. In particular, iminosugars are widely known as glycosidases and glycosyl transferases inhibitors [1].

The use of simple carbohydrates as starting materials for their preparation still offers many advantages. Compared to five- and six-membered iminosugars (e.g. polyhydroxylated pyrrolidines and piperidines), the synthesis of seven-membered analogues (polyhydroxylated azepanes) received little attention, albeit these compounds displayed interesting biological properties [2]. Therefore, the development of efficient and selective strategies for their preparation is of great interest.

In this context, we present a straightforward approach to pentahydroxylated azepanes **1** bearing five-contiguous stereocenters, three of which derive from the starting key intermediate **2**, a masked dialdehyde obtained from D-mannose.

We envisaged that the reductive amination reaction, widely employed for the preparation of polyhydroxylated piperidines [3], could be also useful in this case. The key step of our approach relied on a "tethered aminohydroxylation" (TA) reaction, introduced by Donohoe in 2001 [4], which we previously exploited for the stereoselective synthesis of 2- and 3-aminosugars from glycals [5]. This reaction, combined with the addition of a vinyl metal to aldehyde **2** [6], allowed the stereoselective introduction of the remaining two stereocenters.



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