

THE SYNTHESIS OF CARBOHYDRATE PROCESSING ENZYME INHIBITORS

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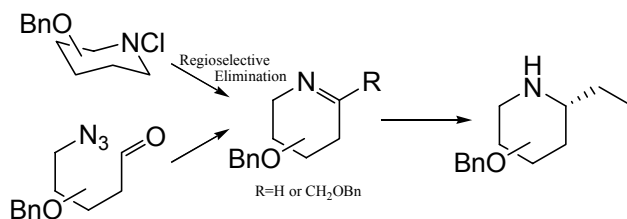
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Iminosugars are carbohydrate mimics in which the ring oxygen has been replaced by a nitrogen atom. Iminosugars have been shown to act as inhibitors of carbohydrate processing enzymes and, as such, have important roles in the possible treatment of lysosomal storage diseases such as Gaucher's disease,^[1] and viral infections such as hepatitis.^[2]

This paper details the synthesis of iminosugars derived from nucleophilic additions to sugar imines. These imines allow introduction of various functional substituents at the pseudo-anomeric centre of the iminosugar at a late stage of the synthesis allowing easy access to a wide variety of species.

Imines were obtained from Staudinger aza-Wittig cyclisations on a variety of 4- or 5-azido sugars (*gluco-*, *galacto-*, *ido-*, *altro-*, *rhamno-*). Elimination of HCl from *N*-chloramines at room or low temperatures gives regioselective access to either ketimine or aldimine, which were identical to those obtained from the Staudinger aza-Wittig reactions.

Stereoselective addition of a variety of nucleophiles (including organometallic, Mukaiyama aldol and Ugi additions) to these imines has been performed giving good stereocontrol and iminosugars with a diverse array of functionality at the pseudo-anomeric centre.



[1] T.D. Butter, R.A. Dwek, F.M. Platt, *Chem. Rev.* **2000**, *100*, 4683-4696

[2] T.M. Chapman, I.G. Davies, B. Gu, T.M. Block, D.I.C. Scopes, P.A. Hay, S. M. Courtney, L. A. McNeill, C.J. Schofield, B.G. Davis, *J. Am. Chem. Soc.* **2005**, *127*, 506-507