



## NMR conformational analysis of glycosylated iminosugars inhibitors of barley β-amylase

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Starch, a polymer of glucose, has an enormous societal and commercial importance, reflected by the huge scale of cereal production per year [1]. On the other hand, the expected increase in world population in next decades is pushing its demand up to levels that will need substantial improvements in crop yields. In the context of a reverse chemical genetic approach, aimed to deepen the understanding of metabolic pathways in barley seeds, three glycosylated iminosugars were prepared as inhibitors of one of the ezymes involved in starch metabolism, the barley  $\beta$ -amylase [2].



Interestingly, observed differences in inhibition potencies could not be fully rationalized on the grounds of their 3D structures of the complexes obtained from X-ray crystallography. In the present work the conformational properties of the three compounds in the free state have been studied by NMR spectroscopy and molecular modelling. Interglycosidic proton-proton distances have been obtained from NOE experiments, and compared with theoretical models obtained from Monte Carlo Stochastic Dynamics (MC/SD) simulations. The data revealed a significant increase in the flexibility of the S-substituted glycosydic linkage, which allowed to rationalize the unexpected reduction in inhibitory activity of **2**.

Tester, R.F.; Karkalas, J. *Polysaccharides II*; Vandamme, E.J., De Baets, S., Steinbuchel, A. Eds.; Biopolymers; Wiley-VCH: Weinhem, 2002.

<sup>[2]</sup> Rejzek, M.; Stevenson, C. E.; Southard, A. M.; Stanley, D.; Denyer, K.; Smith, A. M.; Naldrett, M. J.; Lawson, D. M.; Field, R. A. *Molecular BioSystems* 2011, 7, 718.