NOVEL DI-BRANCHED MONOSACCHARIDES AND IMINO SUGARS

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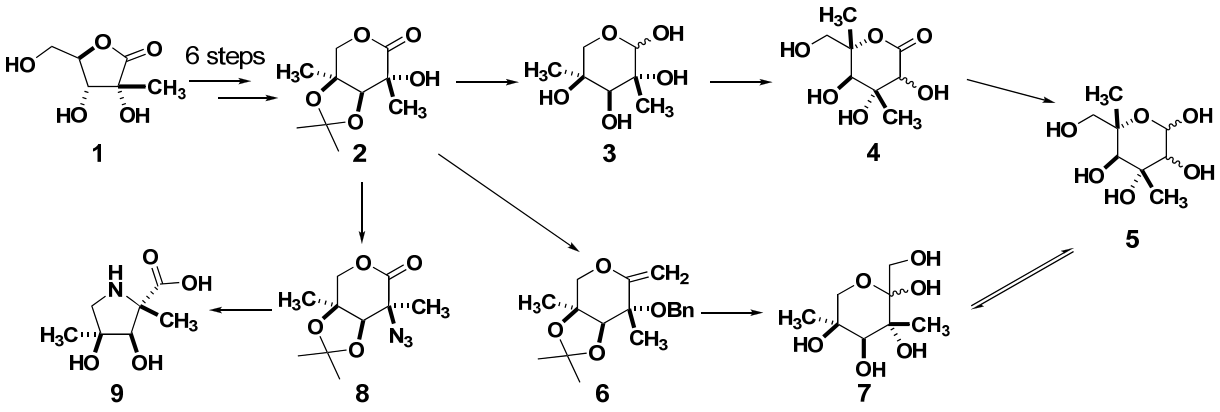
Molecular modelling has indicated that branched glucose analogues may be effective inhibitors of glycogen phosphorylase (GP).[1] GP is involved in glycaemic response and its inhibition is one strategy under investigation against type 2 diabetes.[2] With this in mind, two complementary syntheses of the di-*C*-methyl branched glucose analogue **5** were proposed.

The dimethyl branched lactone **2** can be synthesised in high yield from the readily available branched sugar **1**,[3] utilising the Kiliani reaction.[4] A second Kiliani reaction gives the enantiomeric lactones **4**, which are swiftly converted into the free *gluco* and *manno* configured sugars **5**. Also, protection of **3** followed by treatment with Cp_2TiMe_2 gives **6**,[5] which after dihydroxylation and deprotection affords 3,5-di-*C*-methyl-L-fructose **7** (Scheme 1). It has been demonstrated that many sugars may be interconverted via enzymatic pathways.[6] Therefore, we envisage that treatment of a branched sugar, such as **7**, in a similar fashion will give the desired 3,5-di-*C*-methyl-L-glucose and/or mannose **5** in a single step. This is currently under investigation.



Scheme 1: Divergent syntheses of branched sugars from novel lactone **2**.

Imino sugars, in which the endocyclic oxygen has been replaced by nitrogen, have shown potential as therapeutics for lysosomal storage disorders, provoking exploration into the synthesis of branched analogues.[7] By introduction of an azide functionality, lactone **2** has been used in the synthesis of **9**, a branched hydroxy proline derivative (Scheme 1).

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