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(4→4)-Di(2,3-anhydropentopyranosides), a Novel Class of Potential Enzyme Inhibitors

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Abstract

An easy access in high yields to 4,4`-diepoxydisaccharides, is described reacting epoxy hydroxy enolate pyranosides with the corresponding triflates. This new class of synthons are of interest for further chemical transformations as well as potential enzyme inhibitors.

'Keywords: `Anhydro sugars; Enzyme inhibitors; Disaccharides.

The increased interest in epoxy sugars is not only based on their versatility as intermediates in the synthesis of a variety of modified sugars[1], chiral building blocks[2] or natural products[3], but also on their biological activity as enzyme inhibitors.

There exist several examples in the literature, oxirane ring-containing carbohydrate derivatives to be potential enzyme inhibitors: e.g. 2,3-epoxypropyl-β-D-glycosides of 2-acetamido-2-deoxy-D-glucose and its oligomers are inhibitors of hen's egg-white lysozyme[4-6], 2,3-epoxypropyl-β-D-glucopyranoside irreversibly inhibits yeast hexokinase[7,8], similar derivatives of cellobiose and cellotriose show inhibiting activity against cellulase[9] and the gluco derivative of glycosylceramide inhibits LacCer synthesis[10]. In all these cases, nucleophilic opening of the epoxide ring occurs, while the inhibitors are attached to the active site of the enzyme, resulting in covalent binding to the site.

Recently we have examined a variety of sugar derivatives[11] as possible inhibitors for a new thermostable neutral proteinase, isolated from *Saccharomonospora canescens* and purified by our group[12]. Among all tested compounds, benzyl-2,3-anhydro-β-L-ribopyranoside **1** and benzyl-2,3-anhydro-α-D-ribopyranoside **2** exhibited the highest inhibiting activity[11]. This inhibitory effect of these compounds prompted us to design and synthesize new carbohydrate derivatives with epoxy moieties, and we describe herein a one-pot procedure for the synthesis of a new class of 4,4`-diepoxydisaccharides (**5-8**).

In a representative procedure, **1** was treated with one equivalent of sodium hydride in THF at 0 °C , then benzyl-4-O-tifluoromethanesulfonyl-2,3-anhydro-β-L-ribopyranoside (**3**)[2] was added and the solution stirred for three hours followed by acidic aqueous work up affording

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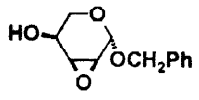
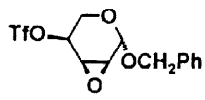
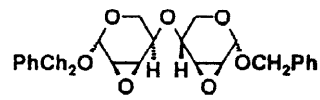
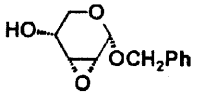
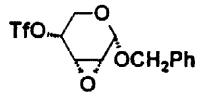
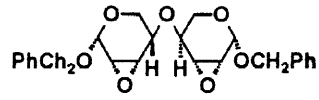
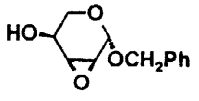
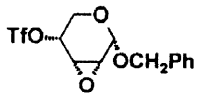
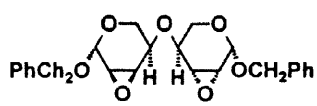
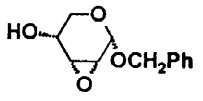
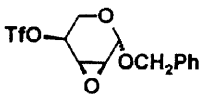
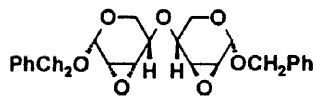
4-O-(benzyl-2,3-anhydro-β-L-ribopyranoside)-(4→4)-benzyl-2,3-anhydro-α-D-lyxopyranoside (**5**). The same procedure was used to synthesize **6-8** in yields of 82-91% (Table1).The structures of the new disaccharides were confirmed unequivocally by mass spectra, elemental analyses ^{1}H and ^{13}C NMR spectra. ^{13}C NMR of **5** in $CDCl_3$, δ: 50.1, 50.2, 52.2, 54.3 (C-2, C-2`, C-3, C3`); 57.9,59.6 (C-5, C-5`); 68.4, 70.3 (C-4, C-4`); 69.9, 70.5 (CH_2Ph, CH_2Ph`); 128.0-128.6, 137.0, 137.5 (Ph, Ph`).

The synthesis of the previously unknown disaccharides gives access to a new class of chiral synthons, which are of interest for further chemical transformation and eventual biological activities.

Table 1. Products and yields for the reaction of epoxypyranosides with their corresponding epoxytriflates.

Reactants		Products	Yield(%)
 1	 3	 5	87
 2	 4	 6	82
 1	 4	 7	91
 2	 3	 8	84

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