Riga Technical University
Faculty of Material Science and Applied Chemistry

ABSTRACTS

of

Riga Technical University

54th International Scientific Conference

Section:

Material Science and Applied Chemistry

October 14-16, 2013, Riga, Latvia

Riga 2013

Synthesis of Isoxazole Glycohybrids

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Keywords **– isoxazole, carbohydrates, 1,3-dipolar reaction, Michael addition, diacetone-α-D-glucose, glycohybrids.**

INTRODUCTION

Isoxazoles are recognized as versatile structural elements in biologically active substances [1]. They are often used as linkers between different pharmacophores. Isoxazoles have found their way in carbohydrate chemistry together with triazoles, which are other prominent azole congeners of the former [2].

DISCUSSION

Herein we report a novel approach to isoxazole- or/and thioether-amine-linked glycoconjugates that is based on the sequential Michael addition – 1,3-dipolar cycloaddition reactions.

As a starting material to prepare the different products of nuclephilic addition we have used inexpensive and commercially available diacetone-α-D-glucose **1**. Its oxydation followed by the Henry reaction with nitromethane provided the diastereomeric mixture of nitroalcohols that were dehydrated into **2** by the Moffatt procedure.

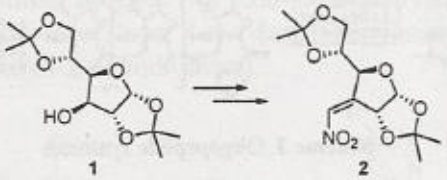

Figure 1. General route for the preparation of Michael acceptors

We have identified glucose-derived nitroalkene **2** as a suitable structural motif that is capable to link a molecule possessing nucleophilic centre and a molecule possessing terminal alkyne.

Michael addition of nucleophiles to corresponding acceptor **2** allows the formation of novel sugar derivatives. Various *O-*, *S-*, *N*-adducts are possible, including the addition of natural amino acid esters, thiol moiety containing sugars, monoamino or diaminosugars. Further, the Michael adducts can be converted either to spirocyclic sugar-piperazinones or they can serve as precursors for isoxazole synthesis.

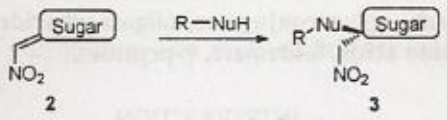

Figure 2. Stereospecific Michael addition to nitroolefine **2**

The key starting material **2** accepts nucleophiles selectively from its *si*-face [3].

The resulting nitromethyl group can be transformed into nitrile oxides and then coupled with suitable terminal alkynes. Both the Michael addition and the 1,3-dipolar cycloaddition occur with excellent isolated yields.

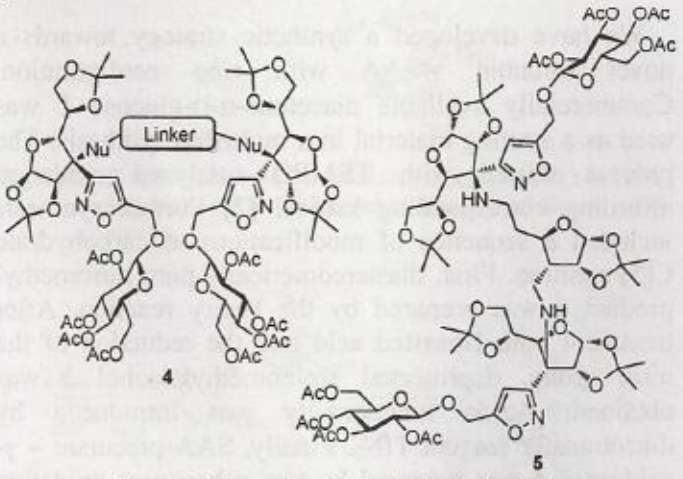

Figure 3. Examples of obtained glycohybrids

The overall process depending on starting material combination yields either disaccharides, trisaccharides or isoxazole glycohybrids of type **4** and **5**.

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