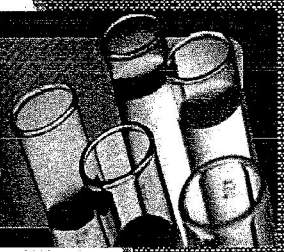
International Symposium organised
in honour of Prof. Alain Krief

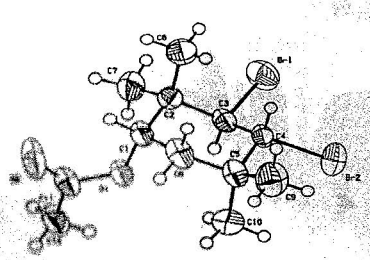
LOST II

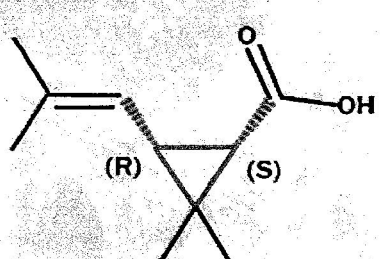
Learning Organic Synthesis Tremendously

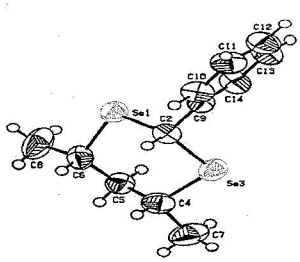


Namur, Belgium

March, 18-20, 2009







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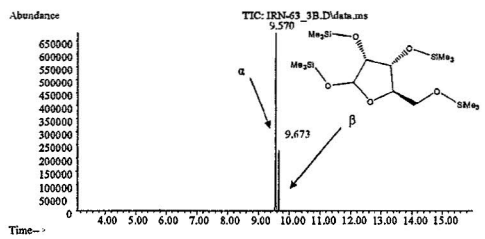
PROGRAM and ABSTRACT

and other acids. One of the highlights is GC-MS analysis of sugar samples which is represented here by an example with ribose (Figure 1).

Figure 1.



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Furan as a masked reactive entity for the generation of reactive oligonucleotides

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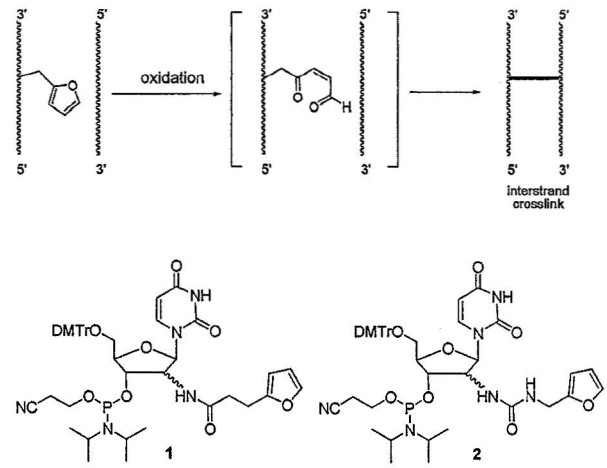
The natural toxicity of furan is due to it's metabolic oxidation to the reactive cis-2-butene-1,4-dial. This process in which a stable furanunit is converted to a reactive functionality is very convenient for the postsynthetic generation of a reactive entity in an oligonucleotide. If the reactive entity is generated after hybridization of the oligonucleotide with its complement, efficient formation of a crosslink is observed.[1]

In order to insert the furan unit in the oligonucleotides, phosphoramidites **1** and **2** are synthesized in the ribo and arabino configuration. Results about incorporation in oligonucleotides and further duplex crosslinking studies will be presented.



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The synthesis of novel glycoamino acids

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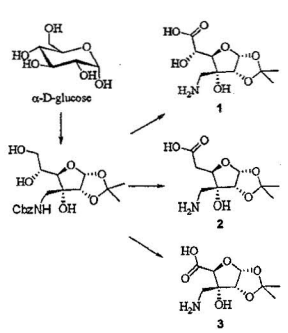
Sugar-amino acids (SAA) are synthetic scaffolds, combining both amino acid functionality and sugar platform in one compound. This provides great versatility for using SAAs as building blocks in peptide and polysaccharide synthesis. Since sugar moiety provides great opportunities for derivatization, SAAs are excellent object for combinatorial chemistry, and were intensively studied recently [1]. Various SAAs and their derivatives show biological activity, can be used as protease and glycosidase inhibitors, as well as peptidomimetics. In carbohydrate chemistry SAAs provide great opportunity to use advanced peptide synthesis methods to obtain polysaccharides. SAA oligomers have shown self-organizing secondary structures, that can contribute to their biological activity [2].



We are presenting here the synthesis of novel SAAs **1**, **2** and **3**, derived from α-D-glucose. Placing -CH_2- linker between functional group and sugar platform will increase the degree of freedom, and would attribute to secondary structures of corresponding oligomers. Free hydroxyl groups can effect secondary structure stabilization and can be used for derivatization of SAAs.

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Synthesis of Novel Disaccharides with Extended Bis-Triazole-Linker

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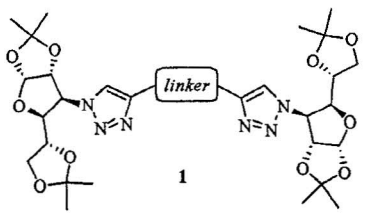
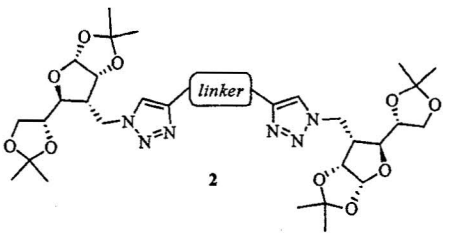
Since discovery of efficient catalysis for Huisgen dipolar cycloaddition between alkynes and azides,[1] this reaction has become a milestone in the field of derivatization of different molecular scaffolds.

Triazoles themselves possess interesting biological activities.[2] Moreover, when attached/fused to sugar or sugar-like scaffolds they show inhibitory effects on the proliferation of leukemia cells[3] and glycosidases.[4] On the other hand, triazole-carbohydrate conjugates have been also studied as antiviral[5] and antitubercular[6] agents, and multidentate ligands.[7]





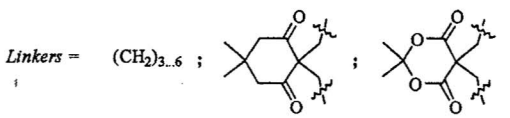
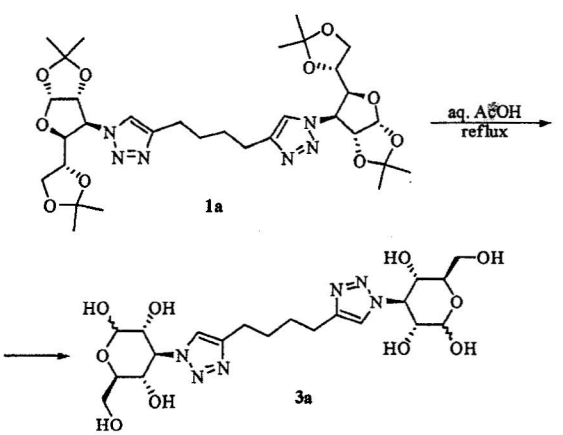


Figure 1.

Herein we report the synthesis of crystalline disaccharides of type **1** and **2** containing either *n*-alkane or cyclic linkers. The products were obtained in good to excellent isolated yields (70...95%) (Figure 1). The reactions between corresponding azides and 1,n-diynes proceeded

Scheme 1.



in 16-36 h at ambient temperature in acetone/water mixture with copper (II) sulfate pentahydrate and sodium ascorbate as the catalytic system. On the other hand, higher reaction temperatures or a change to CuI/DIPEA system gave shorter reaction times.

In order to cleave isopropylidene protecting groups **1** and **2** were refluxed in aqueous acetic acid yielding a mixture of α- and β-anomers of fully deprotected kanosamine derivatives of type **3** (Scheme 1). The latter are fully water soluble and ready for biotests.

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