STEREOSELECTIVE SYNTHESIS OF α-GLYCOSYL-THIOLS AND THEIR CONJUGATES BY CRYO THIOL-ENE PHOTOCOUPLING

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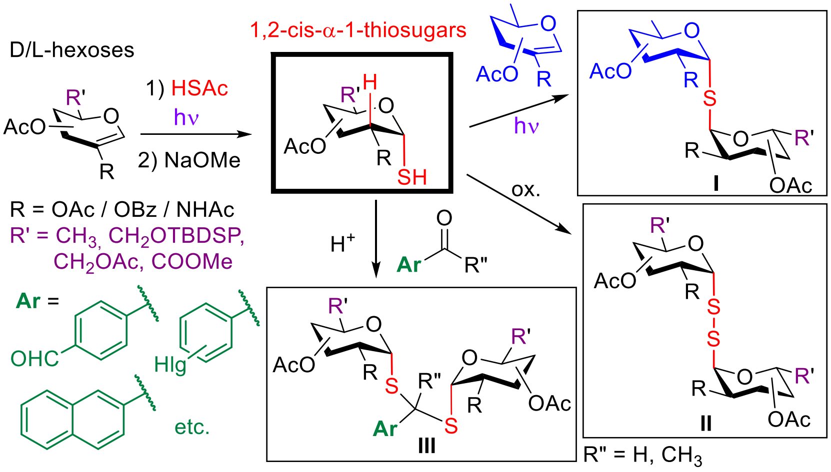
Thio-linked oligosaccharides, due to their high biological stability, are widely utilized as tools for elucidating carbohydrate function in living organisms, and several thioglycosides are currently under investigation as therapeutics. α-Glycosyl thiols can serve as key building blocks for the synthesis of stable thioglycoside mimetics of widespread and biologically relevant α-O-glycosides, however, the stereocontrolled synthesis of 1,2-cis-α-glycosyl thiols is notoriously difficult using classical synthetic methods. To address this problem, we turned to the photocatalyzed thiol-ene reaction, which has been shown to be an efficient method for the synthesis of thioglycosides containing challenging glycosidic bonds [1].

Here, it will be presented that the photoinitiated radical-mediated addition of thioacetic acid to 2-substituted glycals followed by selective S-deacetylation is a general and fully stereoselective method for the synthesis of 1,2-cis-α-glycosyl thiols [2]. The low reactivity of thioacetic acid in the radical reaction was overcome by carrying out the reaction in AcOH or in neat HSAc at -80 °C with UV irradiation, resulting in high yields regardless of the sugar configurations. A self-made spiral vessel reactor was used to achieve efficient irradiation and simultaneous cooling, which allows for large-scale synthesis. By subjecting 1,2-cis-α-1-thiosugars to a second thiol-ene coupling reaction with 2-substituted glycals, trehalose-type symmetrical and unsymmetrical α,α'-thiodi- and oligosaccharides (**I**) were obtained with complete stereoselectivity. Oxidation of α-1-thiosugars provided an easy access to α,α'-diglycosyl disulfides (**II**), while dithioacetal-linked thiodisaccharide mimetics (**III**) were formed by reaction with oxo compounds.



References:
1. A. Borbás, *Eur. J. Chem.* **2020**, *26*, 6090–6101.
2. V. Kelemen, et al., *Eur. J. Chem.* **2019**. *25*(*64*) 14555-14571.