PYRANOSE DEACETYLATION REACTIONS WITH *CANDIDA ANTARCTICA* LIPASE-B RESULTING IN KEY INTERMEDIATES FOR THE SYNTHESIS OF 6'-GALACTOSYLLACTOSE

K. E. Hunt[1,2], A. T. García-Sosa[3], T. Shalima[1], U. Maran[3], R. Vilu[2] and T. Kanger[1]*

[1]Department of Chemistry and Biotechnology, School of Science, Tallinn University of Technology, Akadeemia tee 15, 12618, Tallinn, Estonia

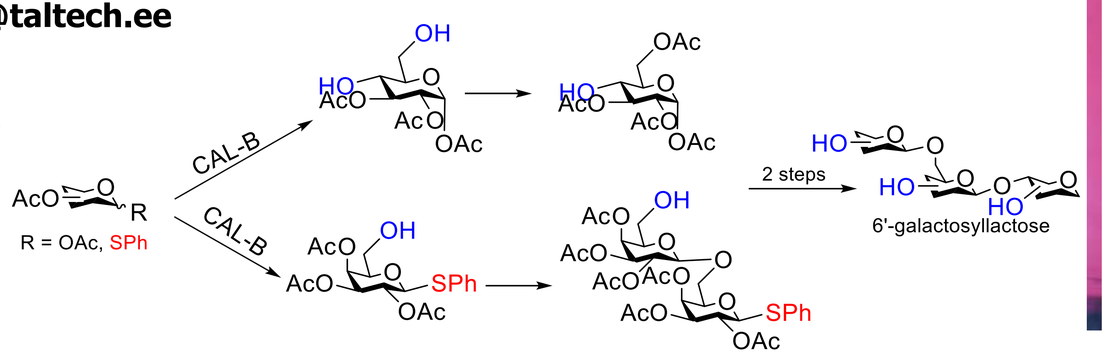
[2]Centre of Food and Fermentation Technologies, Akadeemia tee 15A, 12618 Tallinn, Estonia

[3]University of Tartu, Department of Chemistry, Ravila Street 14a, 50411 Tartu, Estonia

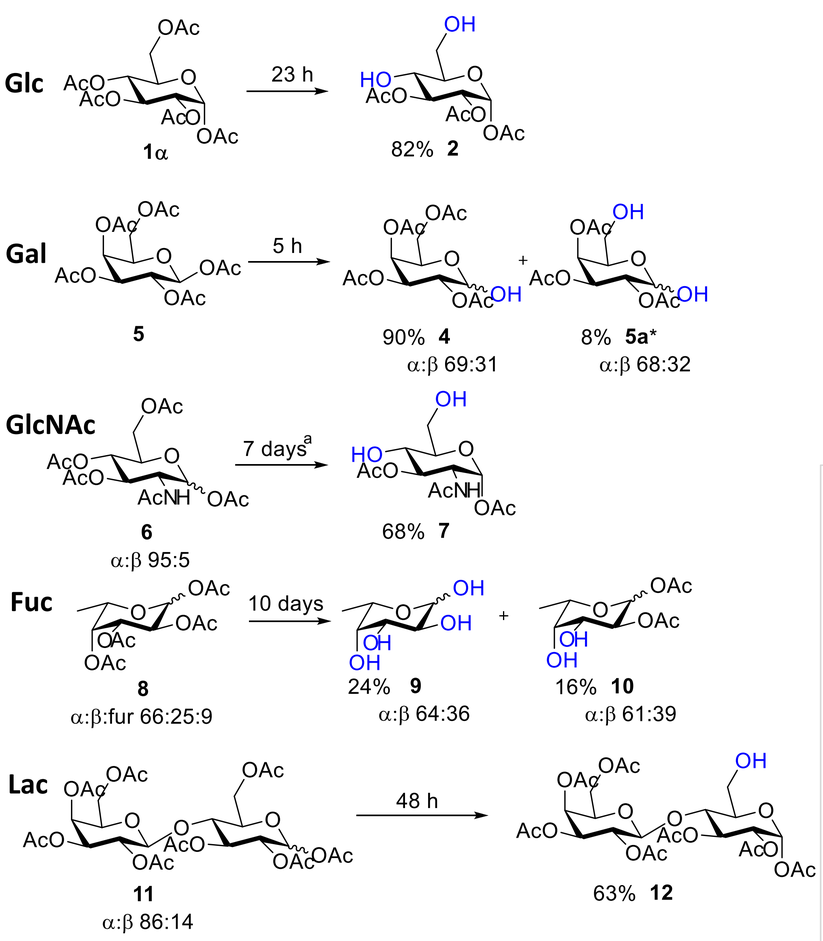
e-mail: kaarel.hunt@taltech.ee

INTRODUCTION

Human milk oligosaccharides (HMOs) are a group of indigestible oligosaccharides mainly found in human milk.[1] HMOs are shown to be beneficial for the development of infants – bacteria digest HMOs thus helping the growth of gut microbiota, can act as decoys for pathogens, alleviate allergic symptoms etc.[2,3] Here we present results for deacetylation reactions with *Candida antarctica* Lipase-B (CAL-B) with HMO building blocks and using those products a deviant HMO, 6'-galactosyllactose, was synthesised.[4]

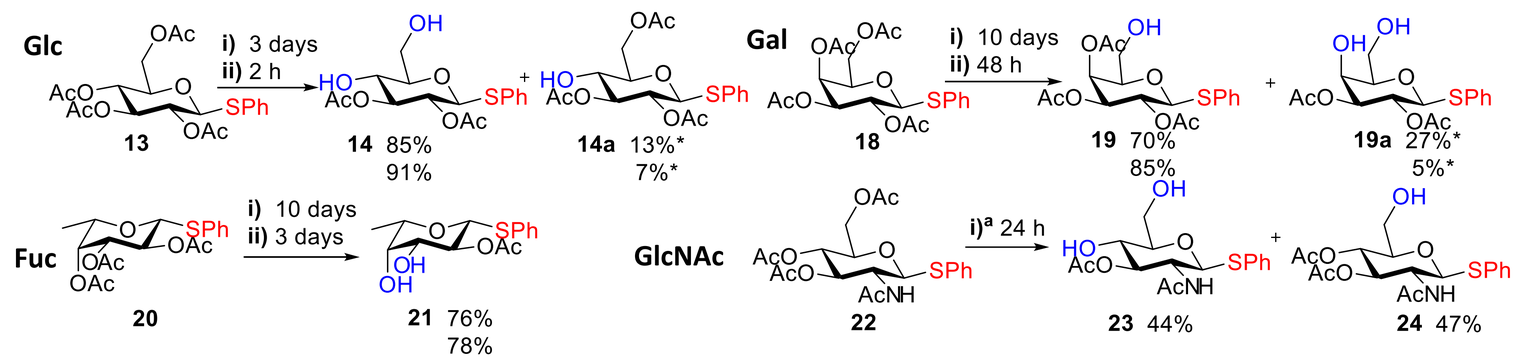


DEACETYLATION OF HMO BUILDING BLOCKS WITH CAL-B



Scheme 1 N435 deacetylation reactions with different peracetylated saccharides. Reaction conditions: saccharide (100 mg), N435 (100 mg), MTBE (10 mL), 45 °C, *n*-BuOH (3.5 equiv); [a] MTBE (20 mL); * mixture of products, dominant shown

Glc – D-glucose; Gal – D-galactose; Fuc – L-fucose; GlcNAc – D-glucosamine; Lac – D-lactose



Scheme 2 Deacetylation reactions with peracetylated thioglycosides. Reaction conditions: **i)** saccharide (100 mg), N435 (100 mg), MTBE (10 mL), 45 °C, *n*-BuOH (3.5 equiv); **ii)** saccharide (100 mg), N435 (200 mg), MTBE (10 mL), reflux, *n*-BuOH (3.5 equiv); [a] MTBE (20 mL); * mixture of products, dominant shown

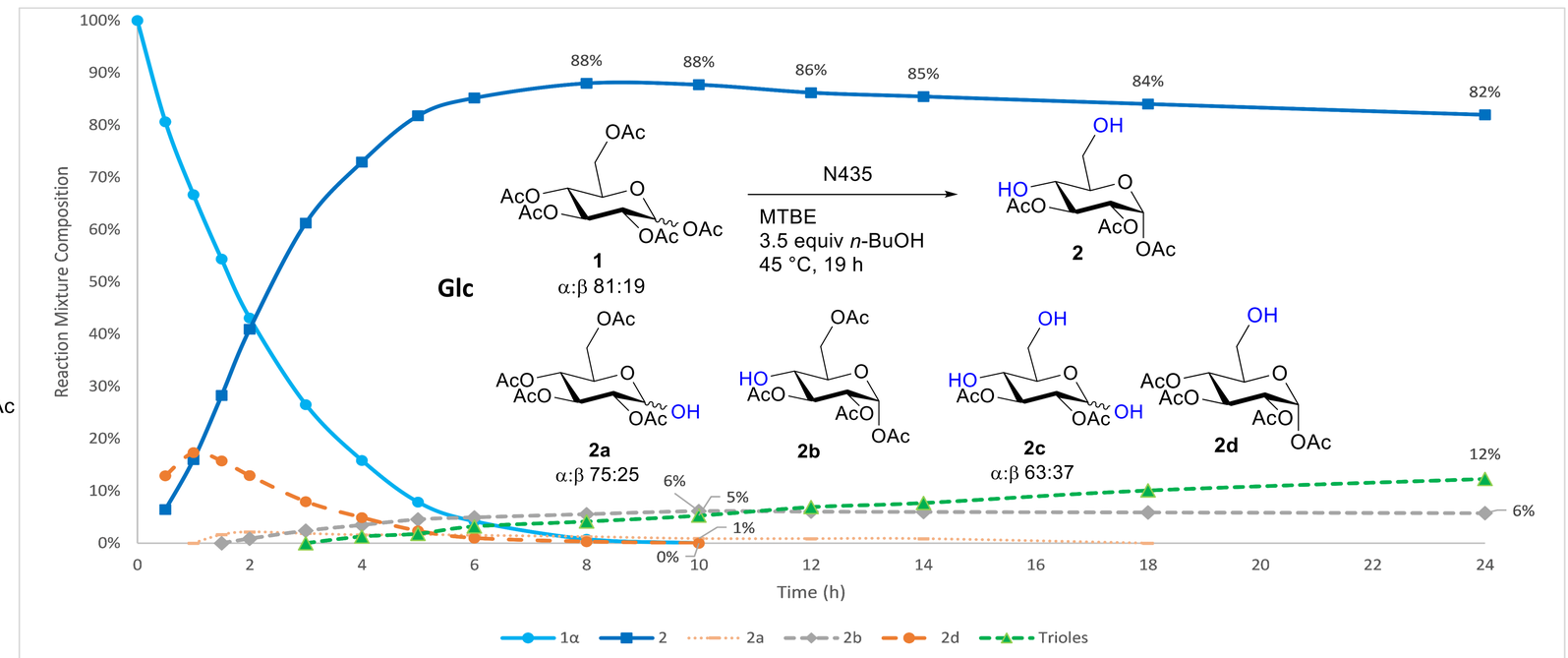


Figure 1 Kinetic study of N435 deacetylation reaction with **1α**. Reaction conditions: **1α** (100 mg), N435 (100 mg), MTBE (10 mL), 45 °C, *n*-BuOH (3.5 eqiuv)

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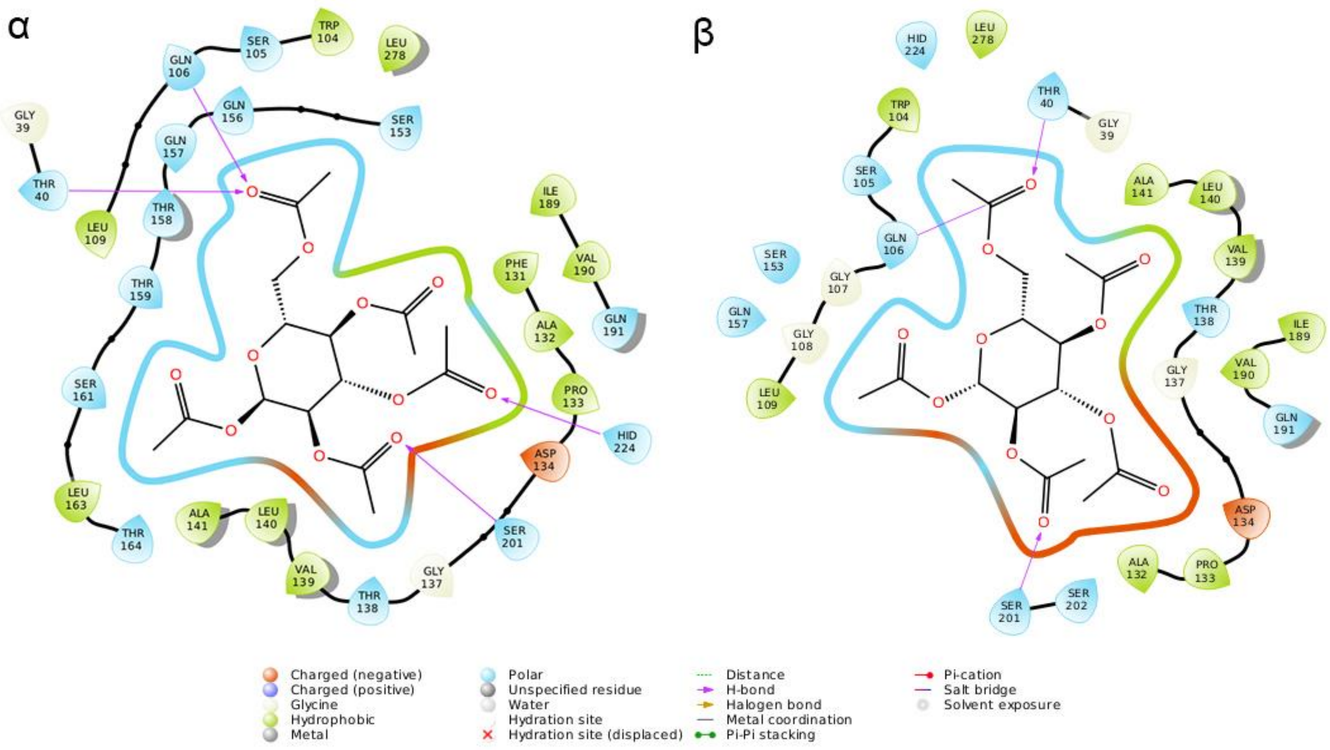
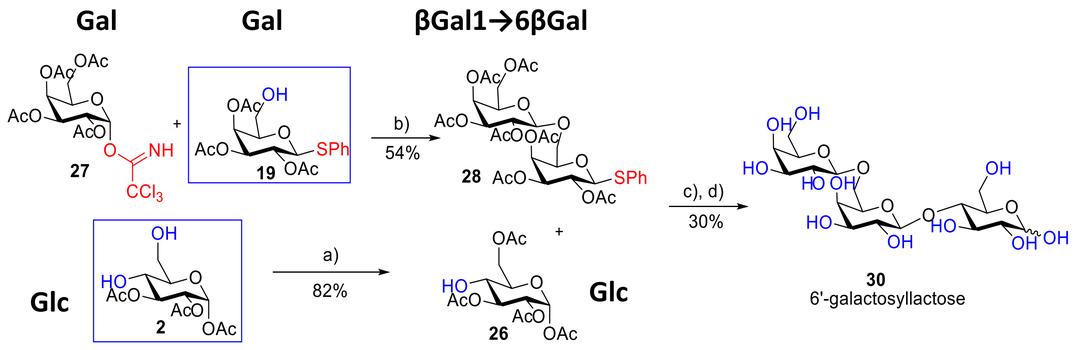


Figure 2 Interactions of α and β anomers of **1** with residues forming the CAL-B (1tca) binding site.

CONCLUSION



Scheme 3 6'-GL synthesis pathway from N435 deacetylated products, which are shown in blue boxes. a) AcCl, Pyridine, DCM, -40 °C -> room temperature, 4 h; b) $BF_3{\cdot}Et_2O$, DCM, 4 Å MS, -20 °C, 60 min; c) TfOH, NIS, DCM, 4 Å MS, -20 °C, 30 min; d) i) NaOMe, MeOH, room temperature, 1 h ii) Amberlite 120 H+, 1 h

Herein we have demonstrated that using immobilised CAL-B different HMO building blocks can be selectively deacetylated. Using two of the products, **2** and **19**, in a simple series of glycosylation reactions a deviant HMO, 6'-galactosyllactose was synthesised.

REFERENCES

1. Appl. Environ. Microbiol., 2012, 78, 4763–4770.
2. J. Dairy Sci., 2017, 100, 7825–7833.
3. Front. Pediatr., 2018, 6, 1–14.
4. Org. Biomol. Chem., 2022, 20, 4724-4735

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