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Extension of the βGal1,1-Transfer to N-Acetyl 5-Thio-Gentosamine by Galactosyltransferase

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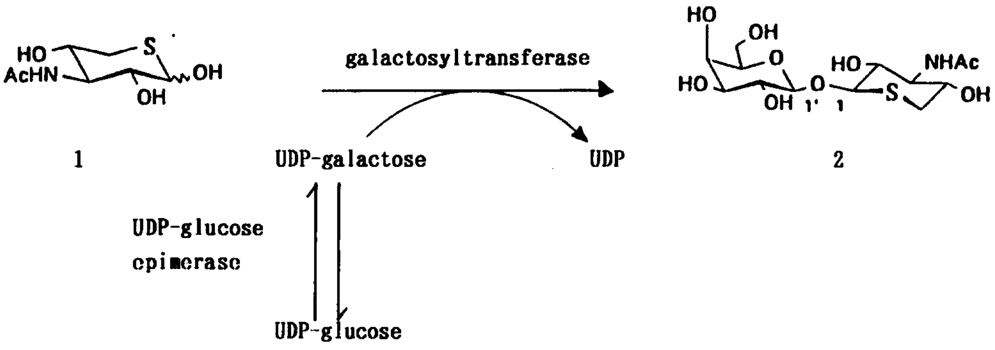
Summary: Galactosyltransferase (GalT) was found to transfer β-galactose to the β-anomeric position of *N*-acetyl-5-thio-gentosamine to afford a novel $\beta,\beta(1,1)$-linked disaccharide in 40% yield.

Galactosyltransferase from bovine milk (GalT, EC 2.4.1.22) has been conveniently used for syntheses of galactose terminated oligosaccharides[1] since stereo- and regioselectivity of the βGal transfer allows simple syntheses compared with chemical methods involving laborious steps for protections and deprotections. Although the transfer by GalT from bovine milk has long been known to be regiospecific at the OH-4 position of glucose analogs, we have previously[2,3] reported a new type of reaction affording a βGal1,1-linked disaccharide. This reaction, namely ***βGal1,1 transfer*** was explained by proposing a new pictorial map for the binding site of GalT.[3] The pictorial map also suggested that this new reaction could be extended to a variety of sugar substrates with or even without[4] *N*-acetyl group at the C-3 position. In this communication, a new substrate 3-acetamido-3-deoxy-5-thio-D-xylose 1 (5-Thio-Xyl3NAc[5]) was investigated in order to extend the scope of this new GalT reaction.

The substrate 1 was prepared according to the reported method[5]. A mixture of 1 (2 mg, 0.01 mmol), UDP-glucose (8 mg, 0.014 mmol), UDP-glucose-4-epimerase (0.5 U, EC 5.1.3.2) and GalT (0.2 U) was incubated at 37 ℃ in Tris-HCl buffer (pH 7.5, 1.5 mL). After 24 hrs the reaction mixture was processed in the reported manner[6] to afford a crude disaccharide (1.5 mg, 40 %). The structure was identified as 1-*O*-(β-D-galactopyranosyl)-3-acetamido-3-deoxy-5-thio-β-D-xylopyranoside 2 by ^{1}H-NMR spectroscopy; no α-anomeric proton was observed, and the two anomeric protons observed at 4.96 ppm (J=8.6 Hz, 5-Thio-Xyl3NAc residue) and 4.69 ppm (J=7.6 Hz, βGal residue) were highly deshielded compared with the β-anomeric proton of βGal1,4βGlcNAc or βGal1,4βGlc (*ca.* 4.4 ppm). Comparing the ^{1}H signals between the β-anomer of 1 and the 5-thio-Xy3NAc residue of 2 indicated substantial deshielding at H-1 (*ca.* 0.3 ppm) and H-2 (*ca.* 0.2 ppm,) after the glycosylation.



1 2

All this information as well as the comparison of the authentic NMR spectra of βGal1,1βGlc3NAc[2] and βGal1,1βXyl3NAc[3] allowed us to assign the structure of 2 as a βGal1,1-linked disaccharide.

Consequently, GalT was found to transfer β-galactose to the β-anomeric position of 1 as well as of Glc3NAc[2] and Xyl3NAc[3]. This means that the replacement of the ring oxygen (*O*) by sulfur (*S*) does not interfer with the βGal1,1-transfer reaction. This result has intensively extended the scope of the new transfer reaction by GalT.

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