Synthesis of an H Type 2 and a Y (Le\(^\uparrow\)) Glycoside from Thioglycoside Intermediates

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Received January 10, 1989.

Key words: synthesis, thioglycoside, H type 2 trisaccharide, Y (Le\(^\uparrow\)) tetrasaccharide

The trisaccharide 2-(p-trifluoroacetamidophenyl)ethyl 2-acetamido-2-deoxy-4-O-[2-O-(\(\alpha\)-L-fucopyranosyl)-\(\beta\)-D-galactopyranosyl]-\(\beta\)-D-glucopyranoside 1 and the tetrasaccharide 2-(p-trifluoroacetamidophenyl)ethyl 2-acetamido-2-deoxy-3-O-(\(\alpha\)-L-fucopyranosyl)-4-O-[2-O-(\(\alpha\)-L-fucopyranosyl)-\(\beta\)-D-galactopyranosyl]-\(\beta\)-D-glucopyranoside 2 were synthesized. Thioglycosides, suitably protected, activated directly with methyl trifluoromethanesulfonate or dimethyl(methylthio)sulfonium tetrafluoroborate or activated after bromine treatment with halophilic reagents, were used as glycosyl donors in the construction of the glycosidic linkages.

The fucosylated glycosides, H type 2 trisaccharide and Y (Le\(^\uparrow\)) tetrasaccharide, are parts of structures found in human glycosphingolipids, and also parts of glycosphingolipids associated with oncogenic transformation [1]. Synthesis of the H type 2 and Y (Le\(^\uparrow\)) determinants as the free saccharides or as glycosides of 8-carboxymethyloctanol and methanol have been described previously [2-8].

The H type 2 and Y (Le\(^\uparrow\)) spacer glycosides reported here can be coupled to proteins or to solid supports to be useful tools in various studies of biological phenomena where carbohydrates are involved. Hydrophobic spacer glycosides of this type are also useful in glycosyltransferase assays [9]. Saccharide 1 was found to be an acceptor for \(\alpha\)(1-3)fucosyltransferase from human colon carcinoma cell lines [10].

The chemical synthesis of oligosaccharides is more complex than the synthesis of other natural biopolymers, such as peptides or proteins and ribo- or deoxyribonucleotides, due to the greater possibility of combining the monosaccharides into oligosaccharides. However, several reasonable strategies can be used for oligosaccharide synthesis.

The use of suitably protected thioglycosides as synthons for the monosaccharide units in oligo- and polysaccharide synthesis has been proved to be successful [11]. The thioalkyl group protects the anomeric centre during the O-protection reactions and effectively reacts

Abbreviations: DMTS, dimethyl(methylthio)sulfonium tetrafluoroborate; Phth, phthaloyl; MBn, \(p\)-methoxybenzyl; ClBn, \(p\)-chlorobenzyl.
with various agents to form an active glycosyl donor. In this paper we present further examples of the use of thioglycosides in oligosaccharide synthesis.

Results

From the retrosynthesis of the oligosaccharides 1 and 2 we designed the monosaccharide synthons to be, for the $\alpha$-fucosyl group ethyl 2,3,4-tri-$\text{O}$-$\text{p}$-chlorobenzyl-1-thio-$\beta$-$\text{L}$-fucopyranoside 3, for the 2-substituted-$\beta$-galactosyl group ethyl 2-$\text{O}$-acetyl-3,4,6-tri-$\text{O}$-$\text{p}$-chlorobenzyl-1-thio-$\beta$-$\text{D}$-galactopyranoside 4, and for the 3,4-substituted-$\beta$-$\text{N}$-acetylglucosaminyl group ethyl 6-$\text{O}$-benzyl-2-deoxy-3-$\text{O}$-$\text{p}$-methoxybenzyl-2-phthalimido-1-thio-$\beta$-$\text{D}$-glucopyranoside 5. The $\text{p}$-chlorobenzyl protective group for thioglycosides 3 and 4 was chosen because of its better crystallization properties [12]. As the starting material for the spacer arm 2-(p-nitrophenyl)ethanol was chosen.

The synthesis of the monosaccharide building blocks was as follows: $\alpha$-$\text{L}$-fucose was treated, successively, with acetic anhydride/pyridine, ethanethiol/boron trifluoride etherate, sodium methoxide/methanol, and $\text{p}$-chlorobenzylchloride/sodium hydride to give thiofucoside 3 in 39% yield. Acetobromogalactose was reacted, successively, with ethanethiol/tetraethylammonium bromide/2,6-lutidine in nitromethane [13], sodium methoxide/methanol, $\text{p}$-chlorobenzyl chloride/sodium hydride, and trimethylsilyl triflate yielding thiogalactoside 4 in 59% yield. The thioglucosimide 5 was prepared as described [14].