Reactivity-based one-pot total synthesis of fucose GM$_1$ oligosaccharide: A sialylated antigenic epitope of small-cell lung cancer

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The total synthesis of the sialic acid-containing antigenic epitope fucose GM$_1$ (Fuc-GM$_1$) by an improved reactivity-based one-pot synthetic strategy is reported. Based on a thioglycoside reactivity database, three saccharide building blocks, 3, 4, and 5, were designed and prepared to incorporate a descending order of reactivity toward thioephilic activation. Using the reactivity-based one-pot synthetic method, the fully protected Fuc-GM$_1$ glycoside 2 was furnished in a facile manner, which was globally deprotected to give the Fuc-GM$_1$ glycoside 1. In addition, using the promoter system 1-(benzensulfinyl)piperidine/trifluoromethanesulfonic anhydride, the product yield was improved and the reaction time was reduced in comparison with the N-iodosuccinimide/trifluoromethanesulfonic acid- and dimethyl (thiomethyl) sulfonium trifluoromethanesulfonate-promoted systems.

Fucose GM$_1$ (Fuc-GM$_1$) ganglioside was first isolated from bovine thyroid tissue in 1979 (1). It is comprised of a hexasaccharide carbohydrate moiety and a ceramide-reducing end component. Within this carbohydrate framework is a tetrasaccharide (sugars a, b, d, and e) bearing a branched sialic acid residue (c) and a terminal fucose (f) (Fig. 1). It is found specifically in the tumor tissue of small-cell lung cancer (SCLC). SCLC accounts for 20% of lung cancer, which remains one of the leading causes of death in the United States (2). Unlike other cancer antigens, Fuc-GM$_1$ has a more restricted distribution in specific tissues in the body. For example, the tumor tissue of small-cell lung cancer (SCLC) is an attractive target for active immunization. Development of an anti-(Fuc-GM$_1$) vaccine and mAb could potentially be of importance for diagnosis and immunotherapy of these tumors (3, 4). However, one of the barriers preventing effective production of an anticancer vaccine is the limited supply of chemically pure Fuc-GM$_1$ oligosaccharide. Despite the development of various oligosaccharide synthetic methods (5–8), the first synthesis of Fuc-GM$_1$ glycoside was reported by Allen and Danishefsky (9) two decades after its initial discovery. This elegant strategy incorporated the sulfonamide glycosidation method (10) in conjunction with a [3 + 3] convergent glycosylation, ultimately leading to the target glycoside. It required protecting group and anomeric leaving group manipulations and encountered a problem with stereoselective formation of the β(1,4) glycosidic bond between a bulky trisaccharide donor and the poor nucleophilic trisaccharide acceptor.

We envisioned that the incorporation of our programmable reactivity-based one-pot strategy (8) in the synthesis of the Fuc-GM$_1$ could simplify this complicated synthetic operation. In brief, the reactivity-based one-pot strategy is based on a developed competitive HPLC assay to assess quantitatively the reactivity of different thioglycosides, the so-called relative reactivity value (RRV). Such information is then used to guide the reactivity-based one-pot synthesis of an oligosaccharide without protecting group manipulation and intermediate isolation (8).

Along with this development, we also report the use of a different thioephilic promoter to improve the efficiency of the reactivity-based one-pot methodology.

Materials and Methods

General. All chemicals were purchased and used without further purification. Dichloromethane (CH$_2$Cl$_2$) was distilled over calcium hydride. Propionitrile (EtCN) was treated with activated molecular sieves (MS) (AW-300) overnight before use. MS used in glycosylation were crushed and flame-activated before use. Reactions were monitored with analytical TLC on silica gel 60 F254 plates and visualized under UV (254 nm) and/or by staining with acidic ceric ammonium molybdate. Flash column chromatography was performed on silica gel (35–77 μm) or iatro beads. $^1$H-NMR spectra were recorded on a Bruker DRX-500 (500 MHz) or DRX-600 (600 MHz) spectrometer at 20°C. Chemical shift (in ppm) was determined relative to either tetramethylsilane in deuterated chloroform (δ = 0 ppm) or acetone in deuterated water (δ = 2.05 ppm). Coupling constants in Hz were measured from one-dimensional spectra. $^{13}$C-Attached Proton Test ($^{13}$C-Apt) NMR spectra were obtained by using the same Bruker NMR spectrometers (125 or 150 Hz) and were calibrated with CDCl$_3$ (δ = 77.00 ppm). Peracetylated lactosyl acetate 11 is commercially available and monosaccharide building blocks 3 (8), 6 (8), 9 (11), 14 (12), and 15 (8) are known compounds. Experimental details for the synthesis of the key thioglycoside building blocks, 4, 5, and 10, the protected Fuc-GM$_1$ 2 and the unprotected Fuc-GM$_1$ 1 are described. The synthesis of the remaining reaction intermediates 7, 8, 12, 13, and 16 and all of the characterization data for 1, 2, 4, 5, 7, 8, 10, 12, 13, and 16 together with their NMR spectra are reported separately in the Supporting Text and Figs. 4–23, which are published as supporting information on the PNAS web site, www.pnas.org.

Abbreviations: RRV, relative reactivity value; Fuc-GM$_1$, fucose GM$_1$; EtCN, propionitrile; MS, molecular sieves; NIS, N-iodosuccinimide; TfOH, trifluoromethanesulfonic acid; DMTST, dimethyl (thiomethyl) sulfonium trifluoromethanesulfonate; BSP, benzensulfinylpiperidine; Tf$_2$O, trifluoromethanesulfonic anhydride; sat. aq., saturated aqueous.

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Disaccharide Building Block (4). Disaccharide precursor 10 (0.27 g, 0.27 mmol) was dissolved in dry pyridine (3 ml), and 1 M hydrazine hydrate (NH₂NH₂·H₂O) in pyr/AcOH mixture (vol/vol = 3:2) (0.81 ml, 0.81 mmol) was added. The reaction mixture was stirred at room temperature for 4 h and then penta-2,4-dione (1 ml) was added. The solvent was removed under reduced pressure, and the residue was dissolved in CH₂Cl₂, washed with H₂O and brine, dried (Na₂SO₄), concentrated, and purified by flash column chromatography purification (hexane/EtOAc, 2:1) to provide the desired disaccharide 4 (0.218 mg, 81%) as a white glassy residue.

Trisaccharide Building Block (5). Sialyl donor 14 (1.4 g, 1.9 mmol), lactoside acceptor 13 (2.8 g, 2.6 mmol), and MS (3 g) were stirred in dry EtCN (15 ml) at room temperature for 2 h under Ar. The mixture was then cooled to −45°C and 0.5 M trimethylsilyl trifluoromethanesulfonate in EtCN (380 µl, 0.19 mmol) was added. The reaction mixture was stirred at −30°C overnight, and then quenched with triethylamine. The reaction mixture was then filtered and concentrated under reduced pressure. The residue was diluted with CH₂Cl₂ and washed with saturated aqueous (sat. aq.) NaHCO₃, H₂O, and brine and dried (Na₂SO₄). The resulting crude mixture was purified by flash column chromatography (gradient eluent hexane/EtOAc, 1:1 → 1:1.5) to yield 5 (1.6 g, 53%) as a colorless glassy residue.

Disaccharide Building Block Precursor (10). Galactosaminyl acceptor 8 (0.3 g, 0.55 mmol), galactosaminyl donor 9 (0.47 g, 0.72 mmol), and MS (0.75 g) were suspended in dry CH₂Cl₂ (3 ml) for 1 h at room temperature under Ar and then cooled to −45°C. N-iodosuccinimid (NIS) (0.16 g, 0.72 mmol) and 0.5 M trifluoromethanesulfonic acid (TfOH) in Et₂O (144 µl, 0.072 µmol) were added. The reaction mixture was stirred at −45°C for 3 h and quenched with sat. aq. NaHCO₃ and solid Na₂S₂O₅. The reaction mixture was filtered and washed with sat. aq. NaHCO₃, H₂O, and brine, dried (Na₂SO₄), and concentrated for flash column chromatography purification (hexane/EtOAc, 2:1) to yield 10 (0.27 g, 45%) as a white glassy solid.

NIS/TfOH Promoted One-Pot Synthesis of Protected Fuc-GM₁ (2). Fucosyl donor 3 (0.158 g, 0.29 mmol), disaccharide building block 4 (0.22 g, 0.225 mmol), and MS (0.75 g) were stirred in dry CH₂Cl₂ (3 ml) at room temperature for 1 h under Ar and cooled to −78°C. This was followed by the addition of NIS (66 mg, 0.29 mmol) and 0.5 M TfOH in Et₂O (58 µl, 0.29 mmol). The reaction mixture was stirred at −70°C for 2 h. After consumption of donor 3 (TLC, hexane/EtOAc, 2.5:1), the trisaccharide acceptor 5 (0.69 g, 0.45 mmol) in dry CH₂Cl₂ (2 ml) was added followed by freshly prepared dimethyl (thiomethyl) sulfonium trifluoromethanesulfonate (DMTST) (0.29 g, 1.125 mmol) in CH₂Cl₂ (1 ml). The reaction mixture was stirred at 0°C overnight and quenched with sat. aq. NaHCO₃ and solid Na₂S₂O₅, filtered, washed with sat. aq. Na₂S₂O₅, sat. aq. NaHCO₃, H₂O, and brine, dried (Na₂SO₄), and concentrated. The crude mixture was purified twice by flash column chromatography (toluene/EtOAc, 1:2, followed by toluene/aceton, 4:1) to provide Fuc-GM₁ 2 (0.23 g, 36%) as a white glassy solid.

Benzensulfinylpiperidine (BSP)/Trifluoromethanesulfonic Anhydride (Tf₂O) Promoted One-Pot Synthesis of Protected Fuc-GM₁ (2). Fucosyl donor 3 (0.092 g, 0.17 mmol), disaccharide building block 4 (0.16 g, 0.16 mmol), BSP (0.018 g, 0.088 mmol), and MS (0.75 g) were stirred in dry CH₂Cl₂ (2 ml) at room temperature for 1 h under Ar. The reaction mixture was cooled to −70°C, followed by the addition of Tf₂O (16 µl, 0.086 mmol), and the temperature was increased gradually from −70°C to −10°C within 1 h. After the donor 3 was consumed, the reaction mixture was cooled to −70°C, which was followed by the addition of the trisaccharide acceptor 5 (0.34 g, 0.22 mmol). Subsequently the second portion of BSP (0.017 mg, 0.08 mmol) and Tf₂O (15 µl, 0.088 mmol) was added. The reaction temperature was increased gradually from −70°C to 0°C in 1 h and the mixture was stirred at 0°C for an additional 4 h. The reaction was quenched with triethylamine.
and the mixture was stirred under H2 (1 atm) at room temperature for 18 h. The reaction mixture was filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (toluene/acetone, 4:1). The protected Fuc-GM1 was subsequently dissolved in MeOH with 10% (wt/vol) of formic acid (3 ml). To the reaction mixture, Pd-black (70 mg) was added. The mixture was stirred for 3 h and neutralized with concentrated HCl. The deacylated residue, which was dissolved in MeOH with 10% (wt/vol) of formic acid, was stirred for 10 h at room temperature and neutralized with Amberlite IR-50 resin. After removal of the protecting groups and design of building blocks. The Fuc-GM1 hexasaccharide was retrosynthetically disconnected into three saccharide building blocks: fucosyl building block 3, disaccharide building block 4, and sialylated trisaccharide building block 5 (Fig. 2). Implementation of reactivity-based one-pot oligosaccharide synthesis requires a descending order of reactivity for these three building blocks. Based on the reactivity database (13), the perbenzylated fucosyl thioglycoside 3 with a RRV of 7.2 × 10^4 was selected as the first donor. The reducing end component is the sialylated trisaccharide building block 5, which is prepared from a lactoside acceptor 13 and sialic acid donor 14. Because 5 is an O-glycoside, a zero RRV can be assumed. The design of the disaccharide building block 4 demanded special concern. Because 4 is used as an acceptor and donor, the presence of a C2-free hydroxyl group on the galactosyl unit as well as a thiotoluene functionality at the anomeric center of the galactosaminy1 unit is required. In theory, its RRV should fall between 7.2 × 10^4 and 0. This criterion could be easily addressed by using appropriate protecting groups.

For an efficient reactivity-based one-pot synthesis, not only is the reactivity value of the thioglycoside building block important, careful selection of the glycosylation promoter is also imperative. Although much success has been observed in our previous one-pot syntheses (14–16), some difficulties occur when either a very reactive donor and/or a poor nucleophilic acceptor is used in glycosylations promoted by NIS/TfOH, mainly because of the competitive formation of an undesired succinimide byproduct (8, 17). To address this problem, a combination of NIS/TfOH and DMTST was used initially to establish the one-pot synthetic route for the target glycoside. Subsequent efforts were focused on the application of a recently developed thioglycoside promoter system, the BSP/Tf2O, to our one-pot synthesis to improve the efficiency of the process (18).

**Syntheses of Building Blocks.** With the synthetic plan in hand, we started the reactivity-based one-pot synthesis of Fuc-GM1 by preparing the three saccharide building blocks 3, 4, and 5.
Perbenzylated fucosyl thioglycoside 3 was prepared by a literature procedure (8). The disaccharide building block 4 can be accessed by glycosylation between a galactosyl donor and a galactosaminyl acceptor. 2-O-Levulinoyl-3,4,6-tri-O-benzyl-1-β-thio-D-galactoside 9 with a RRV of 4,000 was used as the galactosyl donor. The galactosaminyl acceptor should possess a C3-hydroxyl handle, a RRV smaller than 4,000, and a C2-participating group to dictate the β-selective glycosidic bond formation. To address these requirements, we took the advantage of our knowledge on the properties of various protecting groups to design the galactosaminyl thioglycoside 8.

The synthetic route for the galactosaminyl precursor 8 is shown (Scheme 1). Compound 6 was deacetylated by using Zemplén conditions (19), followed by benzylidene formation between the C4/C6 hydroxyls. The remaining C3 hydroxyl was converted to a levulinoyl (Lev) ester, giving the fully protected thioglycoside 7. Subsequent removal of the benzylidene protecting group was followed by reacetylation of C4/C6 hydroxyls and selective Lev deprotection (20), yielding the galactosaminyl acceptor 8. The RRV of 8 was determined to be 3,269 by using the reference method described (8). Because thioglycoside donor 9 is more reactive than 8, a reactivity-based glycosylation was performed in the presence of NIS/TfOH to give the disaccharide precursor 10. Finally, removal of the Lev protecting group afforded the desired disaccharide building block 4 and its RRV was determined to be 2,839.

Sialylated trisaccharide building block 5 was assembled from sialyl phosphite 14 (12) and lactoside acceptor 13. Synthesis of 13 began with the commercially available peracetyl β-lactoside acetate 11 (Scheme 2). 11 was converted to a lactosyl bromide by using 33% hydrogen bromide in acetic acid, followed by reaction with benzyl N-(2-hydroxyethyl)-carbamate in the presence of silver carbonate (Ag 2CO3) to provide an inseparable mixture of the desired β-lactoside and an orthoester byproduct. The acetyl protecting groups of the product mixture were removed and the C3/C4 hydroxyls were protected regioselectively with an isopropylidene acetal in the presence of p-toluene sulfonic acid. At this stage, the desired β-lactoside 12 could be isolated after chromatographic separation. Subsequent perbenzylation of 12 with benzyl bromide (BnBr) and sodium hydride (NaH) was followed by the deprotection of the C3/C4 isopropylidene acetal, giving the target acceptor 13. Regioselective glycosylation of 13 with 14 was promoted by trimethylsilyl trifluoromethanesulfonate in EtCN at -30°C to afford the desired α-(2,3)-sialylated product 5 in 53% isolated yield with only a trace amount of β-isomer (21).

Implementation of Reactivity-Based One-Pot Synthesis of Fuc-GM1 Glycoside. With the desired carbohydrate building blocks, 3, 4, and 5, and their RRV determined, the stage was set for the

Scheme 3. Reagents and conditions for NIS/Tf2O- and DMTST-promoted one-pot reaction: route a (i) NIS, TfOH, CH2Cl2, -70°C, 36%; (ii) DMTST, 0°C, 36%.

Reagents and conditions for BSP/Tf2O-promoted one-pot reaction: route b (i) BSP, Tf2O, CH2Cl2, -70°C to -10°C, 47%; (ii) BSP, Tf2O, CH2Cl2, -70 to 0°C, 47%.

Reagents and conditions for global deprotection: route c (i) Zn dust, acetic anhydride/CH2Cl2, 4-(dimethylamino)pyridine; (ii) NaOMe, CH2Cl2/MeOH; (iii) NaOH, THF/MeOH/H2O; (iv) Pd-black, MeOH with 10% (vol/vol) formic acid, H2 (1 atm), 44% over four steps.
reactivity-based one-pot synthesis of the Fuc-GM1 glycoside (Scheme 3, route a). Perbenzylated fucosyl building block 3 (RRV = 7.2 × 10^4) was coupled with the less reactive disaccharide building block 4 (RRV = 2,839) in the presence of NIS/TfOH (22). After 2 h at −70°C, trisaccharide acceptor 5 was added, followed by the addition of DMTST (23). The second glycosylation required higher reaction temperatures (0°C) and a longer reaction time (1 day). The slow reaction rate was partially attributed to the glycosylation between two large sugar fragments and this had previously been observed during the synthesis of an N-acetyllactosamine octamer (16). In addition, the C4-axial hydroxyl is a weak nucleophile, which further lowered the reaction rate. Nevertheless, the fully protected Fuc-GM1 2 was obtained in 36% isolated yield directly from the building blocks without protecting group manipulation and reaction intermediate isolation. This finding corresponds to an average yield of 60% per glycosylation step.

As access to the one-pot synthesis of the Fuc-GM1 glycoside was accomplished, we turned our attention to improving the efficiency of the established one-pot synthetic protocol. Drawbacks of the present NIS/TfOH and DMTST system were the slow reaction rate (1 day) and moderate yield (36%). To solve this problem, we sought a better promoter. Such a promoter should enable the activation of either a reactive or nonreactive thioglycoside donor without the formation of undesired competitive byproducts. BSP/Tf2O, a recently developed thiophilic reagent (Crich and Smith (18), is compatible to our reactivity-based one-pot glycosylation protocol and acts by in situ conversion of thioglycosides to glycosyl trifluoromethanesulfonates, which then couple with the nucleophilic acceptors efficiently.

To investigate the compatibility of BSP/Tf2O with the present one-pot protocol, we first carried out a reactivity-based glycosylation reaction with a model system (Fig. 3), which incorporated a very active donor and a poor acceptor. This combination was known to be problematic, using the NIS/TfOH promoter system as succinimide byproducts are observed. Thioglycoside acceptor 15 (8) with a RRV of 9.4 was glycosylated with fucosyl donor 3 (RRV = 7.2 × 10^4) in the presence of BSP/Tf2O. Despite the hindered acceptor site of 15, disaccharide product 16 was obtained in 95% isolated yield. Rather interestingly we have also determined that using a substoichiometric amount of BSP/Tf2O provides efficient disaccharide formation. One possible rationalization may be that the reaction pathway produces sulfonium byproducts, which can further promote glycosylations, as shown in Fig. 3. This possibility is supported by the fact that slightly more than half an equivalent of BSP/Tf2O provided a 95% yield of disaccharide product 16. Although no direct evidence for these sulfonium byproducts has been observed, detailed mechanistic studies should shed some light into the reaction pathway. It is also important to note that the reaction also proceeds efficiently with one equivalent of BSP/Tf2O (90%), but the reaction must be quenched at low temperatures (−60°C) with triethylamine for optimal yields. Being encouraged by these results, we further investigated the application of the BSP/Tf2O promoter system to the one-pot synthesis of the Fuc-GM1 (Scheme 3, route b). For the BSP/Tf2O promoted one-pot operation, the first stage glycosylation between fucosyl donor 3 and disaccharide acceptor 4 was completed in 1 h. For the second stage glycosylation between two trisaccharide fragments, the expected longer reaction time (3 h) was needed. The isolated yield of this BSP/Tf2O promoted one-pot reaction was 47%, corresponding to an average of 67% per glycosylation step. In terms of the reaction rate and product yield, the BSP/Tf2O system was substantially better than the NIS/TfOH and DMTST combination in promoting the one-pot glycosylation.

With the development of an improved reactivity-based one-pot synthetic operation, we proceeded to the global deprotection of Fuc-GM1. This process began with the removal of a Troc protecting group and reacylation of the exposed amino functionality by reduction with zinc dust in acetic anhydride. The O-acetyl groups were removed, followed by alkaline hydrolysis of the methyl ester on the sialic acid residue. Unfortunately, the final hydrogenolysis of benzyl and Cbz protecting groups proved problematic by using either the Birch reduction conditions (24) or palladium-catalyzed hydrogenolysis in methanol. After a series of experiments, a successful deprotection was finally accomplished by catalytic transfer hydrogenation using palladium black in methanol with 10% formic acid under hydrogen (1 atm) at room temperature (25). Fully deprotected Fuc-GM1 glycoside 1 was obtained in 44% yield from 2. The target glycoside 1 was characterized with standard NMR spectroscopic methods and high-resolution MS, which were in agreement with the literature reported data (9).

**Conclusion.** The total synthesis of a cancer related and antigenic carbohydrate epitope, the Fuc-GM1 glycoside, was accomplished by an improved reactivity-based one-pot synthetic strategy. Through selection and careful design of various carbohydrate building blocks and application of the BSP/Tf2O promoter system, an efficient reactivity-based one-pot synthetic protocol was successfully developed. Not only does the established one-pot protocol simplify the synthesis of the
Fuc-GM₁ glycoside, application of the BSP/Tf₂O promoter system improves the efficiency of the synthesis by shortening the reaction time and increasing the glycosylation yield. The building blocks and their reactivity developed in this study should find use in the one-pot synthesis of other oligosaccharides. It is reasonable to assume that the incorporation of the BSP/Tf₂O promoter system in our reactivity-based one-pot strategy can apply to the synthesis of more challenging targets.

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Experimental details for the syntheses of 7, 8 12, 13, and 16 and the characterization data for 1, 2, 4, 5, 7, 8, 10, 12, 13, and 16.

**For Deprotected Fuc-GM₁ Glycoside (1).** $^1$H NMR (600 MHz, D$_2$O) $\delta$ 5.07 (d, $J = 3.5$ Hz, 1H), 4.51 (d, $J = 7.5$ Hz, 1H), 4.44 (d, $J = 6.6$ Hz, 1H), 4.37–4.35 (m, 2H), 4.06–4.02 (m, 1H), 3.95 (dd, $J = 10.1$, 2.2 Hz, 1H), 3.92–3.90 (m, 3H), 3.81 (d, $J = 11.4$ Hz, 1H), 3.75–3.41 (m, 29H), 3.20–3.17 (m, 2H), 2.99 (s, 2H), 2.50 (dd, $J = 13.2$, 4.4 Hz, 1H), 1.85 (s, 6H), 1.73 (s, 1H), 1.03 (d, $J = 6.6$ Hz, 3H); $^{13}$C-Apt NMR (150 MHz, D$_2$O) $\delta$ 174.56, 173.80, 173.54, 102.76, 102.14, 101.68, 101.58, 100.89, 98.70, 75.99, 75.39, 74.44, 74.34, 73.65, 72.57, 72.29, 71.83, 71.39, 69.52, 69.10, 68.69, 68.23, 67.99, 67.61, 66.89, 66.29, 62.39, 60.67, 60.45, 60.04, 59.54, 51.16, 51.07, 39.17, 36.86, 22.27, 21.60, 14.92; High Resolution Mass Spectrometry for C$_{45}$H$_{76}$N$_3$O$_{33}$ (M – H)$^-$ calculated 1186.4366, found 1186.4619.

**For Protected Fuc-GM₁ glycoside (2).** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.52 (d, $J = 7.4$ Hz, 2H), 7.36–7.07 (m, 63H), 5.96 (d, $J = 8.8$ Hz, 1H), 5.52–5.47 (m, 2H), 5.09–5.26 (m, 6H), 4.96–4.92 (m, 2H), 4.84–4.72 (m, 6H), 4.68–4.38 (m, 19H), 4.33–4.29 (m, 3H), 4.22–4.15 (m, 4H), 4.10–3.94 (m, 11H), 3.89–3.86 (m, 2H), 3.81 (s, 3H), 3.76–3.73 (m, 2H), 3.67–3.62 (m, 5H), 3.56–3.44 (m, 10H), 3.35–3.26 (m, 2H), 2.34–2.30 (m, 1H), 2.15 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H), 1.96 (s, 3H), 1.92 (s, 3H), 1.90 (s, 3H), 1.88 (s, 3H), 1.03 (s, 3H); $^{13}$C-Apt NMR (150 MHz, CDCl$_3$) $\delta$ 170.65, 170.36, 170.31, 169.81, 169.60, 169.27, 168.58, 156.42, 156.16, 154.10, 139.15, 138.91, 138.70, 138.61, 138.50, 138.29, 138.12, 137.83, 137.78, 136.61, 136.47, 129.56, 128.97, 128.43, 128.40, 128.33, 128.24, 128.20, 128.12, 128.08, 127.97, 127.90, 127.88, 127.81, 127.76, 127.68, 127.64, 127.61,
127.56, 127.52, 127.42, 127.28, 127.26, 127.23, 127.14, 127.07, 127.03, 126.86, 126.75, 126.67, 126.44, 103.50, 102.76, 101.69, 99.12, 97.49, 95.78, 83.46, 82.54, 81.66, 79.04, 78.92, 77.84, 76.46, 76.17, 76.10, 75.93, 75.87, 74.96, 74.87, 74.81, 74.71, 74.52, 74.22, 74.15, 73.97, 73.52, 73.39, 73.22, 73.12, 72.50, 72.45, 72.31, 71.92, 71.62, 70.72, 70.09, 69.09, 69.06, 68.34, 68.20, 68.18, 68.00, 67.87, 67.22, 67.16, 66.44, 62.48, 61.66, 54.91, 53.15, 51.36, 49.34, 47.03, 45.96, 35.59, 29.63, 23.15, 21.22, 20.90, 20.78, 20.58, 20.55, 20.45, 16.82; HRMS for C_{151}H_{168}Cl_{3}N_{3}O_{42}Na (M + Na)^+ calculated 2823.0060, found 2823.0114.

For Disaccharide Building Block (4). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.40–7.25 (m, 17H), 7.09 (d, $J = 7.7$ Hz, 2H), 5.77 (d, $J = 6.6$ Hz, 1H), 5.32 (d, $J = 2.6$ Hz, 1H), 4.92 (d, $J = 11.4$ Hz, 1H), 4.76–4.71 (m, 5H), 4.56 (d, $J = 11.4$ Hz, 1H), 4.47 (d, $J = 11.7$ Hz, 1H), 4.44 (d, $J = 11.7$ Hz, 1H), 4.38 (d, $J = 8.1$ Hz, 1H), 4.13–4.08 (m, 3H), 3.97–3.90 (m, 2H), 3.84–3.78 (m, 5H), 3.73 (t, $J = 6.6$ Hz, 1H), 3.65–3.58 (m, 4H), 3.38 (dd, $J = 9.5, 2.6$ Hz, 1H), 2.32 (s, 3H), 2.03 (s, 6H); $^{13}$C-Apt NMR (125 MHz, CDCl$_3$) $\delta$ 171.53, 170.39, 154.66, 138.45, 137.90, 137.84, 137.71, 132.46, 129.89, 129.51, 128.49, 128.46, 128.34, 128.23, 127.85, 127.82, 127.79, 127.68, 102.63, 95.60, 88.20, 81.14, 74.88, 74.57, 74.47, 73.85, 73.74, 73.48, 72.97, 72.60, 70.04, 69.41, 67.82, 62.24, 52.19, 21.08, 20.77, 20.73; HRMS for C$_{47}$H$_{52}$Cl$_{3}$N$_{3}$O$_{13}$SNa (M + Na)$^+$ calculated 998.2117, found 998.2106.

For Trisaccharide Building Block (5). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.45–7.13 (m, 35H), 5.52 (brs, 1H), 5.41 (brs, 1H), 5.34 (d, $J = 9.9$ Hz, 1H), 5.14 (d, $J = 17.3$ Hz, 2H), 5.00 (d, $J = 10.7$ Hz, 1H), 4.91–4.67 (m, 6H), 4.62–4.39 (m, 6H), 4.36–4.25 (m, 3H), 4.08–3.95 (m, 5H), 3.89–3.85 (m, 3H), 3.74 (s, 3H), 3.71–3.64 (m, 3H), 3.58–3.45 (m, 6H), 3.43–3.27 (m, 3H), 2.78 (brs, 1H), 2.52 (dd, $J = 13.9, 4.0$ Hz, 1H), 2.08 (s, 3H), 2.01
(s, 3H), 1.99 (s, 3H), 1.90 (s, 3H), 1.85 (s, 3H); $^{13}$C-Apt NMR (125 MHz, CDCl$_3$)

$\delta$ 170.61, 170.47, 170.25, 169.92, 169.79, 168.23, 156.04, 138.90, 138.77, 138.46, 138.26, 138.22, 128.36, 128.19, 128.14, 128.13, 128.08, 128.04, 128.03, 127.99, 127.91, 127.72, 127.69, 127.47, 127.43, 127.34, 127.32, 127.30, 127.08, 103.48, 102.13, 98.32, 82.74, 81.69, 78.28, 76.18, 76.11, 75.25, 74.84, 74.78, 73.29, 73.15, 72.88, 72.57, 72.36, 69.04, 68.76, 68.28, 67.84, 67.76, 67.17, 67.10, 67.04, 62.17, 60.27, 52.88, 51.26, 48.93, 46.99, 45.88, 36.26, 22.96, 20.98, 20.69, 20.58, 20.40; HRMS for C$_{84}$H$_{96}$N$_2$O$_{25}$Na (M + Na)$^+$ calculated 1555.6194, found 1555.6247.

4,6-Di-O-Benzylidene-2-Deoxy-2-(2,2,2-Trichloroethoxycarbonylamino)-3-O-Levulinoyl-1-Thio-β-D-Galactopyranoside (7). To a solution of compound 6 (3.00 g, 5.11 mmol) in MeOH/CH$_2$Cl$_2$ (vol/vol = 1:1, 15 ml) was added NaOMe in MeOH (25% wt/vol, 0.2 mL) and the mixture was stirred at 0 °C for 2 h, followed by neutralization with Amberlite IR-50 resin (1.0 g) and filtration. Solvent was removed under reduced pressure to give the crude deacylated product, which was then dissolved in DMF/CH$_3$CN (vol/vol = 1:1, 20 ml), followed by the addition of benzaldehyde dimethyl acetal (1.5 equiv) and (±)-camphorsulfonic acid (CSA) (0.1 equiv). The mixture was stirred at room temperature for 8 h and then diluted with CH$_2$Cl$_2$ (200 ml), washed with saturated aqueous NaHCO$_3$ (20 ml x 3), and brine (10 ml), dried (MgSO$_4$) and concentrated under reduced pressure. The resulting crude benzylidene was dissolved in CH$_2$Cl$_2$ (20 ml), to which 1-ethyl-3-(3'-)dimethylaminopropyl)carbodiimide·HCl (EDC) (1.5 equiv), 3-(dimethylamino) pyridine (DMAP) (0.5 equiv) and levulinic acid (1.5 equiv) were added. The reaction mixture was stirred at room temperature for 16 h and diluted with CH$_2$Cl$_2$ (200 ml), washed with sat. aq. NaHCO$_3$ (20 ml x 3), dried (MgSO$_4$) and concentrated for flash column chromatography purification (CH$_2$Cl$_2$/EtOAc, 4:1) to give compound 7 (1.65 g, 50% over three steps) as a colorless syrup. $^1$H NMR (500 MHz,
CDCl₃ δ 7.45 (d, J = 7.7 Hz, 2H), 7.34–7.25 (m, 5H), 6.98 (d, J = 7.7 Hz, 2H), 5.39 (s, 1H), 5.27 (d, J = 8.5 Hz, 1H), 5.19 (dd, J = 10.7, 3.0 Hz, 1H), 4.89 (d, J = 9.9 Hz, 1H), 4.70 (d, J = 12.1 Hz, 1H), 4.64 (d, J = 11.7 Hz, 1H), 4.26 (d, J = 12.1 Hz, 1H), 4.19 (d, J = 2.2 Hz, 1H), 3.91 (d, J = 12.1 Hz, 1H), 3.80 (d, J = 9.9 Hz, 1H), 3.50 (s, 1H), 2.57 (q, J = 6.6 Hz, 2H), 2.42 (t, J = 6.6 Hz, 1H), 2.25 (s, 3H), 1.94 (s, 3H); ¹³C-Apt NMR (125 MHz, CDCl₃) δ 206.50, 172.17, 153.69, 138.19, 137.64, 134.01, 129.56, 129.03, 128.01, 127.34, 126.46, 100.79, 95.55, 85.05, 74.25, 73.12, 71.57, 69.48, 69.13, 50.23, 37.71, 29.56, 28.04, 21.16; HRMS for C₂₈H₃₀Cl₃NO₈SNa (M + Na)⁺ calculated 668.0650, found 668.0673.

4,6-Di-O-Benzylidene-2-Deoxy-2-(2,2,2-Trichloroethoxycarbonylamino)-3-O-Levulinoyl-1-Thio-β-D-Galactopyranoside (8). Compound 7 (1.65 g, 2.55 mmol) in 80% aqueous acetic acid (20 ml) was heated at 80 oC for 6 h and the solvent was removed under reduced pressure. The residue was dissolved in CH₂Cl₂ (20 ml), to which pyridine (5 equiv), DMAP (0.05 equiv) and acetic anhydride (3 equiv) were added and the mixture was stirred at room temperature for 2 h. The reaction was quenched with addition of MeOH (10 ml) and the solvent was removed under reduced pressure. After coevaporation with toluene (10 ml x 3), the resulting residue was dissolved in pyridine (10 ml) and 1 M hydrazine hydrate (NH₂NH₂.xH₂O) in pyr/AcOH mixture (vol/vol = 3:2) (2 equiv) was added. The reaction was stirred at room temperature for 4 h and quenched with penta-2,4-dione (2 ml), and the solvent was removed under reduced pressure. The resulting residue was dissolved in CH₂Cl₂ (50 ml), washed with 1 M HCl (10 ml), H₂O (10 ml), and brine (10 ml), dried (Na₂SO₄), and concentrated for flash column chromatography purification (hexane/EtOAc, 2:1) to give compound 8 as a syrup (0.94 g, 70% over three steps). ¹H NMR (500 MHz, CDCl₃) δ 7.42 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 5.43 (d, J = 7.7 Hz, 1H), 5.32 (d, J = 3.3 Hz, 1H), 4.79–4.72 (m, 3H), 4.15 (d, J = 6.2 Hz, 2H), 4.08–3.98 (m, 1H), 3.86 (dd, J = 6.6, 6.2 Hz, 1H), 3.63 (q, J = 9.9 Hz, 1H), 3.14 (d, J = 4.4 Hz, 1H), 2.34 (s, 3H), 2.13 (s, 3H), 2.05 (s, 3H); ¹³C-Apt NMR (125
MHZ, CDCl₃) δ 171.14, 170.57, 154.89, 138.41, 133.04, 129.65, 128.46, 95.71, 86.62, 74.70, 74.65, 71.41, 69.30, 62.30, 53.87, 21.13, 20.77, 20.71; HRMS for C₂₀H₂₄Cl₃NO₈SNa (M + Na)⁺ calculated 566.0180, found 566.0177.

For Disaccharide Building Block Precursor (10). ¹H NMR (500 MHz, CDCl₃) δ 7.44 (d, J = 8.1 Hz, 2H), 7.20 (m, 15H), 7.07 (d, J = 8.1 Hz, 2H), 5.36 (d, J = 3.3 Hz, 1H), 5.32 (d, J = 10.3 Hz, 1H), 5.23 (d, J = 10.3, 8.1 Hz, 1H), 4.91 (d, J = 12.1 Hz, 1H), 4.87 (d, J = 11.8 Hz, 1H), 4.61 (d, J = 12.5 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.53 (d, J = 11.8 Hz, 1H), 4.48 (d, J = 11.8 Hz, 1H), 4.45 (d, J = 12.5 Hz, 1H), 4.43 (d, J = 11.8 Hz, 1H), 4.37 (d, J = 7.7 Hz, 1H), 4.31 (dd, J = 10.3, 3.3 Hz, 1H), 4.09 (dd, J = 11.7, 4.4 Hz, 1H), 4.02 (dd, J = 11.7, 7.7 Hz, 1H), 3.88 (d, J = 2.2 Hz, 1H), 3.80 (dd, J = 7.7, 4.4 Hz, 1H), 3.56–3.63 (m, 2H), 3.49 (dd, J = 6.6, 6.3 Hz, 1H), 3.42–3.45 (m, 1H), 3.38 (dd, J = 10.3, 2.6 Hz, 1H), 2.97 (ddd, J = 17.6, 11.0, 2.6 Hz, 1H), 2.86 (ddd, J = 17.6, 11.0, 2.6 Hz, 1H), 2.47 (ddd, J = 17.3, 5.5, 2.9 Hz, 1H), 2.32 (s, 3H), 2.24 (ddd, J = 17.3, 5.5, 2.9 Hz, 1H), 2.21 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H); ¹³C-Apt NMR (125 MHz, CDCl₃) δ 208.57, 171.35, 170.49, 170.09, 153.87, 138.51, 137.93, 137.85, 137.71, 133.01, 129.40, 129.07, 128.46, 128.44, 128.42, 128.40, 128.14, 127.79, 127.74, 127.71, 127.43, 102.40, 95.86, 84.89, 79.65, 75.94, 75.19, 74.25, 74.06, 73.53, 72.51, 71.80, 71.31, 69.67, 68.33, 63.12, 52.96, 37.53, 29.98, 27.48, 21.09, 20.75, 20.72; HRMS for C₅₂H₅₈Cl₃NO₁₅SNa (M + Na)⁺ calculated 1096.2485, found 1096.2491.

2-(Benzyloxycarbonylamino)-Ethyl 4-O-(3,4-Di-O-Isopropylidene-β-D-Galactopyranosyl)-1-β-D-Glucopyranoside (12). To a stirred solution of peracetyl lactosyl acetate 11 (10.00 g, 14.74 mmol) in AcOH/acetic anhydride (vol/vol = 1:1, 20 ml) was added 33% HBr in AcOH (25 ml) and the mixture was stirred at room temperature for 2 h.
The solution was then poured into water (200 ml) and extracted with CH₂Cl₂ (200 ml x 3). The organic phase was washed with saturated aqueous NaHCO₃ (200 ml x 3), dried (Na₂SO₄), and concentrated under reduced pressure to give the crude lactosyl bromide as a white foamy residue, which was coevaporated with toluene (20 ml x 3). A mixture of HOCH₂CH₂NHCbz (2 equiv), Ag₂CO₃ (1.2 equiv), I₂ (0.05 equiv), and MS (12 g) in dry CH₂Cl₂ (40 ml) was stirred at room temperature for 2 h, to which the lactosyl bromide in dry CH₂Cl₂ (30 ml) was added and the mixture was stirred at room temperature for 16 h. The reaction was quenched with saturated aqueous Na₂S₂O₃ (10 ml) and diluted with CH₂Cl₂ (300 ml). After removal of MS by filtration, the solvent was removed to give a syrup, which was coevaporated with toluene (10 ml x 3). This was dissolved in MeOH (30 ml), and NaOMe (25% wt/vol, 0.4 ml) was added. The solution was stirred at room temperature for 2 h and neutralized with amberlite IR 50 (2.5 g). Subsequent removal of resin by filtration and removal of solvent in vacuum gave a white solid. This white solid was suspended in acetone (30 ml), and 2,2 dimethoxypropane (1.5 equiv) and p-TsOH (0.1 equiv) were added. The reaction mixture was stirred at room temperature for 2 h and quenched with triethylamine (5 ml). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (CH₂Cl₂/MeOH, 7:1) to give compound 12 as a colorless oily residue (2.88 g, 35% over four steps). ¹H NMR (500 MHz, CD₃OD) δ 7.40–7.09 (m, 5H), 5.16 (s, 2H), 4.35 (d, J = 8.1 Hz, 1H), 4.29 (d, J = 8.1 Hz, 1H), 4.17 (dd, J = 5.5, 2.2 Hz, 1H), 4.04 (dd, J = 7.4, 5.5 Hz, 1H), 3.92–3.94 (m, 1H), 3.92–3.72 (m, 5H), 3.65–3.59 (m, 1H), 3.57–3.50 (m, 2H), 3.44 (dd, J = 8.1, 7.3 Hz, 1H), 3.40–3.37 (m, 2H), 3.32–3.28 (m, 1H), 3.25 (dd, J = 8.8, 8.0 Hz, 1H), 1.46 (s, 3H), 1.31 (s, 3H); ¹³C-Apt NMR (125 MHz, CD₃OD) δ 158.90, 138.28, 129.45, 129.45, 128.97, 128.82, 111.07, 104.27, 104.12, 80.80, 76.33, 76.12, 75.30, 75.01, 74.78, 74.40, 70.00, 67.45, 62.38, 61.71, 41.95, 28.40, 26.49; HRMS for C₂₅H₃₇NO₁₃Na (M + Na)⁺ calculated 582.2157, found 582.2156.
**Lactoside Acceptor (13).** To a stirred solution of compound **12** (2.88 g, 5.16 mmol) in N,N-dimethylformamide (30 ml) was added BnBr (7.5 equiv) and NaH (60% in mineral oil, 7.5 equiv) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and diluted with EtOAc (400 ml) and quenched with H2O (50 ml). The organic layer was washed with H2O (100 ml), saturated aqueous NaHCO3 (100 ml), and brine (100 ml), dried (Na2SO4) and concentrated to give a pale yellow oil. This was then dissolved in 80% aqueous acetic acid (20 ml) and heated at 80 °C for 2 h. The solution was concentrated for flash column chromatography purification (hexane/EtOAc, 2:1) to give **13** (4.37 g, 80% over two steps) as an colorless oil.

\[
\begin{align*}
\text{H NMR (500 MHz, CDCl3)} & \delta \\
7.36−7.10 & (m, 35H), 5.13 (d, J = 20.2 Hz, 2H), 4.98 (d, J = 11.0 Hz, 1H), 4.85−4.73 (m, 3H), 4.73−4.66 (m, 3H), 4.61−4.52 (m, 3H), 4.45−4.36 (m, 4H), 4.04−3.89 (m, 3H), 3.81−3.28 (m, 13H); \\
\text{13C NMR (125 MHz, CDCl3)} & \delta 154.81, 139.01, 138.30, 138.07, 128.47, 128.38, 128.35, 128.34, 128.32, 128.31, 128.28, 128.02, 127.95, 127.82, 127.66, 127.58, 127.57, 127.54, 127.51, 127.50, 127.24, 127.17, 103.67, 102.51, 82.72, 81.75, 79.96, 76.35, 75.21, 74.96, 74.83, 73.45, 73.42, 73.13, 72.81, 68.72, 68.60, 68.09, 67.24, 51.40; \\
\text{HRMS for C64H69NO13Na (M + Na)+} & \text{calculated 1082.4661, found 1082.4653.}
\end{align*}
\]

**p-Methylphenyl 2,3,6-Tri-O-Benzoyl-4-O-(2,3,4-Tri-O-Benzyl-α-L-Fucopyranosyl)-1-Thio-β-D-Glucopyranoside (16).** A solution of compound **3** (51 mg, 0.10 mmol), compound **15** (51 mg, 0.09 mmol), BSP (0.59 equiv), and MS (0.6 g) in CH2Cl2 (2 ml) was stirred at room temperature for 45 min. The solution was cooled to −70 °C and Tf2O (0.7 equiv) was added. The reaction mixture was heated from −70 °C to −0 °C while stirring over 2 h and quenched with triethylamine (100 µl). After removal of MS by filtration, the filtrate was concentrated directly for flash column chromatography purification (hexane/EtOAc, 3:1) to furnish **16** (82 mg, 95%) as a white glassy residue.
$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.99 (dd, $J$ = 8.3, 1.3 Hz, 2H), 7.81 (dd, $J$ = 8.3, 1.3 Hz, 2H), 7.76 (dd, $J$ = 8.3, 1.2 Hz, 2H), 7.55 (t, $J$ = 7.4 Hz, 1H), 7.42–7.11 (m, 25H), 6.77 (d, $J$ = 7.9 Hz, 2H), 5.61 (t, $J$ = 9.2 Hz, 1H), 5.16(t, $J$ = 9.7 Hz, 1H), 4.98 (dd, $J$ = 11.8, 1.8 Hz, 1H), 4.76–4.74 (m, 4H), 4.70 (d, $J$ = 11.8 Hz, 1H), 4.64 (d, $J$ = 11.8 Hz, 1H), 4.60 (d, $J$ = 11.4 Hz, 1H), 4.56 (dd, $J$ = 12.2, 4.8 Hz, 1H), 4.41 (d, $J$ = 11.8 Hz, 1H), 3.88–3.85 (m, 2H), 3.83–3.79 (m, 2H), 3.62 (q, $J$ = 6.6 Hz, 1H), 3.37 (s, 1H), 2.14 (s, 3H), 0.51 (d, $J$ = 6.6 Hz, 3H); $^{13}$C-Apt NMR (150 MHz, CDCl$_3$) $\delta$ 165.96, 165.90, 165.09, 138.56, 138.33, 138.29, 137.99, 133.89, 133.09, 133.02, 132.98, 129.99, 129.81, 129.73, 129.70, 129.42, 129.37, 129.22, 128.37, 128.33, 128.24, 128.18, 128.07, 127.68, 127.49, 127.40, 100.48, 85.36, 79.14, 77.77, 76.19, 75.58, 75.51, 74.78, 74.29, 72.63, 70.77, 67.62, 62.99, 21.10, 15.90; HRMS for C$_{61}$H$_{58}$O$_{12}$Na (M + Na)$^+$ calculated 1037.3541, found 1037.3554.
Fig. 4. $^1$H NMR spectrum of deprotected Fuc GM$_1$ glycoside 1.
Figure 5. $^{13}$C Apt NMR spectrum of deprotected Fuc-GM$_1$ glycoside 1.
Figure 6. $^1$H NMR spectrum of protected Fuc-GM$_1$ glycoside 2.
Fig. 7. $^{13}$C-Apt NMR spectrum of protected Fuc-GM$_1$ glycoside 2.
Fig. 8. $^1$H NMR spectrum of disaccharide building block 4.
Fig. 9. $^{13}$C-Apt NMR spectrum of disaccharide building block 4.
Fig. 10. NMR spectrum of trisaccharide building block 5.
Fig. 11. $^{13}$C-Apt NMR spectrum of trisaccharide building block 5.
Fig. 12. $^1$H NMR spectrum of 4,6-di-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxyl carbonylamino)-3-O-levulinoyl-1-thio-β-D-galactopyranoside 7.
Fig. 13. $^{13}$C-Apt NMR spectrum of 4,6-di-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxy)carbonylamo)-3-$O$-levulinoyl-1-thio-$\beta$-D-galactopyranoside 7.
Fig. 14. $^1$H NMR spectrum of 4,6-di-O-benzylidenyl-2-deoxy-2-(2,2,2-trichloroethoxyl carbonylamino)-3-O-levulinoyl-1-thio-β-D-galactopyranoside 8.
Fig. 15. $^{13}$C -Apt NMR spectrum of 4,6-di-$O$-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-3-$O$-levulinoyl-1-thio-$\beta$-$D$-galactopyranoside 8.
Fig. 16. $^1$H NMR spectrum of disaccharide building block precursor 10.
Fig. 17. $^{13}$C-Apt NMR spectrum of disaccharide building block precursor 10.
Fig. 18. $^1$H NMR spectrum of 2-(benzyloxycarbonylamino)-ethyl 4-O-(3,4-di-O-isopropylidene-β-D-galactopyranosyl)-1-β-D-glucopyranoside 12.
Fig. 19.  $^{13}$C-Apt NMR spectrum of 2-(benzyloxy carbonylamino)-ethyl 4- O-(3,4-di-O- isopropylidene-β-D-galactopyranosyl)-1-β-D-glucopyranoside 12.
Fig. 20. $^1$H NMR spectrum of lactoside acceptor 13.
Fig. 21. $^{13}$C-Apt NMR spectrum of lactoside acceptor 13.
Fig. 22. $^1$H NMR spectrum of $p$-methylphenyl 2,3,6-tri-$O$-benzoyl-4-$O$-(2,3,4-tri-$O$-benzyl-$\alpha$-$L$-fucopyranosyl)-1-thio-$\beta$-$D$-glucopyranoside 16.
Fig. 23.  $^{13}$C-Apt NMR spectrum of $p$-methylphenyl 2,3,6-tri-$O$-benzoyl-4-$O$-(2,3,4-tri-$O$-benzyl-$\alpha$-$L$-fucopyranosyl)-1-thio-$\beta$-$D$-glucopyranoside 16.