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# SYNTHESIS OF HUMAN MILK OLIGOSACCHARIDES: 2'- AND 3'-FUCOSYLLACTOSE

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**Abstract** – The human milk oligosaccharides 2'-fucosyllactose and 3-fucosyllactose were synthesized using a selectively protected 1-*O*-allyllactosyl acceptor and a 1-*O*-trichloroacetimidate fucosyl donor. This synthesis utilized fewer toxic reagents and milder reaction conditions as compared to previous syntheses.

## INTRODUCTION

The beneficial effects of human breast milk on the survival and health of infants has long been recognized.[1] Advances in separation science and structure analysis have enabled the structural elucidation of approximately 200 different oligosaccharides.[2] Biological studies on human milk and separated oligosaccharide principles have revealed many beneficial properties of human milk oligosaccharides (HMOs), including: (1) forming a protective barrier on the infant's gastrointestinal tract which selectively binds to enteric bacteria and then allows excretion before the pathogen is absorbed through the intestinal wall;[3] (2) providing nutritive support for the growth of beneficial bifidogenic bacteria that assist in digestion;[4] and even (3) possible effects on the development of memory and intelligence.[5] On a global scale, many of the ten million infant mortality cases annually result from diarrhea and are linked to poor access to breast milk, in some cases due to maternal malnutrition.[1] Few other mammals produce the diversity of oligosaccharides associated with the beneficial antimicrobial and prebiotic activities of human milk.

2'-Fucosyllactose (**1**, Scheme 1) is the second-most abundant human milk carbohydrate after lactose, and a specific ligand for inhibiting the diarrhea-causing bacterium *Campylobacter*.[6] Several chemical syntheses of 2'-fucosyllactose have been reported,[7] although these approaches are impractical for large-scale processes or for preparing material for human trials, due to the use of expensive and/or toxic

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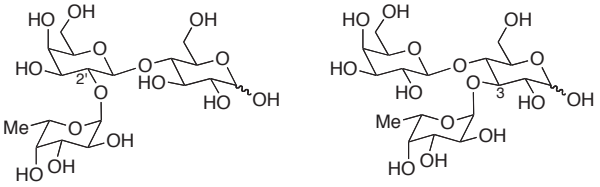
Dedicated in celebration of the 75th birthday of Prof. Dr. Albert Padwa.

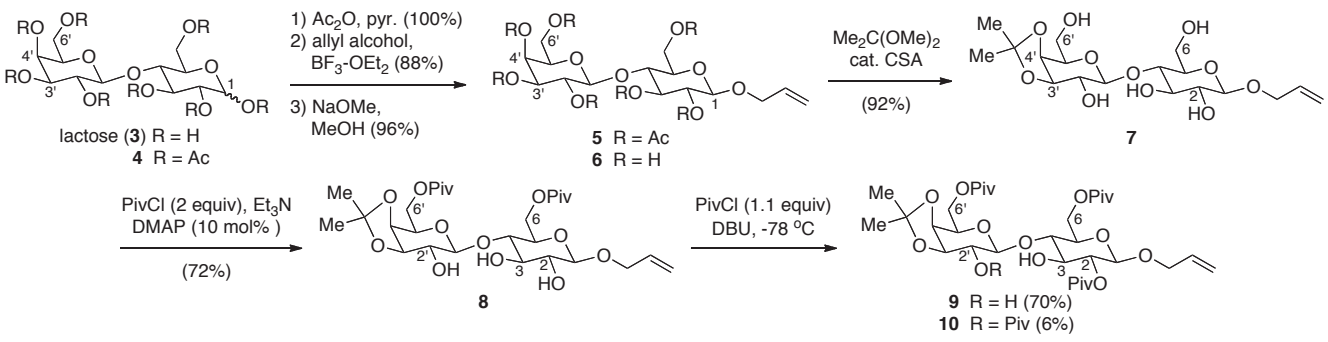
reagents for glycosylations (silver, mercury), malodorous organothiols and -sulfides, and/or alkyl silyl ethers and alkyltin derivatives for protective group manipulations.[8] In the current work, we have sought to synthesize 2'-fucosyllactose without using stoichiometric quantities of toxic reagents, protecting the reducing terminus as an *O*-allyl glycoside, blocking primary and secondary alcohols with ester protective groups whenever possible, and conducting the glycosylation transformation with an *O*-trichloroacetimidate glycosyl donor.[9]




Scheme 1. Human milk trisaccharides

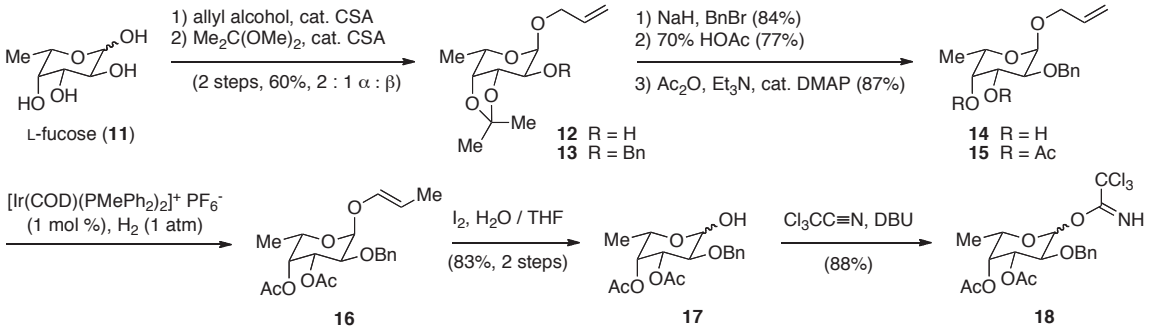
## RESULTS AND DISCUSSION

Our synthesis required regioselective protection of several of the alcohols in lactose for installation of the *alpha*-fucosyl sugar at the 2'-hydroxyl group.[10] To avoid Koenigs-Knorr (mercury- or silver-promoted) glycosylation for the preparation of *O*-allyl lactoside **6** (Scheme 2),[11] we originally explored Fischer (Brønsted acid-catalyzed) glycosylation of lactose with allyl alcohol, but found that superior yields were achieved with $BF_3$-$OEt_2$-promoted glycosylation[12] of the octaacetate **4**, followed by basic methanolysis of intermediate **5** to afford *O*-allyl lactoside **6**. The *cis*-3' and 4'-hydroxyl groups were differentiated by acetonide formation under thermodynamic conditions, followed by pivaloylation of both primary alcohols to give bis-ester **8**. In close concordance with the precedented reactivity of secondary alcohols in the *O*-benzyl lactoside congener (O2 > O2' > O3), low temperature pivaloylation predominantly provided the triester **9** along with small amounts of the tetraester **10**.[13]



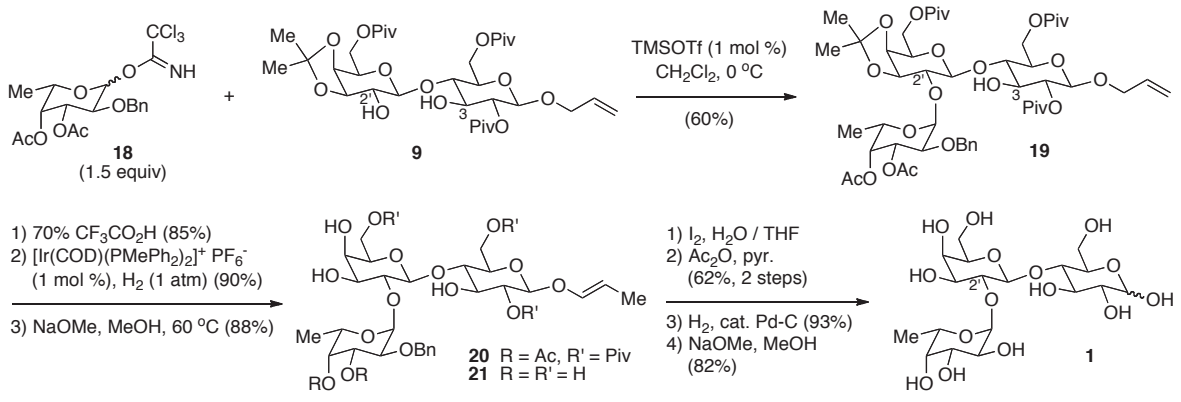

Scheme 2. Synthesis of selectively protected lactose

The fucosyl donor was prepared with a non-participating O2-protective group in order to maximize *alpha*-stereoselectivity in the glycosylation step. Fischer glycosylation of L-fucose (**11**) with allyl alcohol[14] was followed by protection of the *cis*-3' and 4'-hydroxyl groups as the acetonide **12** (Scheme 3). As the *alpha*-anomer of **12** was easily separated, this isomer was used in subsequent steps. Benzylation of the O2-hydroxyl, acidic hydrolysis of the acetonide, and acetylation afforded the fully protected fucose derivative **15**.[15] Iridium-catalyzed isomerization to the 1-propenyl glycoside **16** and subsequent iodohydration of the vinylic ether[16] afforded reducing sugar **17** in good yield, for activation as the *O*-trichloroacetimidate glycosyl donor **18**.[17]



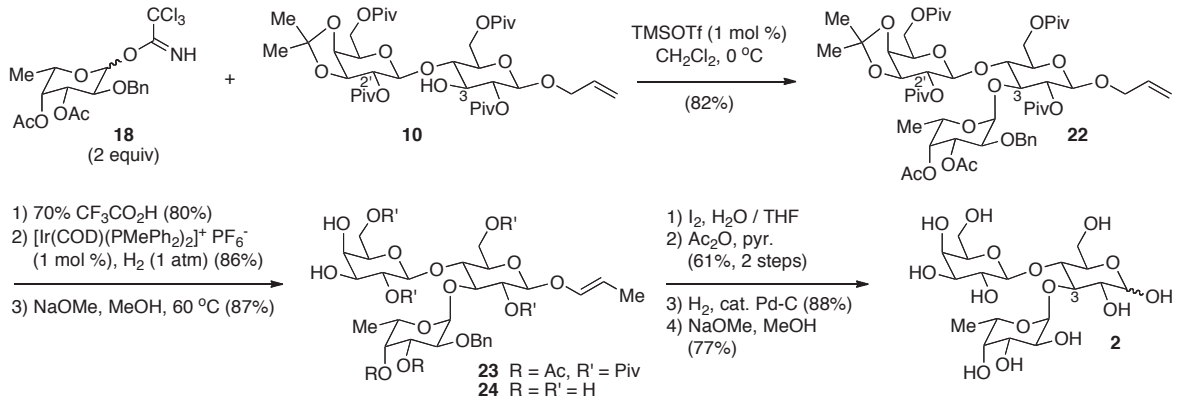

Scheme 3. Synthesis of fucosyl donor **18**

The best results for the glycosylation step were observed when approximately 1.5 equiv of the fucosyl donor **18** (mixture of anomers enriched in the *alpha*-anomer) was added to an ice-cold $CH_2Cl_2$ solution of the lactose acceptor **9** containing 1 mol % TMSOTf (Scheme 4).[18,19] With the non-participating benzyl ether at O2 and acetate esters at O3 and O4 of fucosyl donor **18**, only the *alpha*-anomeric glycoside product **19** was observed, favoring fucosylation at the galactosyl O2' of **9**.[20,21] The origin of this selectivity was attributed to the greater steric bulk of the pivaloate ester adjacent to the glucosyl O3 of **9**, relative to the cyclic acetonide protective group adjacent to O2'.




Scheme 4. Glycosylation of **18** and **9**, and synthesis of 2'-fucosyllactose (**1**)

The order of protective group removal was optimized so that the alkene isomerization step was conducted immediately after removal of the acetonide to afford vinylic glycoside **20**, which was converted into **21** upon basic methanolysis of all pivaloyl and acetyl esters. After iodohydration of the vinylic glycoside of **21**, the acetylation of all hydroxyl groups provided for easier chromatographic purification. The synthesis of 2'-fucosyllactose (**1**) concluded with catalytic hydrogenolysis of the benzyl ether and room temperature basic methanolysis of all acetyl esters. Our synthetic 2'-fucosyllactose exhibited spectroscopic characteristics consistent with those reported in the literature.[7,22] Following an identical strategy initiated by glycosylation of lactose acceptor **10** with fucosyl donor **18** and stepwise deprotection of the trisaccharide **22**, 3-fucosyllactose (**2**) was also prepared in good yield (Scheme 5). For both trisaccharides, initial deprotection of the acetonide has provided a trisaccharide acceptor for a prospective synthesis of higher-order HMOs.




Scheme 5. Synthesis of 3'-fucosyllactose (**2**)

Important features of our synthesis were the avoidance of stoichiometric metal reagents in all steps, the complete stereoselectivity of the glycosylation step, and high yields for most transformations. In particular, the *O*-allyl glycosides were easily introduced and removed without interference with other functional groups. Furthermore, the ester protective groups generally resulted in crystalline intermediates, so that fewer chromatographic purifications were required compared to other syntheses of these HMOs.

## EXPERIMENTAL

$^1$H NMR and $^{13}$C NMR spectra were recorded on Varian INOVA 600, Unity 600 and INOVA 400 spectrometers. NMR spectra were recorded in solutions of deuterated chloroform ($CDCl_3$) with the residual chloroform (7.27 ppm for $^1$H NMR and 77.23 ppm for $^{13}$C NMR) taken as the internal standard, deuterated methanol ($CD_3OD$) with residual methanol (3.31 ppm for $^1$H NMR and 49.3 ppm for $^{13}$C NMR) taken as the internal standard, or deuterated benzene with residual benzene (7.16 ppm for $^1$H NMR

and 128.23 ppm for $^{13}C$ NMR) taken as the internal standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; ddd, doublet of doublet of doublet; dt, doublet of triplet; app d, apparent doublet; app t, apparent triplet; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer as neat films on sodium chloride discs. Mass spectra (high resolution ESI and APCI) were recorded on a Finnigan LTQ FTMS Mass spectrometer. Optical rotations were measured using a Perkin-Elmer 341 polarimeter (concentration in g/100mL). Thin Layer Chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel $60F_{254}$; 0.25 mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science. All reactions were carried out with anhydrous solvents in oven dried or flame dried and argon-charged glassware. All anhydrous solvents were dried with 4 Å molecular sieves purchased from Sigma-Aldrich and tested for trace water content with Coulometric KF titrator from Denver instruments. All solvents used in extraction procedures and chromatography were used as received from commercial suppliers without prior purification.

**2-Propen-1-yl O-3,4-O-(1-methylethylidene)-β-D-galactopyranosyl(1→4)-β-D-glucopyranoside (7).** Lactose (**3**, 80.0 g, 233 mmol) was dissolved in pyridine (328 mL) with stirring, acetic anhydride (358.0 g, 3.505 mol) was added, and the reaction was stirred for 48 h at room temperature. The solvent was removed by rotary evaporation, toluene was added, and solvents were removed again by rotary evaporation to remove traces of pyridine, acetic anhydride, and/or acetic acid. The crude product was dissolved in water and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, filtered and concentrated to obtain an oil. Repeated washing with hexanes followed by decantation resulted in a white solid. Recrystallization using acetone and hexanes provided β-lactose octaacetate (**4**) as a white solid (158 g, 100%). A portion of this material (20.0 g, 29.4 mmol) and allyl alcohol (2.00 g, 35.3 mmol) were dissolved in $CH_2Cl_2$ (400 mL) and cooled to 0 ºC. $BF_3$•$OEt_2$ (6.20 g, 44.2 mmol) was added, and the reaction was stirred for 30 min. After stirring for 68 h at room temperature, $K_2CO_3$ (12 g) was added, and the mixture was stirred for 30 min. The solids were filtered and the filtrate diluted with water. The aqueous layer was extracted with $CH_2Cl_2$ and the combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated to obtain an oil. Repeated washing with hexanes followed by decantation gave *O*-allyl-β-lactose heptaacetate (**5**) as a white solid (17.5 g, 88%). This compound was dissolved in MeOH (175 mL) at room temperature, and a 0.5 M solution of NaOMe in MeOH (5.2 mL, 2.58 mmol) was added. This solution was stirred for 3.5 h. The reaction mixture was diluted with MeOH and neutralized with Amberlyst 120($H^+$) resin. The solution was filtered from the resin, and the solvent was removed by rotary evaporation to obtain the *O*-allyl-β-lactose (**6**) as a white solid (9.5 g, 96%). This compound was dissolved in

2,2-dimethoxypropane (576 mL), 10-camphorsulfonic acid (CSA, 0.3 g, 1.25 mmol) was added, and the reaction mixture was stirred at room temperature for 108 h. $Et_3N$ (2.5 mL) was then added and the reaction mixture was stirred for 15 min before removing the solvents by rotary evaporation, including addition of toluene and rotary evaporation to remove traces of $Et_3N$ and/or 2,2-dimethoxypropane. A mixture of MeOH and water (250 mL : 50 mL) was added, and the reaction mixture was heated to reflux for 3 h. After cooling, the solvent was removed by rotary evaporation, and traces of water were removed by azeotropic evaporation using toluene, to obtain a white solid. The solid was redissolved using a mixture of EtOAc and $CH_2Cl_2$, and precipitated out using hexanes, filtered and dried to obtain the title compound **7** (9.8 g, 92%), with physical and spectroscopic characteristics consistent with the literature.[11]

**2-Propen-1-yl *O*-6-*O*-(2,2-dimethylpropanoyl)-3,4-*O*-(1-methylethylidene)-β-D-galactopyranosyl(1→4)-β-D-glucopyranoside, 6-*O*-(2,2-dimethylpropanoate (8).** Compound **7** (2.1 g, 4.9 mmol), DMAP (0.06 g, 0.49 mmol) and pyridine (10.5 mL) were dissolved in 1,2-dichloroethane (31 mL), and cooled to 0 ºC. Pivaloyl chloride (1.2 g, 9.9 mmol) was added, and the reaction mixture was stirred for 3 h and then at room temperature for 30 min. The reaction mixture was diluted with water and the aqueous layer was extracted with $CH_2Cl_2$. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated to obtain an oil. Toluene was then added and trace amounts of pyridine was removed by rotary evaporation to obtain a white solid. This solid was washed with pentane and filtered to obtain compound **8** (2.1 g, 72%). Mp 173-175 ºC; $[\alpha]_D^{25}$ +33.4 (c 1.135, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 5.98-5.92 (m, 1H), 5.32 (dd, *J* = 1.2, 17.4 Hz, 1H), 5.23 (d, *J* = 10.8 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.44 (dd, *J* = 3.6, 12.0 Hz, 1H), 4.37-4.34 (m, 1H), 4.36 (d, *J* = 7.8 Hz, 1H), 4.24 (dd, *J* = 8.4, 12.0 Hz, 1H), 4.23 (d, *J* = 8.4 Hz, 1H), 4.18-4.06 (m, 6H), 3.64-3.60 (m, 2H), 3.50 (dd, *J* = 6.0, 9.9 Hz, 1H), 3.45-3.41 (m, 2H), 3.30 (dd, *J* = 9.6 Hz, 1H), 2.56 (s, 1H), 1.53 (s, 3H), 1.34 (s, 3H), 1.22 (s, 9H), 1.21 (s, 9H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.9, 178.5, 133.8, 118.4, 110.8, 103.6, 101.1, 81.5, 78.8, 75.0, 73.9, 73.4, 73.3, 73.2, 71.9, 70.5, 63.6, 63.4, 39.0 (2), 28.2, 27.3, 27.2, 26.4; FT-IR: 3458, 3419, 2978, 1733, 1722, 1286, 1169, 1072, 1020 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{28}H_{46}O_{13}Na$ ($M+Na^+$) 613.2830, found 613.2831.

**2-Propen-1-yl *O*-6-*O*-(2,2-dimethylpropanoyl)-3,4-*O*-(1-methylethylidene)-β-D-galactopyranosyl(1→4)-β-D-glucopyranoside, 2,6-bis-*O*-(2,2-dimethylpropanoate) (9).** Compound **8** (4.2 g, 7.1 mmol) and DMAP (0.086 g, 0.71 mmol) were dissolved in $CH_2Cl_2$ (105 mL), and cooled to -78 ºC. DBU (1.19 g, 7.8 mmol) was added, and the reaction mixture was stirred for 15 min. Pivaloyl chloride (0.94 g, 7.8 mmol) was then added dropwise and the reaction mixture was stirred for 30 min at -78 ºC. The reaction mixture was quenched with MeOH at -78 ºC and then warmed to room temperature. After diluting the reaction mixture with saturated aqueous $NaHCO_3$, the aqueous layer was extracted with $CH_2Cl_2$. The

organic layer was dried over $MgSO_4$, filtered and concentrated. The crude was purified by flash chromatography using 15% acetone in hexanes as eluent to obtain the tripivaloate compound **9** as a white solid (3.37 g, 70%). Mp 160-162 ºC; $[\alpha]_D^{25}$ +24.0 (c 1.025, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 5.86-5.79 (m, 1H), 5.24 (dd, *J* = 1.8, 17.1 Hz, 1H), 5.16 (dd, *J* = 1.2, 10.5 Hz, 1H), 4.87 (dd, *J* = 8.4 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.44 (d, *J* = 8.4 Hz, 1H), 4.41 (dd, *J* = 3.6, 12.0 Hz, 1H), 4.29 (dd, *J* = 4.8, 12.9 Hz, 1H), 4.23 (dd, *J* = 8.4, 12.0 Hz, 1H), 4.14-4.07 (m, 5H), 4.05 (dd, *J* = 6.0, 12.9 Hz, 1H), 3.71 (dd, *J* = 8.4 Hz, 1H), 3.61 (dt, *J* = 3.0, 8.1 Hz, 1H), 3.49 (dd, *J* = 6.0, 9.6 Hz, 1H), 3.44 (d, *J* = 3.0 Hz, 1H), 3.36 (dd, *J* = 9.6 Hz, 1H), 1.51 (s, 3H), 1.33 (s, 3H), 1.21 (s, 9H), 1.19 (s, 9H), 1.19 (2s, 18H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.9, 178.7, 176.9, 133.7, 117.7, 110.8, 103.8, 99.7, 82.7, 78.9, 73.8, 73.5, 73.4, 73.1, 72.1, 71.9, 70.0, 63.6, 63.5, 39.0 (2C), 38.9, 28.2, 27.2 (2C), 26.4; FT-IR: 3463, 2973, 1731, 1284, 1157, 1072 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{33}H_{54}O_{14}Na$ ($M+Na^+$) 697.3406, found 697.3407. The tetrapivaloate **10** was also isolated as a byproduct (0.35 g, 6%) as a white solid. Mp 184-186 ºC; $[\alpha]_D^{25}$ +26.1 (c 1.15, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 5.84-5.78 (m, 1H), 5.23 (dd, *J* = 1.2, 17.1 Hz, 1H), 5.16 (dd, *J* = 1.8, 10.5 Hz, 1H), 5.01-4.98 (m, 1H), 4.86 (app t, *J* = 9.0 Hz, 1H), 4.30-4.24 (m, 3H), 4.17-4.14 (m, 3H), 4.07 (dd, *J* = 3.6, 8.7 Hz, 1H), 3.75 (app t, *J* = 8.4 Hz, 1H), 3.41 (app t, *J* = 9.0, Hz, 1H), 1.53 (s, 3H), 1.31 (s, 3H), 1.21 (4s, 36H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.6, 178.0, 177.1, 176.8, 133.7, 117.6, 111.2, 100.9, 99.6, 81.3, 73.4, 73.1, 72.5 (2C), 72.4, 71.7, 69.9, 63.2, 62.7, 39.0, 38.9, 27.5, 27.4, 27.3, 27.2, 26.4; FT-IR: 3471, 2973, 1735, 1280, 1141, 1056 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{38}H_{62}O_{15}Na$ ($M+Na^+$) 781.3980, found 781.3982.

**2-Propen-1-yl 3,4-*O*-(1-methylethylidene)-α-L-fucopyranoside (12).** L-Fucose (**11**, 25.0 g, 152 mmol) was dissolved in allyl alcohol (250 mL), 10-camphorsulfonic acid (CSA, 0.70 g, 3.0 mmol) was added, and the reaction mixture was heated to reflux for 2 h. Triethylamine (1.0 mL) was then added and the solvents were removed by rotary evaporation. Trace amounts of allyl alcohol were removed by azeotroping with toluene. The resulting semisolid material was dried under vacuum and carried on to the next step without purification. The above crude material was dissolved in 2,2-dimethoxypropane (120 mL) and acetone (120 mL), 10-camphorsulfonic acid (CSA, 0.7 g, 3.0 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h. Triethylamine (2.0 mL) was then added and the solvents were removed by rotary evaporation. The crude product was purified by flash chromatography using 20% EtOAc in hexanes as eluent to obtain the title compound **12** (15.0 g, 40%), its β-anomer (7.5 g, 20%) and the mixed 1-methoxy-1-methylethyl acetal at O2, as the β-anomer (11.0 g, 24%). For **12**: $[\alpha]_D^{25}$ -124.9 (c 1.105, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 5.95-5.88 (m, 1H), 5.30 (dd, *J* = 1.2, 17.1 Hz, 1H), 5.21 (d, *J* = 0.6, 10.5, Hz, 1H), 4.87 (d, *J* = 3.6 Hz, 1H), 4.26-4.20 (m, 2H), 4.14 (dq, *J* = 1.8, 6.6, 13.5 Hz, 1H), 4.08-4.02 (m, 2H), 3.80 (dd, *J* = 3.6, 6.9 Hz, 1H), 1.52 (s, 3H), 1.36 (s, 3H), 1.32 (d, *J* = 6.0 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 133.9, 117.8, 109.4, 96.8, 76.4, 75.8,

69.6, 68.7, 64.1, 28.0, 26.1, 16.4; FT-IR: 3444, 2941, 2935, 2873, 1067, 1025, 867 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{12}H_{20}O_5Na$ ($M+Na^+$) 267.1203, found 267.1200. For the β-anomer: $[\alpha]_D^{25}$ -30.8 (c 0.825, $CHCl_3$); $^1H$ NMR (600 MHz, $CDCl_3$) δ 5.96-5.90 (m, 1H), 5.30 (dd, *J* = 2.4, 17.4 Hz, 1H), 5.21 (d, *J* = 10.8 Hz, 1H), 4.38 (dd, *J* = 2.7, 12.6 Hz, 1H), 4.20 (d, *J* = 8.4 Hz, 1H), 4.08 (dd, *J* = 6.6, 13.2 Hz, 1H), 4.04 (dd, *J* = 6.0, 7.5 Hz, 1H), 4.00 (dd, *J* = 2.4, 5.1 Hz, 1H), 3.85 (dq, *J* = 2.4, 6.0, 13.2 Hz, 1H), 3.56 (dd, *J* = 7.8 Hz, 1H), 1.53 (s, 3H), 1.42 (d, *J* = 6.0 Hz, 3H), 1.35 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) δ 133.9, 118.2, 110.0, 101.1, 78.9, 76.4, 73.7, 70.1, 69.3, 28.4, 26.5, 16.7; FT-IR: 3444, 2984, 2873, 1379, 1066, 1030, 868 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{12}H_{20}O_5Na$ ($M+Na^+$) 267.1203, found 267.1200.

**2-Propen-1-yl 2-*O*-(phenylmethyl)-3,4-*O*-(1-methylethylidene)-α-L-fucopyranoside (13).** Compound **12** (17.8 g, 72.8 mmol) was dissolved in a mixture of THF (150 mL) and DMF (15 mL) (10:1), cooled to 0 ºC, and NaH (2.1 g, 87.4 mmol, 60% in mineral oil) was added. The reaction mixture was stirred at room temperature for 15 min. The reaction mixture was then cooled to 0 ºC, and benzyl bromide (14.9 g, 87.4 mmol) and tetrabutylammonium iodide (TBAI) (25 mg) were added. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with water and the aqueous portion was extracted with hexanes. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by flash chromatography using 5% EtOAc in hexanes as eluent to obtain compound **13** as oil (20.5 g, 84%). $[\alpha]_D^{25}$ -107.1 (c 1.115, $CHCl_3$); $^1H$ NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.28 (t, *J* = 7.2 Hz, 1H), 5.97-5.91(m, 1H), 5.35 (dd, *J* = 1.8, 17.1 Hz, 1H), 5.23 (d, *J* = 10.8 Hz, 1H), 4.81 (d, *J* = 3.6 Hz, 1H), 4.81 (d, *J* = 11.4 Hz, 2H) 4.73 (d, *J* = 12.6 Hz, 2H), 4.36 (dd, *J* = 6.0, 7.8 Hz, 1H), 4.19-4.12 (m, 2H), 4.06 (dd, *J* = 2.4, 5.4 Hz, 1H), 4.01 (ddd, *J* = 0.6, 6.3, 12.6 Hz, 1H), 3.53 (dd, *J* = 3.6, 7.8 Hz, 1H), 1.42 (s, 3H), 1.36 (s, 3H), 1.33 (d, *J* = 6.6 Hz, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) δ 138.4, 133.9, 128.4, 128.0, 127.8, 117.9, 108.8, 96.1, 76.3, 76.2, 76.0, 72.3, 68.4, 63.2, 28.3, 26.5, 16.4; FT-IR: 2984, 2901, 1379, 1074, 869, 735 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{19}H_{26}O_5Na$ ($M+Na^+$) 357.1672, found 357.1669.

**2-Propen-1-yl 2-*O*-(phenylmethyl)-α-L-fucopyranoside (14).** Compound **13** (20.5 g, 61.3 mmol) was dissolved in 70% acetic acid (102 mL), and this mixture was heated at 45 ºC for 4 h. After cooling to room temperature, the reaction mixture was diluted with water and the aqueous layer was extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$ filtered and concentrated by rotary evaporation to obtain compound **14** as an oil (14.0 g, 77%). This compound was carried onto the next step without further purification. $[\alpha]_D^{25}$ -127.9 (c 1.03, $CHCl_3$); $^1H$ NMR (600 MHz, $CDCl_3$) δ 7.36-7.34 (m, 4H), 7.32-7.29 (m, 1H), 5.95-5.88 (m, 1H), 5.32 (d, *J* = 16.5 Hz, 1H), 5.21 (d, *J* = 10.2 Hz, 1H), 4.86 (d, *J* = 3.6 Hz, 1H), 4.66 (d, *J* = 11.4 Hz, 1H), 4.61 (d, *J* = 11.4 Hz, 1H), 4.14 (dd, *J* = 4.8, 12.9 Hz, 1H), 4.02 (d, *J* = 10.2 Hz, 1H), 3.99-3.93 (m, 2H), 3.81 (s, 1H), 3.71 (dd, *J* = 3.6, 9.6 Hz, 1H), 2.66 (s, 1H), 2.48 (s, 1H), 1.27 (d, *J* = 6.6 Hz, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) δ

138.1, 134.0, 128.7, 128.3, 128.2, 117.9, 95.6, 76.5, 72.6, 71.6, 69.5, 68.5, 65.6, 16.2; FT-IR: 3424, 2984, 2901, 1366, 1089, 869, 736 $cm^{-1}$; HRMS (ESI) *m/z* calcd. for $C_{16}H_{22}O_5Na$ ($M+Na^+$) 317.1359, found 317.1353.

**2-Propen-1-yl 2-*O*-(phenylmethyl)-α-L-fucopyranoside, 3,4-bis-*O*-acetate (15).** Compound **14** (14.0 g) was dissolved in pyridine (42 mL), and acetic anhydride (42 mL) and a catalytic amount of *N,N*-dimethylaminopyridine (50 mg) were added. The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with water and the aqueous layer was extracted with hexanes. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by flash chromatography using 10% EtOAc in hexanes as eluent to obtain compound **15** as an oil (15.8 g, 87%). $[\alpha]_D^{25}$ -81.8 (c 1.0, $CHCl_3$); $^1H$ NMR (600 MHz, $CDCl_3$) δ 7.35-7.32 (m, 4H), 7.31-7.27 (m, 1H), 5.95-5.88 (m, 1H), 5.36-5.28 (m, 3H), 5.22 (d, *J* = 10.2 Hz, 1H), 4.88 (d, *J* = 3.6 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H) 4.60 (d, *J* = 12.6 Hz, 1H), 4.18-4.14 (m, 2H), 4.00 (dd, *J* = 6.0, 13.5 Hz, 1H), 3.84 (dd, *J* = 3.6, 10.8 Hz, 1H), 2.13 (s, 3H), 1.99 (s, 3H), 1.10 (d, *J* = 6.6 Hz, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) δ 170.7, 170.2, 138.3, 133.8, 128.5, 128.0, 127.9, 118.1, 96.4, 73.6, 73.0, 71.8, 70.2, 68.7, 64.5, 21.0, 20.8, 16.0; FT-IR: 2983, 2903, 1740, 1238, 1366, 1033, 738, 696 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{20}H_{26}O_7Na$ ($M+Na^+$) 401.1570, found 401.1571.

***trans*-1-Propen-1-yl 2-*O*-(phenylmethyl)-α-L-fucopyranoside, 3,4-bis-*O*-acetate (16).** A solution of the catalyst $[Ir(COD)(PMePh_2)_2]^+PF_6^-$ (0.35 g, 0.41 mmol) in THF (21 mL) was degassed and then stirred for 15 min under an atmosphere of hydrogen (red color of the solution decolorised). This solution was then transferred by cannula into a solution of compound **15** (15.8 g, 41.7 mmol) in THF (316 mL) at room temperature and stirred for 30 min. The reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with hexanes. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation to obtain compound **16** as an oil. The compound was carried forward without further purification. $[\alpha]_D^{25}$ -92.2 (c 1.065, $CHCl_3$); $^1H$ NMR (600 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5H), 6.14 (d, *J* = 12.6 Hz, 1H), 5.36 (dd, *J* = 3.0, 10.5, Hz, 1H), 5.29 (d, *J* = 3.6 Hz, 1H), 5.19-5.14 (m, 1H), 5.03 (d, *J* = 3.0 Hz, 1H), 4.69 (d, *J* = 12.6 Hz, 1H), 4.62 (d, *J* = 12.6 Hz, 1H), 4.13 (dd, *J* = 6.6, 13.2 Hz, 1H), 3.85 (dd, *J* = 3.0, 10.5 Hz, 1H), 2.13 (s, 3H), 1.99 (s, 3H), 1.56 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 6.6 Hz, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) δ 170.6, 170.2, 143.1, 138.1, 128.6, 128.0, 127.9, 104.8, 96.9, 73.2, 73.1, 71.6, 70.1, 65.0, 21.0, 20.8, 16.0, 12.6; FT-IR: 2937, 1741, 1238, 1078, 738, 696 $cm^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{20}H_{26}O_7Na$ ($M+Na^+$) 401.1570, found 401.1563.

**2-*O*-(Phenylmethyl)-α-L-fucopyranose, 3,4-bis-*O*-acetate (17).** Compound **16** from the previous step was dissolved in a mixture of THF (880 mL) and water (220 mL) (4:1). Iodine (21.2 g, 83.5 mmol) was added at room temperature and the brown reaction mixture was stirred for 30 min. The reaction mixture was diluted with EtOAc and the organic layer was washed with saturated aqueous $Na_2S_2O_3$, water and

brine. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by flash chromatography using 10% EtOAc in hexanes as eluent to obtain compound **17** as a solid (11.8 g, 83%, 2 steps). Mp 80-83 ºC; $[\alpha]_D^{25}$ -52.1 (c 1.0, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 7.36-7.26 (m, 7H), 5.31 (dd, *J* = 3.6, 10.2 Hz, 0.7H), 5.28-5.26 (m, 1H), 5.20 (d, *J* = 3.0 Hz, 1H), 4.98 (dd, *J* = 3.6, 10.2 Hz, 1H), 4.89 (d, *J* = 11.4 Hz, 1H) 4.75 (app t, *J* = 6.6 Hz, 1H), 4.70-4.64 (m, 2H), 4.36 (q, *J* = 6.6 Hz, 0.6H), 3.83 (dd, *J* = 3.0, 11.7 Hz, 0.6H), 3.58 (app t, *J* = 9.0 Hz, 1H), 3.21 (s, 0.5H), 2.15-2.14 (m, 4.5H), 2.00 (s, 1.6H), 1.97 (s, 3.0H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.12 (d, *J* = 6.6 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.8, 170.7, 170.3, 138.4, 137.8, 128.7, 128.5, 128.2, 127.9 (2C), 97.5, 91.8, 77.7, 74.9, 74.0, 73.4, 72.9, 71.6, 70.8, 70.1, 69.2, 64.7, 21.0, 20.9, 20.8, 16.3, 16.1; FT-IR: 3405, 2983, 1745, 1736, 1367, 1238, 1050, 729 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{17}H_{22}O_7Na$ ($M+Na^+$) 361.1257, found 361.1253.

**2-*O*-(Phenylmethyl)-α-L-fucopyranose, 3,4-bis-*O*-acetate-1-(2,2,2-trichloroethanimidate) (18).** Compound **17** (5.0 g, 14.7 mmol) was dissolved in $CH_2Cl_2$ (66 mL) at room temperature, and trichloroacetonitrile (10.6 g, 73.8 mmol) was added followed by DBU (0.45 g, 2.9 mmol). The brown reaction mixture was stirred for 20 h. The solvent was removed by rotary evaporation and the crude product was purified by flash chromatography using 10% EtOAc in hexanes containing 2% $Et_3N$ as eluent to obtain compound **18** as a white solid (5.4 g, 76%, α-anomer) and a mixture of α and β-anomers (12%). Mp 150-152 ºC; $[\alpha]_D^{25}$ -84.9 (c 1.225, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 8.6 (s, 1H), 7.34-7.27 (m, 5H), 6.52 (d, *J* = 3.6 Hz, 1H), 5.39-5.36 (m, 2H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.35 (q, *J* = 6.6, 13.2 Hz, 1H), 4.02 (dd, *J* = 2.4, 10.2 Hz, 1H), 2.15 (s, 3H), 2.00 (s, 3H), 1.15 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.6, 170.2, 161.4, 137.9, 128.5, 127.9, 127.6, 94.6, 73.0, 72.7, 71.1, 70.0, 67.5, 21.0, 20.8, 16.1; FT-IR: 3292, 2991, 1743, 1262, 1159, 1027, 798, 638 cm$^{-1}$; HRMS (ESI) *m/z* calcd. For $C_{19}H_{22}Cl_3NO_7Na$ ($M+Na^+$) 504.0354, found 504.0353.

**2-Propen-1-yl *O*-3,4-di-*O*-acetyl-2-*O*-(phenylmethyl)-α-L-fucopyranosyl(1→2)-*O*-6-*O*-(2,2-dimethyl-propanoyl)-3,4-*O*-(1-methylethylidene)-β-D-galactopyranosyl(1→4)-β-D-glucopyranoside, 2,6-bis-*O*-(2,2-dimethylpropanoate) (19).** The lactose acceptor **9** (0.70 g, 1.03 mmol) was dissolved in $CH_2Cl_2$ (3.5 mL), cooled to 0 ºC, and a solution of 0.1 M TMSOTf in $CH_2Cl_2$ (100 μL, 0.01 mmol) was added. A solution of fucosyl donor **18** (anomeric mixture enriched in the *alpha*-anomer, 0.75 g, 1.55 mmol) dissolved in $CH_2Cl_2$ (14 mL) was then added using a syringe pump, over a period of 1 h. When compound **9** was consumed (as monitored by TLC), the reaction was quenched by the addition of $Et_3N$ (0.2 mL) and the solvents were removed by rotary evaporation. The crude product was purified by flash chromatography using 25% EtOAc in hexanes as eluent to obtain trisaccharide **19** as a white solid (0.60 g, 60%). Mp 92-94 ºC; $[\alpha]_D^{25}$ -35.5 (c 1.05, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) 7.33-7.32 (m, 3H), 7.31 (m, 2H), 5.84-5.78 (m, 1H), 5.57 (d, *J* = 3.6 Hz, 1H), 5.33 (d, *J* = 3.6 Hz, 1H), 5.25-5.21 (m, 2H), 5.15 (d,

*J* = 10.2 Hz, 1H), 4.86 (app t, *J* = 8.4 Hz, 1H), 4.69 (dd, *J* = 1.8, 11.7 Hz, 1H), 4.67 (d, *J* = 12.6 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 7.8 Hz, 1H), 4.40-4.36 (m, 3H), 4.29-4.23 (m, 2H), 4.20 (app t, *J* = 6.0 Hz, 1H), 4.13 (dd, *J* = 7.2, 12.0 Hz, 1H), 4.09 (dd, *J* = 1.8, 5.4 Hz, 1H), 4.03-4.00 (m, 3H), 3.84 (dd, *J* = 3.0, 10.8 Hz, 1H), 3.77 (app t, *J* = 6.0, 7.8 Hz, 1H), 3.70 (app t, *J* = 9.0 Hz, 1H), 3.66-3.63 (m, 1H), 3.43 (app t, *J* = 9.3 Hz, 1H), 2.12 (s, 3H), 1.96 (s, 3H), 1.50 (s, 3H), 1.33 (s, 3H), 1.21 (s, 9H), 1.20 (2s, 18H), 1.14 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.7, 177.9, 176.7, 170.7, 169.7, 138.3, 133.7, 128.5, 127.9, 127.8, 117.5, 110.8, 101.2, 99.7, 95.6, 81.4, 79.6, 75.3, 73.6, 73.4, 73.0, 72.9, 72.7, 72.3, 71.9, 69.9, 69.4, 65.0, 63.1, 62.7, 39.0, 38.9 (2C), 28.0, 27.3, 27.2, 26.4, 20.9 (2C), 16.0; FT-IR: 3463, 2973, 1743, 1369, 1241, 1149, 1041 cm$^{-1}$; HRMS (ESI): *m/z* calcd for $C_{50}H_{74}O_{20}Na$ (M+Na$^+$) 1017.4665, found 1017.4648.

***trans*-1-Propen-1-yl *O*-2-*O*-(phenylmethyl)-α-L-fucopyranosyl(1→2)-β-D-galactopyranosyl(1→4)-β-D-glucopyranoside (21).** The trisaccharide **19** (0.5 g, 0.5 mmol) was dissolved in $CH_2Cl_2$ (20 mL) and cooled to 0 ºC. 70% trifluoroacetic acid (2 mL) was added, and the reaction mixture was stirred for 2 h at 0 ºC followed by 2 h at room temperature. The reaction mixture was diluted with water and the aqueous layer was extracted with $CH_2Cl_2$. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated by rotary evaporation to obtain the diol as a white solid (0.41 g, 85%). Mp 204-206 ºC; $[\alpha]_D^{25}$ -34.4 (c 0.605, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 7.42-7.33 (m, 3H), 7.32 (d, *J* = 6.6 Hz, 2H), 5.85-5.78 (m, 1H), 5.36 (dd, *J* = 3.6, 10.5 Hz, 1H), 5.29 (d, *J* = 3.6 Hz, 1H), 5.23 (d, *J* = 17.4 Hz, 1H), 5.16 (d, *J* = 10.8 Hz, 1H), 5.11 (d, *J* = 3.6 Hz, 1H), 4.85 (app t, *J* = 9.0 Hz, 1H), 4.73 (d, *J* = 11.4 Hz, 1H), 4.64 (d, *J* = 10.8 Hz, 1H), 4.48 (s, 1H), 4.44-4.38 (m, 3H), 4.33-4.24 (m, 4H), 4.01 (dd, *J* = 6.0, 13.5 Hz, 1H), 3.93 (dd, *J* = 3.0, 10.5 Hz, 1H), 3.80 (s, 1H), 3.76 (bs, 1H), 3.71 (app t, *J* = 8.4, Hz, 1H), 3.67 (dd, *J* = 3.6, 9.0 Hz, 1H), 3.64-3.59 (m, 4H), 2.15 (s, 3H), 2.03 (s, 3H), 1.21 (s, 18H), 1.20 (s, 9H), 1.13 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.7, 178.0, 176.8, 170.5, 170.0, 136.3, 133.8, 129.0, 128.9, 128.7, 117.5, 101.8, 99.8, 80.6, 79.1, 75.4, 74.9, 72.9 (2C), 72.8, 72.6 (2C), 71.6, 70.3, 69.8, 68.1, 66.6, 63.1, 62.3, 39.0 (2C), 38.9, 27.4, 27.3, 27.2, 21.0, 20.8, 16.2; FT-IR: 3440, 2969, 1743, 1241, 1137, 1072 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{47}H_{70}O_{20}Na$ (M+Na$^+$) 977.4352, found 977.4339. A solution of $[Ir(COD)(PMePh_2)_2]^+PF_6^-$ (3.0 mg, 0.0034 mmol) in THF (0.5 mL) was degassed and then stirred for 15 min under an atmosphere of hydrogen (red color of the solution decolorised). This solution was then transferred by cannula into a solution of the compound above (0.33 g, 0.34 mmol) in THF (7.0 mL) at room temperature, and stirred for 30 min. The reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with hexanes. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation to obtain the vinyl ether **20** as a white solid (0.30 g, 90%). The compound was carried forward without further purification. Mp: 207-209 ºC; $[\alpha]_D^{25}$ -29.6 (c 0.55, $CHCl_3$) $^1$H NMR (600 MHz, $CDCl_3$) δ 7.40-7.36 (m, 3H), 7.34 (m, 2H),

6.14 (dd, *J* = 1.2, 12.3 Hz, 1H), 5.36 (dd, *J* = 3.0, 10.2 Hz, 1H), 5.29 (d, *J* = 2.4 Hz, 1H), 5.11 (d, *J* = 3.6 Hz, 1H), 5.06 (dq, *J* = 6.6, 7.2, 11.7 Hz, 1H), 4.89 (dd, *J* = 8.4, 9.3 Hz, 1H), 4.73 (d, *J* = 11.4 Hz, 1H), 4.64 (d, *J* = 10.8 Hz, 1H), 4.49 (s, 1H), 4.45 (dd, *J* = 4.2, 12.0 Hz, 1H), 4.37 (dd, *J* = 1.8, 12.0 Hz, 1H), 4.34-4.24 (m, 3H), 4.22 (dd, *J* = 7.2 Hz, 1H), 3.93 (dd, *J* = 3.6, 10.5 Hz, 1H), 3.84 (d, *J* = 1.2 Hz, 1H), 3.76-3.71 (m, 2H), 3.68-3.59 (m, 5H), 2.32 (s, 1H), 2.15 (s, 3H), 2.03 (s, 3H), 1.51 (dd, *J* = 1.8, 7.2 Hz), 1.21 (s, 18H), 1.20 (s, 9H), 1.13 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.6, 178.0, 176.8, 170.5, 170.0, 143.6, 136.3, 129.0, 128.9, 128.7, 101.8, 101.1, 99.9, 80.5, 79.0, 75.4, 74.9, 73.0, 72.8, 72.7, 72.6, 71.6, 70.3, 68.1, 66.7, 63.1, 39.0 (2C), 27.4, 27.2 (2C), 21.0, 20.8, 16.2, 12.4; FT-IR: 3448, 2969, 1747, 1241, 1137, 1072 cm$^{-1}$; HRMS (ESI): *m/z* calcd for $C_{47}H_{70}O_{20}Na$ (M+Na$^+$) 977.4352, found 977.4338. Compound **20** (0.27 g, 0.28 mmol) was dissolved in MeOH (1.5 mL), a 0.5 M solution of NaOMe in MeOH (280 μL, 0.14 mmol) was added, and the reaction mixture was heated at 60 ºC for 14 h. An additional 0.5 equiv of a 0.5 M solution of NaOMe in MeOH (280 μL, 0.14 mmol) and the reaction mixture was heated for another 24 h. The reaction was cooled to room temperature, neutralized using Amberlyst 120(H$^+$) resin, filtered and concentrated by rotary evaporation to obtain an oil. Repeated washing of the crude product with hexanes followed by ether and decantation afforded the title compound **21** as a pale yellow solid (0.154 g, 88%). Mp 131-133 ºC; $[\alpha]_D^{25}$ -37.9 (c 0.315, $CHCl_3$); $^1$H NMR (600 MHz, $CD_3OD$) δ 7.39 (d, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 6.25 (d, *J* = 12.0 Hz, 1H), 5.45 (d, *J* = 3.0 Hz, 1H), 5.00 (dq, *J* = 7.2, 13.2 Hz, 1H), 4.79 (d, *J* = 11.4 Hz, 1H), 4.61 (d, *J* = 11.4 Hz, 1H), 4.41 (dd, *J* = 5.4, 7.2 Hz, 1H), 4.15 (q, *J* = 6.6 Hz, 1H), 3.81-3.78 (m, 2H), 3.73-3.68 (m, 3H), 3.65 (dd, *J* = 3.0, 9.6 Hz, 1H), 3.62- 3.57 (m, 4H), 3.49-3.47 (m, 1H), 3.41 (app t, *J* = 9.3, 10.3 Hz, 1H), 3.27-3.22 (m, 4H), 1.46 (d, *J* = 6.6 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); $^{13}$C NMR (150 MHz, $CD_3OD$) δ 146.0, 139.7, 129.6, 129.4, 128.8, 104.7, 103.5, 102.4, 98.7, 77.8, 77.2, 77.0, 76.6, 76.3, 76.2, 74.5, 73.8, 73.2, 71.0, 70.9, 67.6, 62.6, 61.5, 16.6, 12.5; FT-IR 3394, 2927, 2885, 1677, 1400, 1079, 1041 cm$^{-1}$; HRMS (ESI) *m/z* calcd. for $C_{28}H_{42}O_{15}Na$ (M+Na$^+$) 641.2415, found 641.2409.

**2'-Fucosyllactose (1)**. Compound **21** (0.13 g, 0.210 mmol) was dissolved in a mixture of THF (10.8 mL) and water (3.0 mL) (4:1), iodine (0.1 g, 0.4 mmol) was added at room temperature, and the brown reaction mixture was stirred for 30 min. The solvents were removed by rotary evaporation, and the crude product was azeotroped with toluene to remove water. The crude product was dissolved in pyridine (1.73 mL), acetic anhydride (0.86 mL) and DMAP (6 mg) were added, and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with EtOAc, and the organic layer was washed with saturated aq. $Na_2S_2O_3$, saturated aq. $NaHCO_3$, water, and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by flash chromatography using 10% acetone in $CH_2Cl_2$ as eluent to obtain the peracylated compound as a white solid (0.125 g, 62%). Mp 94-96 ºC; $^1$H NMR (600 MHz, $CDCl_3$) δ 7.34-7.31 (m, 3H), 7.28-7.25 (m, 6H),

6.29 (d, *J* = 3.6 Hz, 0.75H), 5.68 (d, *J* = 8.4, 1H), 5.41 (app t *J* = 10.2 Hz, 0.85H), 5.33 (d, *J* = 3.0, 8.1 Hz, 2H), 5.29 (dd, *J* = 3.6, 7.5 Hz, 2H), 5.25 (bs, 2H), 5.23 (app t, *J* = 9.6 Hz, 1H), 5.18-5.14 (m, 2H), 5.10-5.07 (m, 1H), 5.05-5.00 (m, 2H), 4.60 (app t, *J* = 11.4, 12.6 Hz, 2H), 4.56 (app t, *J* = 10.2, 11.1 Hz, 1H), 4.51-4.48 (m, 2H), 4.45-4.40 (m, 3H), 4.38-4.30 (m, 3H), 4.16-4.11 (m, 2H), 4.10-4.04 (m, 3H), 3.95-3.91 (m, 1H), 3.90-3.81 (m, 7H), 2.19 (s, 3H), 2.13-2.10 (m, 12H), 2.08-2.05 (m, 12H), 2.04 (s, 3H), 1.93 (s, 3H), 1.92 (s, 3H), 1.87 (s, 3H), 1.85 (s, 3H), 1.18 (d, *J* = 6.6 Hz, 2H), 1.14 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.7, 170.6, 170.5, 170.4, 170.3, 170.2, 170.1, 169.9, 169.8, 169.5, 169.1, 169.0, 138.1, 128.5, 127.9, 127.5, 101.1, 100.8, 97.5, 97.3, 91.8, 89.1, 74.0, 73.9, 73.6, 73.2, 73.0, 72.9, 72.7, 72.0, 71.7, 71.0, 70.8, 70.4, 61.9, 61.7, 61.2, 61.0, 21.1, 21.0 (2C), 20.9, 20.8, 20.7, 20.6 (2C), 15.8, 15.7; FT-IR 2942, 1751, 1369, 1222, 1045 cm$^{-1}$; HRMS (ESI) *m/z* calcd. for $C_{43}H_{56}O_{24}Na$ (M+Na$^+$) 979.3053, found 979.3047. The above compound (53 mg, 0.055 mmol) was dissolved in a mixture of EtOH (0.8 mL) and EtOAc (0.4 mL), the solution was degassed under argon, and 5% Pd/C (0.045 g) was added. The reaction mixture was degassed again under argon and then was stirred under an atmosphere of hydrogen for 48 h. The catalyst was removed by filtration through a bed of Celite, which was rinsed with EtOH, and the filtrate was filtered again through a Whatman filter. The solvents were removed by rotary evaporation to obtain a white solid (45 mg, 93%). Mp 114-116 ºC; $^1$H NMR (600 MHz, $CDCl_3$) δ 6.30 (d, *J* = 3.6 Hz, 0.75H), 5.68 (d, *J* = 8.4 Hz, 1H), 5.42 (app t *J* = 10.2 Hz, 0.84H), 5.35 (dd, *J* = 3.0, 6.6 Hz, 2H), 5.25-5.22 (m, 3H), 5.14 (dd, *J* = 4.2, 10.8 Hz, 2H), 5.09 (app t, *J* = 8.7 Hz, 1H), 5.04 (dd, *J* = 3.0, 10.2 Hz, 1H), 5.01-4.97 (m, 3H), 4.45-4.42 (m, 2H), 4.38-4.29 (m, 4H), 4.27 (q, *J* = 6.6 Hz, 1H), 4.17-4.12 (m, 2H), 4.09-4.06 (m, 2H), 3.91-3.80 (m, 8H), 2.18 (s, 3H), 2.15 (s, 3H), 2.13-2.10 (m, 12H), 2.08-2.06 (m, 12H), 2.04 (s, 3H), 2.02 (m, 12H), 1.19 (d, *J* = 6.6 Hz, 2H), 1.17 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.7 (2C), 170.6, 170.5 (2C), 170.2, 170.1 (2C), 169.5, 169.0, 100.9, 100.6, 100.1 (2C), 91.9, 89.1, 74.1, 73.9 (2C), 73.8, 73.0, 71.9, 71.4, 71.0 (2C), 70.6, 70.5, 70.4, 69.3, 69.2, 67.6, 67.3, 66.1, 66.0, 62.0, 61.9, 61.1, 60.9, 21.1, 21.0, 20.9, 20.8, 20.7, 20.6, 16.0, 15.8; FT-IR 3486, 2942, 1747, 1373, 1226, 1076 cm$^{-1}$; HRMS (ESI) *m/z* calcd. for $C_{36}H_{50}O_{24}Na$ (M+Na$^+$) 889.2584, found 889.2588. The above compound (42 mg, 0.048 mmol) was dissolved in MeOH (4.2 mL), a 0.5 M solution of NaOMe in MeOH (5 μL, 0.0024 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was neutralized with Amberlite 120(H$^+$) resin, filtered, and the solvent was removed by rotary evaporation. The crude solid obtained was washed with $Et_2O$ and decanted, and dried under vacuum to provide 2'-fucosyllactose (**1**) as a white solid (23 mg, 82%). $[\alpha]_D^{25}$ -48.1 (c 0.625, $H_2O$); after 72 h $[\alpha]_D^{25}$ = -49.3 (c 0.625, $H_2O$); $^1$H NMR (600 MHz, $D_2O$) 5.31 (d, *J* = 3.6 Hz, 1H), 5.22 (d, *J* = 3.6 Hz, 0.5H), 4.64 (d, *J* = 7.8 Hz, 0.5H), 4.52 (d, *J* = 7.8 Hz, 1H), 4.26 (q, *J* = 6.6 Hz, 0.5H), 4.23 (q, *J* = 6.6 Hz, 0.5H), 3.95 (dd, *J* = 1.8, 12.0 Hz, 1H), 3.92- 3.85 (m, 3H), 3.82-3.79 (m, 5H), 3.77-3.65 (m, 6H), 3.60-3.57 (m, 1H), 3.48 (ddd, *J* = 1.8, 5.4, 9.9 Hz, 0.5H), 3.29 (dd, *J* = 9.3 Hz,

0.5H), 1.23 (d, *J* = 6.6 Hz, 1.5H), 1.22 (d, *J* = 6.6 Hz, 1.5H); $^{13}$C NMR (150 MHz, $D_2O$) δ 100.3, 99.4, 96.0, 91.9, 76.4, 76.0, 75.9, 75.4, 75.3, 74.4, 74.0, 73.7, 71.8, 71.4 (2C), 70.5, 69.7 (2C), 69.3, 68.3, 67.0, 61.2, 60.3, 60.1, 15.3; HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{32}O_{15}Na$ ($M+Na^+$) 511.1633, found 511.1636.

**2-Propen-1-yl *O*-2,6-bis-*O*-(2,2-dimethylpropanoyl)-3,4-*O*-(1-methylethylidene)-β-D-galactopyranosyl(1→4)-*O*-[3,4-bis-*O*-acetyl-2-*O*-(phenylmethyl)-α-L-fucopyranosyl-(1→3)]-β-D-glucopyranoside, 2,6-bis-*O*-(2,2-dimethylpropanoate) (22).** The lactose acceptor **10** (0.70 g, 0.92 mmol; accumulated from multiple preparations) was dissolved in $CH_2Cl_2$ (3.5 mL), cooled to 0 ºC, and a solution of 0.1 M TMSOTf in $CH_2Cl_2$ (90 μL, 0.009 mmol) was added. A solution of fucosyl donor **18** (0.89 g, 1.84 mmol) dissolved in $CH_2Cl_2$ (14 mL) was then added using a syringe pump, over a period of 1 h. When compound **10** was consumed (as monitored by TLC), the reaction was quenched by the addition of $Et_3N$ (0.2 mL) and the solvents were removed by rotary evaporation. The crude product was purified by flash chromatography using 25% EtOAc in hexanes as eluent to obtain the trisaccharide **22** as a white solid (0.81 g, 82%). Mp: 96-98 ºC; $[\alpha]_D^{25}$ -14.7 (c 0.955, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 7.34-7.29 (m, 3H), 7.25-7.23 (m, 2H), 5.84-5.78 (m, 1H), 5.37 (d, *J* = 3.6 Hz, 1H), 5.35 (d, *J* = 2.4 Hz, 1H), 5.31 (dd, *J* = 1.8, 10.5 Hz, 2H), 5.22 (dd, *J* = 1.8, 17.1 Hz, 1H), 5.16 (dd, *J* = 1.2, 11.1 Hz, 1H), 5.07 (dd, *J* = 7.8, 9.0 Hz, 1H), 4.96-4.91 (m, 2H), 4.60-4.56 (m, 3H), 4.46 (d, *J* = 11.4 Hz, 2H), 4.39 (d, *J* = 8.4 Hz, 1H), 4.28 (d, *J* = 9.0 Hz, 1H), 4.28-4.25 (m, 1H), 4.19 (dd, *J* = 4.8, 12.0 Hz, 1H), 4.11-4.05 (m, 3H), 3.97-3.93 (m, 2H), 3.87 (dd, *J* = 4.8, 10.5 Hz, 1H), 3.81 (app t, *J* = 9.6 Hz, 1H), 3.47 (dq, *J* = 2.4, 9.6 Hz, 1H), 2.14 (s, 3H), 1.92 (s, 3H), 1.52 (s, 3H), 1.31 (s, 3H), 1.22 (2s, 18H), 1.21 (d, *J* = 6.0 Hz, 3H), 1.16 (s, 9H), 1.04 (s, 9H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.6, 178.1, 176.7, 170.7, 169.6, 138.3, 133.4, 128.2, 127.9, 127.5, 117.9, 111.0, 100.2, 97.1, 77.8, 74.7, 74.4 (2C), 74.1, 73.6, 73.5, 72.9, 72.7, 72.1, 71.7, 70.5, 70.1, 64.3, 62.6, 61.8, 39.1, 38.9, 38.8, 27.9, 27.4 (2C), 27.2, 27.0, 26.4, 21.0, 20.9, 16.3; FT-IR: 2973, 1743, 1241, 1133, 1045 $cm^{-1}$; HRMS (ESI): *m*/*z* calcd. for $C_{55}H_{82}O_{21}Na$ ($M+Na^+$) 1101.5300 found 1101.5300.

***trans*-1-Propen-1-yl *O*-β-D-galactopyranosyl(1→4)-*O*-[2-*O*-(phenylmethyl)-α-L-fucopyranosyl-(1→3)]-β-D-glucopyranoside (24).** The trisaccharide **22** (0.5 g, 0.5 mmol) was dissolved in $CH_2Cl_2$ (20 mL) and cooled to 0 ºC. 70% trifluoroacetic acid (2 mL) was added, and the reaction mixture was stirred for 2 h at 0 ºC followed by 2 h at room temperature. The reaction mixture was diluted with water and the aqueous layer was extracted with $CH_2Cl_2$. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated by rotary evaporation to obtain the diol as a white solid (0.38 g, 80%). Mp 98-100 ºC; $[\alpha]_D^{25}$ -25.9 (c 0.83, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 7.32-7.29 (m, 4H), 7.25-7.23 (m, 1H), 5.85-5.78 (m, 1H), 5.33 (d, *J* = 3.0 Hz, 1H), 5.26 (dd, *J* = 3.0, 10.8 Hz, 1H), 5.23 (dd, *J* = 1.2, 18.0 Hz, 1H), 5.16 (d, *J* = 10.2 Hz, 1H), 5.12 (app t, *J* = 7.8 Hz, 1H), 4.93 (app t, *J* = 7.8 Hz, 1H), 4.88 (q, *J* = 6.6 Hz, 1H), 4.59 (d, *J* = 11.4 Hz, 3H), 4.50-4.39 (m, 6H), 4.26 (dd, *J* = 4.8, 12.6 Hz, 2H), 4.19 (dd, *J* = 4.8, 12.0 Hz, 1H), 4.07 (app t, *J* = 9.6 Hz, 1H), 3.97 (dd, *J* = 6.6, 12.0 Hz, 1H),

3.94 (app t, *J* = 9.6 Hz, 1H), 3.90-3.86 (m, 2H), 3.61 (app t, *J* = 6.6 Hz, 1H), 3.57-3.51 (m, 2H), 3.46 (d, *J* = 3.6 Hz, 1H), 2.69 (d, *J* = 9.6, 1H), 2.12 (s, 3H), 1.93 (s, 3H), 1.72 (s, 1H), 1.24 (s, 9H), 1.21 (s, 9H), 1.18 (s, 9H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.12 (s, 9H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.5, 178.1, 178.0, 176.4, 170.9, 170.8, 138.3, 133.5, 128.3, 127.9, 127.6, 117.9, 100.3, 100.1, 96.9, 74.4, 73.8, 73.6, 73.5 73.1 (2C), 72.8, 72.1, 72.0, 70.7, 70.0, 68.5, 64.5, 62.2, 39.1, 39.0 (2C), 38.8, 27.4, 27.3, 27.2, 21.1, 20.9, 16.0; FT-IR: 3486, 2973, 1739, 1276, 1145, 1045 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{52}H_{78}O_{21}Na$ (M+Na$^+$) 1061.4927 found 1061.4927. A solution of $[Ir(COD)(PMePh_2)_2]^+PF_6^-$ (2.8 mg, 0.0033 mmol) in THF (0.56 mL) was degassed and then stirred for 15 min under an athmosphere of hydrogen (red color of the solution decolorised). This solution was then transferred by cannula into a solution of the compound above (0.35 g, 0.36 mmol) in THF (7.7 mL) at room temperature, and stirred for 30 min. The reaction mixture was diluted with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with hexanes. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation to obtain the vinyl ether **23** as a white solid (0.30 g, 86%). The compound was carried forward without further purification. Mp 100-102 ºC; $[\alpha]_D^{25}$ -26.3 (c 0.96, $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$) δ 7.31-7.30 (m, 4H), 7.26-7.24 (m, 1H), 6.12 (dd, *J* = 1.8, 12.3 Hz, 1H), 5.32 (m, 1H), 5.31 (d, *J* = 3.6 Hz, 1H), 5.25 (dd, *J* = 3.6, 10.5 Hz, 1H), 5.16 (app t, *J* = 7.8 Hz, 1H), 5.09-5.03 (m, 1H), 4.93 (app t, *J* = 9.0 Hz, 1H), 4.87 (q, *J* = 6.0, 7.2 Hz, 1H), 4.61 (d, *J* = 11.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 1H), 4.49-4.41 (m, 6H), 4.21 (dd, *J* = 5.4, 12.0 Hz, 1H), 4.08 (app t, *J* = 9.0 Hz, 1H), 3.97 (app t, *J* = 9.6 Hz, 1H), 3.62-3.53 (m, 3H), 3.46 (d, *J* = 3.0 Hz, 1H), 2.70 (d, *J* = 9.6, 1H), 2.11 (s, 3H), 1.93 (s, 3H), 1.72 (s, 1H), 1.51 (d, *J* = 6.6, 3H), 1.23 (s, 9H), 1.22 (s, 9H), 1.18 (s, 9H), 1.18 (d, *J* = 6.0 Hz, 3H), 1.13 (s, 9H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 178.5, 178.0, 176.4, 170.9, 170.8, 143.5, 138.3, 128.3, 127.9, 127.6, 105.1, 100.2, 100.0, 96.9, 74.1, 73.8, 73.5, 73.3 73.1(2C), 72.8, 72.2, 71.9, 70.7, 68.4, 64.6, 62.2, 61.9, 39.0, 38.9, 27.4, 27.3 (2C), 27.2, 21.1, 20.9, 16.0, 12.4; FT-IR: 3486, 2969, 1739, 1276, 1141, 1076 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{52}H_{78}O_{21}$ (M+Na$^+$) 1061.4927 found 1061.4919. Compound **23** (0.27 g, 0.28 mmol) was dissolved in MeOH (1.5 mL), a 0.5 M solution of NaOMe in MeOH (280 μL, 0.14 mmol) was added, and the reaction mixture was heated at 60 ºC for 14 h. An additional 0.5 equiv of 0.5 M solution of NaOMe in MeOH (280 μL, 0.14 mmol) was added, and the reaction mixture was heated for another 24 h. The reaction was cooled to room temperature, neutralized using Amberlyst 120(H$^+$) resin, filtered and concentrated by rotary evaporation to obtain an oil. Repeated washing of the crude product with hexanes followed by $Et_2O$ and decantation afforded the title compound **24** as a pale yellow solid (0.14 g, 87%). Mp 142-144 ºC; $[\alpha]_D^{25}$ -75.8 (c 0.69, $CHCl_3$); $^1$H NMR (600 MHz, $CD_3OD$) δ 7.48 (d, *J* = 7.2 Hz, 2H), 7.33 (app t, *J* = 7.2 Hz, 2H), 7.26 (app t, *J* = 7.2 Hz, 1H), 6.34 (dd, *J* = 1.2, 12.0 Hz, 1H), 5.70 (d, *J* = 3.6 Hz, 1H), 5.14-5.09 (m, 1H), 4.89 (d, *J* = 11.4 Hz, 1H), 4.66 (d, *J* = 11.4 Hz, 1H), 4.50 (dd, *J* = 7.8 Hz, 1H), 4.40 (d, *J* = 7.2 Hz, 1H), 3.93-3.89 (m, 3H), 3.82-3.79 (m, 4H), 3.75 (dd, 10.5, 1.8 Hz, 1H). 3.65 (dd, *J* = 3.6, 10.6

Hz, 1H), 3.60 (dd, *J* = 4.2, 12.0 Hz, 1H), 3.56 (app t, *J* = 8.4 Hz, 1H), 3.50-3.47 (m, 2H), 3.31-3.30 (m, 1H), 1.56 (d, *J* = 6.6 Hz, 3H), 1.16 (d, *J* = 6.0 Hz, 3H); $^{13}$C NMR (150 MHz, $CD_3OD$) δ 144.0, 137.8, 127.7, 127.4, 126.8, 102.8, 102.0, 101.9, 95.9, 76.1, 75.7, 75.1, 74.5, 72.9, 72.2, 71.9, 71.0, 70.7, 68.3, 68.1, 65.2, 61.2, 59.2, 14.6, 10.5; FT-IR: 3394, 2935, 2885, 1454, 1087 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{28}H_{42}O_{15}Na$ (M+Na$^+$) 641.2415, found 641.2417.

**3-Fucosyllactose (2).** Compound **24** (0.12 g, 0.193 mmol) was dissolved in a mixture of THF (10.0 mL) and water (2.8 mL) (4:1), iodine (0.1 g, 0.4 mmol) was added at room temperature, and the brown reaction mixture was stirred for 30 min. The solvents were removed by rotary evaporation, and the crude product was azeotroped with toluene to remove water. The crude product was dissolved in pyridine (1.6 mL), acetic anhydride (0.8 mL) and DMAP (5 mg) were added, and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with EtOAc, and the organic layer was washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, water, and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude product was purified by flash chromatography using 10% acetone in $CH_2Cl_2$ as eluent to obtain the peracylated compound as a white solid (0.11 g, 61%). Mp 110-112 ºC; $^1$H NMR (600 MHz, $CDCl_3$) δ 7.34-7.23 (m, 9H), 6.28 (d, *J* = 3.6 Hz, 0.7H), 5.60 (d, *J* = 7.8 Hz, 1H), 5.40-5.39 (m, 2H), 5.37-5.36 (m, 2H), 5.27 (d, *J* = 4.2 Hz, 2H), 5.24-5.20 (m, 3H), 5.13-5.05 (m, 3H), 5.00-4.97 (m, 3H), 4.91(q, *J* = 6.0, 7.2 Hz, 1H), 4.63-4.54 (m, 6H), 4.53 (dd, *J* = 4.8, 10.2 Hz, 2H), 4.48 (dd, *J* = 7.2, 14.4 Hz, 2H), 4.33 (app t, *J* = 7.8 Hz, 1H), 4.31 (app t, *J* = 7.8 Hz, 1H), 4.19 (app t, *J* = 7.8 Hz, 1H), 4.13-4.09 (m, 2H), 4.07-4.04 (m, 2H), 4.00 (app t, *J* = 6.6 Hz, 1H), 3.93-3.90 (m, 2H), 3.89-3.85 (m, 3H), 3.65 (bd, 1H), 2.20-2.13 (m, 19H), 2.08-2.05 (3s, 9H), 2.03 (s, 6H), 1.98-1.97 (3s, 8H), 1.91-1.90 (2s, 5H), 1.86 (s, 2H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.8, 170.6, 170.4, 170.1, 169.9, 169.4, 169.3, 169.2, 169.1, 168.8, 138.0, 128.5(2C), 128.2, 128.5, 127.6, 100.7, 100.5, 97.7, 97.4, 92.1, 89.2, 74.5, 74.0, 73.6, 73.5, 73.2, 73.0, 72.9, 72.0(2C), 71.6, 71.5, 71.3, 71.2, 71.1(2C), 70.5(2C), 69.2, 69.1, 66.8(2C), 66.8, 64.5, 61.6, 61.2, 61.0, 60.9, 21.1, 20.9, 20.8, 20.7, 16.0; FT-IR: 2977, 1751, 1373, 1226, 1049 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{43}H_{56}O_{24}Na$ (M+Na$^+$) 979.3053, found 979.3064. The above compound (60 mg, 0.062 mmol) was dissolved in a mixture of EtOH (0.48 mL) and EtOAc (0.24 mL), the solution was degassed under argon, and 5% Pd/C (0.02 g) was added. The reaction mixture was degassed again under argon and then was stirred under an atmosphere of hydrogen for 48 h. The catalyst was removed by filtration through a bed of Celite, which was rinsed with EtOH, and the filtrate was filtered again through a Whatman filter. The solvents were removed by rotary evaporation to obtain a white solid (47 mg, 88%). Mp 134-136 ºC; $^1$H NMR (600 MHz, $CDCl_3$) δ 6.17 (d, *J* = 3.6 Hz, 0.7H), 5.60 (d, *J* = 8.4, 1H), 5.43-5.42 (m, 1.8H), 5.33-5.30 (m, 2H), 5.17-5.05 (m, 7H), 4.97 (dt, *J* = 3.0, 10.5 Hz, 2H), 4.89-4.84 (m, 2H), 4.69 (dd, *J* = 6.6, 11.7 Hz, 1H), 4.66 (dd, *J* = 7.8, 11.7 Hz, 1H), 4.58 (dd, *J* = 1.8, 12.0 Hz, 1H), 4.56 (dd, *J* =

1.8, 12.3 Hz, 1H), 4.44 (app t, *J* = 8.4 Hz, 2H), 4.15 (app t, *J* = 9.6 Hz, 1H), 3.96-3.89 (m, 4H), 3.84-3.80 (m, 4H), 3.68-3.66 (m, 1H), 2.20-2.13 (3s, 8H), 2.15-2.14 (2s, 11H), 2.02-1.97 (4s, 11H), 1.26 (d, *J* = 6.6 Hz, 2.75H), 1.23 (d, *J* = 6.6 Hz, 3.3H); $^{13}$C NMR (150 MHz, $CDCl_3$) δ 170.9, 170.8, 170.7, 170.6(2C), 170.3, 170.2, 170.1, 169.8, 169.3, 169.2(2C), 169.0, 100.8, 99.7, 99.6, 91.6, 89.5, 75.3, 74.2, 73.9, 73.8, 72.3, 72.2, 72.1, 71.9, 71.8(2C), 71.1, 71.0, 70.9, 68.9, 68.8, 66.9, 66.8, 65.2, 65.0, 61.5, 61.3, 21.1, 21.0, 20.8(2C), 20.7(2C), 16.0(2C); FT-IR: 3494, 2962, 1747, 1373, 1226, 1045 cm$^{-1}$; HRMS (ESI): *m/z* calcd. for $C_{36}H_{50}O_{24}Na$ (M+Na$^+$) 889.2584, found 889.2572. The above compound (23 mg, 26 μmol) was dissolved in MeOH (2.3 mL), a 0.5 M solution of NaOMe in MeOH (2.6 μL, 1.3 μmol) was added, and the reaction mixture was stirred at room temperature for 24 h. The reaction mixture was neutralized with Amberlite 120(H$^+$) resin, filtered, and the solvent was removed by rotary evaporation. The crude solid obtained was washed with ether and decanted, and dried under vacuum to provide 3-fucosyllactose (**2**) as a white solid (10 mg, 77%). $[\alpha]_D^{25}$ -29.8 (c 0.45, $H_2O$), after 92 h $[\alpha]_D^{25}$ -22.1 (c 0.45, $H_2O$); $^1$H NMR (600 MHz, $D_2O$) δ 5.44 (d, *J* = 3.6 Hz, 0.5H), 5.38 (d, *J* = 3.6 Hz, 0.5H), 5.18 (d, *J* = 3.6 Hz, 0.5H), 4.84-4.81 (m, 2H), 4.65 (d, *J* = 7.8 Hz, 0.5H), 4.43 (d, *J* = 7.8 Hz, 1H), 3.98-3.93 (m, 2.5H), 3.90-3.86 (m, 3H), 3.84-3.70 (m, 3.5H), 3.66-3.64 (m, 1.5H), 3.62-3.59 (m, 1.5H), 3.50-3.44 (m, 2H), 1.19 (d, *J* = 6.0 Hz, 1.5H), 1.18 (d, *J* = 6.6 Hz, 1.5H); $^{13}$C NMR (150 MHz, $D_2O$) δ 101.9, 98.6, 98.4, 95.9, 92.2, 77.1, 75.6, 75.4, 75.0, 74.8, 72.7 (2C), 72.5, 72.0, 71.2, 71.0, 69.4, 69.3, 69.3, 68.4, 68.1, 66.6, 66.5, 61.6, 59.8 (2C), 15.3; HRMS (ESI): *m/z* calcd. for $C_{18}H_{32}O_{15}Na$ (M+Na$^+$) 511.1633, found 511.1639.

## REFERENCES


1. R. E. Black, S. S. Morris, and J. Bryce, *Lancet*, 2003, **361**, 2226.
2. J. Brand Miller and P. McVeagh, *Br. J. Nutr*., 1999, **82**, 333; C. Kunz, S. Rudloff, W. Baier, N. Klein, and S. Strobel, *Annu. Rev. Nutr*., 2000, **20**, 699; D. S. Newburg, G. M. Ruiz-Palacios, and A. L. Morrow, *Annu. Rev. Nutr*., 2005, **25**, 37; L. Bode, *J. Nutrition*, 2006, **136**, 2127; M. R. Ninonuevo, Y. Park, H. Yin, J. Zhang, R. E. Ward, B. H. Clowers, J. B. German, S. L. Freeman, K. Killeen, R. Grimm, and C. B. Lebrilla, *J. Agric. Food Chem*., 2006, **54**, 7471; S. M. Donovan, *Br. J. Nutr*., 2009, **101**, 1267.
3. G. V. Coppa, L. Zampini, T. Galeazzi, B. Facinelli, L. Ferrante, R. Capretti, and G. Orazio, *Pediatr Res*., 2006, **59**, 377; R. Maria Espinosa, M. Tamiz, and P. Prieto, *Br. J. Nutr*., 2007, **98**, S74.
4. L. Bode, *Nutr. Rev*., 2009, **67**, S183; Y. Vandenplas, *Br. J. Nutr*., 2002, **87**, S293.
5. B. Wang and J. Brand-Miller, *Eur. J. Clin. Nutr*., 2003, **57**, 1351; B. Wang, J. Brand-Miller, P. McVeagh, and P. Petocz, *Am. J. Clin. Nutr*., 2001, **74**, 510.
6. G. M. Ruiz-Palacios, L. E. Cervantes, P. Ramos, B. Chavez-Munguia, and D. S. Newburg, *J. Biol. Chem*., 2003, **278**, 14112; A. L. Morrow, G. M. Ruiz-Palacios, X. Jiang, and D. S. Newburg, *J.*

*Nutrition*, 2005, **135**, 1304.

7. S. A. Abbas, J. J. Barlow, and K. L. Matta, *Carbohydr. Res.*, 1981, **88**, 51; A. Fernandez-Mayoralas, and M. Martin-Lomas, *Carbohydr. Res.*, 1986, **154**, 93; R. K. Jain, R. D. Locke, and K. L. Matta, *Carbohydr. Res.*, 1991, **212**, C1; M. Izumi, O. Tsuruta, S. Harayama, and H. Hashimoto, *J. Org. Chem.*, 1997, **62**, 992; A. Rencurosi, L. Poletti, G. Russo, and L. Lay, *Eur. J. Org. Chem.*, 2003, 1672.
8. For a synthesis using metabolically engineered *E. coli,* see: S. Drouillard, H. Driguez, and E. Samain, *Angew. Chem. Int. Ed.*, 2006, **45**, 1778.
9. R. R. Schmidt and W. Kinzy, *Adv. Carbohydr. Chem. Biochem.*, 1994, **50**, 21; G. Kretzschmar and W. Stahl, *Tetrahedron*, 1998, **54**, 6341; F. Jamois, F. Le Goffic, J. C. Yvin, D. Plusquellec, and V. Ferrières, *Open Glycoscience*, 2008, **1**, 19.
10. Y. Matsuzaki, Y. Ito, and T. Ogawa, *Tetrahedron Lett.*, 1992, **33**, 4025.
11. K. Okamoto, T. Kondo, and T. Goto, *Tetrahedron*, 1987, **43**, 5919.
12. G. Zheng, A. Graham, M. Shibata, J. R. Missert, A. R. Oseroff, T. J. Dougherty, and R. K. Pandey, *J. Org. Chem.*, 2001, **66**, 8709.
13. T. Tomoo, T. Kondo, H. Abe, S. Tsukamoto, M. Isobe, and T. Goto, *Carbohydr. Res.*, 1996, **284**, 207.
14. P. J. Garegg and T. Norberg, *Carbohydr. Res.*, 1976, **52**, 235.
15. H.-J. Vermeer, C.-M. van Dijk, J.-P. Kamerling, and J.-F. G. Vliegenthart, *Eur. J. Org. Chem.*, 2001, 193.
16. S. Inamura, Y. Fujimoto, A. Kawasaki, Z. Shiokawa, E. Woelk, H. Heine, B. Lindner, N. Inohara, S. Kusumoto, and K. Fukase, *Org. Biomol. Chem.*, 2006, **4**, 232; D. Hamza, R. Lucas, T. Feizi, W. Chai, D. Bonnaffé, and A. Lubineau, *ChemBioChem.*, 2006, **7**, 1856; S. Ronchi, F. Compostella, L. Lay, F. Ronchetti, and L. Toma, *Eur. J. Org. Chem.*, 2005, 4459.
17. R. Windmüller and R. R. Schmidt, *Tetrahedron Lett.*, 1994, **35**, 7927; L. Lay, R. Windmüller, S. Reinhardt, and R. R. Schmidt, *Carbohydr. Res.*, 1997, **303**, 39; C. Gege, S. Oscarson, and R. R. Schmidt, *Tetrahedron Lett.*, 2001, **42**, 377; C. Gege, A. Geyer, and R. R. Schmidt, *Eur. J. Org. Chem.*, 2002, 2475; B. La Ferla, D. Prosperi, L. Lay, G. Russo, and L. Panza, *Carbohydr. Res.*, 2002, **337**, 1333; A. Rencurosi, L. Poletti, G. Russo, and L. Lay, *Eur. J. Org. Chem.*, 2003, 1672.
18. R. R. Schmidt and A. Toepfer, *Tetrahedron Lett.*, 1991, **32**, 3353.
19. Only 38% yield of the trisaccharide **19** was obtained when the TMSOTf catalyst was added to a cold (-5 °C) $CH_2Cl_2$ solution of lactosyl acceptor **9** and fucosyl donor **18**.
20. Under otherwise identical conditions, the corresponding 2,3,4-triacetate fucosyl trichloroacetimidate provided only the undesired *beta*-anomer of **19**.

21. The formation of trisaccharide **19** was accompanied by variable amounts of a byproduct which was possibly the tetrasaccharide, from a second fucosylation at O3 of **19**. However, this byproduct could not be fully purified nor characterized, although its production increased with corresponding decreases in the yield of **19** when 2 equiv of fucosyl donor **18** was used in the glycosylation. We did not observe any trisaccharide corresponding to O3-glycosylation alone.
22. T. Rundlöf and G. Widmalm, *Magn. Reson. Chem.*, 2001, **39**, 381; G. A. Jenkins, J. H. Bradbury, M. Messer, and E. Trifonoff, *Carbohydr. Res.*, 1984, **126**, 157; Y. Ishizuka, T. Nemoto, M. Fujiwara, K. Fujita, and H. Nakanishi, *J. Carbohydr. Chem.*, 1999, **18**, 522.