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Recognition of synthetic deoxy and deoxyfluoro analogs of the acceptor α-L-Fuc*p*-(1 → 2)-β-D-Gal*p*-OR by the blood-group A and B gene-specified glycosyltransferases

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ABSTRACT

The disaccharide α-L-Fuc*p*-(1 → 2)-β-D-Gal*p*-O-$(CH_2)_7CH_3$ (**6**), is an acceptor for both glycosyltransferases responsible for the biosynthesis of the A and B blood-group antigens. These enzymes transfer GalNAc and Gal, respectively, with an α-linkage to OH-3 of the Gal residue in **6**. All six possible deoxy and deoxyfluoro analogs of **6**, with modifications on the target Gal residue, were chemically synthesized and kinetically evaluated as both substrates and inhibitors for the A and B glycosyltransferases. Both enzymes will tolerate replacement of the hydroxyl groups at the 3 and 6 positions of the Gal residue. Substitution of OH-4 of the Gal residue, however, abolishes recognition by these glycosyltransferases. The 6-deoxy and 6-fluoro compounds are substrates for both enzymes while the 3-deoxy and 3-fluoro compounds are competitive inhibitors, with K_i values in the range 14–110 μM. Kinetic constants have been determined for the 6-deoxy and 6-fluoro derivatives.

INTRODUCTION

It is now widely recognized that carbohydrates fulfill a number of biologically important roles aside from the energy storage and structural functions historically assigned to them. Reports over the last fifteen years have documented that carbohydrates serve as recognition factors for a number of cellular processes, during both normal cell development and tumor progression[1–3]. The observation that, during carcinogenesis, cell-surface oligosaccharides change in structure has prompted much study on the glycosyltransferases since this class of enzyme is responsible for biological glycosidic bond formation. The activity of these enzymes may therefore be modulated in cancerous cells. Our work in this area has been aimed at developing specific glycosyltransferase inhibitors as tools for studying the effects of modified cell glycosylation[4–8]. Additionally, these inhibitors could be potentially useful as anti-cancer drugs. In this paper we report our findings in

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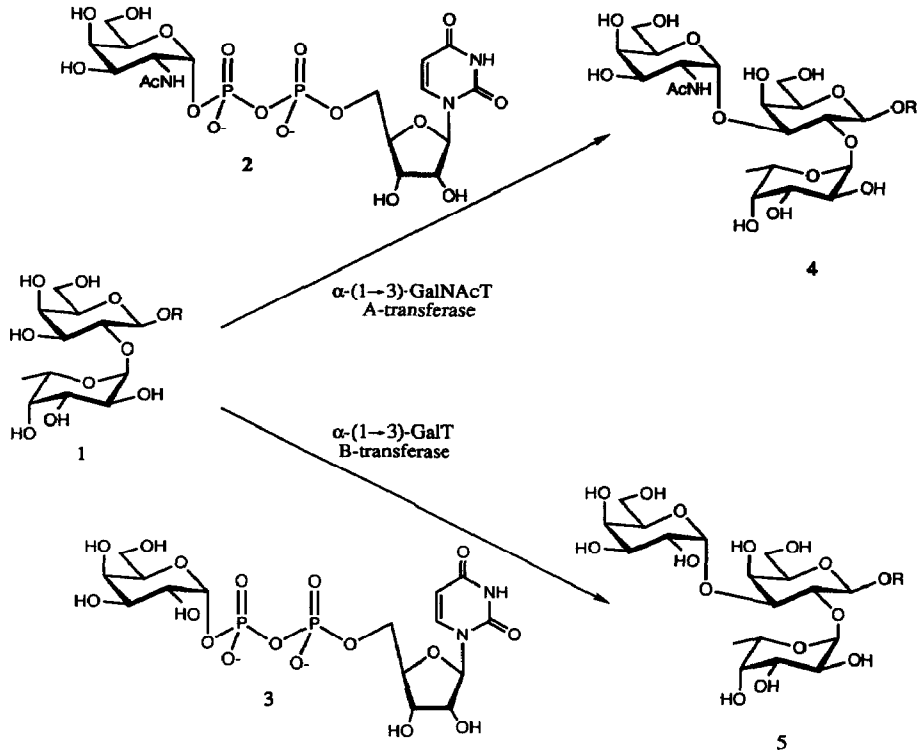


R = carbohydrate residue attached to a glycoprotein or glycolipid

Fig. 1. Biosynthesis of the A and B glood-groups antigens from an O (H) antigen 1.

probing the active site of the glycosyltransferases which are responsible for the biosynthesis of the A and B blood-group antigens.

The trisaccharides α-D-Gal*p*NAc-(1 → 3)[α-L-Fuc*p*-(1 → 2)]-β-D-Gal*p*-OR (**4**) and α-D-Gal*p*-(1 → 3)[α-L-Fuc*p*-(1 → 2)]-β-D-Gal*p*-(1 → 4)-OR (**5**) (where R is a glycoprotein or glycolipid), respectively the A and B blood-group antigens, are ubiquitous biological oligosaccharide structures found not only on the surfaces of red blood cells but also on cells from other tissues and in the cytoplasm[9]. Fig. 1 shows the biosynthetic pathway for these antigens which involves the transfer of either *N*-acetylgalactosamine or galactose from their corresponding UDP derivatives (**2** and **3**) to the galactosyl OH-3 group of the O disaccharide antigen **1**. The enzymes responsible for these transfers are an α-(1 → 3)-*N*-acetylgalactosaminyltransferase (A-transferase, EC 2.4.1.40) and an α-(1 → 3)-galactosyltransferase (B-transferase, EC 2.4.1.37). The widespread occurrence of these carbohydrate antigens as well as the reports that levels of similar α-(1 → 3)-Gal-transferases are elevated in patients with Ehrlich carcinoma[10] and in mouse teratocarcinoma[11] led us to initiate this study. The amino acid sequences of the A- and B-transferases are known to differ at only four residues[12] and they have been recently cloned[12–14].

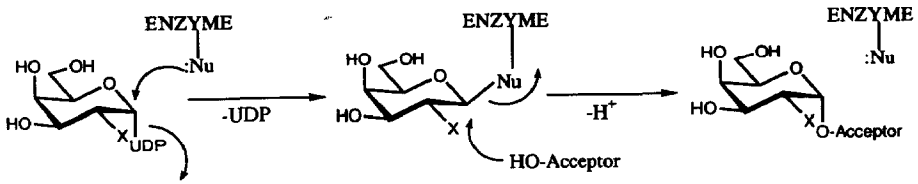


Fig. 2. Hypothetical two-step double-displacement transfer mechanism for the A- and B-transferases: X = OH or NHAc.

While both are morphologically similar to other known glycosyltransferases[15] (a cytoplasmic tail, transmembrane region, and catalytic domain located in the Golgi lumen) they differ from most glycosyltransferases in that they transfer the sugar residue with overall retention of configuration at the anomeric center. The α-sugar nucleotide yields an α-glycosidic linkage.

As a working model (Fig. 2) we hypothesized that the salient features of the transfer involve a two-step double-displacement mechanism. This type of mechanism has been suggested for a number of other enzymes including the glycosidases[16,17]. The first step would be the displacement of UDP from the sugar nucleotide by a nucleophile located in the active site thus forming a covalent glycosyl–enzyme intermediate. Transfer of the sugar residue to the growing oligosaccharide would then be completed by expulsion of the enzyme from the glycosyl–enzyme intermediate by the OH-3 of the acceptor Gal-residue. The hypothesized presence of an essential nucleophile on the enzyme provides a target for possible enzyme deactivation via covalent reaction with an acyl, alkyl, or other group.

The minimum structure recognized by both enzymes is the H disaccharide, α-L-Fuc*p*-(1 → 2)-β-D-Gal*p*-OR[9]. In the present work we chose R to be octyl (**6**) because the presence of this hydrophobic aglycon simplified the enzymatic assays by allowing the use of reverse phase (C_{18}) cartridges to separate and quantitate the product[18]. In order to determine the substrate specificity of these enzymes we synthesized a number of disaccharide analogs of **6** for use as active-site probes. The results of these studies should provide insight into the functional groups present in the active site thus facilitating rational inhibitor design. Below we discuss the preparation and enzymatic evaluation of disaccharides in which the 3, 4, and 6 hydroxyl groups of the galactosyl moiety have been replaced, independently, with hydrogen (**7–9**) and fluorine (**10–12**). Substitutions of hydroxyl groups by either H or F are sterically conservative and can thus provide insights into whether the hydroxyl group removed was involved in critical hydrogen bond interactions with the protein combining site[6,19–21].

RESULTS AND DISCUSSION

Chemical synthesis.—The chemical synthesis of compounds **6–12** followed established synthetic strategy. The general synthetic scheme involved first the synthesis

of a suitably protected galactose residue with OH-2 free, fucosylation under the halide ion conditions developed by Lemieux and co-workers[22], and then deprotection.

Preparation of the unmodified acceptor **6** began with the regioselective benzylation of octyl β-D-galactopyranoside (**13**)[23] with dibutyltin oxide and benzyl bromide to afford **14** in a 60% yield. Benzylidenation of **14** by reaction with zinc chloride and benzaldehyde gave **15** (86%) which was fucosylated using 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide (**16**) to give the protected disaccharide **17** (67%). Hydrogenation of **17** gave **6** (90%).

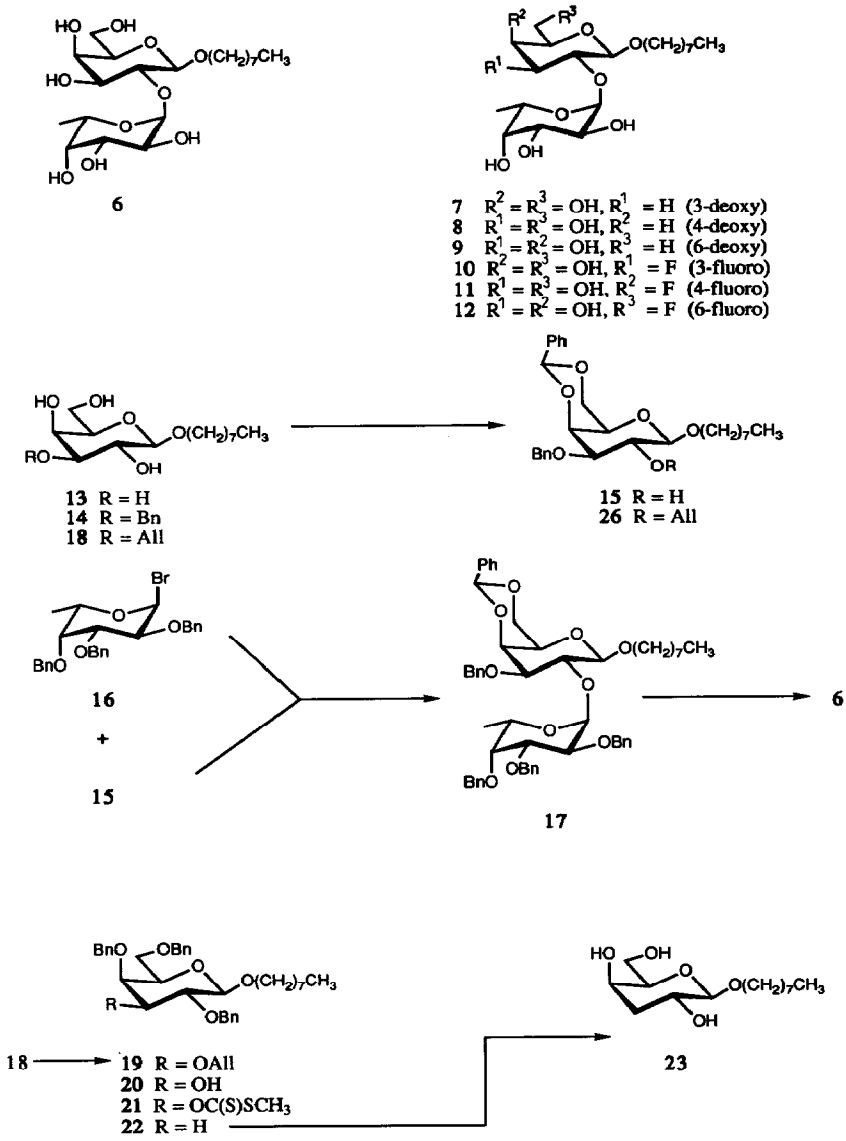
The 3-deoxy analog was prepared by regioselective allylation of **13**, under conditions similar to those for the synthesis of **14**, to give **18** (60%). The remaining hydroxyl groups were protected as benzyl ethers and then the allyl group was removed to provide **20** (70% over two steps). Formation of the xanthate **21** (86%), radical deoxygenation and hydrogenation gave octyl 3-deoxy-β-D-*xylo*-hexopyranoside **23** (62% over the two steps). Benzylidenation of **23** with zinc chloride and benzaldehyde gave **24** (83%) which was converted to **7** by fucosylation and subsequent deprotection (76% from **24**).

The synthesis of the 4-deoxy derivative began with allylation of **15** to give **26** (90%). Regioselective benzylidene ring opening with sodium cyanoborohydride afforded the 4-hydroxy derivative **27** (81%) which was then converted to the xanthate **28** (80%). Radical reduction proceeded in good yield (85%) to give **29**. Deallylation then provided **30** (86%) which was ready for fucosylation. After fucosylation it was not possible to obtain the protected disaccharide in pure form so the partially purified product was debenzylated to produce **8** (39% from **30**) which was purified and characterized.

Benzylidene ring opening of **32** with *N*-bromosuccinimide and subsequent reduction of the 6-bromo derivative **33**, gave the methyl 6-deoxygalactoside **34** in 69% overall yield. Acetylation (96%) followed by treatment of **35** with dichloromethyl methyl ether as described by Glaudemans and Kovac[24] gave chloride **36** (78%) which was glycosylated with octanol, using silver triflate activation, to provide **37** (88%). This fully protected derivative was converted into alcohol **38** (90%) by selective deacetylation with methanolic hydrogen chloride. Fucosylation and then deprotection afforded the 6-deoxy derivative **9** (65% 3 steps).

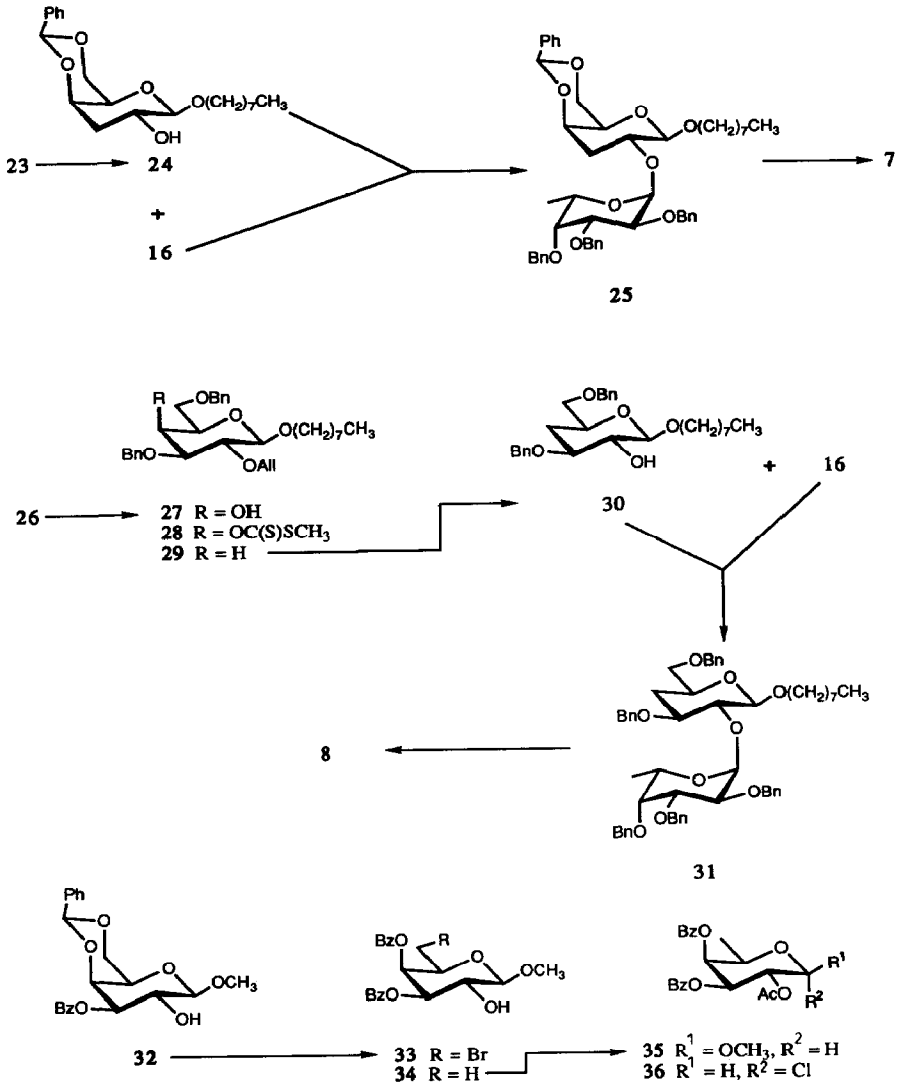
Reaction of peracetate **40** with hydrogen bromide in acetic acid gave bromide **41** (80%) which was reacted with octanol and silver triflate to give glycoside **42** (62%). Zemplén deacetylation produced **43** which was then converted to benzylidene acetal **44** (90% over two steps). The synthesis of the 3-fluoro derivative **10** was completed by fucosylation of **44** (89%) followed by hydrogenation (82%).

The synthesis of the 4-fluoro derivative began with octyl β-D-glucopyranoside which was converted to the fully protected derivative **47** in two steps in 76% yield. Benzylidene ring opening as described for the conversion of **26** to **27**, gave the 4-hydroxy derivative **48** (88%). Alcohol **48** was fluorinated, via its 4-triflate, by



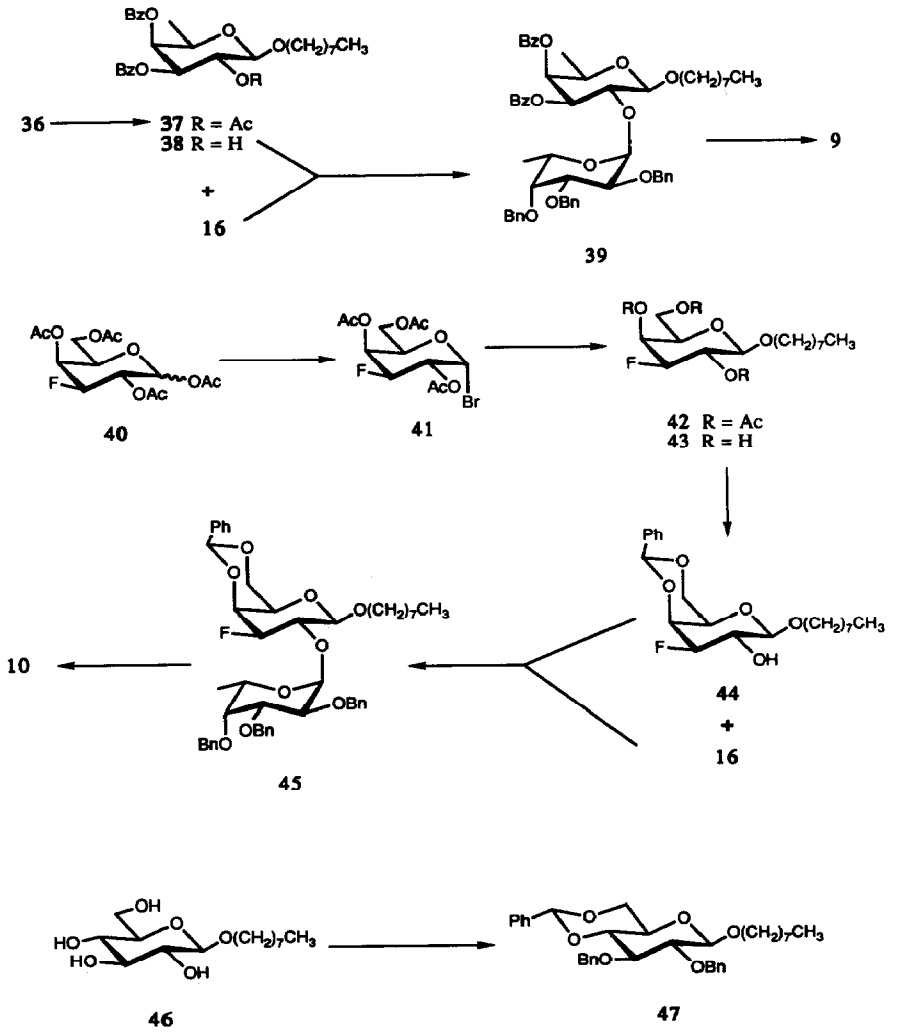
reaction with tetrabutylammonium fluoride (80%). The fluoro galactoside **49** was converted to **50** by hydrogenation (85%) and then protected as the dibenzoate **52** using dibutyltin oxide and benzoyl chloride (37%). A significant amount (50%) of the monobenzoate **51** was also present, but this could be easily converted to **52** by treatment with benzoyl chloride and pyridine (76%). To complete the synthesis, alcohol **52** was fucosylated and deprotected to afford **11** (74%, over two steps).

Bromide **56** was prepared by treatment of 6-deoxy-6-fluoro-1,2:3,4 di-*O*-isopropylidene-α-D-galactopyranose, **54**, first with 90% trifluoroacetic acid, then acetic

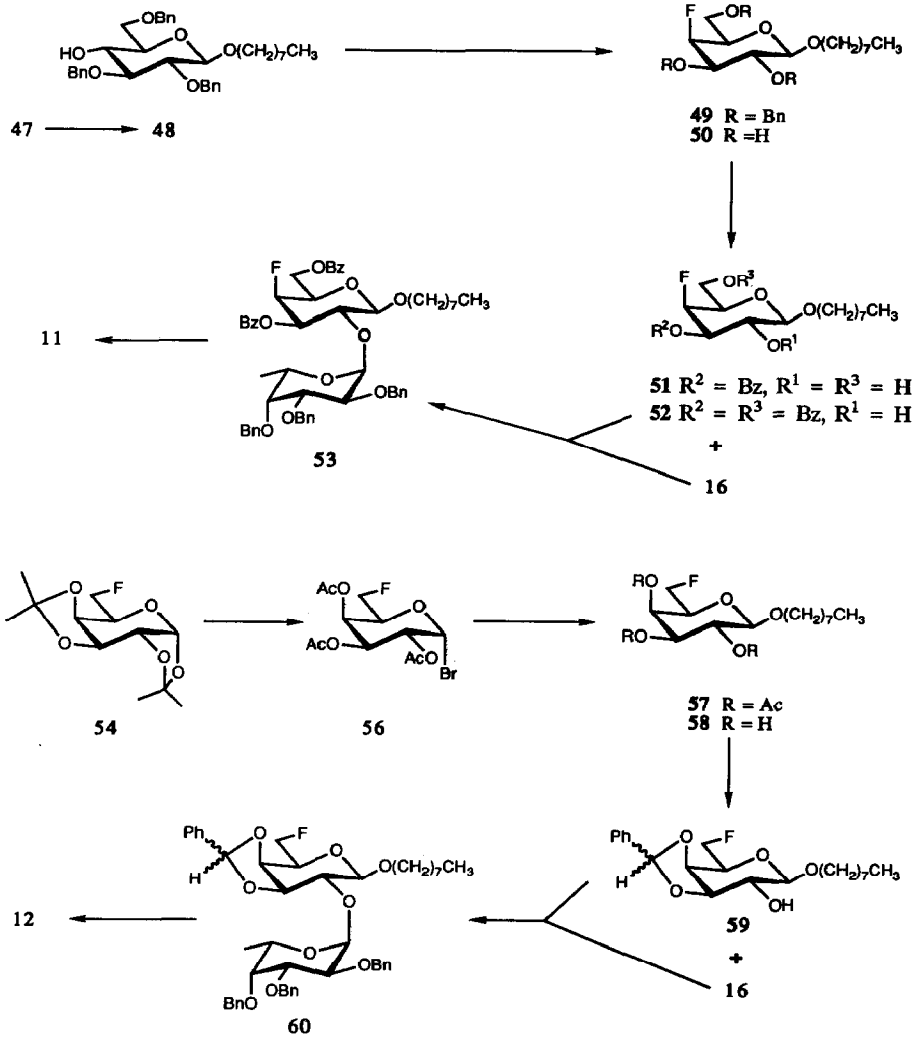


anhydride and pyridine, and finally hydrogen bromide in acetic acid (three steps, 67%). Glycosylation (73%) and then Zemplén deacetylation (90%) gave **58**. The 3,4-diol was protected as a benzylidene acetal by treatment with dimethoxytoluene and *p*-toluenesulfonic acid to give **59** as a mixture of easily separable diastereomers (85%). Fucosylation of **59** (90%) and deprotection gave the 6-fluoro analog **12** (90%).

Enzymatic testing.—The activity of the synthetic disaccharide derivatives described here were determined by a radioactive assay technique which quantitated the rate of transfer of either ^{3}H-labeled Gal or GalNAc, from the corresponding



commercial sugar nucleotides, to hydrophobic octyl acceptors as previously described[18]. Preliminary screening (Table I) of compounds **7–12** as potential acceptors for the GalNAc and Gal transferases in human serum showed that only the disaccharides with an intact 3,4-diol were recognized as substrates. In all cases the relative rates were less than those obtained for the native H disaccharide, **6**. While the 3 modified derivatives are unable to react because of the lack of the galactosyl 3-hydroxyl group, the lack of activity of the 4 modified derivatives demonstrated that this hydroxyl group is crucial for recognition by these enzymes. Calculation of kinetic constants (Table II) for the 6-deoxy and 6-fluoro compounds showed that the V_{max} does not change significantly with the B-transferase, and only slightly so



for the A-transferase. However, the K_m of these compounds with both enzymes are significantly higher than for the corresponding natural sequence **6**.

Results of the evaluation of disaccharides modified at the 3 and 4 positions as potential inhibitors are presented in Table III. The 4-fluoro and 4-deoxy derivatives were, as before, inactive demonstrating that the galactosyl 4-hydroxyl group is crucial for binding to the enzyme. Table IV shows the calculated constants for competitive inhibitors **7** and **10**, the 3-deoxy and 3-fluoro analogs, which were in the range of 14–110 μM. A comparison of these values with the K_m of **6** provides a useful qualitative insight into what groups the enzymes require. A quantitative comparison is not meaningful for enzymes such as these which likely proceed though a two-step mechanism since K_m values need not represent true dissocia-

TABLE I

Relative acceptor activity of disaccharides **6–12** towards the blood group A (GalNAc)- and B (Gal)-transferases in human serum [a]

Substrate	A-Transferase		B-Transferase	
	DPM	Activity (%)	DPM	Activity (%)
Native disaccharide (**6**)	3236	100	3467	100
3-Deoxy (**7**)	43	0	69	0
4-Deoxy (**8**)	47	0.1	85	0.2
6-Deoxy (**9**)	1161	35	835	22
3-Fluoro (**10**)	45	0.3	81	0.1
4-Fluoro (**11**)	39	0	66	0
6-Fluoro (**12**)	1404	43	1084	30
No acceptor	43		78	

[a] Compounds **6–12** were present at a concentration of 2.5 μM for the A-transferase and 10 μM for the B-transferase. Experiments were performed in at least duplicate with variation in replicates of less than 10%.

TABLE II

Calculated kinetic constants [a] for acceptors **6**, **9**, and **12** with the blood group A (GalNAc)- and B (Gal)-transferases in human serum

Substrate	A-Transferase		B-Transferase	
	K_m (μM)	V_{max} (pmol/min)	K_m (μM)	V_{max} (pmol/min)
Natural (**6**)	1.50 ± 0.2	0.61 ± 0.02	21.9 ± 3.4	0.32 ± 0.02
6-Deoxy (**9**)	7.29 ± 1.2	0.98 ± 0.07	68.8 ± 7.5	0.29 ± 0.02
6-Fluoro (**12**)	4.96 ± 0.8	0.45 ± 0.04	55.6 ± 9.5	0.31 ± 0.02

[a] At saturating UDP-GalNAc and UDP-Gal concentrations.

TABLE III

Relative inhibitor ability of disaccharides **7**, **8**, **10**, and **11** towards the blood group A (GalNAc)- and B (Gal)-transferases in human serum

Substrate	Inhibition (%)	
	A-Transferase [a]	B-Transferase [b]
3-Deoxy (**7**)	30%	85%
4-Deoxy (**8**)	2%	0%
3-Fluoro (**10**)	22%	24%
4-Fluoro (**11**)	0%	0%

[a] Concentration of potential inhibitor was 25 μM with acceptor **6** at 2.5 μM. [b] Concentration of potential inhibitor was 100 μM with acceptor **6** at 10 μM.

TABLE IV

Calculated inhibition constants (K_i) [a] of disaccharides **7** and **10** with the blood group A- and B-glycosyltransferases in human serum

Inhibitor	A-Transferase	B-Transferase	Mode of inhibition [b]
3-Deoxy (**7**)	68 ± 9	14 ± 1.5	competitive
3-Fluoro (**10**)	48 ± 9	110 ± 16	competitive

[a] K_i in μM. [b] Both **7** and **10** are competitive inhibitors of both glycosyltransferases.

tion constants. Both **7** and **10** are poor inhibitors for the A-transferase with K_i values an order of magnitude higher than the K_m. Also the 3-fluoro compound (**10**) is a weak inhibitor of the B-transferase. The 3-deoxy compound (**7**) however, appears to be better recognized by the B-transferase, with a K_i below that of the K_m.

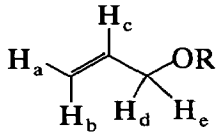
It appears, therefore, that both the A- and the B-transferases will tolerate modifications at the galactosyl 3- and 6-hydroxyl groups without loss of recognition. However, the 4-hydroxyl group is crucial for binding suggesting that it is, according to the terminology of Lemieux[25], a key polar group in the recognition by these enzymes. As well, these results suggest the possibility of a bidentate hydrogen bond between the galactosyl 3,4-diol and an enzymatic carboxylate or amide, as described for other galactose-recognizing proteins[26,27], is not present, or is at least not of critical importance, for recognition by these enzymes. Further studies of these active sites with disaccharides similarly systematically modified by *O*-methylation and amino functionalities is in progress.

EXPERIMENTAL

General methods.—Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 22 ± 2°C. Analytical TLC was performed on Silica Gel 60-F_{254} (E. Merck, Darmstadt) with detection by quenching of fluorescence and/or by charring with H_2SO_4. All commercial reagents were used as supplied and chromatography solvents were distilled prior to use. Column chromatography was performed on Silica Gel 60 (E. Merck 40–60 μm, Darmstadt). Millex-GV (0.22 μm) filter units were from Millipore (Missisauga, ON), C_{18} Sep-Pak sample preparation cartridges were from Waters Associates (Missisauga, ON), and Ecolite scintillation cocktail was from ICN Radiochemicals (St. Laurent, PQ). UDP-[6-^{3}H]-Gal (specific activity 15 Ci/mmol) and UDP-[6-^{3}H]-GalNAc (specific activity 10 Ci/mmol) were from American Radiolabelled Chemicals (St. Louis, MO). UDP-Gal, UDP-GalNAc, and ATP were from Sigma (St. Louis, MO). ^{1}H NMR were recorded at 360 MHz (Bruker WM-360) or 300 MHz (Bruker AM-300) with either internal $(CH_3)_4Si$ (δ 0, $CDCl_3$, CD_3OD) or DOH (δ 4.80, D_2O). ^{13}C NMR were recorded at 75.5 MHz (Bruker AM-300) with internal $(CH_3)_4Si$ (δ 0, $CDCl_3$, CD_3OD) or external 1,4-dioxane (δ 67.4, D_2O). ^{19}F NMR were recorded at 188.3 MHz (Bruker WH-200) or 376.5 MHz (Bruker WH-400) with external $CFCl_3$ (δ 0, $CDCl_3$, CD_3OD, D_2O). ^{1}H data are reported as though they were first order. All ^{13}C shifts assignments are tentative and were assigned based on comparison with published spectra[28–31]. Unless otherwise stated, all reactions were carried out at room temperature and in the processing of mixtures, solutions of organic solvents were washed with equal amounts of aqueous solutions. Organic solutions were dried (Na_2SO_4) prior to concentration under vacuum at < 40°C (bath). Microanalyses were carried out by the analytical services at this department and all samples submitted for elemental analyses were dried overnight under vacuum with P_2O_5 at

56°C (refluxing Me_2CO). Mass spectra were recorded on samples suspended in a matrix of glycerol and HCl using a Kratos AEIMS9 instrument with Xe as the bombarding gas.

Protons of the allyl group present in the compounds described in paper were designated H_a, H_b, H_c, H_d, and H_e as defined below. These protons showed the same coupling constants and thus the same multiplicity pattern in all the compounds examined, only the chemical shifts varied. The observed couplings were as follows: H_a, (dddd, $J_{a,c}$ 10.5, $J_{a,d} = J_{a,e} = J_{a,b} = 1.5 \pm 0.5$ Hz); H_b, (dddd, $J_{b,c}$ 17.0, $J_{b,d} = J_{b,e} = J_{a,b} = 1.5 \pm 0.5$ Hz); H_c, (dddd, $J_{b,c}$ 17.0, $J_{a,c}$ 10.5, $J_{c,d} = J_{c,e} = 5.5$ Hz); H_d, (dddd, $J_{d,e}$ 13.5, $J_{c,d}$ 5.5, $J_{b,d} = J_{a,d} = 1.5 \pm 0.5$ Hz); H_e, (dddd, $J_{d,e}$ 13.5, $J_{c,e}$ 5.5, $J_{a,c} = J_{b,c} = 1.5 \pm 0.5$ Hz).



Octyl 3-O-benzyl-β-D-galactopyranoside (**14**).—Octyl β-D-galactopyranoside[23] (**13**; 10.02 g, 34.32 mmol) and dibutyltin oxide (8.51 g, 34.20 mmol) were refluxed in benzene (250 mL) for 21 h. Water was removed by passing the refluxing solvent through a column of 4A molecular seives. To this solution was added Bu_4NI (12.87 g, 34.88 mmol) and $PhCH_2Br$ (8.2 mL, 69 mmol), and refluxing continued for an additional 21 h. The solution was evaporated to give a brown oil which was dissolved in CH_2Cl_2 and extracted with a saturated solution of $Na_2S_2O_3$. After evaporation, column chromatography of the resulting oil (1:1 CH_2Cl_2–EtOAc) gave **14** (7.8 g, 60%) as a white solid; $[\alpha]_D$ −3.1° (*c* 1.4, $CHCl_3$); R_f 0.46 (1:1 CH_2Cl_2–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.45 (m, 5 H, Ph), 4.74 (s, 2 H, $PhCH_2$), 4.23 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 3.74–4.04 (m, 5 H, H-2, H-4, H-6a, H-6b, OCH_2CH_2), 3.39–3.56 (m, 3 H, OCH_2CH_2, H-5, H-3), 2.77 (d, 1 H, $J_{4,4\text{-OH}}$ 1 Hz, 4-OH), 2.56 (d, 1 H, $J_{2,2\text{-OH}}$ 2.5 Hz, 2-OH), 2.44 (dd, 1 H, $J_{6a,6\text{-OH}}$ 8.5 Hz, $J_{6b,6\text{-OH}}$ 4 Hz), 1.62 (m, 2 H, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ137.72 (Ph quat.), 128.65, 128.13, 127.94 (Ph methine), 103.12 (C-1), 80.16 (C-3), 74.35 (C-5), 72.23 ($PhCH_2$), 71.17 (C-2), 70.19 (OCH_2CH_2), 67.22 (C-4), 62.50 (C-6), 31.85, 29.65, 29.41, 29.25, 25.99, 22.67 (octyl CH_2), 14.11 (octyl CH_3). Anal. Calcd for $C_{21}H_{34}O_6$ (382.50): C, 65.97; H, 8.90. Found: C, 65.69; H, 8.98.

Octyl 3-O-benzyl-4,6-O-benzylidene-β-D-galactopyranoside (**15**).—Galactoside **14** (6.56 g, 17.2 mmol) was dissolved in PhCHO (50 mL) and $ZnCl_2$ (3.79 g, 27.8 mmol) was added. After stirring for 5 h the solution was cooled to 0°C and water (125 mL) was added. Stirring continued for 1 h and then the mixture was diluted with CH_2Cl_2 and extracted with $NaHCO_3$, water, and brine. The organic layer was dried and evaporated under reduced pressure to remove the PhCHO. Column chromatography of the resulting clear oil (3:1 hexane–EtOAc) gave **15** (6.9 g, 86%) as a white solid; $[\alpha]_D$ +32.8° (*c* 1.4, $CHCl_3$); R_f 0.14 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.60 (m, 10 H, Ph), 5.46 (s, 1 H, $PhCHO_2$), 4.76 (s, 2 H,

PhCH_2), 4.30 (dd, 1 H, $J_{6a,6b}$ 12.5, $J_{5,6a}$ 1.5 Hz, H-6a), 4.28 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.12 (dd, 1 H, $J_{3,4}$ 3, $J_{4,5}$ 1 Hz, H-4), 4.02 (dd, 1 H, $J_{6a,6b}$ 12.5, $J_{5,6b}$ 1.5 Hz, H-6b), 3.94 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.44–3.54 (m, 2 H, H-3, OCH_2CH$_2$), 3.34 (br s, 1 H, H-5), 2.43 (br s, 1 H, 2-OH), 1.55–1.70 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (10 H, octyl CH$_2$), 0.88 (t, 3 H J_{vic} 7 Hz, octyl CH$_3$); ^{13}C NMR (CDCl$_3$): δ 138.24, 137.66 (Ph quat.), 128.89, 128.45, 128.10, 127.65 (Ph methine), 102.99 (C-1), 101.15 (PhCHO$_2$), 79.21 (C-3), 73.33 (C-4), 71.54 (PhCH_2), 70.14 (C-2), 69.85 (OCH_2CH$_2$), 69.34 (C-6), 66.73 (C-5), 31.83, 29.55, 29.42, 29.24, 25.99, 22.67 (octyl CH$_2$), 14.11 (octyl CH$_3$). Anal. Calcd for $C_{28}H_{38}O_6$ (470.61): C, 71.46; H, 8.14. Found: C, 71.17; H, 8.00.

Octyl 3-O-benzyl-4,6-O-benzylidene-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (**17**).—Alcohol **15** (50 mg, 0.11 mmol) and Et$_4$NBr (25 mg, 0.12 mmol) were dissolved in CH$_2$Cl$_2$ (4 mL) and DMF (0.5 mL) containing crushed 4A molecular sieves (3 g). The system was purged with Ar and stirred overnight. To this slurry was added freshly prepared 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide[32] (**16**, 0.44 mmol) in CH$_2$Cl$_2$ (3 mL) and the mixture stirred for 2 days under Ar. Methanol (1 mL) was added and stirring continued for 30 min and then the mixture was filtered and taken to dryness. Chromatography of the residue (3:2 hexane–EtOAc) gave the product **17** (63 mg, 67%) as a white solid; $[\alpha]_D$ −50.5° (*c* 0.6, CHCl$_3$); R_f 0.32 (3:2 hexane–EtOAc). ^{1}H NMR (CDCl$_3$): δ 7.17–7.60 (m, 25 H, Ph), 5.64 (d, 1 H, $J_{1',2'}$ 3.5 Hz, H-1'), 5.40 (s, 1 H, PhCHO$_2$), 4.95, 4.86, 4.70, 4.65, 4.58, 4.54, 4.52 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2) 4.45 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.44 (q, 1 H, $J_{5',6'}$ 6.5 Hz, H-5'), 4.29 (dd, 1 H, $J_{6a,6b}$ 12, $J_{5,6a}$ 1 Hz, H-6a), 4.18 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 9.5 Hz, H-2) 4.14 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 3.86–4.06 (m, 4 H, OCH_2CH$_2$, H-2', H-3', H-6b), 3.81 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 3.5 Hz, H-3), 3.64 (br d, 1 H, $J_{3'4'}$ 1.5 Hz, H-4'), 3.39 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.32 (br s, 1 H, H-5'), 1.45–1.60 (m, 2 H, OCH$_2$CH_2), 1.20–1.35 (10 H, octyl CH$_2$), 1.13 (d, 3 H, $J_{5',6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH$_3$); ^{13}C NMR (CDCl$_3$): δ 139.08, 138.88, 138.54, 138.35, 137.78 (Ph quat.), 128.75, 128.27, 128.17, 128.09, 127.77, 127.46, 127.32, 127.29, 127.08, 126.28 (Ph methine), 101.82 (C-1), 100.87 (PhCHO$_2$), 97.01 (C-1'), 81.71 (C-3), 79.55 (C-2), 78.20 (C-4'), 75.99 (C-4), 74.72, 73.05 (PhCH_2), 72.80 (C-3'), 72.47 (PhCH_2), 71.57 (C-2'), 70.59 (OCH_2CH$_2$), 69.42 (C-5'), 69.35 (C-5), 66.39 (PhCH_2), 66.18 (C-6), 31.86, 29.69, 29.33, 26.29, 22.65 (octyl CH$_2$), 16.59 (C-6'), 14.10 (octyl CH$_3$). Anal. Calcd for $C_{55}H_{66}O_{10}$ (887.13): C, 74.47; H, 7.50. Found: C, 74.45; H, 7.60.

Octyl 2-O-(α-L-fucopyranosyl)-β-D-galactopyranoside (**6**).—The protected disaccharide **17** (105 mg, 0.12 mmol) was dissolved in MeOH (10 mL), 5% Pd–C (50 mg) added and the solution stirred under a flow of H_2 overnight. After completion of the reaction, the catalyst was filtered off and the solvent evaporated. The product was purified by redissolution in water and then passing the solution through a Waters C_{18} Sep-Pak cartridge. The cartridge was washed with water and then the product eluted with MeOH. The MeOH eluant was evaporated, the residue redissolved in water, filtered through a 0.22-μm filter, and lyophilized to

give the product **6** (47 mg, 90%) as a white solid. ^{1}H NMR (CD_3OD): 5.10 δ (br s, 1 H, H-1′), 4.21 (m, 2 H, H-1, H-5′), 3.82 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.75 (d, 1 H, $J_{3,4}$ 3 Hz, H-4), 3.50–3.73 (m, 7 H, H-2, H-3, H-6a, H-6b, H-2′, H-3′, H-4′), 3.31–3.50 (m, 2 H, H-5, OCH_2CH_2), 1.52–1.68 (m, 2 H, OCH_2CH_2), 1.22–1.43 (10 H, octyl CH_2), 1.18 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6′), 0.88 (t, 3 H J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ 103.56 (C-1), 101.57 (C-1′), 79.07 (C-2), 76.48 (C-5), 75.74 (C-3), 73.74 (C-3′), 72.56 (C-4′), 71.76 (C-3), 70.78 (OCH_2CH_2), 70.62 (C-2′), 70.38 (C-4), 67.78 (C-5′), 62.38 (C-6), 32.98, 30.98, 30.60, 30.39, 27.29, 23.68 (octyl CH_2), 16.78 (C-6′), 14.41 (octyl CH_3). FABMS: m/z 461 $[M + Na]^+$ and 439 $[M + H]^+$ ($C_{20}H_{38}O_{10}$ requires m/z 438).

Octyl 3-O-allyl-β-D-galactopyranoside (**18**).—Octyl β-D-galactopyranoside[23] (**13**; 6.54 g, 22.39 mmol) and dibutyltin oxide (5.53 g, 22.21 mmol) were refluxed in benzene (250 mL) for 24 h as described for **14**. The solution was cooled to 60°C and then Bu_4NI (8.28 g, 22.43 mmol) and allyl bromide (20 mL, 229 mmol) were added, and heating at 60°C continued for an additional 20 h. The solution was cooled, washed with a saturated solution of $Na_2S_2O_3$, and evaporated. After evaporation, column chromatography of the resulting oil (1:1 CH_2Cl_2–EtOAc) gave **18** (4.51 g, 60%) as a white solid; $[\alpha]_D$ −5.1° (*c* 0.6, $CHCl_3$); R_f 0.26 (1:1 CH_2Cl_2–EtOAc) ^{1}H NMR ($CDCl_3$): δ 5.96 (1 H, H_c allyl), 5.33 (1 H, H_b allyl), 5.23 (1 H, H_a allyl), 4.26 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.21 (m, 2 H, H_d allyl, H_e allyl), 4.04 (ddd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 2, $J_{4,4\text{-OH}}$ 1 Hz, H-4), 3.78–4.01 (m, 3 H, OCH_2CH_2, H-6a, H-6b), 3.73 (ddd, 1 H, $J_{4,5}$ 2, $J_{5,6a}$ 10, $J_{5,6b}$ 9 Hz, H-5), 3.46–3.58 (2 H, H-2, OCH_2CH_2) 3.39 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 3.5 Hz, H-3), 2.46 (d, 1 H, $J_{4,4\text{-OH}}$ 1 Hz, 4-OH), 2.25 (d, 1 H, $J_{2,2\text{-OH}}$ 2.5 Hz, 2-OH), 2.05 (dd, 1 H, $J_{6a,6\text{-OH}}$ 8.5, $J_{6b,6\text{-OH}}$ 4 Hz), 1.57–1.72 (m, 2 H, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 134.79 (CH_2=$CHCH_2O$), 118.02 (CH_2=$CHCH_2O$), 103.12 (C-1), 80.04 (C-3), 74.34 (C-5), 71.08 (CH_2=$CHCH_2O$), 70.91 (C-2), 70.20 (OCH_2CH_2), 66.98 (C-4), 62.44 (C-6), 31.83, 29.63, 29.40, 29.24, 25.97, 22.66 (octyl CH_2), 14.10 (octyl CH_3). Anal. Calcd for $C_{17}H_{32}O_6$ (332.44): C, 61.42; H, 9.70. Found: C, 61.33; H, 9.45.

Octyl 3-O-allyl-2,4,6-tri-O-benzyl-β-D-galactopyranoside (**19**).—Allyl ether **18** (4.41 g, 13.29 mmol) was dissolved in dry DMF (100 mL). Sodium hydride (4.06 g, 80% dispersion in oil, 135.4 mmol) was added and the mixture stirred for 30 min. Benzyl bromide (15 mL, 120 mmol) was added and stirring continued for 15 h. The solution was then cooled to 0°C, water added, and then diluted with CH_2Cl_2 and extracted with $NaHCO_3$ water, and brine. Evaporation of the organic layer gave a brown liquid which was chromatographed (12:1 hexane–EtOAc) to give **19** (5.73 g, 71%) as a colorless oil; $[\alpha]_D$ −3.0° (*c* 1.1, $CHCl_3$); R_f 0.25 (12:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.2–7.4 (m, 15 H, Ph), 5.93 (1 H, H_c allyl), 5.32 (1 H, H_b allyl), 5.17 (1 H, H_a allyl), 4.93, 4.89, 4.74, 4.61, 4.45, 4.39 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.32 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.19 (m, 2 H, H_d allyl, H_e allyl), 3.91 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.85 (dd, 1 H, $J_{3,4}$ 3, $J_{4,5}$ 1 Hz, H-4), 3.74 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 10 Hz, H-2) 3.44–3.62 (m, 4 H, H-5, H-6a, H-6b, OCH_2CH_2), 3.40

(dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3 Hz, H-3), 1.55–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR: δ138.93, 138.75, 138.01 (Ph quat.), 135.06 (CH_2=$CHCH_2O$), 128.56, 128.38, 128.32, 128.20, 128.10, 127.10, 127.86, 127.72, 127.46 (Ph methine), 116.50 (CH_2=$CHCH_2O$), 103.96 (C-1), 81.99 (C-3), 79.54 (C-2), 75.13, 74.39, 73.54 (Ph CH_2), 73.47 (C-5), 73.38 (C-4), 71.92 (CH_2=$CHCH_2O$), 70.02 (OCH_2CH_2), 68.96 (C-6), 31.82, 29.74, 29.43, 29.25, 26.16, 22.65 (octyl CH_2), 14.09 (octyl CH_3). Anal. Calcd for $C_{38}H_{50}O_6$ (602.82): C, 75.72; H, 8.36. Found: C, 75.46; H, 8.33.

*Octyl 2,4,6-tri-*O*-benzyl-β-*D*-galactopyranoside* (**20**).—To a solution of **19** (5.73 g, 9.520 mmol) dissolved in 7:3:1 EtOH–benzene–water (125 mL), tris(triphenylphosphine)rhodium(I) chloride (1.26 g, 1.36 mmol) and 1,4 diazabicyclo[2.2.2]octane (460 mg, 4.10 mmol) were added, and the solution refluxed for 20 h. The solvent was evaporated and the residue dissolved in 9:1 Me_2CO–water (50 mL). Mercuric oxide (50 mg) and $HgCl_2$ (12 g) were added and stirring continued overnight. The mixture was then diluted with CH_2Cl_2 and washed with satd KI, water, and brine. Evaporation of the organic layer followed by chromatography (6:1 hexane–EtOAc) gave **20** (4.54 g, 85%) as a colorless oil; $[\alpha]_D$ +5.7° (*c* 1, $CHCl_3$); R_f 0.20 (6:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.2–7.4 (m, 15 H, Ph), 4.97, 4.78, 4.67, 4.62, 4.50, 4.43 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.33 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.93 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.85 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 3.59–3.70 (m, 4 H, H-3, H-5, H-6a, H-6b), 3.55 (dd, 1 H, $J_{1,2}$ 7.5 Hz, $J_{2,3}$ 10 Hz, H-2), 3.48 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.40 (d, 1 H, $J_{3,3\text{-OH}}$ 4.5 Hz, 3-OH), 1.58–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.59, 138.02 (Ph quat.), 128.51, 128.46, 128.34, 128.22, 128.18, 127.83, 127.70 (Ph methine), 103.84 (C-1), 79.68 (C-2), 75.62 (C-5), 75.02, 74.66 (PhCH_2), 74.16 (C-4), 73.64 (C-3), 73.58 (PhCH_2), 70.07 (OCH_2CH_2), 68.87 (C-6), 31.87, 29.77, 29.46, 29.30, 26.22, 22.70 (octyl CH_2), 14.13 (octyl CH_3). Anal. Calcd for $C_{35}H_{46}O_6$ (562.75): C, 74.70; H, 8.24. Found: C, 74.55; H, 7.93.

*Octyl 2,4,6-tri-*O*-benzyl-3-*O*-[(methylthio)thiocarbonyl]-β-*D*-galactopyranoside* (**21**).—To a solution of **20** (1.01 g, 1.80 mmol) in dry THF (15 mL) was added NaH (162 mg, 80% in oil, 5.4 mmol) and imidazole (32 mg). After stirring for 1 h, CS_2 (1.1 mL, 18.1 mmol) was added, and then 1 h later, MeI (340 μL, 5.5 mmmol) was added, and stirring continued overnight. Evaporation of the solvent gave a yellow liquid which was chromatographed (6:1 hexane–EtOAc) to give **21** (1.0 g, 86%) as a yellow oil; $[\alpha]_D$ +51.9° (*c* 0.9, $CHCl_3$); R_f 0.55 (12:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ7.15–7.45 (m, 15 H, Ph), 5.75 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3 Hz, H-3), 4.85, 4.69, 4.65 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.36–4.5 (m, 3 H, 3 PhCH_2, H-1), 4.18 (br d, 1 H, $J_{3,4}$ 3 Hz, H-4), 3.89–3.99 (m, 2 H, H-2, OCH_2CH_2), 3.68 (br t, 1 H, $J_{5,6a} = J_{5,6b} = 6.5$ Hz, H-5), 3.45–3.63 (m, 3 H, H-6a, H-6b, OCH_2CH_2), 2.54 (s, 3 H, SCH_3) 1.58–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 215.66 (C=S), 138.38, 137.97, 137.91 (Ph quat.), 128.46, 128.37, 128.29, 128.27, 128.09, 127.86, 127.80, 127.75, 127.60 (Ph

methine), 103.76 (C-1), 84.00 (C-3), 76.90 (C-2), 74.87, 74.79, 73.57 (PhCH_2), 73.36 (C-5), 72.90 (C-4), 70.28 (OCH_2CH_2), 68.52 (C-6), 31.86, 29.73, 29.45, 29.30, 26.17, 22.70 (octyl CH_2), 19.16 (SCH_3), 14.13 (octyl CH_3). Anal. Calcd for $C_{37}H_{48}O_6S_2$ (652.91): C, 68.07; H, 7.41; S, 9.82. Found: C, 68.06; H, 7.20; S, 9.76.

*Octyl 2,4,6-tri-O-benzyl-3-deoxy-β-*D*-xylo-hexopyranoside* (**22**).—Compound **21** (717 mg, 1.10 mmol) was dissolved in dry toluene (100 mL) and then tributylstannane (1.5 mL, 5.58 mmol) and AIBN (135 mg, 0.82 mmol) were added. The solution was heated under reflux for 60 min. Evaporation of the solvent followed by chromatography (12:1 hexane–EtOAc) gave **22** (403 mg, 67%) as a colorless oil; $[\alpha]_D$ −26.1° (*c* 0.4, $CHCl_3$); R_f 0.32 (12:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.2–7.4 (m, 15 H, Ph), 4.86, 4.61, 4.56, 4.55, 4.46 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.38 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.36 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 3.95 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.54–3.72 (m, 5 H, H-2, H-4, H-5, H-6a, H-6b), 3.49 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 2.36 (ddd, 1 H, $J_{3a,3e}$ 14.5, $J_{2,3e}$ 5, $J_{3e,4}$ 3 Hz, H-3e), 1.58–1.70 (m, 2 H, OCH_2CH_2), 1.46, (ddd, 1 H, $J_{3a,3e}$ 14.5, $J_{2,3a}$ 2.4, $J_{3a,4}$ 11.5 Hz, H-3a) 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.91, 138.33, 138.25 (Ph quat.), 128.37, 128.30, 128.26, 127.90, 127.87, 127.72, 127.63, 127.58, 127.50 (Ph methine), 105.46 (C-1), 76.48 (C-2), 73.55, 73.21 (PhCH_2), 73.10 (C-5), 72.47 (C-4), 71.11 (PhCH_2), 69.45 (OCH_2CH_2), 69.34 (C-6), 32.83 (C-3), 31.85, 29.78, 29.45, 29.29, 26.21, 22.68 (octyl CH_2), 14.11 (octyl CH_3). Anal. Calcd for $C_{35}H_{46}O_5$ (546.75): C, 76.89; H, 8.48. Found: C, 76.96; H, 8.81.

*Octyl 3-deoxy-β-*D*-xylo-hexopyranoside* (**23**).—Compound **22** (512 mg, 0.94 mmol), was dissolved in MeOH (15 mL) and 5% Pd–C (250 mg) added. The mixture was allowed to stir overnight under a flow of H_2. The catalyst was filtered off, the solvent evaporated, and the residue chromatographed (19:1 CH_2Cl_2–MeOH) to give **23** (237 mg, 92%) as a white solid; $[\alpha]_D$ −55.9° (*c* 0.6, MeOH); R_f 0.30 (19:1 CH_2Cl_2–MeOH). ^{1}H NMR ($CDCl_3$): δ 4.25 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.03 (m, 1 H, H-4), 3.93 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.75–3.90 (m, 3 H, H-2, H-6a, H-6b), 3.46–3.58 (m 2 H, H-5, OCH_2CH_2), 2.29 (ddd, 1 H, J_{gem} 14.5, $J_{2,3e}$ 5.5, $J_{3e,4}$ 3.5 Hz, H-3e), 1.55–1.77 (m, 3 H, H-3a, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 105.75 (C-1), 77.11 (C-2), 70.05 (OCH_2CH_2), 67.88 (C-5), 66.02 (C-4), 63.34 (C-6), 37.14 (C-3), 31.83, 29.68, 29.42, 29.26, 26.01, 22.67 (octyl CH_2), 14.10 (octyl CH_3). Anal. Calcd for $C_{14}H_{28}O_5$ (276.38): C, 60.84; H,10.21. Found: C, 60.74; H, 10.42.

*Octyl 4,6-O-benzylidene-3-deoxy-β-*D*-xylo-hexopyranoside* (**24**).—Galactoside **23** (100 mg, 0.37 mmol) was dissolved in PhCHO (1 mL) and CH_2Cl_2 (2 mL), and $ZnCl_2$ (75 mg, 0.55 mmol) added. After stirring for 3 h the solution was cooled to 0°C and water (2 mL) was added. Stirring was continued for 1 h and then the mixture was diluted with CH_2Cl_2, and extracted with 2 M NaOH (to remove traces of benzoic acid), water, and brine. The organic layer was dried with Na_2SO_4 and evaporated under reduced pressure to remove the PhCHO. Column chromatography of the resulting clear oil (3:1 hexane–EtOAc) gave **24** (112 mg, 83%) as a

white solid; $[\alpha]_D$ −80.4° (*c* 0.5, $CHCl_3$); R_f 0.70 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ7.50–7.62 (m, 2 H, Ph), 7.34–7.44 (m, 3 H, Ph), 5.56 (s, 1 H, PhC*H*O_2), 4.34 (dd, 1 H, $J_{6a,6b}$ 12.5, $J_{5,6a}$ 1 Hz, H-6a), 4.28 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.10 (m, 2 H, H-4, H-6b), 4.02 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OC*H*$_2$CH$_2$), 3.92 (ddd, 1 H, $J_{1,2}$ 8, $J_{2,3e}$ 5, $J_{2,3a}$ 10.5 Hz, H-2), 3.51 (m, 2 H, H-5, OC*H*$_2$CH$_2$), 2.42 (ddd, 1 H, $J_{3a,3e}$ 14, $J_{2,3e}$ 5, $J_{3c,4}$ 2.5 Hz, H-3e), 2.30 (br s, 1 H, 2-OH), 1.73 (ddd, 1 H, $J_{3a,3e}$ 14, $J_{2,3a}$ 10.5, $J_{3a,4}$ 3.5 Hz, H-3a), 1.58–1.70 (m, 2 H, OCH$_2$C*H*$_2$), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR: δ138.06 (Ph quat.), 129.03, 128.23, 126.40 (Ph methine), 105.27 (C-1), 101.37 (Ph*C*HO_2), 73.20 (C-4), 69.70 (O*C*H$_2$CH$_2$), 69.55 (C-6), 69.35 (C-2), 65.81 (C-5), 35.25 (C-3), 31.87, 29.63, 29.47, 29.28, 26.08, 22.70 (octyl CH_2), 14.13 (octyl CH_3). Anal. Calcd for $C_{21}H_{33}O_5$ (365.49): C, 69.20; H, 8.85. Found: C, 69.51; H, 8.85.

Octyl 4,6-O-benzylidene-3-deoxy-2-O-(2,3,4-tri-O-benzyl-α-D-fucopyranosyl)-β-D-xylo-hexopyranoside (**25**).—Alcohol **24** (130 mg, 0.35 mmol) and Et_4NBr (81 mg, 0.39 mmol) were fucosylated as described for **15** using 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide (1.408 mmol). Column chromatography of the mixture (3:1 hexane–EtOAc) gave the disaccharide **25** (241 mg, 88%) as a white solid; ($[\alpha]_D$ −111.51° (*c* 0.5, $CHCl_3$); R_f 0.34 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): 7.10–7.55 (m, 20 H Ph), 5.48 (s, 1 H, PhC*H*O_2), 4.98 (d, 1 H, J_{gem} 11.5 Hz, PhC*H*$_2$), 4.90 (d, 1 H, $J_{1'2'}$ 3.5 Hz, H-1'), 4.60–4.88 (m 5 H, PhC*H*$_2$), 4.47 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.20–4.35 (m, 2 H, H-5', H-6a), 3.88–4.08 (m, 6 H, H-2', H-3', H-6b, H-4, H-2, OC*H*$_2$CH$_2$), 3.65 (1 H, $J_{3'4'}$ 2 Hz, H-4'), 3.32–3.46 (m, 2 H, H-5, OC*H*$_2$CH$_2$), 2.38 (ddd, 1 H, J_{gem} 14, $J_{2,3e}$ 5.5, $J_{3e,4}$ 2.5 Hz, H-3e) 1.75 (ddd, 1 H, $J_{3a,4}$ 3.5, $J_{2,3a}$ 11, J_{gem} 13 Hz, H-3a), 1.55–1.70 (m, 2 H, OCH$_2$C*H*$_2$), 1.20–1.45 (10 H, octyl CH_2), 1.11 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): 138.98, 138.78, 138.58, 137.69 (Ph quat.), 129.16, 128.91, 128.60, 128.29, 128.19, 128.10, 127.93, 127.71, 127.62, 127.42, 127.38, 127.33, 126.37 (Ph methine), 103.18 (C-1), 101.25 (Ph*C*HO_2), 94.27 (C-1'), 79.67 (C-4'), 78.03 (C-3'), 76.38 (C-3), 75.91 (C-2'), 74.72, 73.37, 73.16 (Ph*C*H$_2$), 73.03 (C-4), 69.48 (O*C*H$_2$CH$_2$), 68.99 (C-6), 68.83 (C-5'), 68.25 (C-5), 33.41 (C-3), 31.83, 29.72, 29.49, 29.33, 26.22, 22.62 (octyl CH_2), 16.50 (C-6'), 14.08 (octyl CH_3). Anal. Calcd for $C_{48}H_{60}O_9$ (781.01): C, 73.82; H, 7.74. Found: C, 73.67; H, 7.74.

Octyl 3-deoxy-2-O-(α-L-fucopyranosyl)-β-D-xylo-hexopyranoside (**7**).—The protected disaccharide **25** (150 mg, 0.19 mmol) was dissolved in MeOH (20 mL), 5% Pd–C (75 mg) added, and the solution stirred under a flow of H_2 overnight. The catalyst was filtered off, and the product purified as described for **6** to give **7** (70 mg, 86%) as a white solid. ^1H NMR (CD_3OD): 4.84 (s, 1 H, H-1'), 4.40 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.33 (q, 1 H, $J_{5'6'}$ 6.5 Hz, H-5'), 3.41–4.00 (m, 10 H, H-2, H-4, H-5, H-6a, H-6b, H-2', H-3', H-4', 2 OC*H*$_2$CH$_2$), 2.29 (dt, 1 H, $J_{3e,3a}$ 13, $J_{3e,4} = J_{3e,2} = 4$ Hz, H-3e), 1.50–1.70 (m, 3 H, H-3a, OCH$_2$C*H*$_2$), 1.23–1.45 (10 H, octyl CH_2), 1.18 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): 104.90 (C-1), 96.81 (C-1'), 79.48 (C-2), 73.79 (C-5), 71.73 (C-3'), 70.31 (C-4'), 70.13 (O*C*H$_2$CH$_2$), 69.83 (C-2'), 67.34 (C-4), 66.88 (C-5), 62.81 (C-6), 35.93 (C-3), 33.02,

31.03, 30.61, 30.48, 27.44, 23.70 (octyl CH_2), 16.63 (C-6′), 14.42 (octyl CH_3). FABMS: m/z 445 $[M + Na]^+$ and 423 $[M + H]^+$ ($C_{20}H_{38}O_9$ requires m/z 422).

Octyl 2-O-allyl-4,6-O-benzylidene-3-O-benzyl-β-D-galactopyranoside (**26**).—To a solution of **15** (4.77 g, 10.15 mmol) in dry DMF (75 mL), NaH (730 mg, 30.45 mmol) was added. After stirring for 30 min allyl bromide (3.5 mL, 40.6 mmol) was added and stirring continued for 15 h. The mixture was diluted with CH_2Cl_2 and extracted with water, $NaHCO_3$, and brine. Column chromotography of the resulting oil (3:1 hexane–EtOAc) gave **26** (4.68 g, 90%) as a white solid; $[\alpha]_D$ +29.7° (*c* 1.3; $CHCl_3$); R_f 0.44 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.60 (m, 10 H, Ph), 5.98 (1 H, H_c allyl), 5.48 (s, 1 H, PhC*H*O_2), 5.30 (1 H, H_b allyl), 5.15 (1 H, H_a allyl), 4.80, 4.73 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.41 (1 H, H_d allyl), 4.27 (m, 2 H, H-6a, H_e allyl), 4.29 (d, 1 H, $J_{1,2}$, 8.0 Hz, H-1), 4.07 (dd, 1 H, $J_{3,4}$ 3.8, $J_{4,5}$ 1 Hz, H-4), 3.99 (dd, 1 H, $J_{6a,6b}$ 12.5, $J_{5,6b}$ 1.5 Hz, H-6b), 3.95 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.69 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10 Hz, H-2), 3.48 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.8 Hz, H-3), 3.45 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.28 (br s, 1 H, H-5), 1.62 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.66, 137.97 (Ph quat.), 135.46 (CH$_2$=*C*HCH$_2$O), 128.66, 128.33, 128.08, 127.61, 126.58 (Ph methine), 116.41 (*C*H$_2$=CHCH$_2$O), 103.75 (C-1), 101.33 (Ph*C*HO$_2$), 79.13 (C-3), 78.11 (C-2), 74.25 (C-4), 73.96 (CH$_2$=CH*C*H$_2$O), 72.12 (Ph*C*H$_2$), 70.03 (O*C*H$_2$CH$_2$), 69.29 (C-6), 66.42 (C-5), 31.85, 29.68, 29.43, 29.28, 26.10, 22.68 (octyl CH_2), 14.11 (octyl CH_3). Anal. Calcd for $C_{31}H_{42}O_6$ (510.68): C, 72.91; H, 8.29. Found: C, 72.95; H, 8.18.

Octyl 2-O-allyl-3,6-di-O-benzyl-β-D-galactopyranoside (**27**).—Compound **26** (3.10 g, 6.09 mmol), $NaCNBH_3$ (4.15 g, 66.1 mmol) and Methyl Orange indicator were dissolved in dry THF (40 mL) containing crushed 3A molecular sieves (2 g). The solution was cooled to 0°C and then ethereal HCl was added until the red color of the solution persisted. After 4 h, TLC indicated the reaction was complete and the reaction was quenched by the addtion of $NaHCO_3$. The mixture was filtered, diluted with CH_2Cl_2, and washed with water and brine, and evaporated. Column chromotography of the residue (3:1 hexane–EtOAc) gave **27** (2.54 g, 81%) as a colorless oil; $[\alpha]_D$ −8.5° (*c* 0.8, $CHCl_3$); R_f 0.50 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.40 (m, 10 H, Ph), 5.96 (1 H, H_c allyl), 5.28 (1 H, H_b allyl), 5.16 (1 H, H_a allyl), 4.75, 4.71 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.58 (s, 2 H, PhCH_2), 4.39 (1 H, H_d allyl), 4.27 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.21 (m, 1 H, H_e allyl), 3.99 (ddd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1, $J_{4,4\text{-OH}}$ 2 Hz, H-4), 3.91 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.79 (dd, 1 H, $J_{6a,6b}$ 10, $J_{5,6a}$ 6 Hz, H-6a), 3.70 (dd, 1 H, $J_{6a,6b}$ 10, $J_{5,6b}$ 6 Hz, H-6b), 3.45–3.57 (3 H, H-2, H-5, OCH_2CH$_2$), 3.42 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, H-3), 2.45 (d, 1 H, $J_{4,4\text{-OH}}$ 2 Hz, 4-OH), 1.55–1.65 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.12 (Ph quat.), 135.28 (CH$_2$=*C*HCH$_2$O), 128.47, 128.44, 127.82, 127.78, 127.75 (Ph methine), 116.73 (*C*H$_2$=CHCH$_2$O), 103.71 (C-1), 80.51 (C-3), 78.68 (C-2), 73.94 (CH$_2$=CH*C*H$_2$O), 73.73 (Ph*C*H$_2$), 73.20 (C-5), 72.56 (PhCH_2), 70.02 (O*C*H$_2$CH$_2$), 69.28 (C-6), 67.11 (C-4), 31.84, 29.72, 29.40, 29.27, 26.10, 22.68

(octyl CH_2), 14.11 (octyl CH_3). Anal. Calcd for $C_{31}H_{44}O_6$ (512.69): C, 72.62; H, 8.65. Found: C, 72.29; H, 8.75.

Octyl 2-O-allyl-3,6-di-O-benzyl-4-O-[(methylthio)thiocarbonyl]-β-D-galactopyranoside (**28**).—To a solution of **27** (353 mg, 0.69 mmol) in 20 mL dry THF was added NaH (68 mg, 80% in oil, 2.27 mmol) and imidazole (5 mg). After stirring for 1 h, CS_2 (420 μL, 6.96 mmol) was added and stirring continued for 1 h. At this point, MeI (129 μL, 2.07 mmmol) was added and stirring continued overnight. Evaporation of the solvent gave a yellow liquid which was chromatographed (4:1 hexane–EtOAc) to give **28** (332 mg, 80%) as a yellow oil; $[\alpha]_D$ +23.5° (*c* 0.6, $CHCl_3$); R_f 0.55 (4:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.20–7.40 (m, 10 H, Ph), 6.48 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.93 (1 H, H_c allyl), 5.26 (1 H, H_b allyl), 5.13 (1 H, H_a allyl), 4.78, 4.53, 4.50, 4.45 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.35 (1 H, H_d allyl), 4.35 (1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.22 (1 H, H_e allyl), 3.92 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.76 (dt, 1 H, $J_{5,6a} = J_{5,6b} = 6$, $J_{4,5}$ 1 Hz H-5), 3.43–3.63 (5 H, H-2, H-3, H-6a, H-6b, OCH_2CH$_2$), 2.58 (s, 3 H, SCH_3), 1.62 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 216.61 (C=S), 137.97, 137.83 (Ph quat.), 135.22 (CH$_2$=*C*HCH$_2$O), 128.43, 128.26, 128.03, 127.95, 127.81, 127.63 (Ph methine), 116.70 (*C*H$_2$=CHCH$_2$O), 103.87 (C-1), 79.41 (C-3), 78.65 (C-2), 76.47 (C-4), 74.15 (CH$_2$=CH*C*H$_2$O), 73.85 (Ph*C*H$_2$), 72.89 (C-5), 72.73 (PhCH_2), 70.51 (O*C*H$_2$CH$_2$), 68.69 (C-6), 67.11 (C-5), 31.86, 29.69, 29.40, 29.28, 26.06, 22.69 (octyl CH_2), 19.23 (SCH$_3$), 14.12 (octyl CH_3). Anal. Calcd for $C_{33}H_{46}O_6S_2$ (602.85): C, 65.75; H, 7.69; S, 10.64. Found: C, 65.69; H, 7.57; S, 10.35.

Octyl 2-O-allyl-3,6-di-O-benzyl-4-deoxy-β-D-xylo-hexopyranoside (**29**).—Compound **28** (157 mg, 0.26 mmol) was dissolved in dry toluene (50 mL) and then tributylstannane (1.05 mL, 3.9 mmol) and AIBN (35 mg, 0.21mmol) were added. The solution was heated under reflux for 90 min. Evaporation of the solvent followed by chromatography (99:1 CH_2Cl_2–MeOH) gave **29** (109 mg, 85%) as a colorless oil; $[\alpha]_D$ −19.9° (*c* 0.5, $CHCl_3$); R_f 0.45 (99:1 CH_2Cl_2–MeOH). ^{1}H NMR ($CDCl_3$): δ7.20–7.40 (m, 10 H, Ph), 5.98 (1 H, H_c allyl), 5.29 (1 H, H_b allyl), 5.15 (1 H, H_a allyl), 4.72, 4.66, 4.59, 4.52 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.40 (1 H, H_d allyl), 4.27 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.23 (1 H, H_e allyl), 3.91 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.43–3.63 (5 H, H-3, H-5, H-6a, H-6b, OCH_2CH$_2$), 3.18 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 10 Hz, H-2), 2.08 (ddd, 1 H, $J_{4e,5}$ 1, $J_{3,4e}$ 5, J_{gem} 13 Hz, H-4e), 1.57–1.70 (m, 2 H, OCH$_2$CH_2), 1.20–1.50 (11 H, octyl CH_2, H-4a), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): 138.74, 138.15 (Ph quat.), 135.37 (CH$_2$=*C*HCH$_2$O), 128.36, 128.30, 127.64, 127.56, 127.48 (Ph methine), 116.57 (*C*H$_2$=CHCH$_2$O), 103.78 (C-1), 82.59 (C-3), 78.09 (C-2), 73.73 (CH$_2$=CH*C*H$_2$O), 73.50, 72.55 (PhCH_2), 72.37 (C-6), 70. 93 (C-5), 70.06 (O*C*H$_2$CH$_2$), 34.04 (C-4), 31.80, 29.73, 29.36, 29.23, 26.06, 22.63 (octyl CH_2), 14.08 (octyl CH_3). Anal. Calcd for $C_{31}H_{44}O_5$ (496.69): C, 74.96; H, 8.93. Found: C, 74.68; H, 8.83.

Octyl 3,6-di-O-benzyl-4-deoxy-β-D-xylo-hexopyranoside (**30**).—To a solution of **29** (199 mg, 0.40 mmol) dissolved in 7:3:1 EtOH–benzene–water (20 mL), tris(tri-

phenylphosphine)rhodium(I) chloride (55 mg, 0.06 mmol) and 1,4-diazabicyclo[2.2.2]octane (20 mg, 0.18 mmol) were added, and the solution refluxed for 20 h. The solvent was evaporated and the residue dissolved in 9:1 Me_2CO–water (10 mL). Mercuric oxide (3 mg) and $HgCl_2$ (1 g) were added and stirring continued at room temperature overnight. The mixture was then diluted with CH_2Cl_2 and washed with satd KI, water, and brine. Evaporation of the organic layer followed by chromatography (4:1 hexane–EtOAc) gave **30** (159 mg, 86%) as a colorless oil; $[\alpha]_D$ −8.2° (*c* 0.6, $CHCl_3$); R_f 0.45 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.40 (m, 10 H, Ph), 4.72, 4.65, 4.53 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.21 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.89 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.40–3.68 (6 H, H-2, H-3, H-5, H-6a, H-6b, OCH_2CH$_2$), 2.46 (d, 1 H, $J_{2,2\text{-OH}}$ 1.5 Hz, 2-OH), 2.12 (ddd, 1 H, $J_{4e,5}$ 1.8, $J_{3,4e}$ 4.5, J_{gem} 13 Hz, H-4e), 1.55–1.68 (m, 2 H, OCH$_2$CH_2), 1.43 (dt, 1 H, $J_{3,4a} = J_{4a,5} = 11$, J_{gem} 13 Hz, H-4a), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): 138.46 (Ph quat.), 128.46, 128.43, 127.71 (Ph methine), 103.00 (C-1), 77.94 (C-3), 75.10 (C-5), 73.57, 72.49 (PhCH_2), 71.68 (C-6), 71.31 (C-2), 70.08 (OCH_2CH$_2$), 33.31 (C-4), 31.83, 29.67, 29.40, 29.24, 26.00, 22.66 (octyl CH_2), 14.11 (octyl CH_3). Anal. Calcd for $C_{28}H_{40}O_5$ (456.63): C, 73.65; H, 8.83. Found: C, 73.35; H, 8.28.

*Octyl 4-deoxy-2-*O*-(α-*L*-fucopyranosyl)-β-*D*-xylo-hexopyranoside* (**8**).—Alcohol **30** (101 mg, 0.22 mmol) and Et_4NBr (51 mg, 0.243 mmol) were dissolved in CH_2Cl_2 (4 mL) and DMF (0.5 mL) containing crushed 4A molecular sieves (3 g), and the solution stirred overnight. To this slurry was added freshly prepared 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide (1.105 mmol) in CH_2Cl_2 (3 mL) and the mixture was stirred for 2 days. Methanol (1 mL) was added and stirring continued for 30 min, and then the mixture was filtered and taken to dryness. At this point it was not possible to obtain a pure product, therefore the partially purified product was dissolved in MeOH (10 mL), 5% Pd–C (50 mg) added and the solution stirred under a flow of H_2 overnight. Final purification as described for **6** gave **8** (36 mg, 39%) as a white solid. ^1H NMR (CD_3OD): 5.19 (d, 1 H, $J_{1'2'}$ 2 Hz, H-1'), 4.29 (m, 2 H, H-1, H-5'), 3.88 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.72–3.84 (m, 3 H, H-2', H-3, H-6a), 3.63 (d, 1 H, $J_{3'4'}$ 1.5 Hz, H-3'), 3.44–3.58 (m, 4 H, H-5, H-2, H-4', OCH_2CH$_2$), 3.22 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 10 Hz, H-2) 1.90 (ddd, 1 H, $J_{4e,5}$ 1.5, $J_{3,4e}$ 5, $J_{4e,4a}$ 13 Hz, H-4e), 1.62 (m, 2 H, OCH$_2$CH_2), 1.25–1.45 (11 H, octyl CH_2, H-4a), 1.19 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ 103.36 (C-1), 101.77 (C-1'), 83.42 (C-2), 73.79 (C-4'), 73.76 (C-5), 73.02 (C-3), 71.75 (C-3'), 70.83 (OCH_2CH$_2$), 70.68 (C-2'), 67.83 (C-5'), 65.50 (C-6), 36.49 (C-4), 33.01, 30.99, 30.63, 30.41, 27.30, 23.70 (octyl CH_2), 16.80 (C-6'), 14.42 (octyl CH_3). FABMS: *m/z* 445 $[M + Na]^+$ and 423 $[M + H]^+$ ($C_{20}H_{38}O_9$ requires *m/z* 422).

*Methyl 3,4 di-*O*-benzoyl-6-bromo-6-deoxy-β-*D*-galactopyranoside* (**33**).—Methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranoside (**32**; 3.0 g, 7.78 mmol), *N*-bromosuccinimide (1.73 g, 9.72 mmol) and $BaCO_3$ (7 g) were refluxed in CCl_4 (75 mL) for 30 min. The orange solution was cooled, filtered, evaporated, and the

resulting liquid chromatographed (1:1 hexane–EtOAc) to give **33** (2.74 g, 76%) as a white foam; $[\alpha]_D$ +71.6° (*c* 0.4, $CHCl_3$); R_f 0.65 (1:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.0–7.84 (m, 10 H, Ph), 5.74 (dd, 1 H, $J_{3,4}$ 3.2, $J_{4,5}$ 1 Hz, H-4), 5.20 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.2 Hz, H-3), 4.31 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.96 (m, 2 H, H-2, H-5), 3.57 (s, 3 H, OCH_3), 3.37 (dd, 1 H, $J_{6a,6b}$ 9.5, $J_{5,6a}$ 7 Hz, H-6a), 3.32 (dd, $J_{6a,6b}$ 9.5, $J_{5,6b}$ 6.5 Hz, H-6), 2.48 (br s, 1 H, 2-OH); ^{13}C NMR ($CDCl_3$): δ165.94, 164.44 (C=O), 133.61, 133.26, 129.97, 129.81 (Ph methine), 129.25, 129.07 (Ph quat.), 128.59, 128.28 (Ph methine), 104.27 (C-1), 73.92 (C-5), 73.38 (C-3), 69.73 (C-2), 68.75 (C-4), 57.62 (OCH_3), 28.61 (C-6). Anal. Calcd for $C_{21}H_{21}BrO_7$ (465.30): C, 54.21; H, 4.55; Br, 17.17. Found: C, 54.05; H, 4.64; Br, 17.32.

Methyl 3,4 di-O-benzoyl-6-deoxy-β-D-galactopyranoside (**34**).—Compound **33** (2.43 g, 5.23 mmol), Et_3N (910 μL, 6.53 mmol), and 5% Pd–C (2.25 g) were stirred in 5:1 EtOH–EtOAc (120 mL) under a flow of H_2 for 18 h. The catalyst was filtered off, the solvent evaporated, and the residue chromatographed (1:1 hexane–EtOAc) to give **34** (1.84 g, 91%) as a white solid; $[\alpha]_D$ +100.0° (*c* 0.4, $CHCl_3$); R_f 0.58 (1:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.2–8.1 (m, 10 H, Ph), 5.63 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.34 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, H-3), 4.40 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.05 (ddd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 10, $J_{2,OH}$ 2.5 Hz, H-2), 4.01 (q, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 3.65 (s, 3 H, OCH_3), 2.50 (d, 1 H, $J_{2,2\text{-}OH}$ 2.5 Hz, 2-OH), 1.32 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 166.06, 165.96 (C=O), 133.37, 133.15, 129.25, 129.78 (Ph methine), 129.45 (Ph quat.), 128.49, 128.25 (Ph methine), 104.24 (C-1), 73.75 (C-5), 71.21 (C-3), 69.80 (C-2), 68.68 (C-4), 57.50 (OCH_3), 16.28 (C-6). Anal. Calcd for $C_{21}H_{22}O_7$ (386.41): C, 65.28; H, 5.74. Found: C, 65.28; H, 5.97.

Methyl 2-O-acetyl-3,4 di-O-benzoyl-6-deoxy-β-D-galactopyranoside (**35**).—Alcohol **34** (1.77 g, 4.58 mmol) was dissolved in pyridine (15 mL) and then Ac_2O (5 mL) was added. The mixture was stirred overnight and was quenched by cooling to 0°C and adding MeOH. The solvent was evaporated and the product chromatographed (4:1 hexane–EtOAc) to give the product **35** (1.88 g, 96%) as a white foam; $[\alpha]_D$ +139.4° (*c* 0.8, $CHCl_3$); R_f 0.22 (4:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.2–8.1 (m, 10 H, Ph), 5.67 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.49 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 10.5 Hz, H-2), 5.36 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 3.5 Hz, H-3), 4.54 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.02 (dq, 1 H, $J_{5,6}$ 6.5, $J_{4,5}$ 1 Hz, H-5), 3.60 (s, 3 H, OCH_3), 1.98 (s, 3 H, acetate CH_3), 1.33 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 169.67 (acetate C=O), 165.98, 165.68 (benzoate C=O), 133.40, 133.30, 129.99, 129.76 (Ph methine), 129.27, 129.02 (Ph quat.), 128.57, 128.38 (Ph methine), 102.0 (C-1), 72.24 (C-5), 71.04 (C-3), 69.65 (C-2), 69.17 (C-4), 56.95 (OCH_3), 20.81 (acetate CH_3), 16.27 (C-6). Anal. Calcd for $C_{23}H_{24}O_8$ (428.44): C, 64.48; H, 5.65. Found: C, 64.27; H, 5.67.

2-O-Acetyl-3,4 di-O-benzoyl-6-deoxy-α-D-galactopyranosyl chloride (**36**).—Compound **35** (901 mg, 2.10 mmol), and $ZnCl_2$ (50 mg) were dissolved in $CHCl_3$ (2 mL). To this solution was added $MeOCHCl_2$ (5 mL) and the mixture was refluxed for 45 min. The solvent was evaporated and the product subjected to a rapid chromatographic separation (4:1 hexane–EtOAc) to give **36** (703 mg, 78%) as a

white foam; R_f 0.47 (4:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.30–8.12 (m, 10 H, Ph), 6.50 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.84 (dd, 1 H, $J_{1,2}$ 4, $J_{2,3}$ 10 Hz, H-2), 5.80 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.60 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, H-3), 4.68 (q, 1 H, $J_{5,6}$ 6.5, $J_{4,5}$ 1 Hz, H-5), 2.08 (s, 3 H, acetate CH_3), 1.32 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 170.33 (acetate C=O), 165.72, 165.39 (benzoate C=O), 133.60, 133.35, 129.90, 129.74 (Ph methine), 129.13 (Ph quat.), 128.66, 128.40 (Ph methine), 92.02 (C-1), 70.98 (C-5), 68.47 (C-3), 68.32 (2 C, C-4, C-2), 20.72 (acetate CH_3), 15.87 (C-6).

Octyl 2-O-acetyl-3,4-di-O-benzoyl-6-deoxy-β-D-galactopyranoside (**37**).—Silver triflate (502 mg, 1.95 mmol, dried in vacuo over P_2O_5 for 1 h), was stirred with collidine (125 μL, 1.02 mmol) and 1-octanol (604 μL, 3.84 mmol) in CH_2Cl_2 (10 mL) containing crushed 3A molecular sieves (2.5 g) under N_2 at −30°C for 20 min. To this solution was added dropwise, chloride **36** (549 mg, 1.28 mmol) in CH_2Cl_2 (15 mL). The mixture was stirred under N_2 and warmed to room temperature. After 8 h the reaction was quenched with collidine (200 μL), filtered, and evaporated. The residue was then chromatographed (4:1 hexane–EtOAc) to give the product **37** (590 mg, 88%) as an oil; $[\alpha]_D$ +114.7° (*c* 0.5, $CHCl_3$); R_f 0.51 (4:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.28–8.11 (m, 10 H, Ph), 5.65 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.48 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ Hz, H-2), 5.36 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, H-3), 4.59 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 3.92–4.05 (m, 2 H, OCH_2CH_2, H-5), 3.54 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 1.98 (s, 3 H, acetate CH_3), 1.55–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 13 H, octyl CH_2, H-6). 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 169.54 (acetate C=O), 166.07, 165.73 (benzoate C=O), 133.39, 133.29, 130.06, 129.82 (Ph methine), 129.34, 129.11 (Ph quat.), 128.53, 128.40 (Ph methine), 101.30 (C-1), 72.29 (C-5), 71.13 (C-3), 70.19 (OCH_2CH_2), 69.65 (C-2), 69.36 (C-4), 31.85, 29.53, 29.36, 29.31, 25.91, 22.69 (octyl CH_2), 20.79 (acetate CH_3), 16.35 (C-6), 14.12 (octyl CH_3). Anal. Calcd for $C_{30}H_{38}O_8$ (526.63): C, 68.42; H, 7.27. Found: C, 68.58; H, 7.52.

Octyl 3,4-di-O-benzoyl-6-deoxy-β-D-galactopyranoside (**38**).—Compound **37** (399 mg, 0.76 mmol) was dissolved in 49:1 MeOH–AcCl (9 mL) and stirred for 9 h. The reaction was quenched with $NaHCO_3$ and then diluted with CH_2Cl_2 and extraced with $NaHCO_3$, water, and brine. Chromatography of the residue (4:1 hexane–EtOAc) gave **38** (331 mg, 90%) as an oil; $[\alpha]_D$ +81.4° (*c* 0.4, $CHCl_3$); R_f 0.36 (4:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.20–8.15 (m, 10 H, Ph), 5.65 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 5.38 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, H-3), 4.49 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.07 (ddd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 10, $J_{2,2\text{-OH}}$ 2.5 Hz), 4.02 (m, 2 H, OCH_2CH_2, H-5), 3.62 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 2.38 (d, 1 H, $J_{2,OH}$ 2.5 Hz, 2-OH), 1.58–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 13 H, octyl CH_2, H-6), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 166.03 (C=O), 133.37, 133.13, 130.01, 129.82 (Ph methine), 129.57 (Ph quat.), 128.51, 128.28 (Ph methine), 103.28 (C-1), 73.67(C-5), 71.34 (C-3), 70.59 (OCH_2CH_2), 69.88 (C-2), 69.72 (C-4), 31.85, 29.63, 29.43, 29.28, 25.99, 22.69 (octyl CH_2), 16.36 (C-6), 14.13 (octyl CH_3). Anal. Calcd for $C_{28}H_{36}O_7$ (484.59): C, 69.40; H, 7.49. Found: C, 69.49; H, 7.64.

Octyl 3,4-di-O-benzoyl-6-deoxy-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (**39**).—Alcohol **38** (148 mg, 0.31 mmol) and Et_4NBr (71 mg, 0.34 mmol) were fucosylated as described for compound **15** using 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide (1.224 mmol). Column chromatography of the mixture (3:1 hexane–EtOAc) gave the disaccharide **39** (245 mg, 88%) as an oil; $[\alpha]_D$ −1.3° (*c* 0.2, $CHCl_3$); R_f 0.24 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): 6.9–8.1 (m, 25 H Ph), 5.68 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.57 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5 Hz, H-3), 5.40 (d, 1 H, $J_{1'2'}$ 3.5 Hz, H-1'), 4.98, 4.78 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.60–4.70 (m 3 H, H-1, 2 PhCH_2), 4.44 (q, 1 H, $J_{5'6'}$ 6.5 Hz, H-5'), 4.28–4.38 (m, 3 H, 2 PhCH_2, H-2), 3.94–4.04 (m, 2 H, H-5, OCH_2CH_2), 3.86–3.94 (m, 2 H, H-3', H-2'), 3.68 (s, 1 H, H-4'), 3.62 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 1.55–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.45 (13 H, octyl CH_2, H-6), 1.10 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ166.08, 165.30 (C=O), 138.68, 138.64, 137.82 (Ph quat.), 133.24, 133.17, 129.92, 129.65 (Ph methine), 129.43, 129.31 (Ph quat.), 128.42, 128.39 (Ph methine), 102.04 (C-1), 97.08 (C-1'), 79.37 (C-4'), 77.99 (C-3'), 75.63 (C-2'), 75.50 (C-2), 74.72, 73.22, 72.36 (PhCH_2), 71.41 (C-3), 71.28 (C-4), 70.24 (OCH_2CH_2), 69.22 (C-5), 66.55 (C-5'), 31.82, 29.66, 29.47, 29.30, 26.20, 22.63 (octyl CH_2), 16.55 (C-6), 16.27 (C-6'), 14.08 (octyl CH_3). Anal. Calcd for $C_{55}H_{64}O_{11}$ (901.12): C, 73.31; H, 7.16. Found: C, 73.05; H, 7.01.

Octyl 6-deoxy-2-O-(α-L-fucopyranosyl)-β-D-galactopyranoside (**9**).—To a solution of protected disaccharide **39** (200 mg, 0.22 mmol) in MeOH (10 mL), 5% Pd–C (100 mg) was added and the solution stirred under a flow of H_2 overnight. After completion of the reaction, the catalyst was filtered away and the solvent evaporated. The residue was redissolved in MeOH (20 mL), 1 M NaOH (1 mL) was added, and the mixture stirred overnight. The solution was neutralized with Amberlite IR 120 (H^+) resin, evaporated, and the product purified by chromatography (9:1 CH_2Cl_2–MeOH). Final purification was achieved as described for **6** to give the product **9** (76 mg, 81%) as a white solid; R_f 0.15 (9:1 CH_2Cl_2–MeOH). ^1H NMR (CD_3OD): δ 5.19 (d, 1 H, $J_{1'2'}$ 2 Hz, H-1'), 4.29 (m, 2 H, H-1, H-5'), 3.83 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.56–3.77 (m, 7 H, H-2, H-3, H-4, H-5, H-2', H-3', H-4'), 3.48 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 1.53–1.66 (m, 2 H, OCH_2CH_2), 1.21–1.42 (13 H, octyl CH_2, H-6), 1.18 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ 103.38 (C-1), 101.54 (C-1'), 78.86 (C-2), 75.88 (C-5), 73.74 (C-3), 73.12 (C-4'), 71.76 (2 C, C-3' C-4'), 70.70 (OCH_2CH_2), 70.61 (C-2'), 67.74 (C-5'), 32.99, 30.99, 30.59, 30.38, 27.28, 23.68 (octyl CH_2), 16.77 (C-6'), 16.67 (C-6), 14.40 (octyl CH_3). FABMS: *m/z* 445 $[M + Na]^+$ and 423 $[M + H]^+$ ($C_{20}H_{38}O_9$ requires *m/z* 422).

2,4,6 Tri-O-acetyl-3-deoxy-3-fluoro-α-D-galactopyranosyl bromide (**41**).—1,2,4,6-tetra-*O*-Acetyl-3-deoxy-3-fluoro-D-galactopyranose **40**[33] (0.86 g, 2.44 mmol) was dissolved in CH_2Cl_2 (2 mL) and hydrobromic acid (33% in AcOH, 7 mL) added. The mixture was stirred for 1 h and then evaporated to dryness, coevaporating with dry toluene. The crude product was purified by a rapid chromatographic separa-

tion (3:1 hexane–EtOAc) to give the product **41** (850 mg, 80%) as an oil which solidified on standing; R_f 0.48 (3:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 6.68 (t, 1 H, $J_{1,2} = J_{1,F} = 4$ Hz, H-1), 5.68 (ddd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1, $J_{H4,F}$ 6 Hz, H-4), 5.11 (ddd, 1 H, $J_{1,2}$ 4.0, $J_{2,3}$ 10, $J_{H2,F}$ 12 Hz, H-2) 5.00 (ddd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3.5, $J_{H3,F}$ 48 Hz, H-3), 4.44 (br t, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 4.24 (ddd, 1 H, $J_{5,6a}$ 6.5, $J_{6a,6b}$ 12 Hz, H-6a), 4.11 (ddd, 1 H, $J_{5,6b}$ 6.5, $J_{6a,6b}$ 12, $J_{H6b,F}$ 1 Hz, H-6b), 2.19 (s, 3 H, acetate CH_3), 2.08 (s, 6 H, acetate CH_3).

*Octyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-β-*D*-galactopyranoside* (**42**).—Compound **41** (644 mg, 1.74 mmol), was glycosylated as described for the conversion of **36** to **37**, using silver triflate (669 mg, 2.60 mmol), collidine (167 μL, 1.31 mmol), and octanol (830 μL, 5.22 mmol). The reaction was complete after 30 min. Chromatography of the crude mixture (4:1 hexane–EtOAc) gave the product **42** (448 mg, 62%) as an oil; $[\alpha]_D$ +3.5° (*c* 1.2, $CHCl_3$); R_f 0.38 (4:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 5.55 (ddd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1, $J_{4,F}$ 6 Hz, H-4), 5.28 (ddd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 9.5, $J_{2,F}$ 12 Hz, H-2) 4.61 (ddd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 3.5, $J_{H3,F}$ 47 Hz, H-3), 4.40 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.17 (d, 2 H, $J_{5,6a} = J_{5,6b} = 6.5$ Hz, H-6a, H-6b), 3.88 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.83 (ddt, 1 H, $J_{5,6}$ 6.5, $J_{4,5}$ 1, $J_{5,F}$ 1 Hz), 3.47 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 2.18, 2.12, 2.07 (s, 3 H, acetate CH_3), 1.45–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ170.43 170.02, 169.25 (acetate C=O), 100.77 (d, 1 C, $J_{C1,F}$ 10.6 Hz, C-1), 88.98 (d, 1 C, $J_{C3,F}$ 194.0 Hz, C-3), 70.35 (OCH_2CH_2), 70.03 (d, 1 C, $J_{C2,F}$ 25.7 Hz, C-2), 69.94 (C-5), 67.00 (d, 1 C, $J_{C4,F}$ 16.6 Hz, C-4), 61.37 (d, 1 C, $J_{C6,F}$ 2.4 Hz, C-6) 31.82, 29.42, 29.29, 25.82, 22.66 (octyl CH_2), 20.79, 20.68 (acetate CH_3), 14.09 (octyl CH_3); ^{19}F NMR ($CDCl_3$): δ −200.3 (ddd, 1 F, $J_{H3,F}$ 47, $J_{H2,F}$ 12, $J_{H4,F}$ 5.3 Hz, F-3). Anal. Calcd for $C_{20}H_{36}FO_8$ (423.50): Calculated: C, 56.72; H, 8.57. Found: C, 57.30; H, 8.34.

*Octyl 3-deoxy-3-fluoro-β-*D*-galactopyranoside* (**43**).—Galactoside **42** (338 mg, 0.80 mmol), was dissolved in MeOH (10 mL) and NaOMe (60 mg) was added. After stirring for 48 h, the solution was neutralized by the addition of prewashed Amberlite IR 120 (H^+) resin. Evaporation of the solvent followed by chromatography (19:1 CH_2Cl_2–MeOH) gave the product **43** (218 mg, 92%) as a white solid; $[\alpha]_D$ −19.2° (*c* 0.7, MeOH); R_f 0.11 (19:1 CH_2Cl_2–MeOH). ^{1}H NMR (CD_3OD): δ 4.28 (ddd, 1 H, $J_{3,4}$ 3.5, $J_{2,3}$ 9.5, $J_{H3,F}$ 48.5 Hz, H-3), 4.14 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.01 (dd, 1 H, $J_{H4,F}$ 6.5, $J_{3,4}$ 3.5 Hz, H-4), 3.86 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.62–3.80 (m, 2 H, H-2, H-6a, H-6b), 3.50 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.45 (br t, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 1.58–1.75 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ 104.31 (d, 1 C, $J_{C1,F}$ 11.8 Hz, C-1), 95.01 (d, 1 C, $J_{C3,F}$ 184.8 Hz, C-3), 75.25 (d, 1 C, $J_{C5,F}$ 6.9 Hz, C-5), 71.02 (OCH_2CH_2), 70.98 (d, 1 C, $J_{C2,F}$ 18.1 Hz, C-2), 68.34 (d, 1 C, $J_{C4,F}$ 16.5 Hz, C-4) 62.03 (d, 1 C, $J_{C6,F}$ 3 Hz, C-4), 33.00, 30.80, 30.55, 30.41, 27.09, 23.71 (octyl CH_2), 14.41 (octyl CH_3); ^{19}F NMR (CD_3OD): δ −201.0 (dddd, 1 F, $J_{H3,F}$ 48.5, $J_{H2,F}$ 13, $J_{H4,F}$ 6.5, $J_{H5,F}$ 1 Hz, F-6). Anal. Calcd for $C_{14}H_{27}FO_5$ (294.37): C, 57.13; H, 9.25. Found: C, 56.88; H, 9.16.

Octyl 4,6-O-benzylidene-3-deoxy-3-fluoro-β-D-galactopyranoside (**44**).—Compound **43** (131 mg, 0.45 mmol) and $PhCH(OMe)_2$ (201 μL, 1.34 mmol) were dissolved in MeCN (5 mL) and TsOH (5 mg) added. After stirring for 30 min the reaction was neutralized with Et_3N, evaporated, and chromatographed (3:1 hexane–EtOAc) to give **44** (169 mg, 98%) as a white solid; $[\alpha]_D$ −34.3° (*c* 0.5, $CHCl_3$); R_f 0.13 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.1–7.52 (m, 5 H, Ph), 5.42 (s, 1 H, $PhCHO_2$), 4.4 (ddd, 1 H, $J_{2,3}$ 9, $J_{3,4}$ 3.5, $J_{H3,F}$ 45.5 Hz, H-3), 4.20–4.32 (m, 2 H, H-6a, H-4), 4.18 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 3.92–4.04 (m, 2 H, H-6b, H-2), 3.89 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.42 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.41 (br s, 1 H, H-5), 2.42 (d, 1 H, $J_{2,2\text{-OH}}$ 2-OH), 1.62 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 137.47 (Ph quat.), 129.09, 128.18, 126.36 (Ph methine), 102.44 (d, 1 C, $J_{C1,F}$ 11.3 Hz, C-1), 101.04 ($PhCHO_2$), 91.21 (d, 1 C, $J_{C3,F}$ 191.7 Hz, C-3), 74.14 (d, 1 C, $J_{C4,F}$ 15.8 Hz, C-4), 70.31 (OCH_2CH_2), 69.57 (d, 1 C, $J_{C2,F}$ 18.1 Hz, C-2), 69.01 (C-6), 65.62 (d, 1 C, $J_{C5,F}$ 6.0 Hz, C-5), 31.83, 29.52, 29.41, 29.24, 25.97, 22.67 (octyl CH_2), 14.11 (octyl CH_3); ^{19}F NMR ($CDCl_3$): δ −205.1 (m, 1 F, F-3). Anal. Calcd for $C_{21}H_{31}FO_5$ (382.48): C, 65.95; H, 8.17 Found: C, 65.84; H, 8.49.

Octyl 4,6-O-benzylidene-3-deoxy-3-fluoro-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (**45**).—Alcohol **44** (117 mg, 0.31 mmol) and Et_4NBr (72 mg, 0.34 mmol) were fucosylated as described for compound **15** using 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide (1.27 mmol). Column chromatography of the residue (3:1 hexane–EtOAc) gave the disaccharide **45** (217 mg, 89%) as an oil; $[\alpha]_D$ −84.0° (*c* 0.1, $CHCl_3$); R_f 0.23 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.2–7.6 (m, 20 H Ph), 5.55 (s, 1 H, $PhCHO_2$), 5.36 (d, 1 H, $J_{1'2'}$ 4 Hz, H-1'), 4.99, 4.90 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.64–4.87 (m, 7 H, 6 $PhCH_2$, H-3), 4.21–4.45 (m, 5 H, H-1, H-5', H-2, H-4, H-6a) 4.0–4.11 (m, 2 H, H-6b, H-2') 3.87–3.98 (m, 2 H, H-3', OCH_2CH_2), 3.66 (d, 1 H, $J_{3'4'}$ 2 Hz, H-4'), 3.40 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.36 (br s, 1 H, H-5), 1.45–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 1.12 (d, 1 H, $J_{5',6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 139.15, 138.84, 138.47, 137.39 (Ph quat.), 129.08, 128.34, 128.31, 128.27, 128.20, 128.18, 128.14, 127.59, 127.49, 127.42, 127.36, 126.42 (Ph methine), 101.06 ($PhCHO_2$), 101.00 (d, 1 C, $J_{C1,F}$ 10 Hz, C-1), 97.10 (d, 1 C, $J_{C1',F}$ 5.3 Hz, C-1'), 93.36 (d, 1 C, $J_{C3,F}$ 191 Hz, C-3), 79.41 (C-4'), 78.10 (C-3'), 76.39 (C-2'), 74.78 ($PhCH_2$), 74.49 (d, 1 C, $J_{C4,F}$ 15.8 Hz, C-2), 73.38, 72.77 ($PhCH_2$), 72.11 (d, 1 C, $J_{C2,F}$ 16.5 Hz, C-4), 69.61 (OCH_2CH_2), 69.06 (C-6), 66.45 (C-5'), 65.32 (d, 1 C, $J_{C5,F}$ 6.8 Hz, C-5), 31.87, 29.67, 29.51, 29.34, 26.21, 22.68 (octyl CH_2), 16.60 (C-6'), 14.13 (octyl CH_3); ^{19}F NMR ($CDCl_3$); δ −203 (dt, 1 F, $J_{H3,F}$ 47, $J_{H4,F}$ 6, $J_{H2,F}$ 12.5 Hz, F-3). Anal. Calcd for $C_{48}H_{59}FO_9$ (799.00): C, 72.16; H, 7.44. Found: C, 72.15; H, 7.59.

Octyl 3-deoxy-3-fluoro-2-O-(α-L-fucopyranosyl)-β-D-galactopyranoside (**10**).—The protected disaccharide **45** (166 mg, 0.21 mmol) was dissolved in MeOH (10 mL), 5% Pd–C (100 mg) was added, and the solution stirred under a flow of H_2 overnight. After completion of the reaction, the catalyst was filtered off, the

solvent evaporated, and the product was purified by chromatography (9:1 CH_2Cl_2–MeOH). Final purification of the product was achieved as described for **6** to give the product **10** (75 mg, 82%) as a white solid; R_f 0.20 (9:1 CH_2Cl_2–MeOH). ^{1}H NMR (CD_3OD): δ 5.12 (br s, 1 H, H-1′), 4.66 (ddd, 1 H, $J_{H3,F}$ 48.5, $J_{2,3}$ 9.5, $J_{3,4}$ 3.5 Hz, H-3), 4.37 (m, 2 H, H-1, H-5′), 4.06 (dd, 1 H, $J_{H4,F}$ 7.5, $J_{3,4}$ 3.5 Hz, H-4), 3.98 (ddd, 1 H, $J_{H2,F}$ 7.5, $J_{1,2}$ 8, $J_{2,3}$ 9.5 Hz, H-2), 3.91 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.68–3.79 (m, 4 H, H-6a, H-6b, H-2′, H-3′), 3.63 (br d, 1 H, $J_{3',4'}$ 1 Hz, H-4′), 3.44–3.55 (m, 2 H, H-5, OCH_2CH_2), 1.52–1.68 (m, 2 H, OCH_2CH_2), 1.22–1.43 (10 H, octyl CH_2), 1.18 (d, 3 H, $J_{5',6'}$ 6.5 Hz, H-6′), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ 102.59 (d, 1 C, $J_{C1,F}$ 12.8 Hz, C-1), 99.83 (d, 1 C, $J_{C1',F}$ 6 Hz, C-1′), 96.60 (d, 1 C, $J_{C3,F}$ 184.0 Hz, C-3), 75.15 (d, 1 C, $J_{C5,F}$ 6.9 Hz, C-5), 74.01 (d, 1 C, $J_{C2,F}$ 16.6 Hz, C-2), 73.75 (C-3′), 71.53 (C-4′), 70.78 (OCH_2CH_2), 69.97 (C-2′), 68.50 (d, 1 C, $J_{C4,F}$ 16.5 Hz, C-4), 67.44 (C-5′), 61.94 (d, 1 C, $J_{C6,F}$ 3.1 Hz, C-6), 32.99, 30.97, 30.57, 30.41, 27.38, 23.67 (octyl CH_2), 16.62 (C-6′), 14.40 (octyl CH_3); ^{19}F NMR (CD_3OD): δ −198.4 (dt, 1 F, $J_{H3,F}$ 48.5, $J_{H2,F} = J_{H4,F} = 7.5$ Hz, F-3). FABMS: m/z 463 $[M + Na]^+$ and 441 $[M + H]^+$ ($C_{20}H_{37}FO_9$ requires m/z 440).

Octyl 4,6-O-benzylidene-2,3-di-O-benzyl-β-D-glucopyranoside (**47**).—Octyl β-D-glucopyranoside (**46**, 1.05 g, 3.61 mmol) was dissolved in PhCHO (10 mL) and $ZnCl_2$ (750 mg, 5.41 mmol) was added. After stirring overnight, the solution was cooled to 0°C and water (35 mL) was added. Stirring was continued for 1 h and then the mixture was diluted with CH_2Cl_2 and washed with $NaHCO_3$, water, and brine. The organic layer was dried with Na_2SO_3 and evaporated under reduced pressure to remove the PhCHO. The residue was redissolved in CH_2Cl_2 and extracted with 2 M NaOH to remove traces of benzoic acid. The organic layer was then washed with water and brine, and evaporated. The compound was not characterized, but directly benzylated by dissolving in DMF (25 mL) and adding NaH (650 mg, 80% dispersion in oil, 24.64 mmol). After stirring for 30 min, $PhCH_2Br$ (3 mL, 25.20 mmol) was added and the mixture stirred for 20 h. Methanol was added to decompose the excesss NaH and the mixture diluted with CH_2Cl_2 and then washed with water and brine. After solvent evaporation, column chromatography of the resulting clear oil (9:1 hexane–EtOAc) gave **47** (1.53 g, 76%) as a white solid; $[\alpha]_D$ −39.1° (*c* 1, $CHCl_3$); R_f 0.52 (9:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.23–7.55 (m, 15 H, Ph), 5.60 (s, 1 H, $PhCHO_2$), 4.93 (d, 2 H, J_{gem} 11.5 Hz, 2 $PhCH_2$), 4.82, 4.77 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.52 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.36 (dd, 1 H, $J_{6a,6b}$ 10.5, $J_{5,6a}$ 5 Hz, H-6a), 3.95 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.82 (t, 1 H, $J_{3,4} = J_{4,5} = 10$ Hz, H-4), 3.64–3.77 (m, 2 H, H-3, H-6b), 3.57 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.47 (t, 1 H, $J_{1,2} = J_{2,3} = 8$ Hz, H-2), 3.43 (dt, 1 H, $J_{5,6a}$ 5, $J_{4,5} = J_{5,6b} = 10$ Hz, H-5), 1.55–1.75 (m, 2 H, OCH_2CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.62, 138.47, 137.42 (Ph quat.), 128.94, 128.35, 128.31, 127.25, 128.12, 128.04, 127.71, 127.62, 126.05 (Ph methine), 104.21 (C-1), 101.16 ($PhCHO_2$), 82.22 (C-3), 81.58 (C-2), 80.97 (C-4), 75.36, 75.14 ($PhCH_2$), 70.66 (OCH_2CH_2), 68.88

(C-6), 66.07 (C-5), 31.86, 29.82, 29.43, 29.27, 26.15, 22.69 (octyl CH_2), 14.13 (octyl CH_3). Anal. Calcd for $C_{35}H_{44}O_6$ (560.74): C, 74.97; H, 7.91. Found: C, 74.95; H, 7.87.

Octyl 2,3,6-tri-O-benzyl-β-D-glucopyranoside (**48**).—Compound **47** (1.5 g, 2.68 mmol), $NaCNBH_3$ (1.85 g, 29.5 mmol) and Methyl Orange indicator were dissolved in 25 mL dry THF containing crushed 3A molecular sieves (2 g). The solution was cooled to 0°C and then ethereal HCl was added until the red color of the solution persisted. After 1 h TLC indicated the reaction was complete and the reaction was quenched by the addtion of $NaHCO_3$. The mixture was filtered, diluted with CH_2Cl_2, washed with water and brine, and then evaporated. Column chromotography of the resulting oil (4:1 hexane–EtOAc) gave **48** (1.32 g, 88%) as a colorless oil; $[\alpha]_D$ −22.6° (*c* 0.8, $CHCl_3$); R_f 0.44 (4:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.43 (m, 15 H, Ph), 4.96, 4.93, 4.73, 4.71, 4.61, 4.58 (d, 1 H, J_{gem} 11.5 Hz, PhCH_2), 4.41 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.94 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.77 (dd, 1 H, $J_{5,6}$ 4, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.69 (dd, 1 H, $J_{5,6b}$ 5, $J_{6a,6b}$ 10.5 Hz, H-6b), 3.37–3.63 (m, 5 H, H-2, H-3, H-4, H-5, OCH_2CH$_2$), 2.53 (d, 1 H, $J_{2,2\text{-OH}}$ 2 Hz, 2-OH), 1.59–1.70 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.72, 138.54, 138.03 (Ph quat.), 128.56, 128.44, 128.39, 128.16, 127.99, 127.91, 127.83, 127.73 (Ph methine), 103.75 (C-1), 84.12 (C-3), 81.78 (C-2), 75.28, 74.74 (PhCH_2), 74.07 (C-5), 73.71 (PhCH_2), 71.74 (C-4), 70.47 (OCH_2CH$_2$), 70.47 (C-6), 31.87, 29.83, 29.45, 29.29, 26.23, 22.70 (octyl CH_2), 14.13 (octyl CH_3). Anal. Calcd for $C_{35}H_{46}O_6$ (562.75): C, 74.70; H, 8.24. Found: C, 74.58; H, 8.52.

Octyl 2,3,6-tri-O-benzyl-4-deoxy-4-fluoro-β-D-galactopyranoside (**49**).—To a solution of **48** (1.0 g, 1.78 mmol), in 19:1 CH_2Cl_2–pyridine (50 mL) at 0°C, was added dropwise in CH_2Cl_2 (2 mL) triflic anhydride (1.30 mL, 7.55 mmol). After stirring for 30 min TLC showed the starting material was gone and a new spot (R_f 0.63, 4:1 hexane–EtOAc) appeared. The mixture was then extracted with ice-cold 5% HCl and water, dried with Na_2SO_4, and evaporated to an orange liquid. The product was directly dissolved in dry THF (9 mL), cooled to 0°C, and Bu_4NF (9 mL of a 1.0 M solution in THF) was added. After stirring for 15 h and warming to room temperature, the solvent was removed and the residue chromatographed (4:1 hexane–EtOAc) to give **49** (803 mg, 80%) as a colorless oil; $[\alpha]_D$ −9.0° (*c* 0.3, $CHCl_3$); R_f 0.40 (4:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.20–7.40 (m, 15 H, Ph), 4.69–4.95 (m, 5 H, 4 PhCH_2, H-4), 4.56 (s, 2 H, PhCH_2), 4.37 (dd, 1 H, $J_{1,2}$ 8, $J_{H1,F}$ 1 Hz, H-1), 3.92 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.40–3.78 (m, 6 H, H-2, H-3, H-5, H-6, H-6, OCH_2CH$_2$), 1.58–1.70 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.60, 137.98, 137.84 (Ph quat.), 128.50, 128.44, 128.33, 128.14, 127.88, 127.83, 127.67 (Ph methine), 103.66 (C-1), 86.09 (d, 1 C, $J_{C4,F}$ 183.4 Hz, C-4), 79.04 (C-2), 79.03 (d, 1 C, $J_{C3,F}$ 18.0 Hz, C-3), 75.37, 73.77, 72.49 (PhCH_2), 72.16 (d, 1 C, $J_{C5,F}$ 18.2 Hz, C-5), 70.31 (OCH_2CH$_2$), 67.89 (d, 1 C, $J_{C6,F}$ 5.3 Hz, C-6), 31.86, 29.78, 29.44, 29.27, 26.17, 22.69 (octyl CH_2), 14.11 (octyl CH_3); ^{19}F NMR ($CDCl_3$): δ −217.3

(dt, 1 F, $J_{H4,F}$ 49.4, $J_{H5} = J_{H3,F} = 26.8$ Hz, 4-F). Anal. Calcd for $C_{35}H_{45}FO_5$ (580.74): C, 74.44; H, 8.03. Found: C, 74.70; H, 7.94.

Octyl 4-deoxy-4-fluoro-β-D-galactopyranoside (**50**).—Galactoside **49** (515 mg, 0.91 mmol), was hydrogenated in MeOH (30 mL) with 5% Pd–C (250 mg) as described for **23**. Chromatography (19:1 CH_2Cl_2–MeOH) gave the product **50** (228 mg, 85%) as a white solid; $[\alpha]_D$ −30.3° (*c* 0.6, MeOH); R_f 0.10 (19:1 CH_2Cl_2–MeOH). ^{1}H NMR (CD_3OD): δ 4.65 (dd, 1 H, $J_{3,4}$ 2.5, $J_{H4,F}$ 51 Hz, H-4), 4.21 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.86 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.40–3.75 (m, 6 H, H-2, H-3, H-5, H-6a, H-6b, OCH_2CH_2), 1.55–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ104.64 (C-1), 90.16 (d, 1 C, $J_{C4,F}$ 179.5 Hz, C-4), 75.08 (d, 1 C, $J_{C5,F}$ 18 Hz, C-5), 73.64 (d, 1 C, 18.3 Hz, C-3), 72.57 (C-2), 71.01 (OCH_2CH_2), 61.06 (d, 1 C, $J_{C6,F}$ 6 Hz, C-6), 32.98, 30.77, 30.53, 30.38, 27.05, 23.69 (octyl CH_2), 14.41 (octyl CH_3); ^{19}F NMR (CD_3OD): δ −220.1 (dt, 1 F, $J_{H4,F}$ 51, $J_{H3,F} = J_{H5,F} = 26$ Hz, F-4). Anal. Calcd for $C_{14}H_{27}FO_5$ (294.37): C, 57.13; H, 9.25. Found: C, 57.36; H, 9.54.

Octyl 3,6-di-O-benzoyl-4-deoxy-4-fluoro-β-D-galactopyranoside (**52**).—Compound **50** (101 mg, 0.34 mmol) and dibutyltin oxide (178 mg, 0.68 mmol) were refluxed in dry benzene (30 mL) overnight as described for **14**. The solution was cooled to room temperature and crushed 4A molecular sieves (500 mg) and benzoyl chloride (90 μL, 0.68 mmol) were added. After stirring for 1 h, TLC indicated complete conversion of the starting material to two different products. The solvent was evaporated and the product chromatographed (3:1 hexane–EtOAc) to give **52** (63 mg, 37%) and **51** (68 mg, 50%), both as white solids. The monoester was converted into **52** in 76% yield by dissolution of the purified **51** in CH_2Cl_2 and then addtion of 1.2 equiv of both pyridine and benzoyl chloride. The data below is for compound **52** only, support of structure **51** was the presence of 5 aromatic hydrogens and the large downfield shift of H-3 in the ^{1}H NMR spectrum. $[\alpha]_D$ +9.6° (*c* 0.6, $CHCl_3$); R_f 0.54 (3:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.98–8.15 (m, 4 H, Ph), 4.70–7.62 (m, 6 H, Ph), 5.19 (ddd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 3, $J_{H3,F}$ 27 Hz, H-3), 5.02 (dd, 1 H, $J_{3,4}$ 2.5, $J_{H4,F}$ 50 Hz, H-4), 4.64 (ddd, 1 H, $J_{6a,6b}$ 11, $J_{5,6a}$ 6.5, $J_{H6a,F}$ 1 Hz, H-6a), 4.51 (dd, 1 H, $J_{6a,6b}$ 11, $J_{5,6b}$ 7.5 Hz, H-6b), 4.45 (dd, 1 H, $J_{1,2}$ 7.5, $J_{H1,F}$ 1 Hz, H-1), 3.90–4.12 (m, 3 H, H-2, H-5, OCH_2CH_2), 3.59 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 2.41 (d, 1 H, $J_{2,2\text{-}OH}$ 2-OH), 1.62–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2). 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 166.17, 166.10 (C=O), 133.55, 133.38, 130.04, 129.76 (Ph methine), 129.55, 129.37, (Ph quat.), 128.51 (Ph methine), 103.13 (C-1), 86.31 (d, 1 C, $J_{C4,F}$ 186 Hz, C-4), 73.45 (d, 1 C, $J_{C5,F}$ 18.8 Hz, C-5), 71.18 (d, 1 C, $J_{C3,F}$ 17.2 Hz, C-3), 70.60 (OCH_2CH_2), 69.40 (C-2), 61.93 (d,1 C, $J_{C6,F}$ 5.7 Hz, C-6), 31.83, 29.61, 29.35, 29.25, 25.96, 22.67 (octyl CH_2), 14.11 (octyl CH_3); ^{19}F NMR ($CDCl_3$): −216.4 (dddd, 1 F, $J_{H4,F}$ 50, $J_{H3,F} = J_{H5,F} = 27$, $J_{H1,F}$ 1 Hz, F-4). Anal. Calcd for $C_{28}H_{35}FO_7$ (502.59): C, 66.92; H, 7.02 Found: C, 66.92; H, 6.91.

Octyl 3,6-di-O-benzoyl-4-deoxy-4-fluoro-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (**53**).—Alcohol **52** (139 mg, 0.28 mmol) and Et_4NBr (64

mg, 0.30 mmol) were fucosylated as described for compound **15** using 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide (1.11 mmol). Column chromatography of the residue (CH_2Cl_2) gave the disaccharide **53** (218 mg, 86%) as an oil; $[\alpha]_D$ −84.0° (*c* 0.1, $CHCl_3$); R_f 0.44 (CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 8.0–8.1 (m, 4 H, Ph), 7.40–7.62 (m, 6 H, Ph), 5.42 (d, 1 H, $J_{1'2'}$ 3.5 Hz, H-1'), 5.39 (ddd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 2.5, $J_{H3,F}$ 27 Hz, H-3), 5.06 (dd, 1 H, $J_{3,4}$ 2.5, $J_{H4,F}$ 50.5 Hz, H-4), 4.94, 4.75 (d, 1 H, J_{gem} 11.5 PhCH_2), 4.58–4.69 (m, 4 H, H-1, 3 PhCH_2), 4.50 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 10 Hz, H-2), 4.27–4.42 (m, 4 H, PhCH_2, H-5, H-6a, H-6b), 3.84–4.08 (m, 4 H, H-5, OCH_2CH$_2$, H-3, H-2'), 3.64 (d, 1 H, $J_{3'4'}$ 1.5 Hz, H-4'), 3.47 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 1.60–1.70 (m, 2 H, OCH$_2$CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 1.13 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH$_3$); ^{13}C NMR ($CDCl_3$): δ 166.05, 165.63 (C=O), 138.87, 138.59, 137.88, 133.69, 133.32 (Ph quat.), 129.96, 129.76 (Ph methine), 129.55, 129.10 (Ph quat.), 128.73, 128.48, 128.30, 128.19, 128.08, 127.66, 127.60, 127.43, 127.37 (Ph methine), 101.95 (C-1), 97.22 (C-1'), 86.18 (d, 1 C, $J_{C4,F}$ 185 Hz, C-4), 79.41 (C-4'), 77.90 (C-3'), 75.76 (C-2'), 75.55 (d, 1 C, $J_{C5,F}$ 17 Hz, C-5), 74.84, 73.24, 72.64 (PhCH_2), 70.91 (C-2), 70.74 (d, 1 C, $J_{C3,F}$ 18.0 Hz, C-3), 70.62 (OCH$_2$CH$_2$), 66.69 (C-5'), 61.84 (d, 1 C, $J_{C6,F}$ 6 Hz, C-6), 31.85, 29.70, 29.43, 29.31, 26.19, 22.66 (octyl CH$_2$), 16.57 (C-6'), 14.12 (octyl CH$_3$); ^{19}F NMR ($CDCl_3$): δ −217.1 (dt, 1 F, $J_{H4,F}$ 50.5, $J_{H3,F} = J_{H5,F}$ = 27 Hz, F-4). Anal. Calcd for $C_{48}H_{59}FO_9$ (799.00): C, 72.16; H, 7.44. Found: C, 72.15; H, 7.59.

Octyl 4-deoxy-4-fluoro-2-O-(α-L-fucopyranosyl)-β-D-galactopyranoside (**11**).—To a solution of protected disaccharide **53** (155 mg, 0.17 mmol) in MeOH (10 mL), 10% Pd–C (100 mg) was added, and the solution stirred under a flow of H_2 overnight. After completion of the reaction the catalyst was filtered off and the solvent evaporated. The residue was redissolved in MeOH (20 mL) and 1 M NaOH (1 mL) added, and the mixture stirred overnight. The solution was neutralized with Amberlite IR 120 (H^+) resin, evaporated, and the product further purified as described for **6** to give the product **11** (64 mg, 86%) as a white solid. ^{1}H NMR (CD_3OD): 5.20 (d, 1 H, $J_{1'2'}$ 3 Hz, H-1'), 4.69 (dd, 1 H, $J_{H4,F}$ 50.5, $J_{3,4}$ 2.5 Hz, H-4), 4.38 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.30 (q, 1 H, $J_{5'6'}$ 6.5 Hz, H-5'), 3.88 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 3.54–3.86 (m, 9 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-2', H-3', H-4') 3.52 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH$_2$), 1.50–1.65 (m, 2 H, OCH$_2$CH_2), 1.23–1.45 (10 H, octyl CH$_2$), 1.18 (d, 3 H, $J_{5'6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H J_{vic} 7 Hz, octyl CH$_3$); ^{13}C NMR (CD_3OD): δ103.13 (C-1), 101.47 (C-1'), 90.26 (d, 1 C, $J_{C4,F}$ 181 Hz, C-4), 78.50 (C-2), 75.00 (d, 1 C, $J_{C5,F}$ 18 Hz, C-5), 74.39 (d, 1 C, $J_{C3,F}$ 18.5 Hz, C-3), 73.71 (C-3'), 71.66 (C-4'), 70.92 (OCH$_2$CH$_2$), 70.48 (C-2'), 67.80 (C-5'), 61.00 (d, 1 C, $J_{C6,F}$ 5.5 Hz, C-6), 32.99, 30.92, 30.57, 30.38, 27.25, 23.67 (octyl CH$_2$), 16.75 (C-6'), 14.40 (octyl CH$_3$); ^{19}F NMR (CD_3OD): δ-220.2 (dt, 1 F, $J_{H4,F}$ 50.5, $J_{H3,F} = J_{H5,F}$ = 27.0 Hz, F-4). FABMS: *m/z* 463 $[M + Na]^+$ and 441 $[M + H]^+$ ($C_{20}H_{37}FO_9$ requires *m/z* 440).

1,2,3,4-Tetra-O-acetyl-6-deoxy-6-fluoro-galactopyranose (**55**).—6-Deoxy-6-fluoro-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose[34] (**54**, 1.54 g, 5.88 mmol) was dis-

solved in CH_2Cl_2 (2 mL), 99% CF_3CO_2H (5 mL), and water (500 μL). After stirring for 1 h the mixture was evaporated to dryness. The hydrolyzed product was not characterized, but was dissolved in pyridine (5 mL) and Ac_2O (5 mL), and stirred overnight. Then the mixture was cooled to 0°C and excess Ac_2O decomposed with MeOH. Evaporation of the solvent followed by chromatography (3:1 hexane–EtOAc) gave **55** (1.74 g, 84%) as a white foam containing both anomers (α:β ratio 1:1); R_f 0.20 (3:1 hexane–EtOAc). Partial ^{1}H NMR ($CDCl_3$): δ 6.4 (s, 1 H, H-1α), 5.74 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1β); ^{13}C NMR: δ 92.10 (C-1α), 89.60 (C-1β).

*2,3,4-Tri-*O*-acetyl-6-deoxy-6-fluoro-α-*D*-galactopyranosyl bromide* (**56**).—Peracetate **55** (1.09 g, 3.1mmol), was dissolved in CH_2Cl_2 (5 mL) and hydrobromic acid (33% in AcOH, 10 mL) was added. The mixture was stirred for 2 h and then evaporated to dryness, coevaporating with dry toluene. The crude product was purified by a rapid chromatographic separation (3:1 hexane–EtOAc) to give the product **56** (920 mg, 80%) as a crystalline solid; R_f 0.28 (6:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 6.72 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.58 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 5.43 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 3.5 Hz, H-3), 5.08 (dd, 1 H, $J_{1,2}$ 4, $J_{2,3}$ 10.5 Hz, H-2), 4.33–4.60 (m, 3 H, H-5, H-6a, H-6b), 2.15, 2.10, 2.02 (s, 3 H, acetate CH_3); ^{13}C NMR ($CDCl_3$): δ 170.04, 169.79, 169.68 (acetate C=O), 87.99 (C-1), 80.28 (d, 1 C, $J_{C6,F}$ 174 Hz, C-6), 71.59 (d, 1 C, $J_{C5,F}$ 23.6 Hz, C-5), 67.96 (C-2), 67.77 (C-3), 67.04 (d, 1 C, $J_{C5,F}$ 5.4 Hz, C-4), 20.72, 20.56, 20.51 (acetate CH_3).

*Octyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-fluoro-β-*D*-galactopyranoside* (**57**).—Compound **56** (1.43 g, 3.86 mmol), was glycosylated as described for the conversion of **36** to **37**, using silver triflate (1.49 g, 5.796 mmol), collidine (378 μL, 3.088 mmol), and octanol (1.795 mL, 11.4 mmol). The mixture was complete after 90 min. Chromatography of the crude mixture (6:1 hexane–EtOAc) gave **57** (1.19 g, 73%) as an oil; $[\alpha]_D$ −10.1° (*c* 0.8, $CHCl_3$); R_f 0.36 (6:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$): δ 5.44 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.22 (dd, 1 H, $J_{2,3}$ 10.5, $J_{1,2}$ 8 Hz, H-2), 5.03 (dd, 1 H, $J_{3,4}$ 3.5, $J_{2,3}$ 10.5 Hz, H-3), 4.51 (ddd, 1 H, $J_{5,6a}$ 6.5, $J_{6a,6b}$ 9.5, $J_{H6a,F}$ 46.5 Hz, H-6a), 4.48 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.43 (ddd, $J_{5,6b}$ 5.5, $J_{6a,6b}$ 10, $J_{H6b,F}$ 46.5 Hz, C-6b), 3.87–4.01 (m, 2 H, H-5, OCH_2CH_2), 3.48 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 2.15, 2.08, 1.99 (s, 3 H, acetate CH_3), 1.50–1.65 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 13 H, octyl CH_2, H-6). 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ170.21 170.13, 169.36 (acetate C=O), 101.39 (C-1), 80.86 (d, 1 C, $J_{C6,F}$ 172 Hz, C-6), 71.56 (d, 1 C, $J_{C5,F}$ 23.5 Hz, C-5), 70.94 (C-3), 70.39 (OCH_2CH_2), 69.00 (C-2), 67.21 (d, 1 C, $J_{C4,F}$ 6 Hz, C-4), 31.81, 29.42, 29.29, 29.25, 25.82, 22.66 (octyl CH_2), 20.73, 20.62, 20.59 (acetate CH_3), 14.10 (octyl CH_3); ^{19}F NMR ($CDCl_3$): δ −230.9 (dt,1 F, J_{H6F} 46.5, $J_{H5,F}$ 12.5 Hz, F-6). Anal. Calcd for $C_{20}H_{33}FO_8$ (420.48): C, 57.13; H, 7.91. Found: C, 56.85; H, 7.85.

*Octyl 6-deoxy-6-fluoro-β-*D*-galactopyranoside* (**58**).—Galactoside **57** (1.06 g, 2.54 mmol), was dissolved in MeOH (20 mL) and NaOMe (100 mg) was added. After stirring for 2 h, the solution was neutralized by the addition of prewashed Amberlite IR 120 (H^+) resin. Evaporation of the solvent followed by chromatogra-

phy (19:1 CH_2Cl_2–MeOH) gave **58** (673 mg, 90%) as an oil; $[\alpha]_D$ −13.1° (*c* 0.7, MeOH); R_f 0.11 (19:1 CH_2Cl_2–MeOH). ^1H NMR (CD_3OD): δ 4.58 (ddd, 1 H, $J_{5,6a}$ 5, $J_{6a,6b}$ 9, $J_{H6a,F}$ 46.5 Hz, H-6a), 4.43 (ddd, $J_{5,6b}$ 7, $J_{6a,6b}$ 9, $J_{H6b,F}$ 48 Hz, C-6b), 4.22 (dd, 1 H, $J_{1,2}$ 7.5, $J_{1,6F}$ 1 Hz, H-1), 3.85 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.71–3.82 (m, 2 H, H-4, H-5), 3.23–3.59 (m, 3 H, H-2, H-3, OCH_2CH_2), 1.53–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 13 H, octyl CH_2, H-6). 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ104.91 (C-1), 83.65 (d, 1 C, $J_{C6,F}$ 167.5 Hz, C-6), 74.72 (C-3), 74.70 (d, 1 C, $J_{C5,F}$ 21.9 Hz, C-5), 72.40 (C-2), 70.94 (OCH_2CH_2), 69.94 (d, 1 C, $J_{C4,F}$ 6 Hz, C-4), 32.98, 30.83, 30.52, 30.38, 27.08, 23.69 (octyl CH_2), 14.40 (octyl CH_3); ^{19}F NMR (CD_3OD): δ −230.0 (ddd, 1 F, $J_{H6a,F}$ 46.5, $J_{H6b,F}$ 48, $J_{H5,F}$ 13.5 Hz, F-6). Anal. Calcd for $C_{14}H_{27}FO_5$ (294.37): C, 57.13; H, 9.25. Found: C, 57.09; H, 9.56.

Octyl 3,4-O-benzylidene-6-deoxy-6-fluoro-β-D-galactopyranoside (**59**).—Compound **58** (162 mg, 0.55 mmol) and $PhCH(OMe)_2$ (250 μL, 1.65 mmol) were dissolved in MeCN (20 mL) and TsOH (5 mg) added. After stirring for 2 h the mixture was neutralized with Et_3N, evaporated and chromatographed (3:1 hexane–EtOAc). Both possible diastereomers were present in a 1:1 ratio (179 mg, 85%) and were easily separable by chromatography. Only the faster moving diastereomer was fully characterized and used; $[\alpha]_D$ +19.8° (*c* 0.5, $CHCl_3$); R_f 0.45 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.3–7.5 (m, 5 H, Ph), 6.15 (s, 1 H, $PhCHO_2$), 4.75 (ddd, 1 H, $J_{5,6a}$ 7, $J_{6a,6b}$ 10, $J_{H6a,F}$ 48 Hz, H-6), 4.66 (ddd, $J_{5,6b}$ 4.5, $J_{6a,6b}$ 10, $J_{H6b,F}$ 46.5 Hz, C-6b), 4.46 (dd, 1 H, $J_{3,4}$ 5.5, $J_{2,3}$ 8 Hz, H-3), 4.26 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.13 (dd, 1 H, $J_{3,4}$ 5.5, $J_{4,5}$ 2 Hz, H-4), 4.03 (dddd, $J_{5,6a}$ 7, $J_{5,6b}$ 4.5, $J_{4,5}$ 2, $J_{5H,F}$ 14.5 Hz), 3.96 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.73 (t, 1 H, $J_{1,2} = J_{2,3} = 8$ Hz, H-2), 3.55 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 2.54 (br s, 1 H, 2-OH), 1.61–1.70 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ 138.32 (Ph quat.), 129.26, 128.46, 126.20 (Ph methine), 103.65 (C-1), 102.08 ($PhCHO_2$), 82.38 (d, 1 C, $J_{C6,F}$ 170.5 Hz, C-6), 79.66 (C-3), 73.02 (d, 1 C, $J_{C4,F}$ 7 Hz, C-4), 72.37 (d, 1 C, $J_{C5,F}$ 22 Hz, C-5), 71.06 (C-2), 70.33 (OCH_2CH_2), 31.86, 29.65, 29.41, 29.26, 26.02, 22.69 (octyl CH_2), 14.13 (octyl CH_3); ^{19}F NMR ($CDCl_3$): δ −228.0 (ddd, 1 F, $J_{H6a,F}$ 48, $J_{H6b,F}$ 46.5, $J_{H5,F}$ 14.5 Hz, F-6). Anal. Calcd for $C_{21}H_{31}FO_5$ (382.48): C, 65.95; H, 8.17. Found: C, 65.76; H, 8.06.

Octyl 3,4-O-benzylidene-6-deoxy-6-fluoro-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranoside (**60**).—Alcohol **59** (111 mg, 0.29 mmol) with Et_4NBr (67 mg, 0.32 mmol) was fucosylated as described for compound **15** using 2,3,4-tri-*O*-benzyl-L-fucopyranosyl bromide (1.16 mmol). Column chromatography of the residue (9:1 hexane–EtOAc) gave the disaccharide **60** (208 mg, 90%) as an oil; $[\alpha]_D$ −66.7° (*c* 0.7, $CHCl_3$); R_f 0.75 (3:1 hexane–EtOAc). ^1H NMR ($CDCl_3$): δ 7.18–7.5 (m, 20 H Ph), 6.10 (s, 1 H, $PhCHO_2$), 5.51 (d, 1 H, $J_{1'2'}$ 4 Hz, H-1'), 5.00, 4.89 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.57–4.83 (m, 7 H, 4 $PhCH_2$, H-6a, H-6b, H-3), 4.43 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 4.28 (q, 1 H, $J_{5',6'}$ 6.5 Hz, H-5'), 4.15 (dd, 1 H, $J_{3,4}$ 5.5, $J_{4,5}$ 2 Hz, H-4), 4.09 (dd, 1 H, $J_{2'3'}$ 10.5, $J_{1'2'}$ 4 Hz, H-2'), 3.88–4.04 (m, 4

H, OCH_2CH_2, H-5, H-2, H-3'), 3.63 (d, 1 H, $J_{3',4'}$ 2 Hz, H-4'), 3.45 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 1.50–1.60 (m, 2 H, OCH_2CH_2), 1.20–1.40 (m, 10 H, octyl CH_2), 1.13 (d, 1 H, $J_{5',6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H, J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR ($CDCl_3$): δ138.99, 138.73, 138.33, 138.14 (Ph quat.), 129.26, 128.37, 128.37, 128.33, 128.22, 128.13, 128.10, 127.65, 127.46, 127.35, 126.27 (Ph methine), 103.54 (C-1), 100.81 ($PhCHO_2$), 96.36 (C-1'), 82.40 (d, 1 C, $J_{C6,F}$ 170.5 Hz, C-6), 81.36 (C-3), 79.48 (C-2), 78.00 (C-4'), 76.22 (C-3'), 74.75 ($PhCH_2$), 73.35 (d, 1 C, $J_{C4,F}$ 6.8 Hz, C-4), 73.34, 73.23 ($PhCH_2$), 72.90 (C-2'), 72.12 (d, 1 C, $J_{C5,F}$ 21.9 Hz, C-5), 69.69 (OCH_2CH_2), 66.48 (C-5'), 31.83, 29.74, 29.42, 29.31, 26.18, 22.64 (octyl CH_2), 16.55 (C-6'), 14.09 (octyl CH_3); ^{19}F NMR ($CDCl_3$): δ −228.5 (dt, 1 F, $J_{H6,F}$ 46.5, $J_{H5,F}$ 15 Hz, F-6). Anal. Calcd for $C_{48}H_{59}FO_9$ (799.00): C, 72.16; H, 7.44. Found: C, 72.08; H, 7.56.

Octyl 6-deoxy-6-fluoro-2-O-(α-L-fucopyranosyl)-β-D-galactopyranoside (**12**).—The protected disaccharide **60** (97 mg, 0.12 mmol) was dissolved in MeOH (10 mL) and 10% Pd–C (50 mg) was added, and the solution stirred under a flow of H_2 overnight. After completion of the reaction the catalyst was filtered off, and the product purified as described for **6** to give the product **12** (48 mg, 90%) as a white solid. ^1H NMR (CD_3OD): δ 5.08 (br s, 1 H, H-1'), 4.54 (m, 2 H, H-6a, H-6b), 4.34 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.28 (q, 1 H, $J_{5',6'}$ 6.5 Hz, H-5'), 3.85 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 3.58–3.82 (m, 7 H, H-2, H-3, H-4, H-5, H-2', H-3', H-4'), 3.51 (dt, 1 H, J_{gem} 10, J_{vic} 7 Hz, OCH_2CH_2), 1.52–1.68 (m, 2 H, OCH_2CH_2), 1.22–1.43 (10 H, octyl CH_2), 1.18 (d, 3 H, $J_{5',6'}$ 6.5 Hz, H-6'), 0.88 (t, 3 H J_{vic} 7 Hz, octyl CH_3); ^{13}C NMR (CD_3OD): δ 103.43 (C-1), 101.56 (d, 1 C, $J_{C1',F}$ 4 Hz, C-1'), 83.59 (d, 1 C, $J_{C6,F}$ 167.5 Hz, C-6), 78.82 (C-2), 75.59 (d, 1 C, $J_{C5,F}$ 22 Hz, C-5), 75.37 (C-3), 73.71 (C-3'), 71.72 (C-4'), 70.85 (OCH_2CH_2), 70.57 (C-2'), 70.01 (d, 1 C, $J_{C4,F}$ 6 Hz, C-4), 67.78 (C-5'), 32.98, 30.96, 30.55, 30.37, 27.24, 23.66 (octyl CH_2), 16.76 (C-6'), 14.40 (octyl CH_3); ^{19}F NMR (CD_3OD): δ −232.3 (dt, 1 F, $J_{H6,F}$ 47.5, $J_{H5,F}$ 13.5 Hz, F-6). FABMS: *m/z* 463 $[M + Na]^+$ and 441 $[M + H]^+$ ($C_{20}H_{37}FO_9$ requires *m/z* 440).

Measurement of enzyme kinetics.—Radiochemical assays were based on modification of a previously described method which takes advantage of the use of hydrophobic acceptors and products to facilitate the removal of unreacted radiolabelled donor from reaction products[18]. Human serum used as a source of the A- and B-transferases was prepared by allowing freshly drawn blood to clot at room temperature for 2 h, refrigerating overnight at 4°C and centrifuging to remove blood clots. The serum was then stored frozen at −20°C in 100-μL aliquots until use. Incubations for the A and B assays were carried out in 600-μL plastic microfuge tubes at 37°C.

For the A-transferase, all assays were carried out in a total volume of 66 μL with 50 mM sodium cacodylate buffer, pH 6.9, containing 20 mM $MnCl_2$, 30 μM UDP-GalNAc, 0.2 μCi UDP-[6-^{3}H]GalNAc, and 10 μL of human serum containing the A-transferase (61 μU/mL serum). Under these conditions, the rate of product formation with the native disaccharide **6** was shown to be linear up to a

time of 60 min. Incubations were carried out for 45 min and then quenched by the addition of EDTA (400 μL of a 23 mM solution). The mixtures were transferred to pre-equlibrated[18] C_{18} Sep-Pak cartridges and the unreacted radiolabelled donor removed by washing with dil NH_3 and then water until background counts were obtained. The radiolabelled product was eluted with MeOH (1×3 mL) and quantitated by liquid scintillation[18]. The K_m of **6** was determined to be 1.50 μM under these conditions. Assays to test activity as an acceptor were carried out at concentrations of 2.5 μM. The results are presented in Table I. To test for inhibitory activity, the potential inhibitor (25 μM) was added to **6** at 2.5 μM. The results are recorded in Table III. At concentrations of **6** greater than 25 μM, substrate inhibition was observed. K_m determinations for all compounds were carried out at the following concentrations: 25, 20, 15, 12.5, 10, 7.5, 6.25, 3.13, 1.56, and 0.78 μM. K_i determinations for compound **7** were done with inhibitor concentrations of 25, 50, and 75 μM. For compound **10**, inhibitor concentrations of 44, 88, and 132 μM were used.

For the B-transferase, assay conditions were identical to those described above except that the solution contained 30 μM UDP-Gal, 0.2 μCi UDP-[6-^{3}H]Gal, 250 μM ATP, and 25 μL of human serum containing the B-transferase (12.8 μU/mL serum). Using these conditions, the rate of product formation with the native disaccharide **6** was linear up to a time of 180 min. Incubations were carried out for 120 min. The K_m of **6** was 21.91 μM under these conditions. Assays to test activity as an acceptor were carried out at concentrations of 10 μM. To test for inhibitory activity, the potential inhibitor (100 μM) was added to disaccharide **6** at 10 μM. At concentrations of **6** greater than 50 μM, substrate inhibition was observed. See Tables I and III for results. In determining K_m values, the following substrate concentrations were used. Compound **6**: 50, 37.5, 25, 18.75, 12.5, 6.25, 3.13, and 1.56 μM. Compounds **9** and **12**: 150, 125, 100, 75, 50, 37.5, 25, 18.75, and 12.5 μM. Inhibitor concentrations of 10, 20, and 30 μM were used in the determination of the K_i of **7**. In determining the K_i of **10**, inhibitor concentrations of 60, 150, and 200 μM were used.

Rate data were fitted to the Michaelis–Menten equation using unweighted nonlinear regression with the SigmaPlot 4.0 program to estimate the kinetic parameters shown in Tables II and IV. Compounds **7** and **10** were determined to be competitive inhibitors of **6** by fitting the data to an equation for competitive inhibition using the SigmaPlot 4.0 program.

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