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Synthesis of α-L-Fucopyranosyl Disaccharides with Thioglycosidic Linkages and Characterization of α-L-Fucosidases from Bovine Kidney and Epididymis by their Inhibitory Activities

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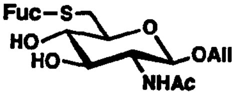
Abstracts: Sulfur-linked disaccharide analogs of three α-L-fucopyranosyl 2-acetamido-2-deoxy-β-D-glucopyranosides and one α-L-fucopyranosyl β-D-galactopyranoside were synthesized by substitution reactions of sulfonates and ring-opening reactions of aziridine as well as oxirane derivatives using 1-thio-α-L-fucopyranose as nucleophile. Fucosidases from bovine kidney and epididymis were inhibited by all of these disaccharide analogs and their Ki values range from 0.65 to 4.9 mM.

INTRODUCTION

Oligosaccharides containing thioglycosidic linkages are well-known and easily available chemical tools for studying behaviours of carbohydrate hydrolases such as exoglycosidases[1] and endoglycosidases,[1,2] because the linkages are not affected enzymatically and the unnatural oligosaccharides behave as inhibitors. α-L-Fucopyranosyl residue is involved in many biologically important oligosaccharides,[3] and α-L-fucosidase (EC3.2.1.15) hydrolyzes the terminal α-L-fucosyl linkage. Gamete recognition between fucose-containing glycoconjugates and α-L-fucosidase was suggested for ascidian[4] and mammal.[5] The most abundant linkages of L-fucose in glycoproteins and glycolipids are α(1→3), α(1→4), and α(1→6) to 2-acetamido-2-deoxy-D-glucose (D-GlcNAc) and α(1→2) to D-galactose (D-Gal). The substrate specificity of α-L-fucosidase differs with its source and has scarcely been reported for the above described α-L-fucosyl GlcNAc and Gal disaccharides except in the case of α-L-fucosidase from human serum.[6] In order to examine the linkage specificity of α-L-fucosidase, four kinds of sulfur-linked disaccharides **1** – **4** were synthesized and a significant difference in their inhibitory activities was observed.



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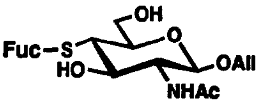

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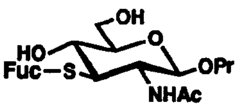

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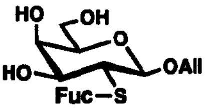
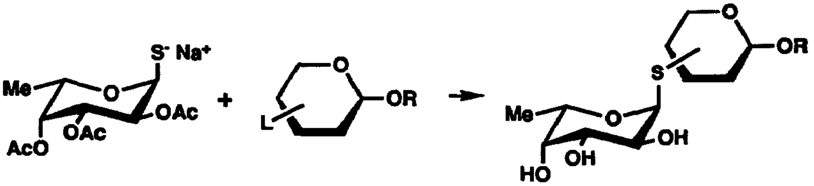


4

Fuc = α-L-fucopyranosyl

RESULTS AND DISCUSSION

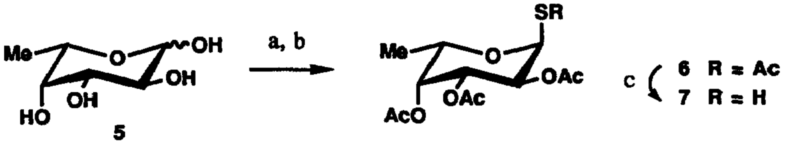
General and effective *O*-glycosylation methods[7] proceed by nucleophilic attack of the hydroxyl group of the acceptor sugar on the electrophilic anomeric carbon of the donor sugar. The formation of the glycosidic linkage by coupling of the donor glycosyloxy anion as nucleophile is limited[7b] and unpractical. On the contrary, thioglycosidic linkage has been formed effectively by the same coupling, *i.e.*, glycosylthio anion as nucleophile, due to higher nucleophilicity of the sulfur atom compared to the oxygen atom. The strategy selected for synthesis of the *S*-linked disaccharides **1** – **4** is shown in Scheme 1, where the acceptor sugars were designed considering their reactivities as electrophile.



L =leaving groups: 6-OTs, 4-OTf, NTs(2,3-aziridine), O (2,3-oxirane)

Scheme 1. Synthetic strategy of S-linked α-L-fucopyranosyl disaccharides.

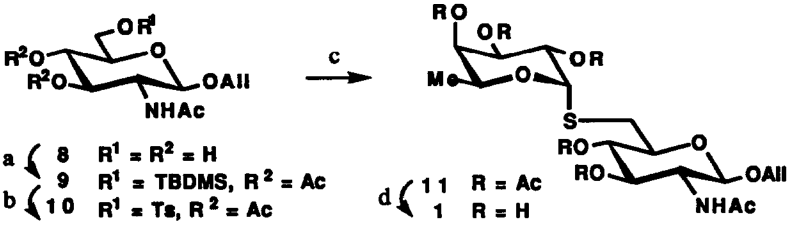
In this strategy the anomeric configuration is maintained during the coupling, because the anomerization of the glycosylthio anion is very slow. In order to utilize this benefit an efficient preparative method of 1-thio-α-L-fucopyranose triacetate (**7**) is necessary. Matta *et al.* reported[8] conversion of L-fucose to the β-anomer of **6** *via* 2-*S*-β-L-fucosyl-2-thiopseudourea and anomerization of the β-anomer of **6** to **7**, which, however, was not isolated. After unsuccessful trials of β-L-fucopyranosyl chloride preparation[9] and addition of thioacetic acid in the presence of *tert*-BuOOH[10] to 2-hydroxy-L-fucal triacetate, the following facile method was found. Condensation of L-fucose (**5**) with thioacetic acid in the presence of hydrogen chloride at room temperature for 4 h, followed by acetylation, gave 1-thio-α-L-fucopyranose tetraacetate (**6**) in 31% yield. The corresponding β-pyranose and α,β-furanose isomers were also formed. Selective *S*-deacetylation of **6** with 2-aminoethanethiol in the presence of DL-1,4-dithiothreitol gave 1-thiol **7** in 89% yield. Both **6** and **7** could be used as nucleophiles for *S*-linked disaccharide synthesis.



Scheme 2. Preparation of 1-thio-α-L-fucopyranose tetraacetate.

Reagents and conditions: (a) AcSH, HCl; (b) Ac_2O, pyridine, DMAP, 31%; (c) 0.5 eq. 1,4-dithiothreitol 1.1 eq. $H_2NCH_2CH_2SH$ / CH_3CN, 56°C, 89%.

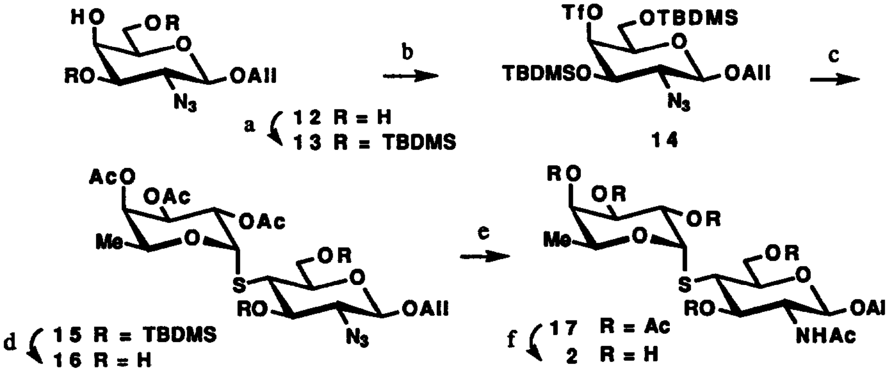
The α(1→6) thiofucosyl linkage was formed as planned highly efficiently by the substitution reaction of a 6-*O*-tosyl derivative (**10**) of GlcNAc in DMF with the thiolate nucleophile, formed by treatment of **6** with sodium hydride, to give **11** in 99% yield. The 6-tosylate **10** was prepared from allyl 2-acetamido-2-deoxy-β-D-glucopyranoside **8** in 35% total yield *via* 6-*tert*-butyldimethylsilyl (TBDMS) ether **9**. *O*-Deacetylation of the disaccharide **11** gave the α(1→6) linked isomer **1** in 31% overall yield from **8**.



Scheme 3. Synthesis of α(1→6) linked disaccharide.

Reagents and conditions: (a) 1) TBDMSCl, imidazole / DMF; 2) Ac_2O, DMAP / pyridine, 61% (2 steps). (b) 1) 60% AcOH, 70°C; 2) TsCl / pyridine, 60% (2 steps). (c) 1)7, NaH / DMF; 2) Ac_2O / pyridine, DMAP, 99%; 3) NaOMe / MeOH, 91%.

For the construction of α(1→4) linkage allyl 2-azido-2-deoxy-β-D-galactopyranoside (**12**) was selected as a precursor of GlcNAc moiety. Its 4-triflate **14** was prepared *via* the corresponding 3,6-bis-*O*-TBDMS derivative **13**, which was deduced to be more reactive than 3,6-di-*O*-pivaloyl analog, which was previously[11] used for preparation of a 4-thio derivative of GlcNAc. The same nucleophilic substitution of **14** with **7** gave the *S*-linked disaccharide **15** in 68% yield including the 4-*O*-triflylation step. *O*-Desilylation of **15**, followed reduction of the azido group with hydrogen sulfide, purification as the peracetate **17** and *O*-deacetylation, gave the α(1→4) linked isomer **2** in 57% total yield.

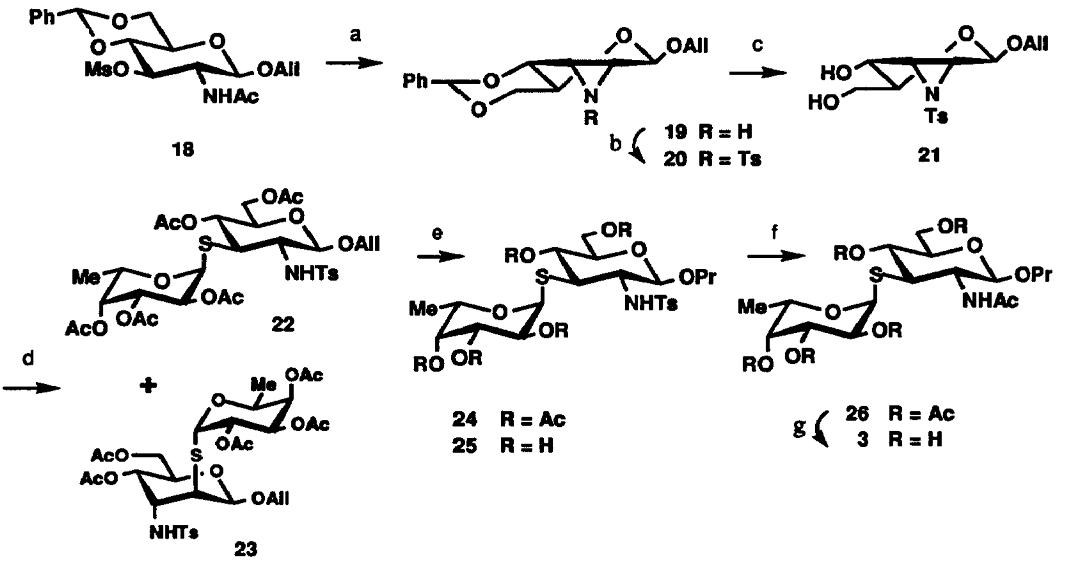


Scheme 4. Synthesis of α(1→4) linked disaccharide.

Reagents and conditions: (a) TBDMSCl, imidazole / DMF, 60°C, 58%. (b) Tf_2O, pyridine, DMAP / CH_2Cl_2. (c) 1) 7,NaH/DMF; 2) Ac_2O / pyridine, DMAP, 68% (3 steps). (d) 1)Bu_4NF / THF; 2) Ac_2O, DMAP / pyridine, 91% (2 steps). (d) 1)H_2S, pyridine, / H_2O; 2) Ac_2O, DMAP / pyridine, 97% (2 steps); 3) NaOMe / MeOH, 65%.

It is rather well known[12] that nucleophilic substitutions at C-3 of GlcNAc derivatives give often cumbersome results. On the other hand, an introduction of benzylthio group at C-3 position *via* 2,3-epimino derivative was reported to be highly regioselective.[12] 4,6-*O*-Benzylidene-2,3-epimino-β-D-allopyranoside (**19**) was prepared in 52% yield (2 steps) *via* the 3-mesylate **18** in the same manner as reported by Meyer zu Reckendorf and Lenzen[13] for the corresponding methyl glycoside. In order to elevate the reactivity of the aziridine ring tosyl group was introduced at the nitrogen (**20**) and *O*-debenzylidenated to give a coupling partner **21** quantitatively.

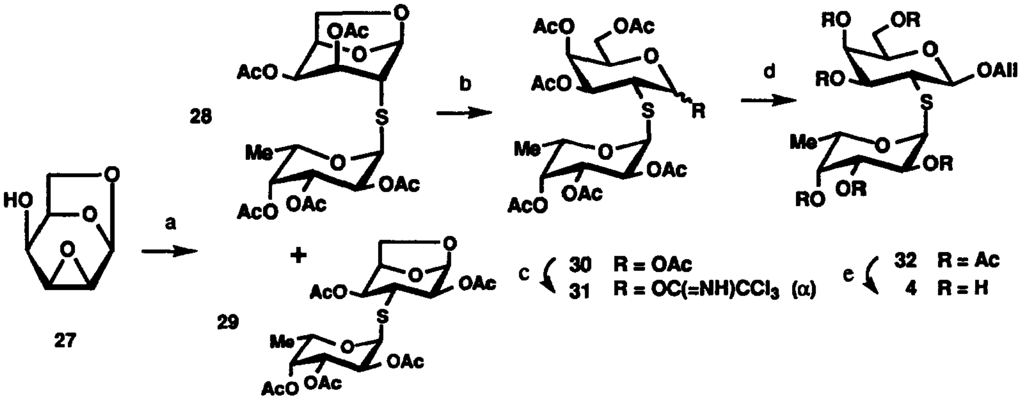
The ring opening reaction of **21** with **6** in the presence of sodium methoxide in methanol at reflux, followed by acetylation, gave a mixture of the desired disaccharide **22** and its D-*altro* isomer **23** with a ratio of 2 : 1 in 92% yield, which were separated on a column of silica gel with toluene-ethyl acetate. *N*-Detosylation under several reported methods,[14] where *O*-allyl group can survive, was unsuccessful. Then, after conversion of the aglycon moiety from allyl to propyl by catalytic hydrogenation, thus obtained α(1→3) linked disaccharide **24** was subjected to Birch reduction, followed by acetylation for purification and *O*-deacetylation, to obtain **3** in 81% total yield.



Scheme 5. Synthesis of α(1→3) linked disaccharide.

Reagents and conditions: (a) MsCl / pyridine, 71%. (b) 1) i-PrONa / i-PrOH-dioxane, reflux, 73%; 2) TsCl / pyridine, 98%. (c) H$^+$resin / 80% MeOH; 60°C, quant. (d) 1) **7**, NaOMe / MeOH, reflux; 2) Ac_2O / pyridine, DMAP, **22**: 63%, **23**: 29% (3 steps). (e) 1) Pd/C, H_2 / MeOH, quant.; 2) NaOMe / MeOH, 90%. (f) 1) Na / NH_3, THF, -78°C; 2) Ac_2O, DMAP / pyridine, 85%. (g) NaOMe / MeOH, 94%.

2-Thio-D-galatopyranoside derivative was prepared in a moderate yield by mercaptonitration[15] of D-galactal triacetate with potassium thiobenzoate in the presence of ceric ammonium nitrate. Although introduction of sulfur atom at C-2 by substitution of triflate or ring-opening reaction of epoxide was reported, no examples of D-*talo* isomer which gives D-galactose derivative was found. Thus the latter possibility was examined using **6** as nucleophile. The coupling of 1,6:2,3-dianhydro-D-talopyranose (**27**) with **6** in highly concentrated solution (2.6 M for **6**) in methanol in the presence of sodium methoxide gave a desired C_2-thiofucosylated D-*galacto* isomer **28** and its C_3-linked D-*allo* isomer **29** in 87% and 7% yields, respectively. The ring-opening reaction in a diluted solution (0.9 M) resulted in a prolonged reaction time and a reduced yield of **28** due to the anomerization of 1-thio-L-fucose. Here the ring-opening reaction seems to proceed under the control of Fürst-Plattner rule.[16] However, it is noteworthy that a distinct reverse regioselectivity in the ring-opening reaction of the corresponding D-*manno* isomer (C-4 epimer) of **27** with benzyl mercaptan was reported.[17] Considering the anomeric configuration of D-galactose in natural glycoconjugates the α(1→2) linked disaccharide **28** was converted to the β-glycoside **32** *via* 1-acetate (**30**) and 1-*O*-trichloroacetimidate (**31**). The glycosidation reaction with allyl alcohol in the presence of boron trifluoride etherate gave the β-glycoside **32** predominately in 90% yield. *O*-Deacetylation of **32** gave the disaccharide **4** quantitatively. Here described synthetic methods, especially by the ring-opening reactions of epimino and oxirane derivatives, proved to be effective for the construction of thioglycosidic oligosaccharides.



Scheme 6. Synthesis of α(1→2) linked disaccharide.

Reagents and conditions: (a) 1) **6**, NaOMe / MeOH, reflux; 2) Ac_2O / pyridine, DMAP, **28**: 87%, **29**: 7%. (b) Ac_2O / AcOH, H_2SO_4, quant. (α:β=88:12). (c) 1) $H_2NNH_2 \cdot AcOH$, DMF, 50°C, 2) CCl_3CN, DBU / CH_2Cl_2 (2 steps, 78%). (d) AllOH, MS4A, $BF_3 \cdot OEt_2$ / CH_2Cl_2, -45°C, 98%. (e) NaOMe / MeOH, quant.

The structures of the above described disaccharide derivatives were confirmed by ^1H- and ^{13}C-NMR data. The position where the 1-thio-α-L-fucopyranosyl residue is introduced is clearly indicated by the higher chemical shift (from 2.8 to 3.4 ppm depending on the position and orientation). The coupling constants of the ring protons, *i.e.* $J_{2,3}$ = 10.3 and $J_{3,4}$ = 10.1 Hz for **22**, $J_{2,3}$ = 5.6 and $J_{3,4}$ = 4.3 Hz for **23**, $J_{3,4}$ = 5.0 Hz for **28** and $J_{3,4}$ = 10.1 Hz for **29**, also support the configuration especially for the ring-opening products.

α-L-Fucosidase are important enzymes in the metabolism of L-fucose-containing biological substances and have been investigated extensively.[18] Human serum α-L-fucosidase[6] is one of the well-characterized glycosidase and was demonstrated to hydrolyze the α(1→2) linkage effectively. On the other hand, commercially available α-L-fucosidases from bovine kidney and epididymis[19] are known to be able to hydrolyze all the four kinds of α-L-fucopyranosyl linkages as well as *p*-nitrophenyl α-L-fucopyranoside, but enzymological kinetic data have not been reported. Thus our synthesized *S*-linked oligosaccharides were examined at first toward these α-L-fucosidases. Inhibitory activities of the *S*-linked oligosaccharides **1** – **4** were examined using *p*-nitrophenyl α-L-fucopyranoside as the substrate, and expressed in the term of Ki values, which were estimated based on the Lineweaver-Burk plot as summarized in Table 1. The most remarkable inhibition was observed for the α(1→3) linked disaccharide **3** with a mode of competitive inhibition. Other *S*-linked disaccharides **1**, **2** and **4** showed mixed inhibition. As preliminary reported[20] 5-thio-α-L-fucopyranosyl analog of **4** shows a potent competitive inhibition (Ki = 30 μM) against α-L-fucosidase from bovine epididymis, the observed mixed inhibition of **4** is deduced to be attributed to the effect of its rather high concentration (Ki = 1.1 mM). Here observed difference in the inhibitory activities of four S-linked α-L-fucopyranosyl disaccharides indicates a usefulness of these disaccharide analogs for characterization of exoglycosidases.

Table 1. Inhibitory activities of sulfur-linked disaccharide analogs **1** – **4** toward α-L-fucosidases

Disaccharide analog	Ki values (mM) and inhibition mode[a]	
	bovine kidney	bovine epididymis
1	4.5 (mixed,[b] α = 9)	4.7 (mixed,[b] α = 7)
2	4.9 (mixed,[b] α = 2)	3.5 (mixed,[b] α = 4)
3	0.65 (competitive)	0.66 (competitive)
4	0.88 (mixed,[b] α = 0.5)	1.1 (mixed,[b] α = 0.5)

[a] The inhibition modes were indicated by Lineweaver-Burk plots and replots of the slope as well as intercept versus the inhibitor concentration.

[b] Linear mixed-type inhibition[21] which may be considered as a mixture of partial competitive inhibition and pure noncompetitive inhibition.

EXPERIMENTAL

General method. Melting points were determined with a Mel-Temp. apparatus and are not corrected. Optical rotations were measured using a 0.5 dm tube and a JASCO DIP-4 Polarimeter. . NMR spectra were recorded at 270 MHz with a JEOL JNM-EX-270 in $CDCl_3$ with tetramethylsilane as a internal standard, unless stated otherwise. Column chromatography was performed on Wakogel C-300 (Wako Pure Chemical Industries, Ltd.)

2,3,4-Tri-*O*-acetyl-1-*S*-acetyl-1-thio-α-L-fucopyranose (6). Into thioacetic acid (100 mL) was introduced hydrogen chloride at 0°C. To the saturated solution was added **5** (9.84 g, 60 mmol) with stirring at 0°C and this temperature was maintained for 10 min. Then the mixture was kept at room temperature for 4 h. After evaporation *in vacuo*, the resulting syrup was acetylated with Ac_2O (50 mL), pyridine (50 mL), and DMAP (catalytic amount) to give **6** (6.56 g, 31%) after workup and chromatography with 10 : 1 hexane-EtOAc. Compound **6** had mp 119-120°C; $[\alpha]_D^{20}$ -156 (c 0.52, $CHCl_3$); ^1H NMR data: δ 6.23 (d, 1 H, $J_{1,2}$ = 5.3 Hz, H-1), 5.48 (dd, 1 H, $J_{2,3}$ = 10.9 Hz, H-2), 5.29 (dd, 1 H, $J_{3,4}$ = 3.2 Hz, $J_{4,5}$ = 1.3 Hz, H-4), 5.03 (dd, 1 H, H-3), 4.06 (q, 1 H, $J_{5,6}$ = 6.4 Hz, H-5), 2.41 (s, 3 H, SAc), 2.18, 2.01, 2.00 (3 s, 9 H, 3 OAc); ^{13}C NMR data: δ 192.2, 170.5, 169.9, 169.6, 81.2, 70.4, 69.3, 69.1, 66.3, 31.5, 20.7, 20.6, 16.1; Anal. Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79. Found: C, 48.12; H, 5.90.

2,3,4-Tri-*O*-acetyl-1-thio-α-L-fucopyranose (7). To a solution **6** (220 mg, 0.632 mmol) and DL-dithiotheritol (44 mg, 0.29 mmol) in acetonitrile (5 mL) was added cysteamine (52 mg, 0.67 mmol) and the solution was kept for 25 min at 55°C. Chloroform was added and the mixture was washed with ice water, dried ($MgSO_4$) and evaporated *in vacuo*. The residue was chromatographed with 1 : 2 hexane-EtOAc to give **7** (172 mg, 89%). Compound **7** had $[\alpha]_D^{20}$ -162 (c 1.00, $CHCl_3$); ^1H NMR data: δ 5.99-5.96 (m, 1 H, H-1), 5.31-5.21 (m, 3 H, H-2, 3, 4), 4.53 (q, 1 H, $J_{5,6}$ = 6.6 Hz, H-5), 2.17, 2.09, 2.01 (3 s, 9 H, 3 Ac), 1.80 (d, 1 H, J = 5.3 Hz, SH), 1.16 (d, 1 H, H-6); ^{13}C NMR data: δ 170.6, 170.1, 77.7, 70.9, 68.1, 67.6, 65.5, 20.9, 20.8, 20.7, 16.0; Anal. Calcd for $C_{12}H_{18}O_7S$: C, 47.05; H, 5.92. Found: C, 47.32; H, 6.03.

Allyl 2-acetamido-3,4-di-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-2-deoxy-α-D-glucopyranoside (9). To a mixture of **8**[22] (3.66 g, 14.0 mmol) and imidazole (2.48 g, 36.4 mmol) in DMF (11 mL) was added a solution of *tert*-butylchlorodimethylsilane (2.74 g, 18.2 mmol) in DMF (5 mL) at 0°C and the solution was kept at this temperature for 30 min. The mixture was treated with Ac_2O (10 mL), pyridine (15 mL), and DMAP to give **9** (3.93 g, 61%) after workup. Compound **9** had mp 212-213°C; $[\alpha]_D^{20}$ -3.2 (c 1.34, $CHCl_3$); ^{1}H NMR data: δ 5.93-5.79 (m, 1 H, OCH$_2$C*H*=CH$_2$), 5.62 (d, 1 H, $J_{2,NH}$ = 8.6 Hz, NH), 5.30-5.17 (m, 3 H, H-3, OCH$_2$CH=C*H*$_2$), 4.99 (t, 1 H, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 9.9 Hz, H-4), 4.63 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H-1), 4.37-4.30 (m, 1 H, OC*H*$_2$CH=CH$_2$), 4.12-4.05 (m, 1 H, OC*H*$_2$CH=CH$_2$), 3.91(dt, 1 H, $J_{2,3}$ = 10.7 Hz, H-2), 3.70 (d, 2 H, $J_{5,6}$ = 4.2 Hz, H-6), 3.53 (dt, 1H, H-5), 2.03, 2.02, 1.95 (3 s, 9 H, 3 Ac), 0.89 (s, 9 H, t-Bu), 0.06, 0.05 (2 s, 6 H, 2 Me); ^{13}C NMR data: δ 171.1, 170.1, 169.3, 133.7, 117.6, 99.5, 74.7, 72.9, 69.4, 69.2, 62.6, 54.5, 25.8, 23.3, 20.7, 18.3, -5.4; Anal. Calcd for $C_{21}H_{37}NO_8Si$: C, 54.88; H, 8.11; N, 3.05. Found: C, 54.60; H, 8.28; N, 2.97.

Allyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-6-*O*-*p*-toluenesulfonyl-β-D-glucopyranoside (10). To 70% acetic acid (15 mL) was added **9** (1.40 g, 3.05 mmol), the mixture was kept for 1.5 h at 70°C and evaporated *in vacuo*. To a solution of the residue in pyridine (5 mL) was added *p*-toluenesulfonyl chloride (0.70 g, 3.7 mmol) with stirring. The mixture was kept at room temperature for 3 h and poured into methanol. The precipitate was filtered and recrystallized from EtOH-hexane to give **10** (0.91 g, 60%). Compound **10** had mp 177-179°C (decomp.); $[\alpha]_D^{24}$ -1.8 (c 1.30, $CHCl_3$); ^{1}H NMR data: δ 7.76, 7.36 (each d, each 2 H, J = 8.3 Hz, aromatic in Ts), 5.89-5.75 (m, 1 H, OCH$_2$C*H*=CH$_2$), 5.60 (d, 1 H, $J_{2,NH}$ = 8.9 Hz, NH), 5.30-5.17 (m, 3 H, OCH$_2$CH=C*H*$_2$, H-3), 4.90 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, H-4), 4.65 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1), 4.29-4.22 (m, 1 H, OC*H*$_2$CH=CH$_2$), 4.15-3.98 (m, 3 H, H-6a, 6b, OC*H*$_2$CH=CH$_2$), 3.82 (dt, 1 H, $J_{2,3}$ = 10.6 Hz, H-2), 3.79-3.72 (m, 1 H, H-5), 2.46 (s, 3 H, Me in Ts), 2.02, 2.00, 1.94 (3 s, 9 H, 3 Ac); ^{13}C NMR data: δ 170.8, 170.2, 169.5, 145.1, 133.3, 132.4, 129.9, 128.0, 117.8, 99.4, 72.0, 71.6, 69.8, 68.9, 68.1, 54.5, 23.3, 21.6, 20.6, 20.5; Anal. Calcd for $C_{22}H_{29}NO_{10}S$: C, 52.90; H, 5.85; N, 2.80. Found: C, 52.82; H, 5.74; N, 2.59.

Allyl 2-acetamido-3,4-di-*O*-acetyl-6-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-6-thio-β-D-glucopyranoside (11). To a solution of **7** (408 mg, 1.33 mmol) in DMF (1 mL) was added sodium hydride (55%, 65 mg, 1.5 mmol) at 0°C. After 2 min, **10** (443 mg, 0.887 mmol) was added to the mixture and kept for 1 h at room temperature. The mixture was treated with Ac_2O (1 mL), pyridine (1 mL), and DMAP to give **11** (55 mg, 99%) after workup and chromatography in 1 : 4 hexane-EtOAc. Compound **11** had $[\alpha]_D^{24}$ -127 (c 1.50, $CHCl_3$); ^{1}H NMR data: δ 6.03 (d, 1 H, $J_{2,NH}$ = 8.5 H, NH), 5.96-5.81 (m, 1 H, OCH$_2$C*H*=CH$_2$), 5.74 (d, 1 H, $J_{1',2'}$ = 5.3 Hz, H-1), 5.34-5.19 (m, 6 H, H-3, H-2',3',4', OCH$_2$CH=C*H*$_2$), 4.92 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.4 Hz, H-4), 4.72 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1), 4.43 (q, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.38-4.31 (m, 1 H, OC*H*$_2$CH=CH$_2$), 4.11-4.04 (m, 1 H, OC*H*$_2$CH=CH$_2$), 3.86 (dt, 1 H, $J_{2,3}$ = 10.6 Hz, H-2), 3.62(dt, 1 H, $J_{5,6a}$ = 8.4 Hz, $J_{5,6b}$ = 3.0 Hz, H-5), 2.76 (dd, 1 H, $J_{6a,6b}$ = 13.9 Hz, H-6a), 2.64 (dd, 1 H, H-6b), 2.17, 2.07, 2.04, 2.03, 1.99, 1.94 (6 s, 18 H, 6 Ac), 1.17 (d, 3 H, H-6'); ^{13}C NMR data: δ 170.6, 170.4, 170.2, 169.9, 169.8, 169.5, 133.5, 117.4, 99.4, 82.8, 74.5, 72.1, 71.9, 70.6, 69.6, 68.3, 67.7, 64.6, 54.6, 30.8, 23.1, 20.7, 20.6, 20.5, 20.4, 15.8; Anal. Calcd for $C_{27}H_{39}NO_{14}S$: C, 51.18; H, 6.20; N, 2.21. Found: C, 51.01; H,6.14; N, 2.25.

Allyl 2-acetamido-2-deoxy-6-*S*-(α-L-fucopyranosyl)-6-thio-β-D-glucopyranoside (1). A solution of **11** (452 mg, 0.713 mmol) and a 1.0 M solution of MeONa in MeOH (0.3 mL) were mixed, and stirred for 20 min at room temperature. The mixture was neutralized with Dowex 50 W-X2 (H^+) resin and filtered. The filtrate was concentrated *in vacuo* to give **1** (274 mg, 91%). Compound **1** had mp 169-171°C; $[\alpha]_D^{24}$ -132 (c 0.75, H_2O); ^{1}H NMR (D_2O): δ 5.94-5.92 (m, 1 H, $OCH_2CH{=}CH_2$), 5.52 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, H-1'), 5.36-5.26 (m, 2 H, $OCH_2CH{=}CH_2$), 4.57 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H-1), 4.39-4.31 (m, 2 H, H-5, $OCH_2CH{=}CH_2$), 4.22-4.15 (m, 1 H, $OCH_2CH{=}CH_2$), 4.08 (dd, 1 H, $J_{2',3'}$ = 10.2 Hz, H-2'), 3.83 (d, 1 H, $J_{4',5'}$ = 3.0 Hz, H-4'), 3.77-3.69 (m, 2 H, H-2, 3'), 3.56-3.35 (m, 3 H, H-3, 4, 5), 3.12 (d, 1 H, $J_{6a,6b}$ = 14.2 Hz, H-6b), 2.83 (dd, 1 H, $J_{5,6b}$ = 8.9 Hz, H-6b), 2.04 (s, 3 H, Ac), 1.25 (d, 3 H, H-6'), ^{13}C NMR (D_2O): δ 174.9, 133.7, 118.6, 100.5, 87.5, 76.4, 74.0, 73.5, 72.0, 70.9, 70.6, 68.1, 67.6, 56.0, 32.3, 22.5, 45.8; Anal. Calcd for $C_{17}H_{29}NO_9S$: C, 48.22; H, 6.90; N, 3.31. Found: C, 48.00; H, 7.09; N, 3.06.

Allyl 2-azido-3,6-di-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-galactopyranoside (13). To a mixture of **12**[22] (584 mg, 2.38 mmol) and imidazole (0.65 g, 9.5 mmol) in DMF (2 mL) was added a solution of *tert*-butylchlorodimethylsilane (0.90 g, 6.0 mmol) in DMF (2 mL). The mixture was stirred for 20 h at 65°C, and diluted with benzene. The organic layer was washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. The residue was chromatographed with 20 : 1 hexane-EtOAc to give **13** (655 mg, 58%). Compound **12** had $[\alpha]_D^{24}$ +4.0 (c 1.91, $CHCl_3$); ^{1}H NMR data: δ 6.01-5.86 (m, 1 H, $OCH_2CH{=}CH_2$), 5.36-5.18 (m, 2H, $OCH_2CH{=}CH_2$), 4.42-4.36 (m, 1 H, $OCH_2CH{=}CH_2$), 4.26 (d, 1 H, $J_{1,2}$ = 7.6 Hz, H-1), 4.17-4.09 (m, 1 H, $OCH_2CH{=}CH_2$), 3.91 (dd, 1 H, $J_{5,6a}$ = 6.8 Hz, $J_{6a,6b}$ = 10.1 Hz, H-6a), 3.82 (dd, 1 H, $J_{5,6b}$ = 5.9 Hz, H-6b), 3.79-3.77 (m, 1 H, H-4), 3.54-3.39 (m, 3 H, H-2, 3, 5), 2.48 (s, 1 H, OH), 0.93, 0.89 (2 s, 18 H, 2 t-Bu), 0.18, 0.13, 0.08 (3 s, 12 H, 4 Me); ^{13}C NMR data: δ 133.6, 117.5, 100.8, 74.5, 73.6, 69.8, 68.2, 64.6, 61.8, 25.8, 25.7, 18.2, 18.0, -4.7, -4.9, -5.4, -5.5; Anal. Calcd for $C_{21}H_{43}N_3O_5Si_2$: C, 53.24; H, 9.15; N, 8.87. Found: C, 52.99; H, 8.68; N, 8.54.

Allyl 2-azido-3,6-di-*O*-*tert*-butyldimethylsilyl-4-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-4-thio-β-D-glucopyranoside (15). To a solution of pyridine (0.7 mL, 8.7 mmol) and DMAP (18 mg, 0.15 mmol) in CH_2Cl_2 (3 mL), was added a solution of trifluoromethanesulfonic anhydride (0.50 mL, 3.0 mmol) in CH_2Cl_2 (2 mL) at 0°C, and after stirred for 30 min at this temperature then **13** (700 mg, 1.48 mmol). The mixture was stirred for 1 h at room temperature, and then diluted with CH_2Cl_2. The organic layer was washed with M hydrochloric acid, aq sodium hydrogencarbonate (saturated), dried ($MgSO_4$), and evaporated in vacuo to give a syrup of triflate **14**. To a solution of **7** (473 mg, 1.43 mmol) in DMF (0.5 mL) was added sodium hydride (55%, 68 mg, 1.6 mmol) at 0°C under argon. After 2 min, a solution of **14** in DMF (1.5 mL) was added to the mixture and kept for 40 min at room temperature. The mixture was treated with Ac_2O (0.3 mL), pyridine (0.3 mL), and DMAP to give **15** (734 mg, 68%) after workup and chromatography with 4 : 1 hexane-EtOAc. Compound **14** had $[\alpha]_D^{23}$ -123 (c 1.02, $CHCl_3$); ^{1}H NMR data: δ 6.02-5.87 (m, 1 H, $OCH_2CH{=}CH_2$), 5.85 (d, 1 H, $J_{1',2'}$ = 4.9 Hz, H-1'), 5.36-5.19 (m, 5 H, H-2', 3', 4', $OCH_2CH{=}CH_2$), 4.53 (q, 1 H, $J_{5',6'}$ = 6.3 Hz, H-5'), 4.40-4.35 (m, 1 H, $OCH_2CH{=}CH_2$), 4.32 (d, 1 H, $J_{1,2}$ = 7.3 Hz, H-1),4.16-4.09 (m, 1 H, $OCH_2CH{=}CH_2$), 3.92 (dd, 1 H, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 11.5 Hz, H-6a), 3.82 (dd, 1 H, $J_{5,6b}$ = 4.5 Hz, H-6b), 3.29-3.16 (m, 3 H, H-2, 3, 5), 2.81 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.4 Hz, H-4), 2.16, 2.05, 1.98 (3 s, 9 H, 3 Ac), 1.10 (d, 3 H, H-6'), 0.94, 0.90 (2 s, 18 H, 2 t-Bu), 0.26, 0.19, 0.08 (3 s, 12 H, 4 Me); ^{13}C NMR data: δ 170.5, 170.0, 169.9, 133.6, 117.5, 101.0, 79.9, 78.2, 72.9, 70.9, 69.8, 68.9, 68.4, 68.3, 65.2, 63.1, 44.4, 26.0, 25.8, 20.8, 20.6, 18.4, 18.2, 15.9, -3.1, -4.4, -5.1, -5.5; Anal. Calcd for $C_{33}H_{59}N_3O_{11}SSi_2$: C, 52.01; H, 7.80; N, 5.51. Found: C, 52.39; H, 7.63; N, 5.34.

Allyl 2-azido-3,6-di-*O*-acetyl-4-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-4-thio-β-D-glucopyranoside (16). A mixture of **13** (693 mg, 0,909 mmol) and M Bu_4NF solution in THF (7 mL) was stirred for 2 h at room temperature, and concentrated *in vacuo*. The residue was treated with Ac_2O (3 mL), pyridine (3 mL), and DMAP to give **16** (513 mg, 91%) after workup and chromatography with 2 : 1 hexane-EtOAc. Compound **16** had $[\alpha]_D^{22}$ -143 (c 1.89, $CHCl_3$); ^1H NMR data: δ 6.00-5.86 (m, 1H, $OCH_2CH{=}CH_2$), 5.65 (d, 1 H, $J_{1',2'}$ = 5.9 Hz, H-1'), 5.37-5.23 (m, 4 H, H-2', 4', $OCH_2CH{=}CH_2$), 5.07 (dd, 1 H, $J_{2',3'}$ = 11.1 Hz, $J_{3',4'}$ = 3.1 Hz, H-3'), 4.91 (dd, 1 H, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 11.2 Hz, H-3), 4.54 (dd, 1 H, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.39 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1), 4.36-4.33 (m, 2 H, H-5', $OCH_2CH{=}CH_2$), 4.22 (dd, 1 H, *J5,6a* = 5.0 Hz, H-6b), 4.18-4.11 (m, 1 H, $OCH_2CH{=}CH_2$), 3.65 (ddd, 1 H, $J_{4,5}$ = 10.9 Hz, H-5), 3.42 (dd, 1 H, $J_{2,3}$ = 9.9 Hz, H-2), 2.92 (t, 1 H, H-4), 2.17, 2.16, 2.12, 2.06, 1.98 (5 s, 15 H, 5 Ac), 1.17 (d, 3 H, $J_{5',6'}$ = 6.6 Hz, H-6'); ^{13}C NMR data: δ 170.5, 170.4, 170.0, 169.8, 169.4, 133.0, 118.3, 100.4, 82.5, 74.2, 71.1, 70.5, 70.4, 68.2, 67.2, 65.9, 65.3, 63.3, 45.4, 20.9, 20.8, 20.7, 20.6, 15.9; Anal. Calcd for $C_{25}H_{35}N_3O_{13}S$: C, 48.62; H, 5.71; N, 6.80. Found: C, 49.01; H, 6.23; N, 6.32.

Allyl 2-acetamido-3,6-di-*O*-acetyl-4-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-4-thio-β-D-glucopyranoside (17). To a solution of **16** (433 mg, 0.701 mmol) in aq 50% pyridine (30 mL) hydrogen sulfide was bubbled for 9 h at room temperature, then the mixture was concentrated *in vacuo*. The residue was treated with Ac_2O (5 mL), pyridine (5 mL), and DMAP to give **17** (432 mg, 97%) after workup and chromatography with EtOAc. Compound **17** had $[\alpha]_D^{24}$ -150 (c 2.09, $CHCl_3$); ^1H NMR data: δ 5.92-5.78 (m, 1 H, $OCH_2CH{=}CH_2$), 5.82 (d, 1 H, $J_{2,NH}$ = 9.2 Hz, NH), 5.68 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, H-1'), 5.29-5.16 (m, 4 H, H-2', 4', $OCH_2CH{=}CH_2$), 5.09 (dd, 1 H, $J_{2',3'}$ = 11.0 Hz, $J_{3',4'}$ = 3.1 Hz, H-3'), 5.04 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 10.7 Hz, H-3), 4.58 (dd, 1 H, $J_{5,6a}$ = 1.6 Hz, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.49 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H-1), 4.40 (q, 1 H, $J_{5',6'}$ = 4.3 Hz, H-5'), 4.34-4.27 (m, 1 H, $OCH_2CH{=}CH_2$), 4.21 (dd, 1 H, $J_{5,6b}$ = 4.3 Hz, H-6b), 4.09 (m, 2 H, H-2, $OCH_2CH{=}CH_2$), 3.70-3.65 (m, 1 H, H-5), 3.03 (t, 1 H, $J_{4,5}$ = 10.7 Hz, H-4), 2.17, 2.12, 2.10, 2.06, 1.99, 1.95 (6 s, 18 H, 6 Ac), 1.17 (d, 3 H, H-6'); ^{13}C NMR data: δ 170.7, 170.4, 170.3, 170.1, 170.0, 169.8, 133.5, 117.5, 99.6, 82.4, 74.1, 72.2, 70.5, 69.4, 68.1, 67.5, 65.7, 63.2, 55.3, 45.1, 23.1, 20.8, 20.7, 20.6, 20.5, 20.4, 15.7; Anal. Calcd for $C_{27}H_{39}NO_{14}S$: C, 51.18; H, 6.20; N, 2.21. Found: C, 50.95; H, 6.23; N, 2.25.

Allyl 2-acetamido-2-deoxy-4-*S*-(α-L-fucopyranosyl)-4-thio-β-D-glucopyrnoside (2). A solution of **17** (879 mg, 1.39 mmol) in MeOH (4 mL) and a 0.5 M solution of MeONa in MeOH (0.3 mL) were mixed, and stirred for 3 h at room temperature. The mixture was neutralized with Dowex 50W-X2 (H^+) resin, and filtered. The filtrate was concentrate *in vacuo* to give **2** (381 mg, 65%). Compound **2** had mp 259-261°C (decomp.); $[\alpha]_D^{24}$ -219 (c 1.08, H_2O); ^1H NMR (D_2O): δ 5.99-5.84 (m, 1 H, $OCH_2CH{=}CH_2$), 5.47 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, H-1'), 5.34-5.25 (m, 2 H, $OCH_2CH{=}CH_2$), 4.55 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H-1), 4.48(q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.38-4.31 (m, 1 H, $OCH_2CH{=}CH_2$), 4.20-4.06 (m, 3 H, H-6a, 2', $OCH_2CH{=}CH_2$), 3.93 (dd, 1 H, $J_{5,6a}$ = 5.3 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6b), 3.83 (d, 1 H, $J_{3',4'}$ = 2.6 Hz, H-4'), 3.76-3.57 (m, 4 H, H-2, 3, 5, 3'), 2.77 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 10.6 Hz, H-4), 2.04 (s, 3 H, Ac), 1.21 (d, 3 H, H-6'); ^{13}C NMR (D_2O): δ 174.9, 133.7, 118.5, 100.3, 85.8, 77.0, 72.0, 71.6, 70.7, 70.5, 68.1, 68.0, 61.8, 57.1, 48.0, 22.5, 15.6; Anal. Calcd for $C_{17}H_{29}NO_9S$: C, 48.22; H, 6.90; N, 3.31. Found: C, 48.19; H, 6.94; N, 3.28.

Allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulfonyl-β-D-glucopyranoside (18). To a solution of allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside[24] (6.51 mg, 18.6

mmol) in pyridine (65 mL) was added methanesulfonyl chloride (2.9 mL, 37.5 mmol) with stirring at 0°C. After 2 h at room temperature, the mixture was poured into ice-water. The precipitate was filtered and washed with water to give **18** (2.93 g, 73%). Compound **18** had mp 200-202°C (decomp.); $[\alpha]_D^{20}$ -44 (c 0.78, $CHCl_3$); ^1H NMR data: δ 7.44-7.35 (m, 5 H, Ph), 5.95-5.81 (m, 2 H, $OCH_2CH{=}CH_2$, NH), 5.54 (s, 1 H, CHPh), 5.33-5.20 (m, 3 H, H-3, $OCH_2CH{=}CH_2$), 5.17 (d, 1 H, $J_{1,2}$ = 8.0 Hz, H-1), 4.39 (dd, 1 H, $J_{3,4}$ = 10.6 Hz, $J_{4,5}$ = 4.9 Hz, H-4), 4.35-4.31 (m, 1 H, $OCH_2CH{=}CH_2$), 4.15-4.08 (m, 1 H, $OCH_2CH{=}CH_2$), 3.80 (t, 1 H, $J_{5,6a}$ = 9.7 Hz, $J_{6a,6b}$ = 9.7 Hz, H-6a), 3.73 (t, 1 H, $J_{5,6b}$ = 9.7 Hz, H-6b), 3.59 (dt, 1 H, H-5), 3.47 (dt, 1 H, $J_{2,3}$ = 9.8 Hz, $J_{2,NH}$ = 8.0 Hz, H-2), 2.93 (s, 3 H, Ms), 2.03 (s, 3 H, OAc); ^{13}C NMR data: δ 171.4, 136.6, 133.4, 129.4, 128.4, 126.0, 118.0, 101.8, 99.5, 79.0, 78.6, 70.7, 68.6, 65.5, 57.1, 38.5, 23.5; Anal. Calcd for $C_{19}H_{25}NO_8S$: C, 53.39; H, 5.89; N, 3.28. Found: C, 53.18; H, 5.98; N, 3.19.

Allyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epimino-β-D-allopyranoside (19). The 3-mesylate **18** (5.92 g, 13.8 mmol) was added to a mixed solution of *i*-PrOH (60 mL) and dioxane (150 mL) containing metallic sodium (1.4 g, 61 mmol) dissolved under reflux. The mixture was boiled for 30 min, poured into ice water, and the product was extracted with $CHCl_3$. The organic layer was dried ($MgSO_4$) and evaporated *in vacuo*. The residue was chromatographed with 2 : 1 hexane-EtOAc to give **19** (2.93 g, 73%). Compound **19** had mp 84-85°C; $[\alpha]_D^{23}$ -5.0 (c 1.01, $CHCl_3$); ^1H NMR ($CDCl_3$, D_2O): δ 7.52-7.30 (m, 5 H, Ph), 6.02-5.88 (m, 1 H, $OCH_2CH{=}CH_2$), 5.58 (s, 1 H, CHPh), 5.37-5.20 (m, 2 H, $OCH_2CH{=}CH_2$), 4.95 (s, 1 H, H-1), 4.38-4.30 (m, 1 H, $OCH_2CH{=}CH_2$), 4.25-4.20 (m, 2 H, H-4, $OCH_2CH{=}CH_2$), 3.79-3.64 (m, 2 H, H-6a, 6b), 2.73 (dd, 1 H, $J_{2,3}$ = 6.6 Hz, $J_{3,4}$ = 2.3 Hz, H-3), 2.58 (d, 1 H, H-2); ^{13}C NMR data: δ 137.4, 133.8, 129.1, 128.2, 126.3, 117.6, 102.5, 98.1, 69.9, 69.3, 60.6, 34.8, 30.5; Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.29; H, 6.60; N, 4.89.

Allyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-(*N*-*p*-toluenesulfonylepimino)-β-D-allopyranoside (20). To a solution of **19** (2.27 g, 7.85 mmol) in pyridine (30 mL) was added TsCl (2.99 g, 15.7 mmol) with stirring at 0°C. The mixture was kept for 2 h at this temperature and the poured into ice water. The precipitate was filtered and washed with water to give **20** (3.40 g, 98%). Compound **20** had mp 154-155°C; $[\alpha]_D^{22}$ -12.3 (c 0.43, $CHCl_3$); ^1H NMR data: δ 7.87 (d, 2 H, *J* = 8.3 Hz, aromatic in Ts), 7.37-7.17 (m, 7 H, aromatic), 5.99-5.85 (m, 1 H, $OCH_2CH{=}CH_2$), 5.47 (s, 1 H, CH-Ph), 5.35-5.22 (m, 2 H, $OCH_2CH{=}CH_2$), 5.04 (s, 1 H, H-1), 4.36-4.29 (m, 1 H, $OCH_2CH{=}CH_2$), 4.17-4.05 (m, 2 H, H-5, $OCH_2CH{=}CH_2$), 3.96-3.92 (m, 1 H, H-4), 3.70-3.57 (m, 2 H, H-6a, 6b), 3.46 (d, 1 H, $J_{2,3}$ =7.3 Hz, H-2), 3.27 (dd, 1 H, $J_{3,4}$ = 2.3 Hz, H-3), 2.44 (s, 3 H, Me in Ts); ^{13}C NMR data: δ 144.7, 136.9, 134.6, 133.2, 129.6, 129.1, 128.0, 128.9, 126.1, 118.1, 101.9, 96.5, 74.3, 70.3, 68.9, 61.6, 42.2, 40.3, 21.7; Anal. Calcd for $C_{23}H_{25}NO_6S$: C, 62.29; H, 5.68; N, 3.16. Found: C, 62.53; H, 5.79; N, 3.11.

Allyl 2,3-dideoxy-2,3-(*N*-*p*-toluenesulfonylepimino)-β-D-allopyranoside (21). A mixture of **20** (2.52 g, 1.69 mmol), Dowex 50W-X2 (H^+) resin (9 g), and 80% MeOH (100 mL) was stirred for 2 h at 60°C. After filtration of undissolved material the filtrate was evaporated *in vacuo*. The residue was chromatographed with 1 : 2 hexane-EtOAc to give **21** (2.10 g, quantitative). Compound **21** had $[\alpha]_D^{22}$ -10.7 (c 3.00, $CHCl_3$); ^1H NMR ($CDCl_3$, D_2O): δ 7.84, 7.37 (each d, each 2 H, *J* = 8.4 Hz, aromatic in Ts), 5.94-5.79 (m, 1 H, $OCH_2CH{=}CH_2$), 5.29-5.16 (m, 2H, $OCH_2CH{=}CH_2$), 4.77 (s, 1 H, H-1), 4.33-4.25 (m, 1 H, $OCH_2CH{=}CH_2$), 4.10-4.02 (m, 1 H, $OCH_2CH{=}CH_2$), 3.98 (m, 1 H, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 8.6 Hz, H-4), 3.77 (m, 1H, $J_{5,6a}$ = 3.5 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 3.66 (m, 1H, $J_{5,6b}$ = 4.8 Hz, H-6b), 3.36 (dd, 1H, $J_{2,3}$ = 7.2 Hz, H-3), 3.31 (ddd, 1 H, H-5), 3.26 (d, 1 H, H-2), 2.46 (s, 3 H, Me in Ts); ^{13}C NMR data: δ 145.2, 133.6, 133.2, 129.9, 128.1, 117.9, 95.8, 72.5, 70.0, 62.6, 62.5, 44,8, 42.8, 21.7; Anal. Calcd for $\mathrm{C_{16}H_{21}NO_6S}$: C, 54.07; H, 5.96; N, 3.94. Found: C, 54.07; H, 6.21; N, 3.67.

Allyl 4,6-di-*O*-acetyl-3-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-3-thio-2-*p*-toluenesulfonamido-β-D-glucopyranoside (22) and 4,6-di-*O*-acetyl-2-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-3-deoxy-2-thio-3-*p*-toluenesulfonamido-β-D-altropyranoside (23). A mixture of **21** (604 mg, 1.69 mmol), **6** (646 mg, 1.85 mmol), and M solution of MeONa in MeOH (1.74 mL) was boiled under argon for 45 min, and then concentrated *in vacuo*. The residue was treated with $\mathrm{Ac_2O}$ (3 mL), pyridine (3 mL), DMAP to give **22** (794 mg, 63%) and **23** (362 mg, 29%) after workup and chromatographed with 3 : 1 - 1 : 1 hexane-EtOAc. Compound **22** had $[\alpha]_D^{27}$ -100 (c 3.22, $\mathrm{CHCl_3}$); ^{1}H NMR data: δ 7.75, 7.29 (each d, each 2 H, J = 7.8 Hz, aromatic in Ts), 5.78 (d, 1 H, $J_{1',2'}$ = 5.7 Hz, H-1'), 5.49-5.37 (m, 1 H, $\mathrm{OCH_2C}H\mathrm{{=}CH_2}$), 5.40 (d, 1 H, $J_{2',3'}$ = 10.9 Hz), 5.26 (d, 1 H, $J_{3',4'}$ = 3.3 Hz, H-4'), 5.11-5.02 (m, 4 H, H-3', NH, $\mathrm{OCH_2CH{=}C}H_2$), 4.94 (t, 1 H, $J_{3,4}$ = 10.1 Hz, $J_{4,5}$ = 8.9 Hz, H-4), 4.40-4.34 (m, 2 H, H-1, H-5'), 4.20 (dd, 1 H, $J_{5,6a}$ = 5.1 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.07 (dd, 1 H, $J_{5,6b}$ = 2.6 Hz, H-6b), 3.98-3.91 (m, 1 H, $\mathrm{OC}H_2\mathrm{CH{=}CH_2}$), 3.70-3.60 (m, 2 H, H-5, $\mathrm{OC}H_2\mathrm{CH{=}CH_2}$), 3.46 (dt, 1 H, $J_{1,2} = J_{2,NH}$ = 7.6 Hz, $J_{2,3}$ = 10.3 Hz, H-2), 3.11 (t, 1 H, H-3), 2.43 (s, 3 H, Me in Ts), 2.16, 2.13, 2.09, 2.06, 1.98 (5 s, 15 H, 5 Ac), 1.15 (d, 3 H, $J_{5',6'}$ = 6.6 Hz, H-6'); ^{13}C NMR data: δ 170.6, 170.4, 170.2, 169.8, 169.0, 143.3, 138.5, 133.2, 129.3, 127.2, 118.1, 100.5, 83.2, 74.1, 70.6, 69.8, 68.4, 68.3, 66.7, 65.7, 62.6, 59.6, 48.7, 21.4, 20.8, 20.7, 20.5, 15.9; Anal. Calcd for $\mathrm{C_{32}H_{43}NO_{15}S_2}$: C, 51.53; H, 5.81; N, 1.88. Found: C, 51.90; H, 6.29; N, 1.75.

Compound **23** had $[\alpha]_D^{24}$ -87 (c 3.18, $\mathrm{CHCl_3}$); ^{1}H NMR data: δ 7.75, 7.35 (each d, each 2 H, J = 8.3 Hz, aromatic in Ts), 5.92-5.80 (m, 1 H, $\mathrm{OCH_2C}H\mathrm{{=}CH_2}$), 5.76 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, H-1'), 5.30-5.10 (m, 6 H, H-2', 3', 4', NH, $\mathrm{OCH_2CH{=}C}H_2$), 5.01 (dd, 1 H, $J_{3,4}$ = 4.3 Hz, $J_{4,5}$ = 7.9 Hz, H-4), 4.97 (d, 1 H, $J_{1,2}$ = 2.0 Hz, H-1), 4.42 (q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.32-4.26 (m, 1 H, $\mathrm{OC}H_2\mathrm{CH{=}CH_2}$), 4.19 (dd, 1 H, $J_{5,6a}$ = 5.3 Hz, $J_{6a,6b}$ = 12.1 Hz, H-6a), 4.13 (dd, 1 H, $J_{5,6b}$ = 4.1 Hz, H-6b), 4.04-3.84 (m, 3 H, H-3, 5, $\mathrm{OC}H_2\mathrm{CH{=}CH_2}$), 3.40 (dd, 1 H, $J_{2,3}$ = 5.6 Hz, H-2), 2.45 (s, 3 H, $\mathrm{CH_3\text{-}C_6H_4}$), 2.18, 2.07, 2.06, 2.00, 1.80 (5 s, 15 H, 5 Ac), 1.17 (d, 3 H, H-6'); ^{13}C NMR data: δ 170.6, 170.5, 170.1, 169.8, 168.6, 144.2, 136.4, 133.3, 129.9, 127.1, 117.7, 97.5, 84.3, 71.2, 70.9, 69.8, 68.3, 67.7, 66.2, 65.7, 62.9, 53.5, 49.3, 21.5, 20.8, 20.7, 20.6, 20.4, 15.8; Anal. Calcd for $\mathrm{C_{32}H_{43}NO_{15}S_2}$: C, 51.53; H, 5.81; N, 1.88. Found: C, 51.65; H, 6.01; N, 1.75.

***n*-Propyl 4,6-di-*O*-acetyl-3-S-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-3-thio-2-*p*-toluenesulfonamido-β-D-glucopyranoside (24).** A mixture of **22** (470 mg, 0.630 mmol) and 10% Pd-C (100 mg) in MeOH (5 mL) was stirred under $\mathrm{H_2}$ for 24 h at room temperature, then filtered through Celite. The filtrate was concentrated *in vacuo*. The residue was chromatographed 1 : 2 hexane-EtOAc to give **24** (486 mg, quantitative). Compound **24** had $[\alpha]_D^{24}$ -98 (c 1.90, $\mathrm{CHCl_3}$); ^{1}H NMR data: δ 7.76, 7.30 (each d, each 2 H, J = 8.4 Hz, aromatic in Ts), 5.76 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, H-1'), 5.39 (dd, 1 H, $J_{2',3'}$ = 11.0 Hz, H-2'), 5.24 (d, 1 H, $J_{3',4'}$ = 3.5 Hz, H-4'), 5.07 (dd, 1 H, H-3'), 4.99 (d, 1 H, $J_{2,NH}$ = 7.3 Hz, NH), 4.94 (t, 1 H, $J_{3,4}$ = 10.2 Hz, $J_{4,5}$ = 8.7 Hz, H-4), 4.40 (d, 1 H, $J_{1,2}$ = 7.3 Hz, H-1), 4.36 (q, 1 H, $J_{5',6'}$ = 6.3 Hz, H-5'), 4.22 (dd, 1 H, $J_{5,6a}$ = 5.1 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.07 (dd, 1 H, $J_{5,6b}$ = 3.1 Hz, H-6b), 3.62 (ddd, 1 H, H-5), 3.50 (dt, 1 H, J_d = 9.3 Hz, J_t = 7.1 Hz, $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 3.40 (dt, 1 H, $J_{2,3}$ = 10.6 Hz, H-2), 3.17 (t, 1 H, H-3), 3.00 (dt, 1H, J_t = 6.9 Hz, $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 2.43 (s, 3 H, Me in Ts), 2.16, 2.12, 2.09, 2.06, 1.98 (5 s, 15 H, 5 OAc), 1.30-1.18 (m, 2 H, $\mathrm{OCH_2C}H_2\mathrm{CH_3}$), 1.14 (d, 3 H, H-6'), 0.70 (t, 3 H, J = 7.4 Hz, $\mathrm{OCH_2CH_2C}H_3$); ^{13}C NMR data: δ 170.6, 170.4, 170.2, 169.8, 169.0, 143.4, 138.6, 129.3, 127.2, 101.6, 83.1, 74.1, 71.3, 70.6, 68.5, 68.3, 66.8, 65.8, 62.7, 59.6, 48.7, 22.3, 21.4, 20.9, 20.8, 20.7, 20.5, 15.9, 10.2; Anal. Calcd for $C_{32}H_{45}NO_{15}S_2$: C, 51.40; H, 6.07; N, 1.87. Found: C, 51.27; H, 6.20; N, 1.73.

***n*-Propyl 2-deoxy-3-*S*-(α-L-fucopyranosyl)-3-thio-2-*p*-toluenesulfonamido-β-D-glucopyranoside (25).** A solution of **24** (433 mg, 0.579 mmol) in MeOH and a 0.5 M solution of MeONa in MeOH (0.5 mL) was mixed and stirred for 20 min at room temperature. The mixture was neutralized with Dowex 50W-X2 (H^+) resin and filtered. The filtrate was concentrated *in vacuo* to give **25** (281 mg, 90%). Compound **25** had mp 195-198°C; $[\alpha]_D^{24}$ -145 (c 1.06, MeOH); ^1H NMR (CD_3OD): δ 7.76, 7.32 (each d, each 2 H, J = 8.3 Hz, aromatic in Ts), 5.56 (d, 1 H, $J_{1',2'}$ = 5.4 Hz, H-1'), 4.39 (q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.20 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.07 (dd, 1 H, $J_{2',3'}$ = 9.6 Hz, H-2'), 3.85-3.30 (m, 8 H, H-2, 4, 5, 6a, 6b, 3', 4', $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 3.05-2.86 (m, 1 H, $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 2.75 (dd, 1 H, J = 9.9 Hz, J = 11.6 Hz, H-3), 1.28-1.10 (m, 2 H, $\mathrm{OCH_2C}H_2\mathrm{CH_3}$), 1.23 (d, 3 H, H-6'), 0.69 (t, 3 H, J = 7.4 Hz, $\mathrm{OCH_2CH_2C}H_3$); ^{13}C NMR (CD_3OD): δ 143.8, 141.6, 130.1, 128.0, 104.0, 88.2, 80.1, 73.3, 72.2, 72.1, 70.5, 69.8, 69.1, 62.9, 61.0, 55.2, 23.4, 21.4, 16.6, 10.6; Anal. Calcd for $C_{22}H_{35}NO_{10}S_2$: C, 49.15; H, 6.56; N, 2.61. Found: C, 48.87; H, 6.62; N, 2.40.

***n*-Propyl 2-acetamido-4,6-di-*O*-acetyl-3-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-deoxy-β-D-glucopyranoside (26).** To a solution of **25** (310 mg, 0.576 mmol) in liquid ammonia (80 mL) and THF (50 mL), cooled at -78, was added metallic sodium (300 mg). The mixture was stirred for 45 min at this temperature. After addition of NH_4Cl until discharge of the blue color, liquid ammonia was distilled off, then concentrated *in vacuo*. The residue was treated with Ac_2O, pyridine, and DMAP to give **26** (314 mg, 86%) after workup and chromatography with 1 : 3 hexane-EtOAc. Compound **26** had mp 176-178°C; $[\alpha]_D^{24}$ -119 (c 1.0, $CHCl_3$); 5.80 (d, 1 H, $J_{2,NH}$ = 7.6 Hz, NH), 5.74 (d, 1 H, $J_{1',2'}$ = 5.5 Hz, H-1'), 5.28 (d, 1 H, $J_{3',4'}$ = 3.3 Hz, H-4'), 5.20 (dd, 1 H, $J_{2',3'}$ = 11.1 Hz, H-2'), 5.09 (dd, 1 H, H-3'), 4,99 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.88 (dd, 1 H, $J_{3,4}$ = 11.5 Hz, $J_{4,5}$ = 9.9 Hz, H-4), 4.40 (q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.23 (dd, 1 H, $J_{5,6a}$ = 5.0 Hz, $J_{6a,6b}$ = 11.4 Hz, H-6a), 4.06 (dd, 1 H, $J_{5,6b}$ = 2.6 Hz, H-6b), 3.81 (dt, 1 H, J_d = 9.6 Hz, J_t = 6.6 Hz, $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 3.76 (t, 1 H, $J_{2,3}$ = 11.4 Hz, H-3), 3.74-3.68 (m, 1 H, H-5), 3.44 (dt, 1 H, J_t = 6.8 Hz, $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 3.26 (dt, 1 H, H-2), 2.16, 2.08, 2.07, 2.03, 1.99 (5 s, 18 H, 6 Ac), 1.62-1.52 (m, 2 H, $\mathrm{OCH_2C}H_2\mathrm{CH_3}$), 1.18 (d, 3 H, H-6'), 0.90 (t, 3 H, J = 7.3 Hz, $\mathrm{OCH_2CH_2C}H_3$); ^{13}C NMR data: δ 170.8, 170.7, 170.4, 170.3, 169.8, 169.2, 100.1, 82.0, 74.2, 71.4, 70.5, 68.3, 68.2, 67.7, 65.2, 62.6, 58.6, 45.9, 23.5, 22.6, 20.8, 20.7, 20.6, 20.5, 16.0, 10.3; Anal. Calcd for $C_{27}H_{41}NO_{14}S$: C, 51.02; H, 6.50; N, 2.20. Found: C, 50.97; H, 6.52; N, 2.20.

***n*-Propyl 2-acetamido-2-deoxy-3-*S*-(α-L-fucopyranosyl)-β-D-glucopyranoside (3).** A solution of **26** (326 mg, 0.513 mmol) in MeOH (1 mL) and a 0.5 M solution of MeONa in MeOH (1 mL) were mixed and stirred for 1 h at room temperature was concentrated *in vacuo* to give **27** (206 mg, 94%). Compound **3** had mp 247-248°C; $[\alpha]_D^{24}$ -220 (c 0.45, H_2O); ^1H NMR (D_2O): δ 5.38 (d, 1 H, $J_{1',2'}$ = 5.6 Hz, H-1), 4.53 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1), 4.68 (q, 1 H, $J_{5',6'}$ = 6.3 Hz, H-5'), 4.04 (dd, 1 H, $J_{2',3'}$ = 10.6 Hz, H-2'), 3.94 (dd, 1 H, $J_{5,6a}$ = 1.7 Hz, $J_{6a,6b}$ = 12.3 Hz, H-6a), 3.92-3.81 (m, 3 H, H-2, 4', $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 3.76 (dd, 1 H, $J_{5,6b}$ = 4.6 Hz, H-6b), 3.71 (dd, 1 H, $J_{3',4'}$ = 3.5 Hz, H-3'), 3.61-3.51 (m, 2 H, H-5, $\mathrm{OC}H_2\mathrm{CH_2CH_3}$), 3.45 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, H-4), 2.80 (t, 1 H, H-3), 2.05 (s, 3 H, Ac), 1.60-1.52 (m, 2 H, $\mathrm{OCH_2C}H_2\mathrm{CH_3}$), 1.21 (d, 3 H, H-6'), 0.87 (t, 3 H, J = 7.4 Hz, $\mathrm{OCH_2CH_2C}H_3$); ^{13}C NMR (D_2O): δ 174.5, 102.5, 87.5, 78.7, 72.5, 72.0, 70.5, 68.1, 67.8, 61.5, 55.8, 52.8, 22.4, 15.7, 10.0; Anal. Calcd for $C_{17}H_{31}NO_9S$: C, 47.99; H, 7.34; N, 3.29. Found: C, 47.51; H, 7.45; N, 3.08.

3,4-Di-*O*-acetyl-2-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-1,6-anhydro-2-thio-β-D-galactopyranose (28) and 2,4-di-*O*-acetyl-3-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-1,6-anhydro-3-thio-β-D-idopyranose (29). A mixture of **6** (383 mg, 1.10 mmol), **27**[25] (144 mg, 1.00 mmol), and a 2.9 M solution of MeONa in MeOH (0.38 mL) was stirred for 2 h at 95°C under argon. The mixture was treated with Ac_2O (2 mL), pyridine (2 mL), and DMAP to give **28** (465 mg, 87%) and **29** (39 mg, 7%) after workup and chromatography with 2 : 1 - 1 : 1 hexane-EtOAc. Compound **28** had mp 173-174 °C; $[\alpha]_D^{24}$ -187 (c 1.46, $CHCl_3$); ^1H NMR data: δ 5.95 (d, 1 H, $J_{1',2'}$ = 5.3 Hz, H-1'), 5.48 (s, 1 H, H-1), 5.34 (t, 1 H, $J_{3,4}$ = 5.0 Hz, $J_{4,5}$ = 4.3 Hz, H-4), 5.31 (dd, 1 H, $J_{2',3'}$ = 11.0 Hz, H-2'), 5.29 (d, 1 H, $J_{3',4'}$ = 3.3 Hz, H-4'), 5.21 (dd, 1 H, $J_{2,3}$ = 1.0 Hz, H-3), 5.14 (dd, 1 H, H-3'), 4.49-4.45 (m, 2 H, H-5, 5'), 4.41 (d, 1 H, $J_{6a,6b}$ = 7.3 Hz, H-6a), 3.74 (dd, 1 H, $J_{5,6d}$ = 5.6 Hz, H-6b), 3.13 (s, 1 H, H-2), 2.16, 2.11, 2.10, 2.06, 1.99 (5 s, 15 H, 5 Ac), 1.16 (d, 3 H, $J_{5',6'}$ = 6.6 Hz, H-6'); ^{13}C NMR data: δ 170.4, 170.0, 169.9, 169.8, 169.2, 101.9, 82.4, 72.5, 70.8, 70.7, 68.4, 67.4, 65.5, 64.9, 64.8, 46.9, 20.9, 20.7, 20.6, 20.5, 15.9; Anal. Calcd for $C_{22}H_{30}O_{13}S$: C, 49.43; H, 5.66. Found: C, 49.32; H, 5.66.

Compound **29** had mp 159-160°C; $[\alpha]_D^{24}$ -203 (c 0.76, $CHCl_3$); ^1H NMR data: δ 5.93 (d, 1 H, $J_{1',2'}$ = 5.0 Hz, H-1'), 5.45 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1), 5.30 (d, 1 H, $J_{3',4'}$ = 2.0 Hz, H-4'), 5.20-5.13 (m, 2 H, H-2',3'), 5.08 (dd, 1 H, $J_{3,4}$ = 10.1 Hz, $J_{4,5}$ = 3.5 Hz, H-4), 4.67 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, H-2), 4.56 (t, 1 H, $J_{5,6b}$ = 5.0 Hz, H-5), 4.47 (q, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.10 (d, 1 H, $J_{6a,6b}$ = 7.9 Hz, H-6a), 3.76 (dd, 1 H, H-6b), 3.19 (t, 1 H, H-3), 2.17, 2.13, 2.04, 2.00 (4 s, 15 H, 5 Ac), 1.21 (d, 3 H, H-6'); ^{13}C NMR data: δ 170.4, 170.3, 169.9, 169.8, 169.7, 99.1, 82.4, 73.9, 73.0, 72.9, 70.6, 68.2, 68.0, 65.4, 64.9, 41.4, 20.8, 20.7, 20.6, 20.5, 15.8; Anal. Calcd for $C_{22}H_{30}O_{13}S$: C, 49.43; H, 5.66. Found: C, 49.15; H, 5.44.

1,3,4,6-Tetra-*O*-acetyl-2-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-thio-D-galactopyranose (30). A solution of **28** (1.26 g, 2.36 mmol) in Ac_2O-AcOH-H_2SO_4 (7 : 3 : 0.07 v/v; 3 mL) was stirred at room temperature for 1 h. Sodium acetate (500 mg) was then added and the solution was concentrated *in vacuo*. The residue was dissolved in EtOAc and the solution was washed with brine dried (MgSO4), and evaporated in vacuo. The residue was chromatographed with 1 : 1 hexane-EtOAc to give **30** (1.56 g, quantitative) as a 88 : 12 mixture of α and β anomers. Compound **30** had mp 219-221°C; $[\alpha]_D^{22}$ -119 (c 1.13, $CHCl_3$); ^1H NMR data: δ 6.21 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.88 (d, 1 H, $J_{1',2'}$ = 4.6 Hz, H-1'), 5.39 (d, 1 H, $J_{3,4}$ = 3.6 Hz, H-4), 5.28-5.27 (m, 1 H, H-4'), 5.27 (dd, 1 H, $J_{2,3}$ = 11.5 Hz, H-3), 5.19-5.09 (m, 2 H, H-2', 3'), 4.43 (q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.27 (t, 1 H, $J_{5,6}$ = 6.9 Hz, H-5), 4.08(d, 2 H, H-6), 3.35(dd, 1 H, H-2), 2.19, 2.16, 2.15, 2.03, 2.02, 1.99 (6 s, 21 H, 7 Ac), 1.20 (d, 3 H, H-6'); ^{13}C NMR data: δ 170.4, 170.3, 170.1, 170.0, 169.8, 168.8, 92.7, 83.4, 70.7, 70.3, 68.6, 68.1, 68.0, 66.7, 65.1, 61.2, 42.0, 20.8, 20.6, 20.5, 20.4, 15.9; Anal. Calcd for $C_{26}H_{36}O_{16}S$: C, 49.05; H, 5.70. Found: C, 48.86; H, 5.81.

***O*-{3,4,6-Tetra-*O*-acetyl-2-S-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-thio-α-D-galactopyranosyl}trichloroacetimidate (31).** A mixture of **30** (617 mg, 0.812 mmol) and $NH_2NH_2\cdot$AcOH (152 mg, 1.65 mmol) in DMF was stirred for 20 min at 50°C, and diluted with EtOAc. The mixture was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed with 3 : 5 hexane-EtOAc to give the corresponding hemiacetal (372 mg, 65%). A solution of this hemiacetal (543 mg, 0.913 mmol) in CH_2Cl_2 (1 mL), stirred under argon, was treated successively with CCl_3CN (0.90 mL, 9.0 mmol) and DBU (50 μL) at 0°C. After being stirred for 1 h at 0°C, the mixture was directly chromatographed with 4 : 1 - 1 : 1 hexane -EtOAc to give **31** (598 mg, 89%). Compound **31** had mp 181-182 °C; $[\alpha]_D$ -84 (c 1.07, $CHCl_3$); ^1H NMR data: δ 8.78 (s, 1 H, NH), 6.41 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1), 5.91 (d, 1 H, $J_{1',2'}$ = 4.5 Hz, H-1'), 5.45 (d, 1 H, $J_{3,4}$ = 3.1 Hz, H-4), 5.33 (dd, 1 H, $J_{2,3}$ = 11.7 Hz, H-3), 5.31 (m, 1 H, H-4), 5.19 (dd, 1 H, $J_{2',3'}$ = 10.8 Hz, H-2'), 5.12 (dd, 1 H, $J_{3,4}$ = 2.8 Hz, H-3'), 4.49 (q, 1 H, $J_{5',6'}$ = 6.3 Hz, H-5'), 4.42 (t, 1 H, $J_{5,6a}$ = 6.3 Hz, $J_{5,6b}$ = 7.3 Hz, H-5), 4.14 (dd, 1 H, $J_{6a,6b}$ = 11.5 Hz, H-6a), 4.07 (dd, 1 H, H-6b), 3.43 (dd, 1 H, H-2), 2.17, 2.16, 2.04, 2.03, 2.01, 1.99 (6 s, 18 H, 6 Ac), 1.21 (d, 3 H, H-6'); ^{13}C NMR data: δ 170.4, 170.3, 170.2, 170.0, 169.9, 169.8, 160.6, 96.8, 83.4, 70.6, 70.4, 69.2, 68.2, 68.1, 66.8, 65.0, 61.4, 42.4, 20.7, 20.6, 20.5, 20.4, 15.9; Anal. Calcd for $C_{26}H_{34}Cl_{3}NO_{15}S$: C, 42.26; H, 4.64; N, 1.90. Found: C, 42.25; H, 4.76; N, 1.80.

Allyl 3,4,6-tri-*O*-acetyl-2-*S*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-2-thio-β-D-galactopyranoside (32) and α-anomer. To a mixture of **31** (816 mg, 1.10 mmol), allyl alcohol (0.45 mL, 6.6 mmol), and MS 4A (2 g), stirred under argon at -45°C, was added a solution of $BF_3 \cdot OEt_2$ (34 mL, 0.28 mmol) in CH_2Cl_2 (0.3 mL) and filtered through Celite. The filtrate was evaporated *in vacuo*. The residue was chromatographed with 1 : 1 - 1 : 2 hexane-EtOAc to give **32** (634 mg, 90%) and its α-anomer (56 mg, 8%). Compound **33a** had $[\alpha]_D^{21}$ -189 (c 1.15, $CHCl_3$); ^{1}H NMR data: δ 6.03-5.92 (m, 1 H, $OCH_2CH{=}CH_2$), 5.90 (d, 1 H, $J_{1',2'}$ = 5.1 Hz, H-1'), 5.38-5.19 (m, 5 H, H-4, 3', 4', $OCH_2CH{=}CH_2$), 5.14 (dd, 1 H, $J_{2',3'}$ = 10.7 Hz, H-2'), 4.99 (dd, 1 H, $J_{2,3}$ = 11.8 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.60 (q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.41 (d, 1 H, $J_{1,2}$ = 9.1 Hz, H-1), 4.41-4.36 (m, 1 H, $OCH_2CH{=}CH_2$), 4.19 (dd, 1 H, $J_{5,6a}$ = 6.6 Hz, $J_{6a,6b}$ = 11.0 Hz, H-6a), 4.14-4.11 (m, 1 H, $OCH_2CH{=}CH_2$), 4.12 (dd, 1 H, $J_{5,6b}$ = 6.9 Hz, H-6b), 3.85 (t, 1 H, H-5), 3.09 (dd, 1 H, H-2), 2.16, 2.13, 2.05, 2.03, 2.01, 2.00 (6 s, 18 H, 6 Ac), 1.16 (H-6'); ^{13}C NMR data: δ 170.4, 170.3, 170.2, 170.1, 170.0, 169.9, 133.3, 118.6, 100.5, 82.4, 73.7, 70.9, 70.8, 70.4, 68.4, 68.2, 66.1, 65.1, 61.4, 44.1, 20.6, 20.5, 20.3, 15.7; Anal. Calcd for $C_{27}H_{38}O_{15}S$: C, 51.10; H, 6.04. Found: C, 51.20; H, 6.40.

Compound **33b** had mp 162-163°C; $[\alpha]_D^{21}$ -107 (c 0.58, $CHCl_3$); 5.99 (m, 2 H, H-1', $OCH_2CH{=}CH_2$), 5.38-5.17 (m, 7 H, H-3, 4, 2', 3', 4', $OCH_2CH{=}CH_2$), 4.93 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H-1), 4.47 (q, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 4.26-4.00 (m, 5 H, H-5, 6a, 6b, $OCH_2CH{=}CH_2$), 3.30 (dd, 1 H, $J_{2,3}$ = 11.2 Hz, H-2), 2.16, 2.12, 2.05, 2.02, 2.01, 2.00 (6 s, 18 H, 6 Ac), 1.19 (d, 3 H, $J_{5',6'}$ = 6.6 Hz, H-6'); ^{13}C NMR data: δ 170.4, 170.2, 170.1, 169.9, 133.0, 118.3, 71.5, 70.7, 69.0, 68.1, 67.4, 66.8, 64.7, 61.9, 42.0, 20.6, 20.5, 20.4, 15.9, Anal. Calcd for $C_{27}H_{38}O_{15}S$: C, 51.10; H, 6.04. Found: C, 51.00; H, 6.04.

Allyl 2-*S*-(α-L-fucopyranosyl)-2-thio-β-D-galactopyranoside (4). A solution of **32** (596 mg, 0.939 mmol) in MeOH (2 mL) and a 0.5 M solution of MeONa in MeOH (0.3 mL) were mixed and stirred for 2 h at room temperature. The mixture was neutralized with Dowex 50W-X2 (H^+) resin and filtered. The filtrate was concentrated *in vacuo* to give **4** (371 mg, quantitative). Compound **34** had mp 171-172°C; $[\alpha]_D^{21}$ -177 (c 0.66, H_2O); ^{1}H NMR data: δ 6.08-5.98 (m, 1 H, $OCH_2CH{=}CH_2$), 5.59 (d, 1 H, $J_{1',2'}$ = 5.5 Hz, H-1'), 5.43-5.27 (m, 2 H, $OCH_2CH{=}CH_2$), 4.56 (d, 1 H, $J_{1,2}$ = 8.9 Hz, H-1), 4.46 (q, $J_{5',6'}$ = 5.6 Hz, H-5'), 4.39-4.37 (m, 1 H, $OCH_2CH{=}CH_2$), 4.30-4.23 (m, 1 H, $OCH_2CH{=}CH_2$), 4.08 (dd, 1 H, $J_{2',3'}$ = 10.2 Hz, H-2'), 3.90-3.66 (m, 7 H, H-3, 4, 5, 6a, 6b, 3', 4'), 2.83 (t, 1 H, $J_{2,3}$ = 10.9 Hz, H-2), 1.22 (d, 3 H, H-6'); ^{13}C NMR data: δ 134.0, 118.9 ($OCH_2CH{=}CH_2$), 101.4, 86.9, 75.3, 73.8, 72.1, 71.1, 70.7, 68.4, 68.2, 68.0, 61.4, 49.0, 15.9 Anal. Calcd for $C_{15}H_{26}O_9S$: C, 47.11; H, 6.85. Found: C, 47.11; H, 7.14.

Measurement of inhibition activity. α-L-Fucosidases from bovine kidney and bovine epididymis were purchased from Sigma Chemical Co. and *p*-nitrophenyl α-L-fucopyranoside from Seikagaku Kogyo Co. Enzyme assay was performed by essentially the same method as that of Evans *et al.*[26] Inhibition assay was performed at 25°C for 30-40 min in 20 mM citrate buffer (pH 5.5 for bovine kidney and pH 5.8 for bovine epididymis, 300 μL), which contained the following assay components: *p*-nitrophenyl α-L-fucopyranoside (0.07-0.33 mM), the *S*-linked disaccharide **1**, **2**, **3** (each 0-6.7 mM, two intermediate points) or **4** (0-1 mM, two intermediate points), α-L-fucosidase (0.8-1.1 units/mL for bovine kidney and 1.4 units/mL for bovine epididymis). After addition of 50 mL glycine buffer (pH 10.0, 500 μL), UV absorption at 400 nm was measured. The data expressed by Lineweaver-Burk plot and replots of the slope *versus* the inhibitor concentration and the intercept *versus* the inhibitor concentration indicate the modes of inhibition and give the Ki values as well as the coefficient α.

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   The coefficient α is defined as shown in the following system of the linear mixed-type inhibition, where E, S, I, and P mean enzyme, substrate, inhibitor, and product, respectively.

$$\begin{tikzcd}
E + S \arrow[r, shift left, "K_s"] & ES \arrow[l, shift left] \arrow[r, "k_p"] & E + P \\
+ & + & \\
I \arrow[d, shift left] & I \arrow[d, shift left] & \\
EI + S \arrow[u, shift left, "K_i"] \arrow[r, shift left, "\alpha K_s"] & ESI \arrow[l, shift left] \arrow[u, shift left, "\alpha K_i"'] &
\end{tikzcd}$$

$$K_s = [E][S] / [ES]$$

$$K_i = [E][I] / [EI]$$

$$v = k_p[ES]$$

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