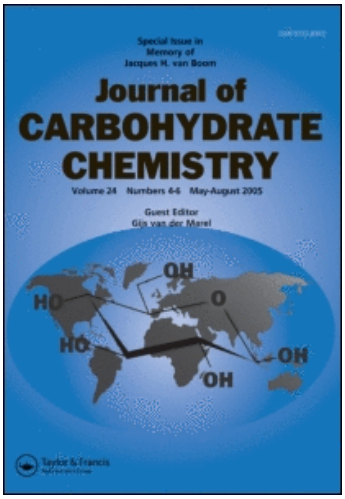

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Regioselective Glycosylation of *N*-Protected l-Rhamno(fuco) pyranosylamines: Preparation and Spectroscopic Characterization of Building Blocks for Neoglycoconjugate Syntheses.

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REGIOSELECTIVE GLYCOSYLATION OF *N*-PROTECTED L-RHAMNO(FUCO) PYRANOSYLAMINES: PREPARATION AND SPECTROSCOPIC CHARACTERIZATION OF BUILDING BLOCKS FOR NEOGLYCOCONJUGATE SYNTHESES.

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ABSTRACT

The regioselective glycosylations of *N*-2-bis(ethoxycarbonyl)vinyl-β-L-rhamno- (**1**) and fucopyranosylamine (**2**) with tetra-*O*-acetyl-α-D-glycopyranosyl bromides were performed. In this way the *N*-protected disaccharide and trisaccharide β-D-Glc*p*-(1→3)-β-L-Rha*p* (**3**), β-D-Glc*p*-(1→4)-β-L-Rha*p* (**5**), β-D-Gal*p*-(1→3)-β-L-Rha*p* (**7**), β-D-Gal*p*-(1→4)-β-L-Rha*p* (**9**), β-D-Glc*p*-(1→3)-β-L-Fuc*p* (**11**), β-D-Glc*p*-(1→2)-β-L-Fuc*p* (**13**), and β-D-Gal*p*-(1→3)-[β-D-Gal*p*-(1→2)]-β-L-Rha*p* (**14**) glycosylamines were obtained. The structures of compounds **3**, **5**, **7**, **9**, **11**, **13**, and **14** are supported by the preparation of the corresponding per-*O*-acetyl derivatives and by spectroscopic (IR, NMR, and MS) data.

INTRODUCTION

Glycosylamines are valuable building blocks in the synthesis of neoglycoconjugates and other compounds of biological and synthetic interest such as glycosylisothiocyanates, *N*-nucleosides and glycosylaminoheterocycles.[1-10] The latter

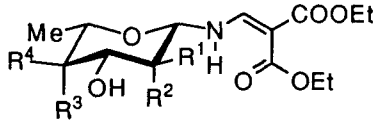
two can also be interesting from a pharmacological point of view.[11] The data on oligosaccharide glycosylamines are limited. The usual strategy for obtaining oligosaccharide glycosylamines involves the reduction of the corresponding azide[12-13] or the treatment of the reducing oligosaccharide with aqueous ammonium bicarbonate.[2,14-16] In both cases the corresponding oligosaccharides are used as precursors. We have recently reported[17,18] the synthesis of *O*-protected glycosylaminomethylenemalonates of oligosaccharides through glycosylation reactions using *N*-alkenylglycosylamines as glycosyl acceptors. The *N*-protecting ethoxycarbonylvinyl group is easy to remove under mild conditions which do not produce cleavage of the glycosidic bonds in oligosaccharides[19].

Oligosaccharides are frequently obtained through glycosylation reactions on suitable partially *O*-protected sugars.[20] Direct regioselective glycosylation of unprotected mono and disaccharides may represent a valuable tool for the syntheses of oligosaccharides,[21] although in some instances, complex mixtures of products difficult to isolate are produced. In this regard transient dibutylstannylene acetals and tributyltin ethers have proved to be particularly useful.[22]

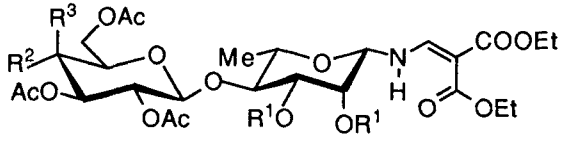
As a part of our programme on the synthesis of glycosylamines and glycosyl isothiocyanates, we now report the regioselective glycosylation of the *N*-protected L-rhamno (**1**) and L-fucopyranosylamine (**2**) with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco(galacto)pyranosyl bromides. In these reactions the regioselectivity will be due only to differences in the reactivity between secondary hydroxyl groups. The carbohydrate moieties of the new compounds represent the repeating unit of several capsular polysaccharides[23-25] that would be of potential interest for immunological studies. They are also related to the structure of several glycopeptidolipid antigens of pathogenic *Mycobacterium* species.[26] In addition the L-fucosylamine is an inhibitor of the lactose transport system of *Escherichia coli*.[27]

RESULTS AND DISCUSSION

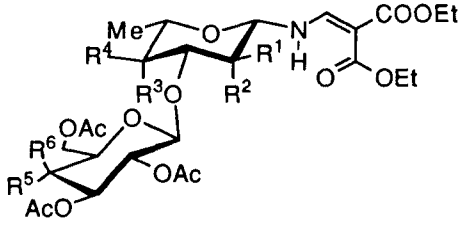
Regioselective glycosylation of unprotected sugars is a convenient method for oligosaccharide syntheses when a marked difference of reactivity exists between the hydroxyl groups. This method has been applied to the syntheses of 2-amino-2-deoxy oligosaccharides[28] but, as far as we know, there are no precedents of its use in oligosaccharide glycosylamine synthesis. A study[6] on the selective benzoylation of an *N*-alkenylrhamnopyranosylamine has shown that the 3-hydroxyl group is consistently more



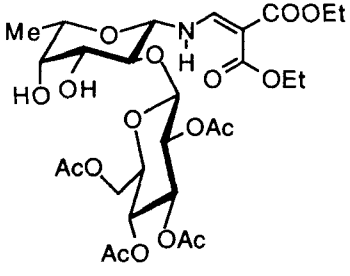
1 $R^1=R^3=H$ $R^2=R^4=OH$
2 $R^1=R^3=OH$ $R^2=R^4=H$



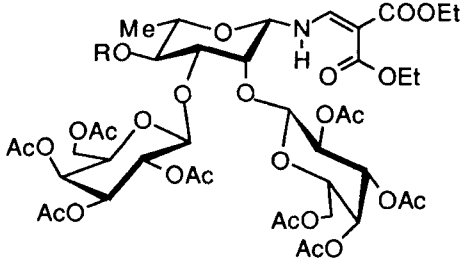
	R^1	R^2	R^3
5	H	OAc	H
6	Ac	OAc	H
9	H	H	OAc
10	Ac	H	OAc



	R^1	R^2	R^3	R^4	R^5	R^6
3	H	OH	H	OH	OAc	H
4	H	OAc	H	OAc	OAc	H
7	H	OH	H	OH	H	OAc
8	H	OAc	H	OAc	H	OAc
11	OH	H	OH	H	OAc	H
12	OAc	H	OAc	H	OAc	H



13



14 R=H
15 R=Ac

reactive towards the acylation than either the 2- or the 4-hydroxyl group, which do not have a marked difference of reactivity between them. This observation suggested that, under mild conditions, a similar order of reactivity might prevail in the reaction of glycosyl halides with the same L-rhamnopyranosylamine derivative. Accordingly, the *N*-ethoxycarbonylvinyl-L-rhamno- (**1**) and L-fuco- (**2**) pyranosylamines were glycosylated[29] at low temperature using acetobromoglucose and acetobromogalactose as glycosyl donors. In these reactions a 6:3:8 donor:acceptor:promoter molar ratio was used (see experimental), and in every case, the glycosylation occurred with a complete 1,2-*trans* stereoselectivity. The new products and the yields are shown in Table 1. The compounds isolated after the glycosylations of the L-rhamno derivative **1** (entries 1 and 2) indicated that, as in the case of benzoylations,[6] the HO-3 appears to be the most reactive hydroxyl group. In the case of the L-fucosylamine derivative **2** (entry 3) the most reactive hydroxyl group also appears to be the HO-3, the regioselectivity being higher than in the case of the L-rhamno compound **1**. In this reaction a second disaccharide derivative was detected; its NMR data were in accordance with the structure **13**; however, the product could not be fully purified. In the three reactions (entries 1-3), a part (20 - 25%) of the starting material was recovered unaltered and several trisaccharide glycosylamine derivatives were detected (TLC, NMR and MS) but only the β-D-Gal*p*-(1→3)-[β-D-Gal*p*-(1→2)]-β-L-Rha*p* *N*-alkenylglycosylamine **14** (entry 2) could be isolated and characterised.

Compounds **3, 5, 7, 9, 11,** and **14** were conventionally acetylated to give **4, 6, 8, 10, 12,** and **15,** respectively. The structures (**3 - 15**) were based on analytical and UV, IR, ^{1}H(Tables 2 and 3), ^{13}C(Table 4) NMR, and MS spectroscopic data. Thus, the resonances for the carbon atoms which are glycosylated (C-3 in **3, 7,** and **11**, C-4 in **5** and **9**, C-2 in **13**, and C-2 and C-3 in **14**) undergo a strong deshielding (Δδ 10-12 ppm) when they are compared with the signals for the same atoms in the starting materials **1** and **2**,[6] as reported for other glycosyl derivatives.[18, 30] These Δδ practically disappear on acetylation (see Table 4). The glycosylation positions were also confirmed by comparison of the chemical shifts for the resonances of the protons corresponding to non- glycosylated positions before (C*H*OH) and after (C*H*OAc) acetylation (see Table 2). A small amount of **14** was acetylated with Ac_2O-Py to give **15**. After evaporation of these reagents, the ^{1}H and COSY spectra confirmed the 2 and 3 as glycosylation positions; the resonance for H-4 in **15** appeared as a triplet at 4.89 ppm, whereas in **14** the same proton resonated at 3.43 ppm. The $J_{1,2}$ values (7.5-8.3 Hz) for the rings B and C of **3 - 15** were in the range for antiperiplanar protons and, together with the chemical shifts of the C-1 (rings B and C) resonance (98.5-103.1 ppm),[17, 30] indicated that the glycosyloxy moieties have the β configuration. The $^4C_1$(D) conformation for the D-*gluco*

TABLE 1

Regioselective Glycosylations of **1** and **2**

Entry	Acceptor	Donor	Products (yield)			Total yield[a]
			Disaccharides		Trisaccharides	
1	**1**	Acetobromoglucose	**3**(30%)	**5**(24%)	Detected	54%
2	**1**	Acetobromogalactose	**7**(30%)	**9**(20%)	**14** (5%)	55%
3	**2**	Acetobromoglucose	**11**(44%)	**13** (Detected)	Detected	44%

a. of isolated products

and D-*galacto* rings (B, C) and the $^1C_4$(L) conformation for the L-*rhamno* or L-*fuco* ring (A) in chloroform solutions of **3 - 15** were evident from the $^3J_{H,H}$ values (Table 3), except in the case of the *O*-unprotected L-*rhamno* ring (A) of compounds **3** and **5,** where the $^1C_4$(L) conformation is somewhat distorted in the C-3, C-4 region, as $J_{2,3}$ is 1.7 Hz instead of the characteristic value (≈ 3.3 Hz).[6,31] The enamino moiety of **3 - 15** had the hydrogen bond shown in the structure, as is deduced from the two ^{13}C NMR signals at ≈ 168.0 (C=O chelated) and 165.8 ppm (C=O free),[17, 18] and from the IR bands at ≈1725 (C=O free), ≈ 1650 (C=O chelated) and ≈ 1615 cm^{-1} (C=C and NH).[32] The $J_{NH,1}$ values (8.0-9.2 Hz) observed for **3 - 15** are indicative of an *anti* relationship between the corresponding protons. This conformation is similar to that described for *N*-acyl-α-D-ribofuranosylamines[33] and other *N*-alkenylglycosylamines.[17, 18]

The EIMS of the acetyl derivatives **4, 6, 8, 10,** and **12** contained the molecular ions, and showed the same fragmentation pathways described for other N-alkenylglycosylamines.[6,17,34] Thus, the losses of EtO$^\bullet$ (peak A), and enamino group (peak B), and the peaks at *m/z* 216 ($C_9H_{14}O_5N$, peak C), 187 [$H_2NCH{:}C(CO_2Et)_2^{\bullet+}$, peak D], and 142 (D-EtO$^\bullet$, peak E) were significant signals (see Experimental). The peak *m/z* 331 corresponding to the tetra-*O*-acetyl-D-gluco(galacto)pyranosyl[17] group was also observed.

EXPERIMENTAL

General methods. Melting points are uncorrected. Optical rotations were measured at 20 - 25 °C, using 1 cm cell. UV spectra were measured in dichloromethane with a Philips PU 8720 spectrometer. FTIR spectra were recorded for KBr discs. ^1H

TABLE 2

Relevant ^1H NMR chemical shifts (δ,ppm) for the sugars rings of compounds **3 - 15** in $CDCl_3$

Comp.	Ring[a]	H-1	H-2	H-3	H-4	H-5	H-6	H-6'
3[b]	A	4.62dd	4.20dd	3.56dd	3.64t	3.40dq	1.35d(3H)	-
	B	4.72d	5.04dd	5.31t	5.02t	3.78ddd	←---- 4.30-4.08m ----→	
4[c]	A	4.71dd	5.40dd	3.86dd	5.02t	3.51dq	1.31-1.25m(3H)	-
	B	4.61d	4.91dd	←---- 5.22-5.00m ----→		3.72-3.60m	4.31dd	4.31-4.15m
5[c]	A	4.50dd	3.95dd	3.75-3.57m	3.44t	3.38-3.27m	1.31d(3H)	-
	B	4.81d	4.83dd	5.16t	4.98t	3.75-3.57m	←---- 4.20-4.07m ----→	
6[b]	A	4.73dd	5.38dd	5.18dd	3.59t	3.52m	1.35-1.25m(3H)	-
	B	4.68d	4.96dd	5.17t	5.07t	3.76m	←---- 4.27-4.18m ----→	
7[b]	A	4.60dd	4.11dd	3.52dd	3.63t	3.41m	1.35d(3H)	-
	B	4.63d	5.24dd	5.06dd	5.40d	3.95dd	←---- 4.27-4.16m ----→	
8[b]	A	4.70dd	5.53dd	3.88dd	5.06t	3.52m	1.33-1.20m(3H)	-
	B	4.59d	5.09dd	4.94dd	5.35d	3.85-3.90m	4.25-4.11m	4.17dd
9[b]	A	4.59dd	4.11dd	3.53dd	3.61t	3.40m	1.20-1.10m(3H)	-
	B	4.65d	5.23dd	5.05dd	5.40d	3.96m	4.08dd	4.26-4.15m
10[b]	A	4.66dd	5.33-5.27m	4.93dd	3.52t	3.45m	1.10d(3H)	-
	B	4.55d	5.07dd	4.98dd	5.32-5.27m	3.87t	4.17-4.10m	4.01dd
11[c]	A	4.32t	3.82t	3.57dd	←---- 3.87-3.60m ----→		1.30d(3H)	-
	B	4.65d	5.00t	5.26t	5.04t	3.87-3.60m	←---- 4.17-4.07m ----→	
12[b]	A	4.46t	5.14t	4.01dd	5.25dd	3.78dq	1.19d(3H)	-
	B	4.65d	4.88dd	5.17t	5.14t	3.73-3.69m	4.35dd	4.08dd
13[b]	A	4.70dd	3.61t	←-------	3.73-3.66m	-------→	1.21-1.39m(3H)	-
	B	4.60d	5.06dd	5.25t	5.10t	3.83-3.80m	←---- 4.30-4.10m ----→	
14[b]	A	4.51bd	4.31-4.10m	3.49dd	3.43t	3.36m	1.35d(3H)	-
	B	4.93d	5.30dd	5.05-5.01m	5.42d	3.98t	←---- 4.31-4.10m ----→	
	C	4.69d	5.18dd	5.05-5.01m	5.37d	3.88t	4.31dd	4.12dd
15[b]	A	4.53bd	4.35-4.20m	3.74dd	4.89t	3.47m	1.23d(3H)	-
	B	4.95d	5.35dd	5.06dd	5.43-5.42m	3.96-3.91m	4.35-4.20m	4.06dd
	C	4.67d	5.17dd	5.02dd	5.43-5.42m	3.96-3.91m	4.35-4.20m	4.17dd

a. For **3-13** ring A and B refers to the rhamno(fuco) residue and the gluco(galacto) residue respectively. In the case of **14** and **15** ring A is the rhamno moiety and rings B and C are the galacto residues joined to positions 2 and 3, respectively. b. 500 MHz. c. 200 MHz.

TABLE 3

Relevant ^{1}H NMR measured coupling constanst (J, Hz) for the sugar rings of compounds **3 - 15** in $CDCl_3$

Comp.	Ring[a]	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
3[b]	A	<1	1.7	9.6	9.6	6.1	-	-
	B	7.9	9.3	9.3	9.3	2.5	6.4	-
4[c]	A	<1	2.9	10.1	10.1	6.4		-
	B	8.3	9.6	9.6	9.6	2.4	-	12.9
5[c]	A	<1	1.7	8.6	8.6	6.5		-
	B	8.0	9.7	9.7	9.7	-	-	-
6[b]	A	<1	3.3	9.4	9.4	-	-	-
	B	8.1	9.6	9.6	9.6	-	-	-
7[b]	A	<1	3.0	9.3	9.3	6.1	-	-
	B	7.5	10.9	3.4	0.0	-	-	-
8[b]	A	<1	3.2	9.3	9.3	-	-	-
	B	7.9	10.5	3.0	0.0	-	-	11.4
9[b]	A	<1	3.1	9.2	9.2	-	-	-
	B	7.8	10.4	3.4	0.0	5.2	-	11.5
10[b]	A	<1	-	9.5	9.5	5.8	-	-
	B	8.0	10.5	3.2	-	-	7.3	11.3
11[c]	A	8.0	8.0	3.3	-	7.1	-	-
	B	8.0	9.2	9.2	9.2	-	-	-
12[b]	A	9.5	9.5	2.9	0.8	6.0	-	-
	B	7.5	9.1	9.1	9.1	4.3	2.4	12.4
13[b]	A	9.0	9.0	-	-	-		
	B	8.5	9.6	9.6	9.6	-	-	-
14[b]	A	≈0.0	2.2	9.3	9.0	5.9	-	-
	B	7.8	10.3	3.2	0.0	7.1	7.1	-
	C	7.6	10.3	2.7	0.0	7.2	7.2	11.4
15[b]	A	≈0.0	2.8	9.6	9.6	6.1	-	-
	B	7.8	10.6	3.5	0.0	-	6.7	12.2
	C	7.9	10.5	3.3	0.0	-	6.1	11.4

a, b, c. See footnotes of Table 2

TABLE 4

Relevant ^{13}C NMR chemical shifts (δ,ppm) for the sugars rings of compounds **3 -14** in $CDCl_3$

Comp.	Ring[a]	C-1	C-2	C-3	C-4	C-5	C-6
3[d]	A	85.2	69.1	84.4	69.9	72.0	17.4
	B	101.1	71.3	73.2	68.2	72.0	61.8
4[d]	A	84.3	70.6	75.9	71.9	71.7	17.2
	B	100.6	70.1	72.3	68.0	71.6	60.9
5[d]	A	85.3	71.9	73.3	80.8	71.6	17.5
	B	101.0	70.4	72.6	68.2	71.8	61.9
6[d]	A	84.0	73.2	69.7	75.8	72.7	17.6
	B	100.6	71.0	72.6	68.5	71.4	61.9
7[c]	A	85.1	69.1	84.6	71.2	73.6	17.4
	B	101.6	68.9	70.0	66.6	70.2	61.4
8[c]	A	84.5	71.9	75.7	72.1	72.0	17.2
	B	101.1	68.6	70.6	66.6	70.8	60.8
9[b]	A	85.1	71.2	73.1	84.6	70.2	17.4
	B	101.6	68.9	69.9	66.6	70.1	61.4
10[c]	A	84.0	73.2	69.6	75.6	72.7	17.7
	B	101.9	68.6	70.3	66.7	70.8	60.9
11[d]	A	88.0	69.0	85.6	71.3	72.0	16.1
	B	100.9	70.1	72.1	68.2	72.0	61.9
12[b]	A	87.3	69.2[e]	76.2	69.0[e]	71.4	16.2
	B	98.5	71.1	72.8	67.8	71.7	61.7
13[c]	A	88.6	82.9	71.4	72.4	72.2	16.2
	B	101.9	71.2	73.4	67.9	71.9	61.4
14[c]	A	85.6	84.7	84.8	70.9	73.7	17.5
	B	101.2	69.4	70.7	66.7	70.6	61.3
	C	103.1	68.8	70.7	66.5	70.6	61.1

a. See footnote [a] of Table 2; b. 125.7 MHz; c. 75.4 MHz; d. 50.3 MHz; e. Assignments may be interchanged.

NMR spectra were obtained at 200 and 500 MHz for solutions in $CDCl_3$. Assignments were confirmed by decoupling, H/D exchange, and homonuclear 2D COSY correlated experiments.

^{13}C NMR spectra were recorded at 50.3, 75.4, and 125.7 MHz for solutions in $CDCl_3$. Proton decoupled APT[35] and heteronuclear 2D correlated spectra were obtained to assist in carbon signal assignments. EIMS (70 eV) were measured with a KRATOS MS-80RFA instrument, with an ionising current of 100 μA, an accelerating voltage of 4 KV

and a resolution of 1000 (10% valley definition). The elemental composition of the ions was determined with a resolution of 10,000 (10% valley definition). The FABMS spectra were recorded with the same instrument. Ions were produced by a beam of xenon atoms (6 - 7 KeV) using a matrix consisting of glycerol or thioglycerol and NaI as salt. In the HRFABMS, $(CsI)_{37}Cs$ was used as reference. TLC was performed on Silica Gel HF_{254} (Merck), with detection by UV light, or charring with sulphuric acid. Silica Gel 60 (Merck, 230 mesh) was used for preparative chromatography.

Regioselective glycosylation of L-rhamno (1) and L-fucopyranosylamine (2). A solution of acetobromoglucose(galactose) (1.23 g, 3 mmol) in dry acetonitrile (15 mL) was transferred under N_2 to a mixture of acceptor[6] (**1** or **2**, 0.50 g, 1.5 mmol), mercury (II) cyanide (1.01 g, 4 mmol), mercury (II) bromide (1.44 g, 4 mmol), and molecular sieves (3 Å). The reaction mixture was stirred under N_2 for 48 h at -10 °C, and then filtered through celite and concentrated. The filtrate was diluted with chloroform (30 mL) and washed with aqueous 10% potassium iodide, saturated aqueous sodium hydrogencarbonate, and water, dried ($MgSO_4$), and concentrated. The purification was performed by column chromatography on silica gel (10:1→ 5:1, dichloromethane:acetone). The following compounds were prepared in this manner.

***N*-2-bis(ethoxycarbonyl)vinyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-rhamnopyranosylamine (3) and *N*-2-bis(ethoxycarbonyl)vinyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-rhamnopyranosylamine (5).** The reaction of **1** and acetobromoglucose gave **3** (0.30 g, 30%) and **5** (0.24 g, 24%).

Compound **3** had mp 175-177 °C (from dichloromethane:acetone); $[\alpha]_D$ +19° (*c* 1.0, chloroform); λ_{max} 225.4 and 275.2 nm (ε_{mM} 5.2 and 22.5); ν_{max} 3543 (OH), 3310 (NH), 1755 (C=O), 1720 (C=O free),[32] 1659 (C=O chelated), 1609 (NH and C=C), 1233 (C-O-C). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.63 (dd, 1H, $J_{NH,1}$ = 9.1 Hz, NH), 8.08 (d, 1H, $J_{NH,=CH}$ = 12.2 Hz, =CH), 4.30-4.08 (m, 4H, $2CH_2CH_3$), 3.14 (d, 1H, $J_{H,OH}$ (C=O), 1730 (C=O chelated), 1675, 1607 (NH and C=C), 1231 (C-O-C). ^1H NMR (200 MHz) Tables 2 and 3 and δ 9.63 (dd, 1H, $J_{NH,1}$ = 9,2 Hz, NH), 8.08 (d, 1H, $J_{NH,=CH}$ = 12.2 Hz, =CH), 4.20 - 4.07 (m, 4H, $2CH_2CH_3$), 3.15 (bs, 2H, 2OH), 2.08, 2.08, 2.04, and 2.01 (4s, each 3H, $4COCH_3$), 1.36 - 1.26 (m, 6H, $2CH_2CH_3$). ^{13}C NMR (50.3 MHz), = 2.7 Hz, OH), 2.74 (d, 1H, $J_{H,OH}$ = 2.9 Hz, OH), 2.07, 2.06, 2.05, and 2.04 (4s, each 3H, 4 $COCH_3$), 1.31 and 1.29 (2t, each 3H, $J_{H,H}$ = 7.2 Hz, $2CH_2CH_3$). ^{13}C NMR (50.3 MHz), Table 4 and δ 170.7, 170.0, 169.3 (4 $COCH_3$), 167.7 (CO chelated),[17] 165.8 (CO free), 157.8 (=CH), 93.0 (=C), 60.1, 59.9 (2 CH_2CH_3), 20.6, 20.5, 20.5, 20.4 (4 $COCH_3$),14.3 and 14.1 ($2CH_2CH_3$). FABMS: *m/z* 686 (100%, $[M+Na]^{+\bullet}$) and 664 (82,$[M+H]^{+\bullet}$).

Anal. Calcd for $C_{28}H_{41}NO_{17}$: C, 50.68; H, 6.18; N, 2.11. Found: C, 50.58; H, 6.41; N, 2.46.

Compound **5** has mp 78-80 °C (from dichloromethane-acetone); $[\alpha]_D$ -7° (*c* 1.1, chloroform); λ_{max} 227.2 and 275.2 nm (ε_{mM} 6.2 and 15.9). ν_{max} 3488 (OH, NH), 1755 Table 4 and δ 170.1, 169.4, 169.3 (4 $COCH_3$), 167.9 (CO chelated), 165.7 (CO free), 157.9 (=CH), 93.1 (=C), 60.1, 60.0 (2CH_2CH_3), 20.7, 20.6, 20.5 (2C) (4 $COCH_3$), 14.3 and 14.1 (2 CH_2CH_3). FABMS: *m/z* 686 (100%, $[M+Na]^{+\cdot}$) and 664 (22, $[M+H]^{+\cdot}$).

Anal. Found: C, 50.86; H, 6.35; N, 2.40.

***N*-2-bis(ethoxycarbonyl)vinyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-L-rhamnopyranosylamine (7), *N*-2-bis(ethoxycarbonyl)vinyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-L-rhamnopyranosylamine (9), and *N*-2-bis(ethoxycarbonyl)vinyl-2,3-di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-L-rhamnopyranosylamine (14).** The reaction of **1** and acetobromogalactose gave **7** (0.30g, 30%), **9** (0.20 g, 20%), and **14** (5%).

Compound **7** had mp 93-95 °C (from dichloromethane-acetone); $[\alpha]_D$ +24° (*c* 1.0, chloroform). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.68 (dd, 1H, $J_{NH,1}$ = 8.8 Hz, NH), 8.07 (d, 1H, $J_{NH,=CH}$ = 13.6 Hz, =CH), 4.27 - 4.16 (m, 4H, 2CH_2CH_3), 2.19, 2.09, 2.03, and 2.01 (4s, each 3H, 4$COCH_3$), 1.32 and 1.30 (2t, each 3H, $J_{H,H}$ = 7.2 Hz, 2CH_2CH_3). ^{13}C NMR (75.4 MHz), Table 4 and δ 170.5, 170.1, 170.0, 169.9 (4$COCH_3$), 167.7 (CO chelated), 165.8 (CO free), 157.8 (=CH), 93.2 (=C), 60.4, 59.9 (2 CH_2CH_3), 20.7, 20.5, 20.4 (2C) (4 $COCH_3$), 14.3 and 14.2 (2 CH_2CH_3). FABMS: *m/z* 686 (100%, $[M+Na]^{+\cdot}$) and 664 (33, $[M+H]^{+\cdot}$).

Anal. Found: C, 50.74; H, 6.18, N, 2.01.

Compound **9** had mp 77-79 °C (from dichloromethane-acetone); $[\alpha]_D$ -17° (*c* 0.7, chloroform). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.69 (dd, 1H, $J_{NH,1}$ = 8.8 Hz, NH), 8.07 (d, 1H, $J_{NH,=CH}$ = 13.8 Hz, =CH), 4.26 - 4.15 (m, 4H, 2CH_2CH_3), 3.00 (bs, 1H, OH-2), 2.18, 2.09, 2.02, and 2.01 (4s, each 3H, 4 $COCH_3$), 1.31 and 1.30 (2t, each 3H, $J_{H,H}$ = 7.1 Hz, 2 CH_2CH_3). ^{13}C NMR (125.7 MHz), Table 4 and δ 170.4, 170.1, 170.0, 169.9 (4 $COCH_3$), 167.7 (CO chelated), 165.8 (CO free), 157.8 (=CH), 93.2 (=C), 60.0, 59.9 (2 CH_2CH_3), 20.7, 20.5, 20.4 (2C) (4 $COCH_3$), 14.3 and 14.2 (2 CH_2CH_3). FABMS: *m/z* 686 (100%, $[M+Na]^{+\cdot}$) and 664 (22, $[M+H]^{+\cdot}$).

Anal. Found: C, 51.06; H, 6.06, N, 1.75.

Compound **14** was an amorphous solid; $[\alpha]_D$ +20° (*c* 0.4, chloroform). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.44 (m, NH), 7.97 (d, 1H, $J_{NH,=CH}$ = 13.7 Hz, =CH), 4.31 - 4.10 (m, 4H, 2CH_2CH_3), 2.22, 2.16, 2.14, 2.06, 2.04, 2.01, and 1.98 (8s, each 3H, 8$COCH_3$), 1.31 and 1.28 (2t, each 3H, $J_{H,H}$ = 7.1 Hz, 2CH_2CH_3). ^{13}C NMR (75.4 MHz), Table 4 and δ 170.3, 170.1, 169.9, 169.8, and, 169.7 (8 $COCH_3$), 166.9 (CO chelated), 166.1 (CO free), 157.9 (=CH), 93.6 (=C), 59.9, 59.7 (2 CH_2CH_3), 20.8, 20.7, 20.6 (2C), 20.5(2C), 20.4, and, 20.3 (8 $COCH_3$), 14.3 and 14.2 (2 CH_2CH_3). FABMS: *m/z* 1016 (100%, $[M+Na]^{+\cdot}$) and 994 (8, $[M+H]^{+\cdot}$).

***N*-2-bis(ethoxycarbonyl)vinyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-fucopyranosylamine (11) and *N*-2-bis(ethoxycarbonyl)vinyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-fucopyranosylamine (13).** The reaction of **2** and acetobromoglucose gave **11** (0.4 g, 44%) and **13** (detected).

Compound **11** has mp 171-173 °C (from dichloromethane-acetone); $[\alpha]_D$ -10.5° (*c* 1.1, chloroform); λ_{max} 227.3 and 276.8nm (ε_{mM} 4.3 and 19.8). ν_{max} 3549 (OH), 3300 (NH), 1751 (C=O), 1724 (C=O free), 1669 (C=O chelated), 1611 (NH and C=C), 1229 (C-O-C). ^{1}H NMR (200 MHz): Tables 2 and 3 and 9.45 (dd, 1H, $J_{NH,1}$ = 8.0 Hz, NH), 8.09 (d, 1H, $J_{NH,=CH}$ = 14.9 Hz, =CH), 4.24 - 4.12 (m, 4H, 2 CH_2CH_3), 2.08, 2.07, 2.05, and 2.02 (4s, each 3H, 4$COCH_3$), and 1.36 - 1.26 (m, 6H, 2 CH_2CH_3). ^{13}C NMR (50.3 MHz), Table 4 and δ 170.4, 170.0, 169.5, 169.2 (4 $COCH_3$), 168.4 (CO chelated), 165.7 (CO free), 157.9 (=CH), 92.3 (=C), 60.0, 59.8 (2 CH_2CH_3), 20.7, 20.6, 20.4 (2C) (4 $COCH_3$), 14.3 and 14.2 (2 CH_2CH_3). FABMS: *m/z* 686 (100%, $[M+Na]^{+\cdot}$) and 664 (98, $[M+H]^{+\cdot}$).

Anal. Found: C, 50.74; H, 6.18; N, 2.01.

Acetylation of 3, 5, 7, 9, 11 and 14. Each of these products (0.05 g, 0.075 mmol, each) was conventionally acetylated with acetic anhydride (0.3 mL) in pyridine (0.3 mL) for 24 h at rt. After partitioning between dichloromethane and water, the organic layer was successively washed with 1M sulphuric acid, aqueous sodium hydrogencarbonate, and water, dried, and evaporated. The new compounds were isolated as syrups.

2,4-Di-*O*-acetyl-*N*-2-bis(ethoxycarbonyl)vinyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-rhamnopyranosylamine (4). 0.04 g, 70%, $[\alpha]_D$ = - 132° (*c* 0.5, dichloromethane). ^{1}H NMR (200 MHz): Tables 2 and 3 and δ 9.45 (dd, 1H, $J_{NH,1}$ = 8.5 Hz, NH), 8.09 (d, 1H, $J_{NH,=CH}$ = 13.2 Hz, =CH), 4.31 - 4.15 (m, 4H, 2 CH_2CH_3), 2.23, 2.12, 2.11, 2.03, 2.03, and 2.00 (6s, each 3H, 6 $COCH_3$), and 1.31 - 1.25 (m, 6H, 2 CH_2CH_3). ^{13}C NMR (50.3 MHz): Table 4 and δ 170.7, 170.3, 170.0, 169.3, 169.1, 168.9 (6 $COCH_3$), 167.8 (CO chelated), 165.5 (CO free), 157.0 (=CH), 93.6 (=C), 60.1, 59.9 (2CH_2CH_3), 20.8, 20.7, 20.5, 20.3(3C) (6 $COCH_3$), 14.3 and 14.1 (2 CH_2CH_3). EIMS: *m/z* 747 (1, M^+), 702 (1, peak A)[6, 34], 561 (1, peak B), 331 (40, $C_{14}H_{19}O_9^+$), 216 (3, peak C), 187 (2, peak D), 169 (96, 331-2AcOH-CH_2CO), 142 (5, peak E), 60 (18, AcOH), and 43 (100, Ac). Found $M^{+\cdot}$ 747.2624. $C_{32}H_{45}NO_{19}$ requires 747.2585.

Anal. Calcd for $C_{32}H_{45}NO_{19}$: C, 51.40; H, 6.02; N, 1.87. Found: C, 51.41; H, 6.38; N, 1.87.

2,4-Di-*O*-acetyl-*N*-2-bis(ethoxycarbonyl)vinyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-rhamnopyranosylamine (6). 0.04 g, 70%, $[\alpha]_D$ = +2° (*c* 0.5, dichloromethane-acetone 2:1). ^{1}H NMR (500 MHz): Tables 2 and 3 and δ 9.52 (dd, 1H, $J_{NH,1}$ = 8.5 Hz, NH), 8.09 (d, 1H, $J_{NH,=CH}$ = 13.2 Hz, =CH), 4.31 - 4.17 (m, 4H, 2

CH_2CH_3), 2.29, 2.11, 2.09, 2.04, 2.00, and 1.99 (6s, each 3H, 6 $COCH_3$), and 1.25 - 1.40 (m, 6H, $2CH_2CH_3$). ^{13}C NMR (50.3 MHz): Table 4 and δ 170.4, 170.2, 170.1, 169.7, 169.3, 169.2 (6 $COCH_3$), 167.6 (CO chelated), 165.2 (CO free), 157.0 (=CH), 93.8 (=C), 60.1, 59.9 ($2CH_2CH_3$), 20.7, 20.6(3C), 20.5, 20.4 (6 $COCH_3$), 14.3 and 14.1 (2 CH_2CH_3). EIMS: *m/z* 747 (1, $M^{+\cdot}$), 702 (1, peak A), 561 (1, peak B), 331 (12, $C_{14}H_{19}O_9^+$), 216 (1, peak C), 187 (1, peak D), 169 (37, 331-2AcOH-CH_2CO), 142 (1, peak E), 60 (20, AcOH), and 43 (100, Ac). Found $M^{+\cdot}$ 747.2574

Anal. Found: C, 51.28; H, 6.19; N, 1.87.

2,4-Di-*O*-acetyl-*N*-2-bis(ethoxycarbonyl)vinyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-L-rhamnopyranosylamine (8). 0.04 g, 75%, $[\alpha]_D = +4°$ (*c* 0.5, chloroform). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.42 (dd, 1H, $J_{NH,1}$ = 8.8 Hz, NH), 8.02 (d, 1H, $J_{NH,=CH}$ = 13.6 Hz, =CH), 4.23, 4.20 (2q, each 2H, $J_{H,H}$=7.1 Hz, $2CH_2CH_3$), 2.28, 2.24, 2.12, 2.06, 2.04, and 1.98 (6s, each 3H, 6 $COCH_3$), and 1.33 - 1.20 (m, 6H, $2CH_2CH_3$). ^{13}C NMR (75.4 MHz), Table 4 and δ 170.3, 170.3, 170.1, 170.0, 169.3, 169.0 (6 $COCH_3$), 167.8 (CO chelated), 165.6 (CO free), 156.9 (=CH), 94.2 (=C), 60.1, 59.9 (2 CH_2CH_3), 20.8, 20.6, 20.4 (each 2C, 6 $COCH_3$), 14.3 and 14.2 (2 CH_2CH_3). EIMS: *m/z* 747 (2, $M^{+\cdot}$), 702 (4, peak A), 561 (2, peak B), 331 (25, $C_{14}H_{19}O_9^+$), 169 (35, 331-2AcOH-CH_2CO), 216 (14, peak C), 187 (2, peak D), 142 (10, peak E), 60 (15, AcOH), and 43 (100, Ac). Found $M^{+\cdot}$ 747.2587.

Anal. Found: C, 51.46; H, 6.14; N, 1.88.

2,3-Di-*O*-acetyl-*N*-2-bis(ethoxycarbonyl)vinyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-L-rhamnopyranosylamine (10). 0.04 g, 70%, $[\alpha]_D = 0°$ (*c* 0.5, chloroform). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.45 (dd, 1H, $J_{NH,1}$ = 8.0 Hz, NH), 7.94 (d, 1H, $J_{NH,=CH}$ = 13.2 Hz, =CH), 4.10 - 4.17 (m, 4H, $2CH_2CH_3$), 2.22, 2.20, 2.09, 2.00, 1.92, and 1.91 (6s, each 3H, 6 $COCH_3$), and 1.25 - 1.18 (m, 6H, 2 CH_2CH_3).^{13}C NMR (75.4 MHz), Table 4 and δ 170.4, 170.1 (3C), 169.7, 169.3 (6 $COCH_3$), 168.2 (CO chelated), 165.2 (CO free), 157.1 (=CH), 93.8 (=C), 60.1, 59.9 (2 CH_2CH_3), 20.7 (2C), 20.6, 20.5, 20.4, 20.3 (6 $COCH_3$), 14.3 and 14.1 (2 CH_2CH_3). EIMS: *m/z* 747 (2, $M^{+\cdot}$), 702 (4, peak A), 561 (1, peak B), 331 (57, $C_{14}H_{19}O_9^+$), 216 (1, peak C), 187 (1, peak D), 169 (50, 331-2AcOH-CH_2CO), 142 (4, peak E), 60 (13, AcOH), and 43 (100, Ac). Found $M^{+\cdot}$ 747.2595.

Anal. Found: C, 51.23; H, 6.34; N, 1.89.

2,4-Di-*O*-acetyl-*N*-2-bis(ethoxycarbonyl)vinyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-L-fucopyranosylamine (12). 0.04 g, 70% $[\alpha]_D = -10.8°$ (*c* 1.0, dichloromethane). ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.28 (dd, 1H, $J_{NH,1}$ = 9.2 Hz, NH), 7.96 (d, 1H, $J_{NH,=CH}$ = 13.5 Hz, =CH), 4.26, 4.21(2q, each 2H, $J_{H,H}$ = 7.1Hz, 2 CH_2CH_3), 2.15, 2.05, 2.04, 2.03, 2.02, and 1.99 (6s, each 3H, 6 $COCH_3$), 1.34, and 1.31

(2t, each 3H, 2 CH_2CH_3). ^{13}C NMR (125.7 MHz), Table 4 and δ 170.4, 170.4, 170.1, 169.7, 169.3, 169.2 (6 $COCH_3$), 167.6 (CO chelated), 165.8 (CO free), 157.5 (=CH), 94.0 (=C), 60.2, 60.0 (2 CH_2CH_3), 20.6 (2C), 20.5 (3C) 20.4 (6 $COCH_3$), 14.3 and 14.2 ($2CH_3$). EIMS: *m/z* 747 (5, $M^{+\cdot}$), 702 (8, peak A), 561 (20, peak B), 331 (3, $C_{14}H_{19}O_9^+$), 216 (1, peak C), 187 (1, peak D),169 (12, 331-2 AcOH-CH_2CO), 142 (1, peak E), 60 (17, AcOH), and 43 (100, Ac). Found $M^{+\cdot}$ 747.2584.

Anal. Found: C, 51.41; H, 6.38; N, 1.88.

4-*O*-acetyl-*N*-2-bis(ethoxycarbonyl)vinyl-2,3-di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-L-rhamnopyranosylamine (15). 0.06 g, 80%. ^1H NMR (500 MHz): Tables 2 and 3 and δ 9.38 (dd, 1H, $J_{NH,1}$ = 8.1 Hz, NH), 7.99 (d, 1H, $J_{NH,=CH}$ = 13.5 Hz, =CH), 4.32 - 4.21 (m, 4H, $2CH_2CH_3$), 2.26, 2.18, 2.13, 2.10, 2.05 (2C), 2.04, 2.02, and 2.01 (9s, each 3H, $9COCH_3$), 1.35 and 1.31 (2t, each 3H, $J_{H,H}$ = 7.1 Hz, $2CH_2CH_3$).

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