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Tri-*O*-benzoyl-β-L-rhamnopyranosyl and β-L-fucopyranosyl isothiocyanates. Partially protected β-L-rhamnopyranosylenamines

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ABSTRACT

Regioselective benzoylations of *N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**1**) yielded 2,3-di-*O*- (**3**), 3,4-di-*O*- (**4**), and 3-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**5**) together with the tri-*O*-benzoylated derivative **2**. Syntheses of 2,3,4-tri-*O*-benzoyl-β-L-rhamno- (**7**) and -β-L-fuco-pyranosyl isothiocyanate (**13**) from **2** and L-fucopyranosylamine, respectively, are described. *N*-Phenacyl-*N'*-(2,3,4-tri-*O*-benzoyl-β-L-rhamno- (**8**) and -β-L-fuco-pyranosylthiourea (**14**) were prepared from **7** and **13**, respectively, by reaction with phenacylamine. Conformational properties and MS data of the prepared compounds are discussed.

INTRODUCTION

Glycosylamines and glycosyl isothiocyanates are valuable intermediates[1–3] in syntheses of *neo*glycoproteins, *N*-nucleosides, glycosylthioureas, and glycosylaminoheterocycles of biological and pharmaceutical interest[4–7]. A great deal of effort has been devoted to the development of techniques[8–10] for attaching oligosaccharides to larger molecules. In this regard, the synthesis of glycosylamine oligosaccharides plays an important role. The preparation of glycosylamines of several reducing oligosaccharides, by treatment of the sugar with aqueous ammonium hydrogen carbonate, has been reported[11–13]. Recently, we have performed syntheses of *O*-protected gentiobiosylenamines[14] and of *O*- and *N*-protected 2-amino-2-deoxygentiobiosides[15] by glycosylation reactions using the corresponding 6-*O*-trityl derivatives as glycosyl acceptors.

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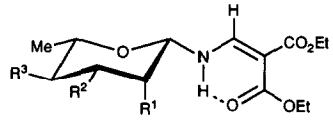
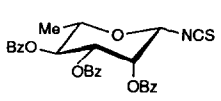
On the other hand, partially *O*-protected carbohydrates are useful intermediates in the synthesis of more complex structures such as oligosaccharides. Several methods have been developed for the synthesis of these types of compounds, including approaches via organotin derivatives[16], regioselective direct substitution[17,18], or partial deacylation of per-*O*-acyl sugars by both chemical[19] and enzymatic[20–22] methods. We have also reported the synthesis of partially *O*-protected glycosylenamines by deprotection of 6-*O*-trityl derivatives[2,14] or by regioselective benzoylation of the corresponding glycosylenamines[23,24]. Their transformations into partially protected glycosyl isothiocyanates, glycosylthioureas, glycosylaminoheterocycles, and *N*-nucleosides has also been described[2]. These compounds are useful as glycosyl acceptors in glycosylation reactions.

L-Rhamnose and L-fucose occur widely through Nature and constitute building blocks of bacterial and plant polysaccharides[25–28], most of which are antigenic and responsible for the specific immunological properties of types, species, or groups of bacteria. L-Rhamnose and/or L-fucose are carbohydrate epitopes[29–31].

For the above reasons, we consider of interest the synthesis of *O*-protected L-rhamno- and L-fuco-pyranosylenamines and derivatives. This paper describes the regioselective benzoylation of *N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**1**) and the concomitant preparation of partially *O*-protected rhamnopyranosylenamines (**3–5**) which may be used as acceptors in glycosylation reactions, providing substrates suitable for *N*-deprotection[23–32]. The synthesis of 2,3,4-tri-*O*-benzoyl-β-L-rhamno- and -β-L-fuco-pyranosylamine hydrochlorides and their conversion into the corresponding glycosyl isothiocyanates (**7** and **13**) are also reported. These isothiocyanates were transformed into the glycosylthioureas **8** and **14**.



	1	2	3	4	5	6
R^1	OH	OBz	OBz	OH	OH	OAc
R^2	OH	OBz	OBz	OBz	OBz	OAc
R^3	OH	OBz	OH	OBz	OH	OAc



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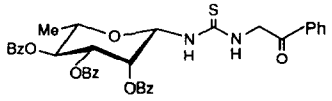

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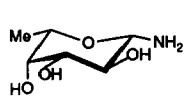

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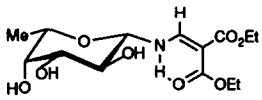

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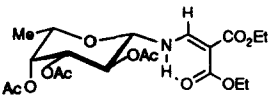

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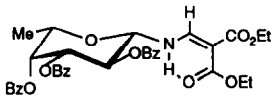

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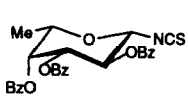

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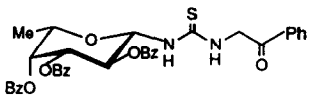

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RESULTS AND DISCUSSION

The results of the treatment of **1** with 2–6 equiv of benzoyl chloride at −14°C and room temperature are shown in Table 1.

The yields of the benzoylated derivatives show that the relative reactivity of the three hydroxyl functions is HO-3 > HO-4 ≈ HO-2. The high value for the reactivity of HO-3 is in accordance with the data reported for methyl α-L-rhamno- and α-D-manno-pyranoside[17]. The low reactivities of HO-4 and HO-2 may be due to the axial position of HO-2 and to the steric hindrance through *gauche* interactions with the 5-methyl and the bulky 1-acylvinyl group, respectively. Additionally, assuming that HO-3 is esterified first, another *gauche* interaction with a benzoyloxy group can be considered. The HO-2 in **1** is slightly less reactive than HO-4

TABLE I

Selective benzoylation of 1 and of each hydroxyl group

Entry	Temp. (°C)	Time (h)	BzCl (eq)	Products and isolated yields (%)						HO (Σ%)		
				1	2	3	4	5	Total	HO-2	HO-3	HO-4
1	−14	1	2	35		4	5	44	88	4	53	5
2	−14	24	3	16		5	10	56	88	5	71	10
3	[a]	1	3.5		16	21	26	25	88	37	88	42
4	[a]	2	4.5		46	5	8	26	85	51	85	54
5	[a]	24	6		70				70	70	70	70

[a] Room temperature.

TABLE II

Relevant ^{1}H NMR chemical shifts (δ, ppm) for the sugar rings of compounds **2–14**

Compound	H-1	H-2	H-3	H-4	H-5	H-6
2 [a]	5.02dd	5.07–5.13m	5.45–5.46m	5.07–5.13m	3.89dq	1.37d
2 [b]	5.65dd	5.89dd	5.75dd	5.41t	4.19dq	1.34d
2 [d]	3.94dd	5.99dd	5.68dd	5.98t	3.43m	1.25d
3 [c]	4.98dd	5.85dd	5.29dd	3.88t	3.67m	1.50d
3 [d]	3.87dd	5.79dd	5.23dd	3.69t	3.23m	1.35d
4 [c]	4.85dd	4.46dd	5.35dd	5.62t	3.75–3.94m	1.36d
5 [c]	4.71dd	4.28dd	5.03dd	3.95t	3.50–3.60m	1.39d
6 [a]	4.79dd	4.99–5.10m	5.41–5.50m	4.99–5.10m	3.61dq	1.32d
7 [c]	5.20dd	5.95dd	5.53dd	5.61t	3.91dq	1.46d
8 [c]	6.15bs	5.97m	← 5.59–5.74m →		4.12m	1.48d
10 [b]	4.40t	← 3.29–3.53m →			3.65c	1.24d
11 [c]	4.49t	5.28t	5.11dd	5.18dd	3.92dq	1.22d
12 [c]	4.81t	5.78dd	5.69dd	5.76dd	4.19dq	1.33d
13 [c]	5.31d	5.86dd	5.56dd	5.75dd	4.15dq	1.37d
14 [a]	5.78–5.82m	5.68t	← 5.78–5.82m →		4.33dq	1.44d

[a] In $CDCl_3$, 500 MHz. [b] In $(CD)_3)_2SO$, 200 MHz. [c] In $CDCL_3$, 200 MHz. [d] In C_6D_6, 500 MHz.

(entries 2–4) in contrast with the reactivities described for L-rhamno- and D-manno-pyranoside; this fact may be attributed to the close *gauche* enamino group. The main differences in reactivity are observed at low temperatures (entries 1 and 2). This selectivity is in agreement with the data reported for other enaminosugars[18,23]. Increases of temperature, reaction time, and moles of benzoyl chloride cause a diminution of regioselectivity and there is no selectivity in the conditions of entry 5. The best yields for **3** and **4** (21 and 26%, respectively) were obtained after reaction of **1** with 3.5 mol of benzoyl chloride, 1 h at room temperature (entry 3), and for **5** (56%) with 3 mol of benzoyl chloride, 24 h at −14°C (entry 2). Treatment of **1** with 6 mol of benzoyl chloride, 24 h at room temperature, yielded the tribenzoate **2**, which was not characterized previously. Compound **6**[33] was prepared for spectroscopic studies. The structures of **2–6** were assigned on the basis of analytical, UV, IR, ^{1}H and ^{13}C NMR, and MS data (see Experimental and Tables II–IV).

The chemical shifts for the resonance of the NH (9.34–9.68 ppm) and one C=O group (165.5–168.1 ppm) and the high value for $J_{NH,=CH}$ (12.2–13.7 Hz), indicative of antiperiplanar protons, are in agreement[14,32] with a chelated structure. This fact is also confirmed[14,34] by the low stretching frequencies for NH (3256–3290 cm^{-1}) and CO ($\sim$ 1665 cm^{-1}). For the partially protected L-rhamnosylenamines (**3–5**) the signals for the resonances of H-4 in **3**, H-2 in **4**, and H-2 and H-4 in **5** are in the range 3.88–4.46 ppm for C*H*OH, and the coupling constants $J_{1,2}$, $J_{2,3}$, $J_{3,4}$ and $J_{4,5}$ (Table III) are in agreement with the data reported[34,35] for related compounds. These results are consistent with a $^1C_4$ conformation. The β-anomeric configuration was unequivocally assigned by an X-ray analysis[36] on compound **2**. For the

TABLE III

Relevant ^1H NMR coupling constants (J, Hz) for the sugar rings of compounds **2–14**

Compound	$J_{1,NH}$	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
2 [a]	8.6	1.3			9.7	6.1
2 [b]	8.5	~1	3.2	9.8	9.8	7.8
2 [d]	9.1	1.3	3.4	10.2	10.2	6.2
3 [c]	8.5	~1	3.4	9.6	9.5	6.0
3 [d]	7.2	~1	3.4	9.8	9.8	6.5
4 [c]	8.7	~1	3.7	10.1	10.1	7.7
5 [c]	9.5	~1	3.1	9.6	9.6	6.0
6 [c]	8.9	1.4			10.4	6.2
7 [c]		1.3	3.1	9.3	9.3	6.2
8 [c]						6.0
10 [b]	8.4	8.4			~0	7.2
11 [c]	9.5	9.5	9.5	3.2	0.7	6.4
12 [c]	8.2	8.2	10.0	2.7	0.8	6.7
13 [c]		8.5	10.6	3.5	0.9	6.5
14 [a]		9.3	9.3			6.3

[a] In $CDCl_3$, 500 MHz. [b] In $(CD_3)_2SO$, 200 MHz. [c] In $CDCl_3$, 200 MHz. [d] In C_6D_6, 500 MHz.

peracylated compounds **2** and **6**, the J values in Me_2SO and C_6D_6 (Table III) are in agreement with the $^1C_4$ conformation; however, the ^1H NMR spectra for $CDCl_3$ solutions were markedly different with an accidental coincidence of chemical shifts, and only $J_{1,2}$ and $J_{4,5}$ (Table III) could be measured.

In order to corroborate the predominant conformer, theoretical calculations on different conformations of **2** and **5** were carried out *. The total energies, theoretical coupling constants, and H-dihedral angles for the different conformations are listed in Table V. For both compounds **2** and **5**, the minimum energies correspond to the $^1C_4$ conformation; the theoretical coupling constants are in very good agreement with the experimental ones, and confirm the $^1C_4$ conformation as preponderant in chloroform solution. The PLUTO drawings[42] of the most stable conformations of compounds **2** and **5** are shown in Fig. 1.

No transbenzoylation was observed when solutions in chloroform of **3–5** were kept at room temperature for 48 h.

The mass spectra of **2–6** showed molecular ions and losses of EtO· (peak A) and enamino group (peak B). The base peaks were always m/z 105 (Bz^+), and prominent fragments at m/z 122 ($BzOH^+$) and 77 (Ph^+) were observed. The peaks at m/z 216 (C, $C_9H_{14}O_5N$), 187 [D, $H_2NCH{:}C(CO_2CH_2CH_3)_2$], and 142 (E, 187 – EtO·), described[14,24] for the diethoxycarbonylvinylamino group, were also found.

* These conformations were modelled using the program SYBYL[37]. The final structures obtained by SYBYL geometrical optimization were performed by the program PCMODEL[38] which uses a modified Allinger[39] MM2 force field. The theoretical coupling constants were calculated with the Osawa and Jaime 3JHH program[40] that is set up for the use of the generalized Karplus equation[41].

TABLE IV

Relevant ^{13}C NMR chemical shifts (δ, ppm) for compounds **2–14**

Compound	Sugar ring						NCS	C=S
	C-1	C-2	C-3	C-4	C-5	C-6		
2 [c]	81.7	70.1 [e]	71.8	70.6 [e]	72.7	17.6		
3 [c]	84.5	70.3 [e]	74.3	70.5 [e]	74.8	17.7		
4 [c]	85.6	68.2	74.3	70.4	72.1	17.4		
5 [c]	85.5	69.0	76.6	69.8	73.9	17.4		
6 [c]	84.1	69.3	70.9 [e]	69.5 [e]	72.2	17.3		
7 [c]	82.8	69.9	71.3 [e]	70.4 [e]	73.1	17.5	145.4	
8 [c]	81.2	70.1	71.1 [e]	71.9 [e]	72.4	17.7		182.3
10 [b]	88.5	70.0	72.4	71.3	73.8	17.0		
11 [c]	87.3	68.0	70.9	69.8	71.0	16.0		
12 [a]	87.8	69.1	71.6	70.7	71.7	16.2		
13 [d]	84.1	69.9	71.7	70.5	72.1	16.1	143.7	
14 [a]	83.1	69.5	71.3	71.0	71.6	16.2		182.8

[a] In $CDCl_3$, 125.7 MHz. [b] In $(CD_3)_2SO$, 50.3 MHz. [c] In $CDCl_3$, 50.3 MHz. [d] In $CDCl_3$, 75.4 MHz. [e] Values are interchangeable.

L-Fucopyranosylamine[43] (**9**) was prepared from L-fucose, using a modification of the method reported for other glycosylamines[44]. The reaction of **9** with diethyl ethoxymethylenemalonate gave *N*-(2,2-diethoxycarbonylvinyl)-β-L-fucopyranosylamine (**10**). Treatment of **10** with an excess of benzoyl chloride gave the tribenzoate **12**. The triacetate **11** was prepared for characterisation purposes. The NMR data of **11** and **12** are included in Tables II–IV. The mass spectra of **10–12** were similar to those described above for **2–6**; however, the spectrum of **12** did not contain peak A.

The *N*-deprotection of **2** and **12** with chlorine in dichloromethane[2,32] followed by treatment with thiophosgene in a basic medium[2] yielded 2,3,4-tri-*O*-benzoyl-β-L-rhamnopyranosyl (**7**) and -β-L-fucopyranosyl isothiocyanate (**13**), respectively. Compounds **7** and **13** showed ν_{NCS} 2020–2025 cm^{-1}, δ ~ 144 ppm for NCS, and

TABLE V

Calculated energies and coupling constants (J_{ab}, Hz) and dihedral angles (H-a–C–C–H-b) for compounds **2** and **5**

Compound	Conformation	*E* (kcal/mol)	$J_{1,2}$ (H-1–C–C–H-2)	$J_{2,3}$ (H-2–C–C–H-3)	$J_{3,4}$ (H-3–C–C–H-4)	$J_{4,5}$ (H-4–C–C–H-5)
2	$^4C_1$	62.53	4.8 (48°)	3.4 (51°)	2.9 (67°)	1.4 (71°)
	$^1C_4$	35.77	1.2 (57°)	3.2 (52°)	9.5 (174°)	9.2 (176°)
	$B_{O,3}$	43.24	3.4 (35°)	6.2 (30°)	4.0 (59°)	1.2 (99°)
	$^2S_5$	64.60	6.8 (25°)	2.0 (63°)	1.1 (83°)	7.1 (149°)
5	$^4C_1$	29.04	4.4 (53°)	3.1 (54°)	2.5 (70°)	1.3 (73°)
	$^1C_4$	16.02	1.2 (56°)	3.0 (53°)	8.9 (169°)	9.1 (175°)
	$B_{O,3}$	27.06	4.6 (51°)	4.6 (43°)	2.9 (130°)	9.2 (177°)
	$^2S_5$	21.17	5.2 (18°)	4.9 (40°)	4.2 (58°)	1.5 (105°)

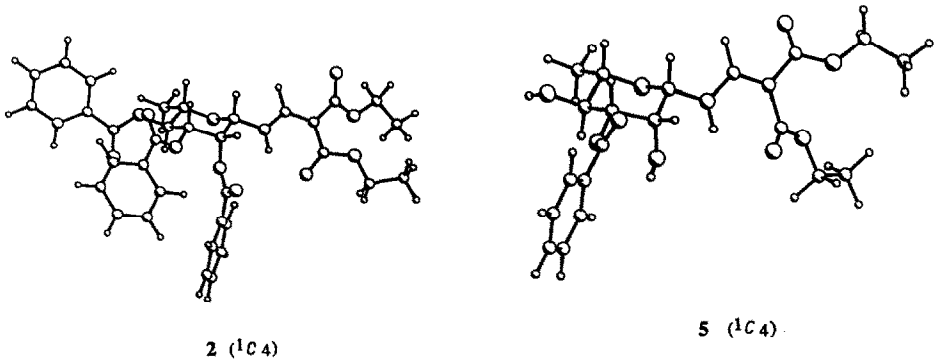

Fig. 1. PLUTO drawings of the most stable conformations of compounds **2** and **5**.

the mass spectra had a peak at m/z 459 corresponding to a loss of NCS from M^+ as reported for related glycosyl isothiocyanates[2,45].

The reactions of **7** and **13** with phenacylamine hydrochloride yielded the *N*-phenacyl-*N'*-(2,3,4-tri-*O*-benzoyl-β-D-glycopyranosyl)thioureas (**8** and **14**). Their structures were based on analytical, IR, ^1H and ^{13}C NMR, and MS data. Thus, **8** and **14** showed an IR band at 1694–1697 cm^{-1} ($\nu_{C=O}$ of phenacyl group), proton resonances of CH_2 at 4.98–5.02 ppm, and carbon resonances at ~53 (CH_2), ~182.5 (CS), and ~194 ppm (CO), characteristic of phenacylglycosylthioureas[44]. The mass spectra had a peak corresponding to the loss of the thiourea moiety ($M^+ - 193$), and the described peaks for poly-*O*-benzoyl sugar derivatives[2,18] (see Experimental).

The $^3J_{H,H}$ values of **7–8** and **10–14** indicated the $^1C_4$ conformation to be preponderant in solution in chloroform or dimethyl sulphoxide.

EXPERIMENTAL

General methods.—Melting points are uncorrected. FTIR spectra were recorded from KBr discs. ^1H NMR spectra were obtained at 200 and 500 MHz for solutions in $CDCl_3$ and $(CD_3)_2SO$. Assignments were confirmed by decoupling, H–D exchange, and homonuclear 2D correlated experiments. ^{13}C NMR spectra were recorded at 50.3, 75.4, and 125.7 MHz for solutions in $CDCl_3$ and $(CD_3)_2SO$. Proton-decoupled APT[46] and heteronuclear 2D correlated spectra were obtained to assist in signal assignments. EI mass spectra (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 10000 (10% valley definition). The FABMS spectra were recorded with the same instrument. Ions were produced by a beam of Xe atoms (6–7 keV), using a matrix consisting of glycerol or thioglycerol and NaI as salt. In the FABHRMS, $(CsI)_{37}Cs$ was used as reference. TLC was performed on Silica Gel HF_{254} (Merck), with detection by UV

light, or charring with H_2SO_4. Silica Gel 60 (Merck, 230 mesh) was used for preparative chromatography.

Benzoylation of N-*(2,2-diethoxycarbonylvinyl)-β-*L*-rhamnopyranosylamine* (**1**).—(*a*) To a stirred solution of **1** (2.5 g, 7.5 mmol) in dry pyridine (7 mL) at room temperature was gradually added benzoyl chloride (2.8 mL, 26 mmol) in pyridine (7 mL) with simultaneous cooling of the mixture under running tap water. The mixture was kept at r.t. for 1 h, then poured into ice–water (150 mL), and extracted with CH_2Cl_2. The organic layer was washed successively with satd aq $NaHCO_3$, aq H_2SO_4, and water, dried, and evaporated. The resulting syrup (1.53 g) was chromatographed on silica gel and eluted with ether–hexane (2:1 → 5:1) to give, as white solids, the following compounds: 2,3,4-tri-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**2**; 0.80 g, 16%), $R_f \sim 0.65$; 3,4-di-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**4**; 1.06 g, 26%), $R_f \sim 0.60$; 2,3-di-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**3**; 0.83 g, 21%), $R_f \sim 0.50$; and 3-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-L-rhamnopyranosylamine (**5**; 0.81 g, 25%), $R_F \sim 0.46$.

Compound **2** had: mp 160–162°C (from EtOH); $[\alpha]_D^{33} + 57°$ (*c* 1, CH_2Cl_2); λ_{max} 275 and 242 nm (ϵ_{mM} 26.8 and 24.5); ν_{max} 3256 (NH), 1732 (C=O free), 1707 (C=O), 1664 (C=O chelated), 1609 (NH and C=C), 1258 (C–O–C, aromatic), and 708 cm^{-1} (CH aromatic). NMR data: ^1H (500 MHz, $CDCl_3$), Tables II, III, and δ 9.41 (dd, 1 H, $J_{NH,=CH}$ 13.5 Hz, NH), 7.14–8.13 (m, 16 H, 3Bz, =CH), 4.13 and 4.02 (2 q, each 2 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2), 1.20 and 1.10 (2 t, each 3 H, 2 CH_3CH_2); ^1H (500 MHz, C_6D_6), Tables II, III, and δ 9.98 (dd, 1 H, $J_{NH,=CH}$ 13.1 Hz, NH), 8.22–6.92 (m, 15 H, 3 Bz), 8.15 (d, 1 H, =CH), 4.20–4.14 and 3.92–3.84 (2 m, each 2 H, 2 CH_3CH_2), 1.08 and 0.90 (2 t, each 3 H, $^3J_{H,H}$ 7.1 Hz, 2 CH_3CH_2); ^1H [200 MHz, $(CD_3)_2SO$], Tables II, III, and δ 9.34 (dd, 1 H, $J_{NH,=CH}$ 13.6 Hz, NH), 8.12 (d, 1 H, =CH), 8.06–7.20 (m, 15 H, 3 Bz), 4.04 (q, 4 H, 2 CH_3CH_2), 1.20 and 1.08 (2 t, each 3 H, $^3J_{H,H}$ 7.5 Hz, 2 CH_3CH_2); ^{13}C (50.3 MHz, $CDCl_3$), Table IV and δ 167.5 (CO chelated), 165.5 and 165.4 (3 CO of Bz and CO free), 157.6 (=CH), 128.2–134.4 (18 C of Ph), 94.0 (=C), 60.0 (2 CH_2), 14.0 and 14.3 (2 CH_3). Mass spectrum: *m/z* 645 (1, M^+), 600 (1, peak A), 459 (1, peak B), 337 (1, 459 − BzOH), 216 (1, peak C), 187 (1, peak D), 142 (1, peak E), 122 (45, $BzOH^+$), 105 (100, Bz^+), and 77 (43, Ph^+). Anal. Calcd for $C_{35}H_{35}NO_{11}$: C, 65.00; H, 5.45; N, 2.12. Found: C, 65.40; H, 5.70; N, 2.30.

Compound **3** had: mp 77–79°C (from ether–hexane); $[\alpha]_D^{19} - 26°$ (*c* 1, CH_2Cl_2); λ_{max} 275 and 233 nm (ϵ_{mM} 10.6 and 11.8); ν_{max} 3500–3250 (OH, NH), 1726 (C=O free), 1700 (C=O), 1663 (C=O chelated), 1609 (NH and C=C), 1262 (C–O–C), and 708 cm^{-1} (CH aromatic). NMR data: ^1H (200 MHz, $CDCl_3$), Tables II, III, and δ 9.43 (dd, 1 H, $J_{NH,=CH}$ 13.1, NH), 8.12–7.26 (m, 10 H, 2 Bz), 8.12 (d, 1 H, =CH), 4.17 and 4.06 (2 q, each 2 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2), 1.27 and 1.16 (2 t, each 3 H, 2CH_3CH_2); ^1H (500 MHz, C_6D_6), Tables II, III, and δ 9.40 (dd, 1 H, $J_{NH,=CH}$ 10.4 Hz, NH), 6.94–8.15 (m, 16 H, 3 Bz, =CH), 4.11–4.14 and 3.85–3.88 (2 m, each 2 H, 2 CH_3CH_2), 1.05 and 0.90 (2 t, each 3 H, $^3J_{H,H}$ 7.4, 7.1 Hz, 2 CH_3CH_2); ^{13}C

(50.3 MHz), Table IV and δ 167.5 (CO chelated), 166.2 (2 CO of Bz), 165.4 (CO free), 156.9 (=CH), 133.6 and 133.4 (2 C-4″ of Ph), 129.9 and 129.7 (4 C, 2 C-2″,6″ of Ph), 128.8 (2 C, 2 C-1″ of Ph), 93.7 (=C), 59.9 (2 CH_2), 14.2 and 14.0 (2 CH_3). Mass spectrum: *m/z* 541 (1, M^+), 496 (1, peak A), 355 (2, peak B), 233 (3, 355 − BzOH), 216 (2, peak C), 187 (2, peak D), 170 (3), 142 (4, peak E), 122 (47, $BzOH^+$), 105 (100, Bz^+), and 77 (23, Ph^+). Anal. Calcd for $C_{28}H_{31}NO_{10}$: C, 62.10; H, 5.77; N, 2.60. Found; C, 61.98; H, 5.60; N, 2.35.

Compound **4** had: mp 90–92°C (from ether–hexane); $[\alpha]_D^{19}$ + 11° (*c* 1, CH_2Cl_2); λ_{max} 274 and 232 nm (ϵ_{mM} 26.3 and 28.6); ν_{max} 3500–3250 (OH, NH), 1726 (C=O free), 1665 (C=O chelated), 1605 (NH and C=C), 1260 (C–O–C), and 710 cm^{-1} (CH aromatic). NMR data ($CDCl_3$): ^1H (500 MHz), Tables II, III, and δ 9.68 (dd, 1 H, $J_{NH,=CH}$ 13.7, NH), 8.12 (d, 1 H, =CH), 8.00–7.25 (m, 10 H, 2 Bz), 4.29–4.16 (m, 4 H, 2 CH_3CH_2), 1.32 and 1.31 (2 t, each 3 H, $^3J_{H,H}$ 7.3, 7.5 Hz 2 CH_3CH_2); ^{13}C (50.3 MHz), Table IV and δ 167.8 (CO chelated), 165.6 (2 CO of Bz), 157.7 (=CH), 133.2–128.3 (10 C, 2 C-1″,2″,3″,4″,5″,6″ of Ph), 93.5 (=C), 60.1 and 59.9 (2 CH_2), 14.3 and 14.1 (2 CH_3). Mass spectrum: *m/z* 541 (1, M^+), 496 (1, peak A), 355 (2, peak B), 233 (3, 355 − BzOH), 216 (2, peak C), 187 (2, peak D), 170 (2), 142 (4, peak E), 122 (40, $BzOH^+$), 105 (100, Bz^+), and 77 (21, Ph^+). Anal. Calcd for $C_{28}H_{31}NO_{10}$; C, 62.10; H, 5.77; N, 2.60. Found: C, 62.37; H, 5.43; N, 2.52.

Compound **5** had: mp 88–90°C (from EtOH); $[\alpha]_D^{22}$ − 34° (*c* 1, CH_2Cl_2); λ_{max} 275 and 230 nm (ϵ_{mM} 20.8 and 14.0); ν_{max} 3450 (OH), 3290 (NH), 1700 (C=O free), 1696 (C=O), 1665 (C=O chelated), 1603 (NH and C=C), 1256 (C–O–C), and 712 cm^{-1} (CH aromatic). NMR data ($CDCl_3$): ^1H (200 MHz), Tables II, III, and δ 9.63 (dd, 1 H, $J_{NH,=CH}$ 12.2 Hz, NH), 8.08 (d, 1 H, =CH), 8.74–7.26 (m, 5 H, Bz), 4.17 (q, 4 H, $^3J_{H,H}$ 7.0 Hz, $2CH_3CH_2$), 1.23 (t, 6 H, 2 CH_3CH_2); ^{13}C (50.3 MHz), Table IV and δ 168.1 (CO chelated), 166.3 (CO of Bz), 165.7 (CO free), 157.8 (=CH), 133.5 (C-4″ of Ph), 129.7 (2 C, C-2″,6″ of Ph), 129.1 (C-1″ of Ph), 128.4 (2 C, C-3″,5″ of Ph), 93.1 (=C), 60.1 and 59.9 (2 CH_2), 14.4 and 14.1 (2 CH_3). Mass spectrum: *m/z* 437 (1, M^+), 392 (1, peak A), 251 (1, peak B), 216 (11, peak C), 187 (10, peak D), 142 (29, peak E), 122 (41, $BzOH^+$), 15 (100, Bz^+), and 77 (23, Ph^+). Anal. Calcd for $C_{21}H_{27}NO_9$: C, 57.66; H, 6.22; N, 3.20. Found: C, 57.63; H, 6.35; N, 2.95.

(*b*) When the reaction was performed with **1** (3.0 g, 9.0 mmol) in dry pyridine (10.5 mL) and benzoyl chloride (4.5 mL, 40.5 mmol) as in (*a*), **2** (2.65 g, 46%), **3** (0.203 g, 5%), **4** (0.361 g, 8%), and **5** (1.00 g, 26%) were obtained.

(*c*) To a stirred solution of **1** (0.95 g, 2.85 mmol) in dry pyridine (1.9 mL) at 0°C was gradually added benzoyl chloride (1.9 mL, 17.0 mmol) in dry pyridine (8.5 mL). The mixture was kept at room temperature for 48 h, then poured into ice–water (100 mL), and extracted with CH_2Cl_2. The organic layer was treated as in (*a*) and the crude product was recrystallised from EtOH to give **2** (1.28 g, 70%).

(*d*) To a solution of **1** (1.0 g, 3.0 mmol) in dry pyridine (2 mL) at 0°C was added benzoyl chloride (1.0 mL, 9.0 mmol) in dry pyridine (4.7 mL). The mixture was

kept for 24 h at −14°C, poured into ice–water (100 mL), and then worked up by the same procedure as in (*a*). The crude product was chromatographed on silica gel (eluted with ether–hexane, 2:1 → 5:1), to yield **3** (0.129 g, 8%), **4** (0.178 g, 10%), and **5** (0.769 g, 56%). The aqueous layer was washed with ether and concentrated to dryness; **1** (0.156 g, 16%) was isolated.

(*e*) To a solution of **1** (0.5 g, 1.5 mmol) in pyridine (1 mL) at 0°C was added benzoyl chloride (0.33 mL, 3 mmol) in dry pyridine (1.6 mL). The mixture was kept at −14°C for 24 h. The mixture, processed as in (*c*), gave **3** (0.062 g, 4%), **4** (0.077 g, 5%), and **5** (0.289 g, 44%); **1** (0.289 g, 35%) was recovered.

*N-(2,2-Diethoxycarbonylvinyl)-β-*L*-fucopyranosylamine* (**10**).—L-Fucose (5 g, 30.5 mmol) was dissolved in ice-cold dry NH_3-satd MeOH (150 mL) with NH_3 gas bubbling through. The solution was hydrogenated at room temperature and 50 atm for 15 days. The resulting white solid (L-fucosylamine; 3.6 g, 72%) was removed by filtration. This solid (0.4 g, 2.45 mmol) was dissolved in MeOH (5 mL) and diethyl ethoxymethylenemalonate (1 mL, 4.94 mmol) was added. The mixture was allowed to stand at room temperature for 7 days and then concentrated to dryness. Column chromatography (CH_2Cl_2–MeOH, 20:1) of the residue gave **10** (0.744 g, 91%) which, after recrystallisation from CH_2Cl_2–MeOH, had mp 116–118°C, $[\alpha]_D^{21}$ − 15° (*c* 1.05, CH_2Cl_2); λ_{max} 274 and 219 nm (ϵ_{mM} 11.0 and 24.1); ν_{max} 3486 (OH), 3298 (NH), 1728 and 1699 (C=O free), 1663 (C=O chelated), 1605 (NH and C=C), and 1244 cm^{-1} (C–O–C). NMR data [$(CD_3)_2SO$]: ^1H (200 MHz), Tables II, III, and δ 9.19 (dd, 1 H, $J_{NH,=CH}$ 13.9 Hz, NH), 8.06 (d, 1 H, =CH), 5.27, 4.85 and 4.56 (3 d, each 1 H, $^2J_{H,H}$ 7.2 Hz, 3 OH), 4.13 and 4.03 (2 q, each 2 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2), 1.24 and 1.21 (2 t, each 3 H, 2 CH_3CH_2); ^{13}C (50.3 MHz), Table IV and δ 168.0 (CO chelated), 165.3 (CO free), 158.4 (=CH), 90.6 (=C), 59.6, 59.5 (2 CH_2), 14.6 and 14.7 (2 CH_3). Mass spectrum: *m/z* 333 (23, M^+), 288 (17, peak A, 216 (51, peak C), 187 (20, peak D), and 142 (100, peak E). Anal. Calcd for $C_{14}H_{23}NO_8$; C, 50.45; H, 6.90; N, 4.20. Found: C, 50.59; H, 7.02; N, 4.50.

*2,3,4-Tri-*O*-acetyl-*N*-(2,2-diethoxycarbonylvinyl)-β-*L*-fucopyranosylamine* (**11**).—Compound **10** (0.3 g, 0.9 mmol) was acetylated conventionally with Ac_2O (1.5 mL) in pyridine (2 mL) for 48 h at 0°C. The resulting oil was dissolved in ether and precipitated with hexane to give **11** as an amorphous hygroscopic solid (0.315 g, 76%); $[\alpha]_D^{32}$ + 0.95° (*c* 1.05, CH_2Cl_2); λ_{max} 274 nm (ϵ_{mM} 23.3); ν_{max} 3272 (NH), 1748, 1718 (C=O free), 1672 (C=O chelated), 1613 (NH and C=C), 1225 and 1240 cm^{-1} (C–O–C). NMR data (Cl_3CD): ^1H (200 MHz), Tables II, III, and δ 9.23 (dd, 1 H, $J_{NH,=CH}$ 14.2 Hz, NH), 7.98 (d, 1 H, =CH), 4.30 and 4.23 (2 q, each 2 H, $^3J_{H,H}$ 7.1 Hz, 2 CH_3CH_2), 2.21 (s, 3 H, Ac *ax*), 2.05 and 2.02 (2 s, each 3 H, 2 Ac *eq*), 1.34 and 1.31 (2 t, each 3 H, 2 CH_3CH_2); ^{13}C (50.3 MHz), Table IV and δ 170.4, 169.9, 169.7 (3 CO of Ac), 167.7 (CO chelated), 165.5 (CO free), 157.5 (=CH), 94.0 (=C), 60.2 and 59.9 (2 CH_2), 14.2 and 14.1 (2 CH_3). Mass spectrum: *m/z* 414 (23, peak A), 273 (77, peak B), 171 (84, 273 − AcOH − CH_2CO), 153 (84, 273 − 2AcOH), 111 (100, 153 − CH_2CO), 216 (91, peak C), 187 (7, peak D), and 142 (47, peak E); 459.1742 (25%, M^+; Calcd for $C_{20}H_{29}NO_{11}$ 459.1740).

2,3,4-Tri-O-benzoyl-N-(2,2-diethoxycarbonylvinyl)-β-L-fucopyranosylamine (**12**). —To a solution of **10** (1.0 g, 3.0 mmol) in dry pyridine (2 mL) at 0°C was gradually added benzoyl chloride (6 mL, 54 mmol). The reaction mixture was allowed to stand at room temperature for 96 h, poured into ice–water (100 mL), and then worked up as for (*a*). The dried organic layer was evaporated to dryness and the crude product was chromatographed on silica gel (ether–petroleum ether, 1:1 → 2:1) to give **12** (1.28 g, 70%), which, after recrystallisation (from ether–hexane, 1:1), had mp 97–100°C; $[\alpha]_D^{20}$ − 70° (*c* 1.03, CH_2Cl_2); λ_{max} 275 and 242 nm (ϵ_{mM} 25.0 and 24.4); ν_{max} 3284 (NH), 1728 (C=O free), 1694 (C=O), 1660 (C=O chelated), 1610 (NH and C=C), 1586 and 1263 (C–O–C), and 710 cm^{-1} (CH aromatic). NMR data ($CDCl_3$): ^1H (200 MHz), Tables II, III, and δ 9.47 (dd, 1 H, $J_{NH,=CH}$ 12.5 Hz, NH), 8.15–7.21 (m, 16 H, 3 Bz, =CH), 4.29 and 4.16 (2 q, each 2 H, $^3J_{H,H}$ 7.3 Hz, 2 CH_3CH_2), 1.37 and 1.27 (2 t, each 3 H, 2 CH_3CH_2); ^{13}C (125.7 MHz), Table IV and δ 167.6 (CO chelated), 165.8 and 165.5 (3 CO of Bz), 165.4 (CO free), 157.6 (=CH), 133.5–128.2 (18 C, 3 Ph), 94.2 (=C), 60.2 and 59.9 (2 CH_2), 14.2 and 14.1 (2 CH_3). Mass spectrum: *m/z* 645 (1, M^+), 459 (1, peak B), 354 (1, 459 − Bz), 216 (1, peak C), 187 (1, peak D), 142 (1, peak E), 122 (43, $BzOH^+$), 105 (100, Bz^+), and 77 (39, Ph^+). Anal. Calcd for $C_{35}H_{35}NO_{11}$; C, 65.0; H, 5.45; N, 2.20. Found: C, 65.02; H, 5.54; N, 2.40.

2,3,4-Tri-O-benzoyl-β-L-rhamno- and -fuco-pyranosyl isothiocyanate (**7** *and* **13**). —Chlorine was bubbled through a solution of **2** or **12** (0.4 g, 0.62 mmol) in CH_2Cl_2 (5 mL) until total consumption of the starting material was observed by TLC (ether–hexane, 4:1). The solution, which contained the corresponding glycopyranosylamine hydrochloride, was used without further purification. To a mixture of the above solution and $CaCO_3$ (0.25 g, 2.53 mmol) in water (2 mL) was added thiophosgene (0.14 mL, 1.9 mmol). The mixture was stirred vigorously for 28 h at room temperature and then filtered. The organic layer was washed with water, dried over $CaCl_2$, and evaporated to dryness. The resulting syrup was chromatographed on silica gel (ether–petroleum ether, 1:1) to give **7** or **13**, respectively.

Compound **7** (0.35 g, 55%) had: mp 55–57°C (from ether–hexane, 1:1); $[\alpha]_D^{22}$ + 182° (*c* 1.03, CH_2Cl_2); λ_{max} 284, 275, and 232 nm (ϵ_{mM} 6.0, 8.1, and 39.5); ν_{max} 2020 (NCS), 1728 (C=O), 1601 (C=C aromatic), 1260 (C–O–C), and 710 cm^{-1} (CH aromatic). NMR data (Cl_3CD): ^1H (200 MHz), Tables II, III, and δ 8.12–7.22 (m, 15 H, 3 Bz); ^{13}C (50.3 MHz), Table IV, δ 165.3 (3 CO of Bz), and 133.2–128.1 (18 C, 3 Ph). Mass spectrum: *m/z* 459 (12, M^+ − NCS), 337 (1, 459 − BzOH), 232 (1, 337 − Bz), 215 (12, 459 − 2 BzOH), 122 (56, $BzOH^+$), 105 (100, Bz^+), and 77 (36, Ph^+). Anal. Calcd for $C_{28}H_{23}NO_7S$; C, 64.98; H, 4.48; N, 2.71. Found: C, 64.96; H, 4.63; N, 3.00.

Compound **13** (0.26 g, 81%) had: mp 58–60°C after recrystallisation (from ether–hexane, 1:1); $[\alpha]_D^{21}$ − 174° (*c* 1, CH_2Cl_2); λ_{max} 278, 275, and 244 nm (ϵ_{mM} 10.7, 13.2, and 66.5); ν_{max} 2025 (NCS), 1726 (C=O), 1601 (C=C aromatic), 1265 (C–O–C) and 708 cm^{-1} (CH aromatic). NMR data ($CDCl_3$): ^1H (200 MHz),

Tables II, III, and δ 8.13–7.26 (m, 15 H, 3 Bz); ^{13}C (75.4 MHz), Table IV and δ 165.7, 165.4, and 165.0 (3 CO of Bz), and 133.5–128.2 (18 C of Ph). Mass spectrum: *m/z* 459 (12, M^+ – NCS), 337 (5, 459 – BzOH), 232 (2, 337 – Bz), 215 (6, 459 – BzOH), 122 (27, $BzOH^+$), 105 (100, Bz^+), and 77 (17, Ph^+). Anal. Calcd for $C_{28}H_{23}NO_3S$: C, 64.98; H, 4.48; N, 2.71. Found: C, 65.10; H, 4.60; N, 3.04.

N-*Phenacyl*-N'-*[2,3,4,-tri*-O-*benzoyl*-β-L-*rhamno- and -fuco-pyranosyl]thiourea* (**8** *and* **14**).—A solution of phenacylamine hydrochloride (0.053 g, 0.31 mmol) in water (2 mL) was neutralised with $NaHCO_3$ (0.026 g, 0.31 mmol) and gradually added to a solution of **7** or **13** (0.159 g, 0.31 mmol) in acetone (4 mL) under N_2. The resulting solution was kept at room temperature for 1.5 h (**8**) or 0.5 h (**14**) and then concentrated in vacuo. The residue was partitioned between CH_2Cl_2 and water. The dried organic layer was evaporated to dryness and the crude product was chromatographed on silica gel (ether–hexane, 4:1) to give **8** or **14**, respectively.

Compound **8** (0.14 g, 70%) had mp 172–175°C after recrystallisation (from ether–hexane); $[\alpha]_D^{21}$ + 100° (*c* 1.07, CH_2Cl_2); λ_{max} 238 nm (ϵ_{mM} 41.6); ν_{max} 3347 (NH), 1730 (CO ester), 1694 (CO ketone), 1601, 1540 (C=C aromatic), 1277 and 1263 (C–O–C and C=S), 712 cm^{-1} (CH aromatic). NMR data ($CDCl_3$): ^1H (200 MHz), Tables II, III, and δ 8.07–7.14 (m, 17 H, 3 Bz, NH, N'H), 4.98 (bs, 2 H, CH_2); ^{13}C (50.3 MHz), Table IV and δ 194.3 (CO ketone), 165.9, 165.6, and 165.2 (3CO of Bz), 134.4–128.1 (24 C of Ph), 51.9 (CH_2). Mass spectrum: *m/z* 459 (6, M^+ – $NHCSNHCH_2COPh$), 337 (2, 459 – BzOH), 232 (3, 337 – Bz), 215 (1, 459 – 2BzOH), 122 (36, BzOH), 105 (100, Bz^+), and 77 (58, Ph^+). Anal. Calcd for $C_{36}H_{32}N_2O_8S$: C, 66.25; H, 4.91; N, 4.29. Found: C, 66.20; H, 4.45; N, 4.20.

Compound **14** (0.079 g, 76%) was an amorphous solid; $[\alpha]_D^{21}$ – 123° (*c* 1.06, $CHCl_3$); λ_{max} 244 nm (ϵ_{mM} 38.6); ν_{max} 3343 (NH), 1726 (CO ester), 1697 (CO ketone), 1600, 1528 (C=C aromatic), 1288 and 1263 (C–O–C, C=S), and 710 cm^{-1} (CH aromatic). NMR data ($CDCl_3$): ^1H (500 MHz) Tables II, III, and δ 8.08–7.47 (m, 22 H, 4 Ph, NH, N'H), 5.02 (bs, 2 H, CH_2); ^{13}C (75.4 MHz), Table IV and δ 193.5 (CO, ketone), 165.7 and 165.4 (3CO of Bz), 129.9–127.9 (24C of Ph), 54.2 (CH_2). Mass spectrum: *m/z* 459 (4, M^+ – $NHCSNHCH_2COPh$), 337 (2, 459 – BzOH), 232 (1, 337 – Bz), 215 (3, 459 – 2BzOH), 122 (21, $BzOH^+$), 105 (100, Bz^+), and 77 (33, Ph^+): FABMS *m/z* 785.0975 [18%, $(M + Cs)^+$; calcd for $C_{36}H_{32}N_2O_8SCs$ 785.0933].

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