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REGIOSELECTIVE BENZOYLATIONS OF GLYCOPYRANOSYLAMINES: SYNTHESIS OF PARTIALLY PROTECTED GLYCOPYRANOSYL ISOTHIOCYANATES*†

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ABSTRACT

Regioselective benzoylations of *N*-(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine (**1**) yielded 2,3,6-tri-*O*- (**3**) and 3,6-di-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine (**4**), whereas, from the β-D-*gluco* analogue **5**, the 2,3,6-tri- (**7**), 3,6-di- (**8**), and 2,6-di-*O*-benzoyl (**9**) derivatives were obtained together with the fully esterified compounds (**2** and **6**). Treatment of **3** with bromine and of **7** with chlorine gave the 2,3,6-tri-*O*-benzoyl-β-D-glycopyranosylamine hydrohalides (**10** and **11**, respectively), which reacted with thiophosgene to afford 2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl isothiocyanate (**12**) and the β-D-*gluco* analogue **14**, respectively. 3,6-Di-*O*-benzoyl-β-D-galactopyranosyl isothiocyanate (**13**) was prepared from **4** by successive treatments with bromine and thiophosgene.

INTRODUCTION

Selectively protected monosaccharide derivatives are useful in the synthesis of oligosaccharides[1]. Glycosylamines[2] and glycosyl isothiocyanates[3–6] are valuable intermediates in the syntheses of *N*-nucleosides, glycosylthioureas, and glycosylaminoheterocycles of biological and pharmaceutical interest[7]. Hitherto, the regioselective benzoylation of hexopyranosylamines has not been reported and there are no data on partially protected sugar isothiocyanates.

We now report on the regioselective benzoylations of *N*-(2,2-diethoxycarbonylvinyl)-β-D-galacto- and -β-D-gluco-pyranosylamines (**1** and **5**), the

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preparation of 2,3,6-tri-*O*-benzoyl-β-D-galacto- and -β-D-gluco-pyranosylamine hydrohalides (**10** and **11**), and their conversion into the corresponding glycosyl isothiocyanates (**12** and **14**). 3,6-Di-*O*-benzoyl-β-D-galactopyranosyl isothiocyanate (**13**) is also described.

RESULTS AND DISCUSSION

The results of the treatment of *N*-(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine[8] (**1**) with 2–4.5 mol of benzoyl chloride in pyridine at 0° are shown in Table I. In general, primary hydroxyl groups are esterified more readily than are secondary hydroxyl groups[9]. The resistance of the axial HO-4 in **1** to esterification accords with other results for galactopyranosides[1]. Significantly, the order of reactivity HO-3 > HO-2 > HO-4 for the benzoylation of **1** agrees with that for mesylation of methyl β-D-galactopyranoside[1,10]. The low reactivity of HO-2 may be due to steric hindrance through *gauche* interaction with the bulky 1-substituent. The yields and selectivities for **3** (3 mol of BzCl) and **4** (2 mol of BzCl) are better than those reported for related glycosyl derivatives[1,10,11]. Treatment of **1** with 4.5 mol of benzoyl chloride yielded the tetrabenzoate **2**, which was not characterized previously[12].

The structures of **2–4** were assigned on the basis of analytical, i.r., and ^{1}H- and ^{13}C-n.m.r. data (see Experimental). The signals for H-4 in **3** and H-2,4 in **4** were in the range δ 3.91–4.35 for *CH*OH. The $J_{4,5}$ value of **2** and **3** was ~0 Hz, as for related galactopyranosyl compounds[12,13].

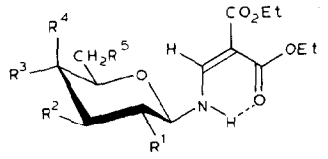
An acyl group in a sugar derivative deshields the α-carbon and shields the β-carbon[14,15]. These effects were observed in **2–4** (see Experimental).

Benzoylations of *N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine[8] (**5**) under different conditions afforded mixtures of the tetra- (**6**), 2,3,6-tri- (**7**), 3,6-di- (**8**), and 2,6-di-benzoate (**9**). The best yield of **7** was obtained after the reaction of **5** with 3.1 mol of benzoyl chloride at −15°. The order of reactivity on benzoylation of **5** was HO-6 > HO-2 ≃ HO-3 > HO-4. The low reactivity of HO-4

TABLE I

SELECTIVE BENZOYLATIONS OF *N*-(2,2-DIETHOXYCARBONYLVINYL)-β-D-GALACTO- (**1**) AND -GLUCO-PYRANOSYLAMINE (**5**)

	Temp. (degrees)	*BzCl (mol)*	*Benzoylated derivative and yield (%)*			
			Tetra	*2,3,6-Tri*	*3,6-Di*	*2,6-Di*
1	0	2	**2** (6)	**3** (11)	**4** (54)	Not isolated
1	0	3	**2** (12)	**3** (64)	**4** (24)	
1	20	4.5	**2** (84)			
5	0	3	**6** (5)	**7** (27)	**8** (19)	**9** (19)
5	−30	3		**7** (20)	**8** (14)	**9** (16)
5	−15	3.1	**6** (10)	**7** (57)	**8** (8)	**9** (7)
5	20	6	**6** (75)			



	1	2	3	4	5	6	7	8	9
R^1	OH	OBz	OBz	OH	OH	OBz	OBz	OH	OBz
R^2	OH	OBz	OBz	OBz	OH	OBz	OBz	OBz	OH
R^3	H	H	H	H	OH	OBz	OH	OH	OH
R^4	OH	OBz	OH	OH	H	H	H	H	H
R^5	OH	OBz	OBz	OBz	OH	OBz	OBz	OBz	OBz

has been observed in glucose[16] and α-glucosides[1], and it may be due to steric hindrance through *gauche* interaction with CH_2OBz (assuming that HO-6 is esterified first) and HO(BzO)-3. However, HO-2 is somewhat more reactive than HO-3 in α- and β-glucopyranosides[1,11].

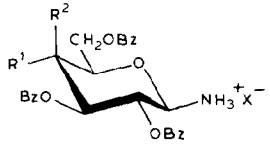
The structures of **6–9** were based on analytical, u.v., i.r., and ^1H- and ^{13}C-n.m.r. data (see Experimental).

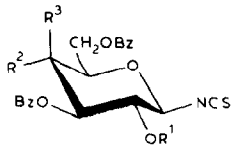
Comparison of the δ values for the ^{13}C resonances of sugar moieties in **6–9** showed that the benzoyl group shielded the β-carbons, whereas the α-carbons were slightly shielded (*i.e.*, C-3, **9** *vs.* **5**) or deshielded (*i.e.*, C-2, **8** *vs.* **5**). It has been reported[17] that esterification shifts for the signals of α-carbons are unpredictable, although the effects on β-carbon resonances are consistent.

No transbenzoylations were observed when solutions of **3**, **4** (methyl sulphoxide), and **7–9** (chloroform) were kept for 48 h at room temperature.

Treatment of **3** with bromine and of **7** with chlorine in chloroform[12,18] or dichloromethane gave, in good yields, the corresponding tri-*O*-benzoyl-β-D-glycopyranosylamine hydrohalides (**10** and **11**), the analytical, i.r., ^1H- and ^{13}C-n.m.r. data of which were consistent with the structures proposed. No transbenzoylation occurred during deprotection of the amine group.

2,3,6-Tri-*O*-benzoyl-β-D-galacto- (**12**) and -β-D-gluco-pyranosyl isothiocyanates (**14**) were obtained by reaction of **10** and **11**, respectively, with





10 $R^1 = H, R^2 = OH, X = Br$
11 $R^1 = OH, R^2 = H, X = Cl$

12 $R^1 = Bz, R^2 = H, R^3 = OH$
13 $R^1 = R^2 = H, R^3 = OH$
14 $R^1 = Bz, R^2 = OH, R^3 = H$

thiophosgene in the presence of calcium carbonate. 3,6-Di-*O*-benzoyl-β-D-galactopyranosyl isothiocyanate (**13**) was prepared by the reaction of **4** with bromine followed by treatment with thiophosgene, without isolation of the intermediate galactopyranosylamine. Partially protected glycosyl isothiocyanates cannot be obtained by selective deacylation[19]. Compounds **12–14** had $\nu_{C=S}$ at 2040–2060 cm^{-1} and ^{13}C resonances at δ 142.6–144.5 characteristic of the isothiocyanate group[4,12].

The $^3J_{H,H}$ values for **2–4** and **6–13** indicated the presence of $^4C_1$(D) conformations in solution in methyl sulphoxide or chloroform.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured at 22 ±3°, using 1- and 10-cm cells. I.r. spectra were recorded for KBr discs. Assignments of the ^1H-n.m.r. (200 MHz) spectra were confirmed by decoupling experiments, H/D exchange, and by using Eu(fod)$_3$ as shift reagent[20,21]. ^{13}C-N.m.r. (50.3 MHz) spectra were obtained for solutions in $CDCl_3$ and $(CD_3)_2SO$. Proton-decoupled APT[22] (attached proton test) spectra and "off-resonance" spectra were used to assist in signal assignments. T.l.c. was performed on Silica Gel HF_{254} (Merck), with detection by u.v. light, iodine vapour, or charring with sulphuric acid. Silica Gel 60 (Merck, 230 mesh) was used for flash column chromatography.

Benzoylation of N-*(2,2-diethoxycarbonylvinyl)-β-*D-*galactopyranosylamine*[8] (**1**). — (*a*) To a stirred solution of **1** (1 g, 2.9 mmol) in pyridine (2 mL) at 0° was gradually added benzoyl chloride (0.66 mL, 5.8 mmol) in pyridine (3 mL). The mixture was kept for 24 h at 0°, then poured into ice–water (400 mL) to give a white powder (1.22 g), column chromatography (benzene–methanol, 20:1) of which gave 2,3,4,6-tetra-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine (**2**; 0.14 g, 6%), R_F 0.91; 2,3,6-tri-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine (**3**; 0.21 g, 11%), R_F 0.65; 3,6-di-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine (**4**; 0.85 g, 54%), R_F 0.29; and traces of other products (R_F <0.25).

Compound **2** had m.p. 123–124° (from ethanol), $[\alpha]_D^{22}$ +74° (*c* 0.5, chloroform); ν_{max} 3290 (NH), 1720 (C=O), 1670 (C=C), 1600 (NH, C=C aromatic), 1270 (C–O–C), 710 and 690 cm^{-1} (CH aromatic). ^1H-N.m.r. data [$(CD_3)_2SO$]: δ 9.49 (dd, 1 H, $J_{NH,CH}$ 14.6, $J_{1,NH}$ 8.8 Hz, NH), 8.28 (d, 1 H, =CH), 8.21–7.33 (m, 20 H, 4 Bz), 6.05–5.89 (m, 3 H, H-2,3,4), 4.85 (t, 1 H, $J_{5,6} = J_{5,6'}$ = 6.4, $J_{4,5}$ 0 Hz, H-5), 4.60 (dd, 1 H, $J_{6,6'}$ 11.6 Hz, H-6), 4.59 (t, 1 H, $J_{1,2}$ 8.8 Hz, H-1), 4.48 (dd, 1 H, H-6′), 4.15 and 4.11 (2 q, 4 H, $^3J_{H,H}$ 7.2 Hz, 2 CH_3CH_2), 1.22 and 1.21 (2 t, 6 H, 2 CH_3CH_2); ^{13}C, δ 166.7, 165.2, 165.1, 164.9, 164.7, 164.5 (6 C=O), 157.1 (HC=), 134.0–128.4 (24 C, 4 Ph), 93.1 (C=), 85.9 (C-1), 72.0 (C-5), 71.7 (C-3), 69.4 (C-2), 68.7 (C-4), 62.0 (C-6), 59.5, 59.4 (2 CH_2), 14.2 and 14.1 (2 CH_3).

Anal. Calc. for $C_{42}H_{39}NO_{13}$: C, 65.88; H, 5.13; N, 1.83. Found: C, 65.57; H, 5.14; N, 1.96.

Compound **3** had m.p. 178–180° (from ethanol), $[\alpha]_D^{22}$ +33° (*c* 0.6, chloroform); $\lambda_{max}^{CH_2Cl_2}$ 272 and 232 nm (ε_{mM} 24.2 and 37.1); ν_{max} 3400 (OH), 3240 (NH), 1710, 1690 (C=O), 1640 (C=C), 1590 (NH, C=C aromatic), 1250 (C–O–C), and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 9.28 (dd, 1 H, $J_{NH,CH}$ 13.7, $J_{1,NH}$ 8.6 Hz, NH), 8.14 (d, 1 H, HC=), 8.04–7.45 (m, 15 H, 3 Bz), 5.89 (d, $J_{4,OH}$ 6.5 Hz, OH), 5.76 (t, 1 H, $J_{1,2} = J_{2,3}$ = 8.6 Hz, H-2), 5.52 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 5.34 (t, 1 H, H-1), 4.52 (m, 2 H, H-6,6′), 4.39 (t, 1 H, $J_{5,6} = J_{5,6'}$ = 6.2, $J_{4,5}$ 0 Hz, H-5), 4.35 (dd, 1 H, H-4), 4.12 and 4.05 (2 q, 4 H, 2 CH_3CH_2), 1.18 and 1.16 (2 t, 6 H, 2 CH_3CH_2); ^{13}C, δ 166.8, 165.5, 165.2, 165.0, 164.5, (5 C=O), 157.0 (HC=), 133.8–128.5 (18 C, 3 Ph), 92.6 (C=), 85.2 (C-1), 74.0 (2 C, C-3,5), 69.4 (C-2), 66.1 (C-4), 63.5 (C-6), 59.4, 59.2 (2 CH_2), 14.1 and 14.0 (2 CH_3).

Anal. Calc. for $C_{35}H_{35}NO_{12}$: C, 63.53; H, 5.33; N, 2.12. Found: C, 63.11; H, 5.32; N, 2.06.

Compound **4** was amorphous, $[\alpha]_D^{22}$ +44° (*c* 2.6, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 272 and 232 nm (ε_{mM} 23.4 and 31.9); ν_{max} 3450 (OH), 3260 (NH), 1700 (C=O), 1640 (C=C), 1590 (NH, C=C aromatic), 1250 (C–O–C), and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 9.31 (dd, 1 H, $J_{NH,CH}$ 13.6, $J_{1,NH}$ 8.5 Hz, NH), 8.13 (d, 1 H, HC=), 8.10–7.46 (m, 10 H, 2 Bz), 5.81 (d, 1 H, $J_{H,OH}$ 5.8 Hz, OH), 5.47 (d, 1 H, $J_{H,OH}$ 6.6 Hz, OH), 5.00 (dd, 1 H, $J_{2,3}$ 8.6, $J_{3,4}$ 2.7 Hz, H-3), 4.81 (t, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 4.42 (m, 2 H, H-6,6′), 4.21–3.91 (m, 7 H, H-2,4,5, 2 CH_3CH_2), 1.24 and 1.21 (2 t, 6 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2); ^{13}C, δ 167.5, 165.5, 165.4, 164.7 (4 C=O), 157.9 (HC=), 133.4–128.5 (12 C, 2 Ph), 91.1 (C=), 88.0 (C-1), 76.5 (C-3), 73.7 (C-5), 67.2 (C-2), 66.1 (C-4), 63.8 (C-6), 59.3 and 59.1 (2 CH_2), 14.2 and 14.1 (2 CH_3).

Anal. Calc. for $C_{28}H_{31}NO_{11}$: C, 60.32; H, 5.60; N, 2.51. Found: C, 60.36; H, 5.66; N, 2.52.

(*b*) When the reaction was performed with **1** (3 g, 8.6 mmol) and benzoyl chloride (3 mL, 25.8 mmol) as in (*a*), **2** (12%), **3** (64%), and **4** (24%) were obtained.

(*c*) To a stirred solution of **1** (1.3 g, 8.6 mmol) in pyridine (10 mL) at 0° was added gradually benzoyl chloride (4.5 mL, 38.7 mmol). After 24 h at room temperature, the mixture was poured into ice–water (700 mL), and the crude product was recrystallised from ethanol to give **2** (5.5 g, 84%).

Benzoylation of N-*(2,2-diethoxycarbonylvinyl)-β-*D-*glucopyranosylamine*[8] (**5**). — (*a*) Following a procedure similar to that described above for **1, 5** (0.5 g, 1.42 mmol) and benzoyl chloride (0.5 mL, 4.29 mmol) at 0° gave a mixture of products. Column chromatography (benzene–methanol, 20:1) yielded 2,3,4,6-tetra-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine (**6**; 0.05 g, 5%), R_F 0.80; 2,3,6-tri-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine (**7**; 0.25 g, 27%), R_F 0.50; and an amorphous solid (0.30 g, 38%) which, on t.l.c. (benzene–methanol, 12:1), yielded 3,6-di-*O*-benzoyl- (**8**; 0.04 g, 19%) and 2,6-di-*O*-benzoyl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine (**9**; 0.04 g, 19%).

Compound **6** had m.p. 145–146° (from ethanol), $[\alpha]_D^{22}$ +22° (*c* 0.65, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 275 and 233 nm (ε_{mM} 20.5 and 37.5); ν_{max} 3285 (NH), 1720 (C=O), 1660 (C=C), 1610 (NH, C=C aromatic), 1220 (C–O–C), 710 and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data ($CDCl_3$): δ 9.42 (dd, 1 H, $J_{NH,CH}$ 12.8, $J_{1,NH}$ 8.8 Hz, NH), 8.00 (d, 1 H, HC=), 8.03–7.20 (m, 20 H, 4 Bz), 6.03 (t, 1 H, $J_{3,4} = J_{2,3}$ = 8.8 Hz, H-3), 5.76 (t, 1 H, $J_{4,5}$ 8.8 Hz, H-4), 5.61 (t, 1 H, $J_{1,2}$ 8.8 Hz, H-2), 4.93 (t, 1 H, H-1), 4.85 (dd, 1 H, $J_{6,6'}$ 12.8, $J_{5,6}$ 3.2 Hz, H-6), 4.50 (dd, 1 H, H-6'), 4.30–4.20 (m, 1 H, H-5), 4.26 and 4.14 (2 q, 4 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2), 1.31 and 1.22 (2 t, 6 H, 2 CH_3CH_2); ^{13}C [$(CD_3)_2SO$], δ 168.4–165.8 (6 C=O), 158.6 (HC=), 134.4–128.9 (24 C, 4 Ph), 90.9 (C=), 88.1 (C-1), 79.1 (C-3), 77.0 (C-5), 73.2 (C-2), 69.9 (C-4), 61.1 (C-6), 59.5 and 59.3 (2 CH_2), 14.5 and 14.4 (2 CH_3); ^{13}C ($CDCl_3$), δ 167.3, 165.5, 165.2, 165.2, 164.9, 164.8 (6 C=O), 157.1 (HC=), 134.6–127.2 (24 C, 4 Ph), 94.9 (C=), 87.4 (C-1), 74.0 (C-3), 72.6 (C-5), 71.1 (C-2), 68.9 (C-4), 62.6 (C-6), 60.1 and 59.9 (2 CH_2), and 14.1 (2 CH_3).

Anal. Calc. for $C_{42}H_{39}NO_{13}$: C, 65.88; H, 5.13; N, 1.83. Found: C, 65.72; H, 5.13; N, 1.78.

Compound **7** had m.p. 148–150° (from ether), $[\alpha]_D^{22}$ −37° (*c* 0.6, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 275 and 233 nm (ε_{mM} 18.9 and 31.3); ν_{max} 3480 (OH), 3280 (NH), 1725 (C=O), 1665 (C=C), 1610 (NH, C=C aromatic), 1270 (C–O–C), 715 and 695 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data ($CDCl_3$): δ 9.33 (dd, 1 H, $J_{NH,CH}$ 13.0, $J_{1,NH}$ 9.0 Hz, NH), 8.02 (d, 1 H, HC=), 8.10–7.42 (m, 15 H, 3 Bz), 5.63 (t, 1 H, $J_{3,4} = J_{2,3}$ = 9.0 Hz, H-3), 5.43 (t, 1 H, $J_{1,2}$ 9.0 Hz, H-2), 4.78 (t, 1 H, H-1), 4.58 (dd, 1 H, $J_{6,6'}$ 12.8, $J_{5,6'}$ 1.1 Hz, H-6'), 4.23 and 4.11 (2 q, 4 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2), 3.90 (m, 1 H, H-5), 3.88 (t, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.65 (bs, 1 H, OH), 1.29 and 1.22 (2 t, 6 H, 2 CH_3CH_2) (values of H-4 and H-5 were obtained by extrapolation to zero concentration of $Eu(fod)_3$; $J_{3,4}$ and $J_{4,5}$ were measured in the presence of the same europium salt); ^{13}C, δ 167.1, 165.9, 165.7, 165.4, 165.1 (5 C=O), 157.6 (HC=), 134.2–129.1 (18 C, 3 Ph), 94.1 (C=), 87.1 (C-1), 76.4 (C-3), 75.3 (C-5), 71.0 (C-2), 68.6 (C-4), 63.1 (C-6), 60.1, 59.9 (2 CH_2), 14.2 and 14.1 (2 CH_3).

Anal. Calc. for $C_{35}H_{35}NO_{12}$: C, 63.53; H, 5.33; N, 2.12. Found: C, 62.98; H, 5.66; N, 2.11.

Compound **8** was an amorphous solid, $[\alpha]_D^{25}$ −12°, $[\alpha]_{578}^{25}$ −14°, $[\alpha]_{546}^{25}$ −16°, $[\alpha]_{436}^{25}$ −28°, $[\alpha]_{365}^{25}$ −55° (*c* 0.6, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 273 and 270 nm (ε_{mM} 19.1 and 24.9); ν_{max} 3425 (OH), 3280 (NH), 1720, 1700 (C=O), 1660 (C=C), 1610 (NH, C=C aromatic), 1270 (C–O–C), 720 and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data ($CDCl_3$): δ 9.39 (dd, 1 H, $J_{NH,CH}$ 14.0, $J_{NH,1}$ 8.0 Hz, NH), 8.06 (d, 1 H, HC=), 8.05–7.27 (m, 10 H, 2 Bz), 5.35 (t, 1 H, $J_{2,3} = J_{3,4}$ = 8.0 Hz, H-3), 4.67 (dd, 1 H, $J_{6,6'}$ 12.1, $J_{5,6}$ 3.7 Hz, H-6), 4.60 (t, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.57 (dd, 1 H, $J_{5,6'}$ 1.6 Hz, H-6'), 4.16 and 4.10 (2 q, 4 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_2CH_3), 3.85–3.80 (m, 4 H, H-2,5, 2 OH), 3.76 (t, 1 H, $J_{4,5}$ 8.0 Hz, H-4), 1.27 and 1.23 (2 t, 6 H, 2 CH_3CH_2); ^{13}C, δ 168.4, 167.5, 167.0, 165.7 (4 C=O), 158.2 (HC=), 133.4–128.3 (12 C, 2 Ph), 92.9 (C=), 88.7 (C-1), 78.5 (C-3), 76.1 (C-5), 72.0 (C-2), 68.5 (C-4), 63.4 (C-6), 60.1, 59.9 (2 CH_2), 14.1 and 14.0 (2 CH_3).

Anal. Calc. for $C_{28}H_{31}NO_{11}$: C, 60.32; H, 5.60; N, 2.51. Found: C, 59.98; H, 5.53; N, 2.24.

Compound **9** was an amorphous solid, $[\alpha]_D^{25}$ −115°, $[\alpha]_{578}^{25}$ −122°, $[\alpha]_{546}^{25}$ −143° (*c* 0.5, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 273 and 233 nm (ε_{mM} 29.8 and 35.7); ν_{max} 3420 (OH), 1720 (C=O), 1660 (C=C), 1610 (NH, C=C aromatic), 1275 (C–O–C), 720 and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data ($CDCl_3$): δ 9.29 (dd, 1 H, $J_{CH,NH}$ 13.2, $J_{1,NH}$ 9.3 Hz, NH), 8.05 (d, 1 H, HC=), 8.05–7.36 (m, 10 H, 2 Bz), 5.17 (t, 1 H, $J_{2,3} = J_{1,2}$ = 9.3 Hz, H-2), 4.72 (dd, 1 H, $J_{6,6'}$ 13.0, $J_{5,6}$ 4.2 Hz, H-6), 4.64 (t, 1 H, H-1), 4.58 (dd, 1 H, $J_{5,6'}$ 1.8 Hz, H-6'), 4.19, 4.10 (2 q, 4 H, $^3J_{H,H}$ 7.0 Hz, 2 CH_3CH_2), 3.93 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 3.74 (ddd, 1 H, $J_{4,5}$ 9.3 Hz, H-5), 3.70 (bs, 2 H, 2 OH), 3.63 (t, 1 H, H-4), 1.26 and 1.21 (2 t, 6 H, 2 CH_3CH_2); ^{13}C, δ 167.5, 167.1, 166.0, 165.6 (4 C=O), 157.6 (HC=), 133.5–128.3 (12 C, 2 Ph), 94.0 (C=), 87.2 (C-1), 75.9 (C-3), 74.7 (C-5), 73.2 (C-2), 70.0 (C-4), 63.2 (C-6), 60.2, 59.9 (2 CH_2), 14.1 and 14.0 (2 CH_3).

Anal. Calc. for $C_{28}H_{31}NO_{11}$: C, 60.32; H, 5.60; N, 2.51. Found: C, 59.94; H, 5.61; N, 2.33.

(*b*) When the reaction was carried out as (*a*), but at −30°, **7** (20%), **8** (14%), and **9** (16%) were isolated.

(*c*) To a stirred solution of **5** (4 g, 11.36 mmol) in pyridine (9.2 mL) at −15° was added gradually a solution of benzoyl chloride (4.1 mL, 35.2 mmol) in pyridine (13.4 mL). The mixture was kept for 24 h at 0°, then worked-up conventionally. Crystallisation of the product from ether gave **7** (2.40 g, 32%). Column chromatography (benzene–methanol, 20:1) of the mother liquor gave **6** (0.87 g, 10%), **7** (1.90 g, 25%), and a mixture of **8** and **9** that was resolved by t.l.c. (benzene–methanol, 12:1) to give **8** (0.50 g, 8%) and **9** (0.45 g, 7%).

(*d*) A solution of **5** (2 g, 6.88 mmol) in pyridine (6 mL) was stirred and cooled at 0°. Then benzoyl chloride (4.8 mL, 18.37 mmol) was gradually added. The mixture was kept for 24 h at room temperature, then worked-up conventionally. Crystallisation of the product from ethanol gave **6** (4.0 g, 75%).

*2,3,6-Tri-*O*-benzoyl-β-*D*-galactopyranosylamine hydrobromide* (**10**). — To a solution of **3** (1.28 g, 1.93 mmol) in chloroform (3 mL) was added gradually a solution of bromine (0.5 g, 3.13 mmol) in chloroform (12.5 mL) and water (0.06 mL, 3.3 mmol). The mixture was kept for 48 h at room temperature, concentrated to ~6 mL, and stored at ~5° to give **10** (0.84 g, 78%), m.p. >140° (dec.), $[\alpha]_D^{22}$ +59° (*c* 1, methyl sulphoxide); $\lambda_{max}^{CH_2Cl_2}$ 280, 272, and 229 nm (ε_{mM} 2.7, 3.4, and 28.3); ν_{max} 3450 (OH), 3100–2400 ($^+NH_3$), 1700 (C=O), 1580 (C=C aromatic), 1250 (C–O–C), and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 9.15 (bs, 3 H, $^+NH_3$), 8.08–7.47 (m, 15 H, 3 Bz), 6.06 (bs, 1 H, OH), 5.74 (dd, 1 H, $J_{2,3}$ 10.2, $J_{1,2}$ 8.7 Hz, H-2), 5.54 (dd, 1 H, $J_{3,4}$ 2.9 Hz, H-3), 5.13 (d, 1 H, H-1), and 4.57–4.40 (m, 4 H, H-4,5,6,6'); ^{13}C, δ 165.6, 165.1, 165.1 (3 C=O), 133.5–128.5 (18 C, 3 Ph), 78.8 (C-1), 74.8 (C-5), 73.9 (C-3), 68.4 (C-2), 65.7 (C-4), and 63.7 (C-6).

Anal. Calc. for $C_{27}H_{26}BrNO_8$: C, 56.65; H, 4.58; N, 2.45. Found: C, 56.72; H, 4.51; N, 2.32.

H, H-4,5), and 3.75 (bs, 1 H, OH); ^{13}C, δ 167.0, 166.6, 164.8 (3 C=O), 144.2 (N=C=S), 133.5–128.3 (18 C, 3 Ph), 83.7 (C-1), 76.6 (C-3), 75.5 (C-5), 71.8 (C-2), 68.7 (C-4), and 68.2 (C-6).

Anal. Calc. for $C_{28}H_{23}NO_8S$: C, 63.06; H, 4.36; N, 2.62. Found: C, 63.39; H, 4.24; N, 2.69.

3,6-Di-O-benzoyl-β-D-galactopyranosyl isothiocyanate (**13**). — To a solution of **4** (0.22 g, 0.39 mmol) in chloroform (1.3 mL) was gradually added a solution of bromine (0.06 g, 0.39 mmol) in chloroform (1.5 mL) and water (0.39 mmol). The mixture was kept at room temperature for 48 h, and then concentrated. Chloroform was added to the syrupy residue and evaporated several times until no bromine was detected. To a mixture of this residue, chloroform (5 mL), calcium carbonate (0.12 g, 1.2 mmol), and water (3 mL) was added thiophosgene (0.1 mL, 1.3 mmol). The mixture was stirred vigorously for 48 h and then filtered, and the organic layer was washed with water, dried ($CaCl_2$), and concentrated to dryness. Preparative t.l.c. (benzene–ether, 5:2) gave **13** (0.06 g, 36%), isolated as an amorphous solid; $\lambda_{max}^{CH_2Cl_2}$ 280, 273, and 233 nm (ε_{mM} 4.0, 4.5, and 25.8); ν_{max} 3470 (OH), 2050 (N=C=S), 1720 (C=O), 1600, 1580 (C=C aromatic), 1225 (C–O–C), 715 and 690 cm^{-1} (CH aromatic). ^1H-N.m.r. data ($CDCl_3$): δ 8.06–7.30 (m, 10 H, 2 Bz), 5.11 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 3.4 Hz, H-3), 4.91 (d, 1 H, $J_{1,2}$ 8.9 Hz, H-1), 4.63 (dd, 1 H, $J_{6,6'}$ 11.4, $J_{5,6}$ 6.7 Hz, H-6), 4.48 (dd, 1 H, $J_{5,6'}$ 6.7 Hz, H-6'), 4.30–4.20 (m, 4 H, H-2,4, 2 OH), and 4.00 (t, $J_{4,5}$ 0 Hz, H-5); ^{13}C, δ 166.5, 166.4 (2 C=O), 142.6 (N=C=S), 133.6–128.3 (12 C, 2 Ph), 86.3 (C-1), 75.3 (C-3), 74.2 (C-5), 70.1 (C-2), 66.9 (C-4), and 62.7 (C-6).

Anal. Calc. for $C_{21}H_{19}NO_7S$: C, 58.73; H, 4.46; N, 3.26. Found: C, 58.63; H, 4.10; N, 2.68.

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2,3,6-Tri-O-benzoyl-β-D-glucopyranosylamine hydrochloride (**11**). — Chlorine was passed through a solution of **7** (2 g, 3 mmol) in dichloromethane (80 mL) until a solid mass resulted. The precipitate was collected and washed with dichloromethane to give **11** (1.46 g, 92%), m.p. 157–160° (dec.), $[\alpha]_D^{25}$ +75°, $[\alpha]_{578}^{25}$ +77°, $[\alpha]_{546}^{25}$ +90°, $[\alpha]_{436}^{25}$ +167°, $[\alpha]_{365}^{25}$ +289° (*c* 0.6, methyl sulphoxide); $\lambda_{max}^{CH_3OH}$ 280, 272, and 227 nm (ε_{mM} 2.5, 3.1, and 21.5); ν_{max} 3410 (OH), 3100–2600 ($^+NH_3$), 1720 (C=O), 1600, 1580 (C=C aromatic), 1270 (C–O–C), 715 and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. [$(CD_3)_2SO$]: δ 9.29 (bs, 3 H, $^+NH_3$), 8.11–7.43 (m, 15 H, 3 Bz), 5.64 (t, 1 H, $J_{2,3} = J_{3,4}$ = 8.8 Hz, H-3), 5.36 (t, 1 H, $J_{1,2}$ 8.8 Hz, H-2), 5.27 (d, 1 H, H-1), 4.69 (dd, 1 H, $J_{6,6'}$ 12.5, $J_{5,6}$ <1 Hz, H-6), 4.49 (dd, 1 H, $J_{5,6'}$ 5.0 Hz, H-6'), 4.41 (s, 1 H, OH), 4.23 (m, 1 H, H-5), and 3.93 (t, 1 H, $J_{4,5}$ 8.8 Hz, H-4); ^{13}C, δ 165.7, 165.4, 164.9 (3 C=O), 133.6–128.6 (18 C, 3 Ph), 78.8 (C-1), 76.0 (C-3), 75.4 (C-5), 71.2 (C-2), 67.3 (C-4), and 63.3 (C-6).

Anal. Calc. for $C_{27}H_{26}ClNO_8$: C, 61.42; H, 4.96; N, 2.65. Found: C, 61.35; H, 4.97; N, 2.66.

When solutions of **10** and **11** in methyl sulphoxide were kept at room temperature for more than 24 h, transbenzoylation reactions were observed.

Tri-O-benzoyl-β-D-glycopyranosyl isothiocyanates. — To a mixture of the glycosylamine hydrohalide (**10** or **11**, 2.5 mmol) in chloroform (17.5 mL) and calcium carbonate (7.5 mmol) in water (6 mL) was added thiophosgene (3.8 mmol). The mixture was stirred vigorously for 48 h, then filtered. The organic layer was washed with water, dried ($MgSO_4$ or $CaCl_2$), and concentrated to dryness, and the residue was crystallised from ether. The following compounds were prepared in this manner.

2,3,6-Tri-*O*-benzoyl-β-D-galactopyranosyl isothiocyanate (**12**; 0.72 g, 54%), m.p. 150–152°, $[\alpha]_D^{21}$ +2° (*c* 0.5, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 280, 273, and 228 nm (ε_{mM} 3.2, 3.7, and 28.3); ν_{max} 3490 (OH), 2040 (N=C=S), 1730, 1715, 1690 (C=O), 1600, 1580 (C=C aromatic), 1270 (C–O–C), 715 and 680 cm^{-1} (CH aromatic). ^{1}H-N.m.r. ($CDCl_3$): δ 8.07–7.25 (m, 15 H, 3 Bz), 5.92 (dd, 1 H, $J_{2,3}$ 10.3, $J_{1,2}$ 9.1 Hz, H-2), 5.35 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 5.28 (d, 1 H, H-1), 4.74 (dd, 1 H, $J_{6,6'}$ 11.6, $J_{5,6}$ 6.1 Hz, H-6), 4.55 (dd, 1 H, $J_{5,6'}$ 6.1 Hz, H-6'), 4.37 (t, 1 H, $J_{4,OH}$ 3.2, $J_{4,5}$ 0 Hz, H-4), 4.12 (t, 1 H, H-5), and 2.75 (d, 1 H, OH); ^{13}C, δ 166.4, 165.5, 164.9 (3 C=O), 143.0 (N=C=S), 133.0–128.0 (18 C, 3 Ph), 84.4 (C-1), 74.6, 73.9 (C-5, C-3), 69.8 (C-2), 67.1 (C-4), and 63.1 (C-6).

Anal. Calc. for $C_{28}H_{23}NO_8S$: C, 63.06; H, 4.34; N, 2.62. Found: C, 63.25; H, 4.10; N, 2.68.

2,3,6-Tri-*O*-benzoyl-β-D-glucopyranosyl isothiocyanate (**14**; 1.04 g, 78%), m.p. 197–199°, $[\alpha]_D^{25}$ +46°, $[\alpha]_{578}^{25}$ +47°, $[\alpha]_{546}^{25}$ +54°, $[\alpha]_{436}^{25}$ +97°, $[\alpha]_{365}^{25}$ +162° (*c* 0.94, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 281, 273, and 235 nm (ε_{mM} 2.7, 3.2, and 23.7); ν_{max} 3480 (OH), 2040 (N=C=S), 1730, 1700 (C=O), 1600, 1580 (C=C aromatic), 1220 (C–O–C), 715 and 690 cm^{-1} (CH aromatic). ^{1}H-N.m.r. ($CDCl_3$): δ 8.11–7.30 (m, 15 H, 3 Bz), 5.60–5.46 (m, 2 H, H-2,3), 5.26 (m, 1 H, H-1) 4.77 (dd, 1 H, $J_{6,6'}$ 12.6, $J_{5,6}$ 3.9 Hz, H-6), 4.64 (dd, 1 H, $J_{5,6'}$ 1.7 Hz, H-6'), 3.95–3.83 (m, 2

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