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Stereocontrolled preparation of 2-,3- and 4-isothiocyanato aldopyranose derivatives

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Abstract

The regio- and stereocontrolled introduction of an isothiocyanato group into the positions 2, 3 and 4 of glycopyranose derivatives starting from glycosides, glycosylamines, and aminosugars is reported. Isothiocyanato sugars with D-*gluco*, D-*allo* and D-*manno* configurations have been prepared.

1. Introduction

Of the sugar isothiocyanates, the glycosyl derivatives are the most well-known compounds, and have been widely used in different syntheses of glycoconjugates, whose sugar moiety is a monosaccharide to trisaccharide glycosyl radical.[1] In recent years, various synthetic methods for both pyranoid[1c,2] and furanoid[3] glycosyl isothiocyanates have been reported. However, the data on the introduction of an NCS group onto a non-glycosydic position of a sugar,[4] onto a polyol chain,[5] or onto the secondary positions of sugar moieties of *C*-nucleosides[6] are limited, in spite of the interest of deoxy-isothiocyanato derivatives in the preparation of guanidinosugars,[5] macrocycles,[7] several glycomimetics,[1c,8] and pseudonucleosides.[4c] Frequently, there are problems of formation of mixtures of diastereomers,[1c] or of reactions between the NCS group and a neighbouring hydroxyl group[6c] in the described synthetic methods for deoxy-isothiocyanato sugars.

In this paper we report on the stereocontrolled introduction of an isothiocyanato group into different secondary positions of D-glycopyranose rings. We have chosen, as carbohydrate derivatives, glycosides, and glycosylamines, potentially useful for glycoconjugates and macrocycles syntheses, and as configurations, D-*gluco*, D-*allo* and D-*manno*. The stereocontrol is based mainly on the use of S_N2 reactions.

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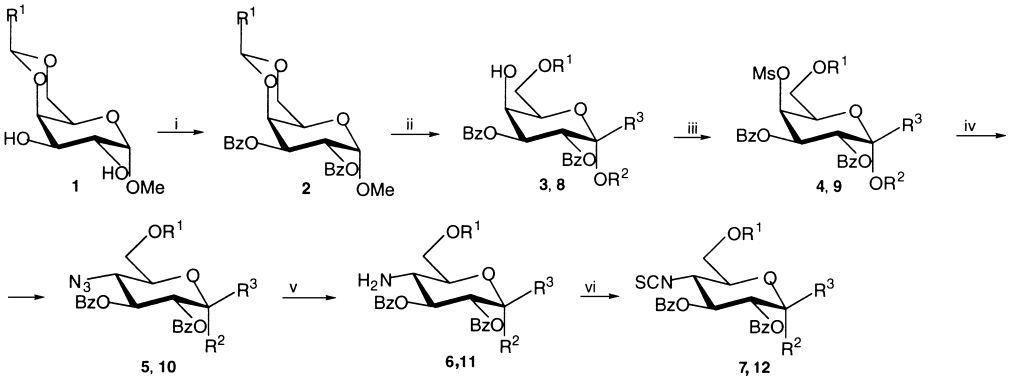
2. Results and discussion

For the introduction of the NCS group onto the position 4 of a D-glucopyranose ring, we have started from the α-methyl-D-galactopyranoside derivative **1**,[9] and from the partially *O*-benzoylated-β-D-galactopyranosylamine derivative **8**[10] (Scheme 1). Conventional *O*-benzoylation with benzoyl chloride of **1** gave the di-*O*-benzoylderivative **2**. The regioselective ring opening of the 4,6-acetal ring of **2** with sodium cyanoborohydride in DMF and trifluoroacetic acid produced the partially *O*-protected D-galactoglycoside **3**. The chemical shifts for the resonances of H-2 and H-3 in compounds **2** and **3** were in agreement with the presence of the benzoyl groups (see Table 1 and Experimental). The IR spectrum of **3** showed the OH band at 3300 cm^{-1}, and the corresponding ^1H NMR spectrum had the signal for H-4 at 4.45 ppm (C*H*OH), and the value for $J_{4,5}$ was roughly 0 Hz, as is described[11] for related D-galactopyranosyl derivatives.



Reagents and conditions. (i) ClBz/Py, rt; (ii) $NaCNBH_3$/TFA, 0°C; (iii) ClMs, rt; (iv) NaN_3, 60-70 °C; (v) H_2/Pd/C, rt; (vi) Cl_2CS, rt.

	1-2	3-7	8-12
R^1	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4CH_2$	Bz
R^2	-	OMe	H
R^3	-	H	NH-CH=$C(CO_2Et)_2$

Scheme 1.

Treatment of the D-galactopyranosyl compounds **3** and **8**, with the hydroxyl group on C-4 being free, with mesyl chloride gave, in good yield, the corresponding 4-methanesulphonyl esters **4** and **9**, which by reaction with sodium azide in hexamethylphosphoramide (HMPT) at 60–70°C produced the 4-azido-4-deoxyglucopyranosyl compounds **5** and **10** in high yield. No appreciable elimination products were observed in the formation of **5** and **10**, nor were compounds coming from the internal nucleophilic attack of the NH (enamino group) on C-4[11] formed in the case of **10**. Catalytic hydrogenation of **5** and **10** produced the 4-aminosugars **6** and **11**, which by reaction with thiophosgene in a basic medium gave the 4-deoxy-4-isothiocyanatoglucoside **7** or glucosylenamine **12**, respectively.

The structures of compounds **4**–**7** and **9**–**12** were supported by analytical and spectroscopic data. The chemical shifts for the resonances of H-4 in compounds **4** and **9** showed a downfield

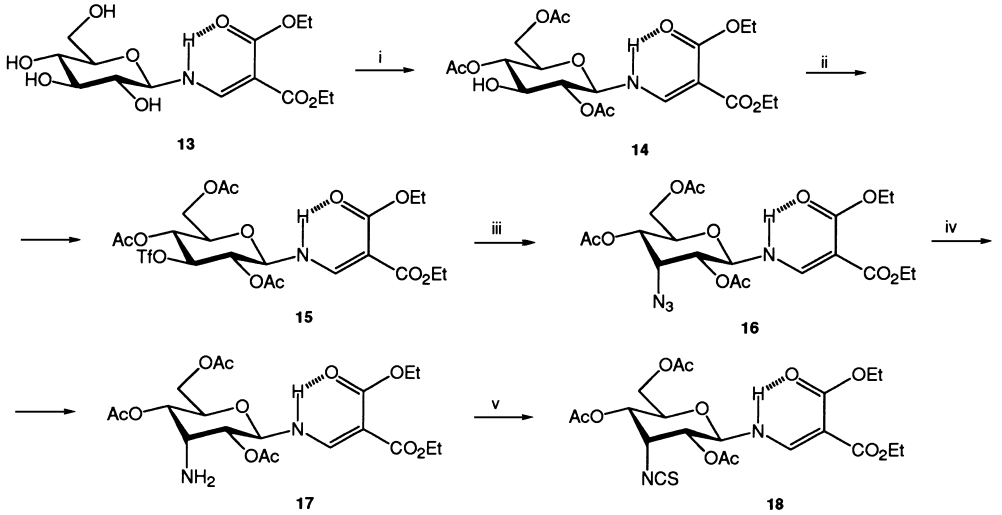
Table 1
Relevant NMR data for compounds **2**–**7**, **9**–**12**, **14**, **16**, **18**, **21**, **22** and **24** in $CDCl_3$

	δ(ppm)									$J_{H,H}$(Hz)			
	H-2	H-3	H-4	H-5	C-2	C-3	C-4	C-5	NCS	1,2	2,3	3,4	4,5
2[a]	5.78		4.64	3.89	69.0	69.0	74.1	62.0	-	1.6	-	1.2	-
3[b]	5.72-5.66		4.45	4.13	69.0	71.0	69.2	68.1	-	3.2	-	-	0.2
4[b]	5.59	5.78	5.45	4.31	68.4	68.2	76.6	67.0	-	3.6	10.9	3.0	-
5[b]	5.21-5.16	5.91	4.04	3.93-3.79	71.9	70.9	60.3	69.2	-	-	-	10.0	10.0
7[b]	5.13	5.98	4.32	4.01	71.4	70.3	56.4	69.3	138.1	3.6	10.1	10.1	10.1
9[b]	5.78	5.59	5.49	4.35	68.3	71.0	74.2	72.2	-	8.9	10.4	3.1	0.6
10[a]	5.38	5.70	3.89	3.78	71.1	73.4	60.5	74.4	-	9.5	9.5	9.5	9.5
12[b]	5.45	5.87	4.27-4.24	3.99	70.9	72.9	57.1	74.6	141.3	9.5	9.5	9.5	10.1
14[b]	4.96	3.81	4.95	3.73	73.6	72.9	70.2	73.5	-	9.0	9.0	10.0	10.0
16[b]	4.96	4.46	4.93	4.14-4.10	69.4	60.7	66.9	71.2	-	9.1	3.2	3.2	10.0
18[b]		4.91-4.86		4.13	68.3	58.1	66.0	71.6	141.7	8.8	-	-	9.9
21[b]	3.86	5.34	5.29	4.08	58.9	69.5	65.0	70.6	-	2.0	3.7	9.3	9.3
22[a]	3.94	5.09	5.23	3.83	59.4	71.7	64.8	73.2	-	1.3	3.8	9.8	9.8
24[b]	4.26	5.28	5.39	4.05	57.5	69.2	64.9	70.7	140.2	2.0	4.0	10.0	10.0

[a]300MHz for ^1H, 75.4 MHz for ^{13}C. [b]500 MHz for ^1H, 125.7 MHz for ^{13}C.

shift of ≈1 ppm when they were compared with the same signal for **3** and **8**, supporting the formation of the sulphonic ester. Compounds **5** and **10** had the IR absorption at ≈2100 cm^{-1} for the azido group, and the vicinal coupling constants values $J_{3,4}$ and $J_{4,5}$, roughly 10 Hz, supported the formation of the D-glucopyranosyl ring. The presence of the isothiocyanato group in **7** and **12** was based on the IR band at ≈2041 cm^{-1}, and on the NMR resonances at ≈140 (N*C*S), ≈57 (C-4), and 4.30 ppm (H-4), which are characteristic[1c] of the isothiocyanato-sugars.

A suitable starting material to prepare 3-deoxy-3-isothiocyanato-D-allopyranosylamines is the *N*-protected D-glucopyranosylamine **13**[10] (Scheme 2). The regioselective acetylation of **13** with acetic anhydride and pyridine, using a molar ratio 1:3 (**13**: Ac_2O) at –20°C, produced a mixture of acetylated products, whose NMR spectra showed that the 2,4,6-tri-*O*-acetyl **14** and 2,3,6-tri-*O*-acetyl derivatives are the preponderant compounds. After the mixture was boiled in ethyl ether, transacylation took place and **14** was obtained as sole crystalline product. Its IR spectra had the



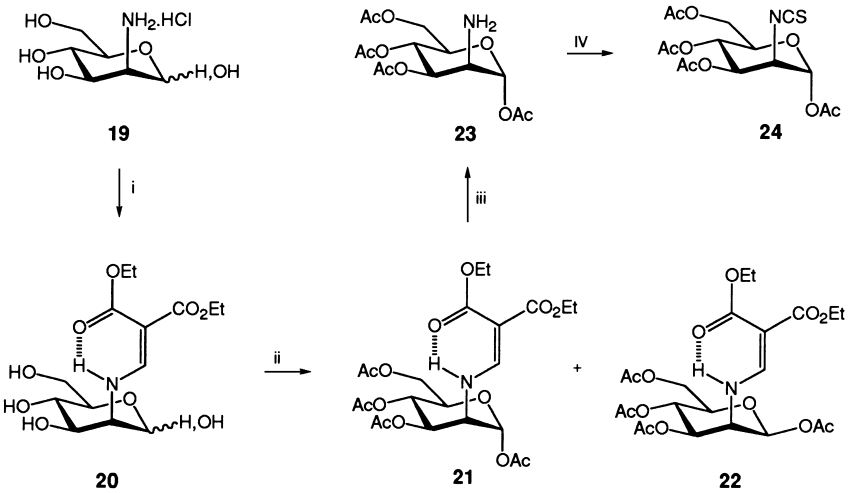
Scheme 2. Reagents and conditions. (i) Ac_2O/Py, –20°C; (ii) Tf_2O/Py, –15°C; (iii) NaN_3, rt; (iv) H_2/Pd/C, rt; (v) Cl_2CS, rt

OH band at 3420 cm^{-1}, and the resonance for H-3 appeared at 3.81 ppm, showing a coupling between H-3 and the hydroxyl group of 5.0 Hz.

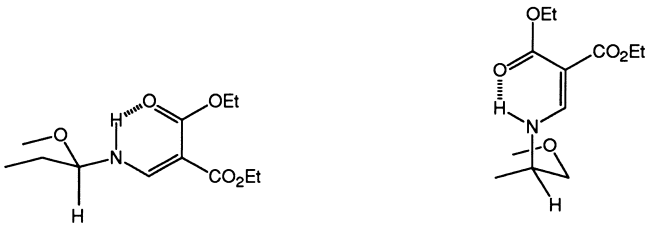
Treatment of **14** with trifluoromethanesulphonic anhydride gave the 3-*O*-trifyl-D-glucopyranosylamine derivative **15**. The C-3 configuration of **15** was inverted by reaction with sodium azide, producing the 3-azido-3-deoxy-D-allopyranosylamine **16**. Catalytic [$Pd(OH)_2$] hydrogenation of the latter gave the amino derivative **17**. This was directly reacted with thiophosgene to produce the 3-deoxy-3-isothiocyanato-D-allopyranosylamine derivative **18**.

The spectroscopic data of **16** supported both the introduction of the azido group (IR absortion at 2130 cm^{-1}, and H-3 and C-3 resonances at 4.46 and 60.7 ppm, respectively) and the D-*allo* configuration ($J_{2,3} = J_{3,4} = 3.2$ Hz). In the case of compound **18**, the presence of the NCS group was confirmed by the ^{13}C resonances at 141.7 (NCS) and 58.1 ppm (C-3), and by the IR band at 2047 cm^{-1} (NCS).

As the 2-amino-2-deoxy monosaccharides are the most readily available aminosugars, to introduce an isothiocyanato group into the position 2 of the D-mannopyranose ring we started from 2-amino-2-deoxy-D-mannose hydrochloride **19** (Scheme 3). The reaction of this aminosugar with diethyl ethoxymethylene malonate produced the *N*-protected D-mannosamine **20**, with an α:β ratio of 3:1. Acetylation of **20** with acetic anhydride gave a mixture of the tetra-*O*-acetyl-derivatives anomers **21** and **22**, the α:β anomers ratio being 4:1. This mixture was resolved by column chromatography to obtain the α (**21**, 41%) and β (**22**, 11%) anomers as pure products. The following reactions were performed on the major α anomer. The NMR spectra of compounds **20**–**22** contained the characteristic[1b] signals of the enamino group (see Experimental); the $J_{1,2}$ value for the α-anomer **21** (2.0 Hz) and for the β-anomer **22** (1.3 Hz) were very close to that described[12] for related pairs of anomers with D-*manno* configuration. In all the compounds having the enamino group (**9**, **10**, **12**, **14**, **16**, **18**, **21** and **22**), the δ values for NH (9.18–9.62 ppm), for a CO_2Et group (167.4–168.4, C=O chelated) and the IR absorptions at 1650–1670 cm^{-1} (C=O chelated) were indicative[13] of the hydrogen bond shown in Fig. 1. The $J_{1,NH}$ ($J_{2,NH}$ for **21** and **22**) value of these compounds was in the range 8.9–9.9 Hz, indicating *trans* relationship between the corresponding protons (Fig. 1).



Scheme 3. Reagents and conditions. (i) $EtOCH{=}C(CO_2Et)_2$, Na_2CO_3, rt; (ii) Ac_2O/Py, –20°C; (iii) Cl_2/CH_2Cl_2, 0°C; (iv) Cl_2CS, rt



9, 10, 12, 14, 16, 18 **21, 22**

Figure 1. Conformation of the CH–NH bond

The *N*-deprotection of **21** with chlorine in dichloromethane yielded the *O*-acetylated aminosugar **23**, which by reaction with thiophosgene produced the 2-deoxy-2-isothiocyanato D-*manno* derivative **24** with a 75% overall yield from **21**. The NCS group of **24** was evident from the IR absorption at 2062 cm^{-1}, and from the resonances of NCS (140.2 ppm), C-2 (57.5 ppm), and H-2 (4.26 ppm). All the vicinal coupling constant values of the mannopyranose ring were indicative[12] that, in solution in chloroform, the $^4C_1$ conformation is little distorted, in spite of the presence of the polar NCS group in axial disposition on C-2.

3. Conclusion

For the regio- and stereocontrolled introduction of an isothiocyanato group into secondary positions of glycopyranose rings, the reaction of *O*-protected aminosugar derivatives with thiophosgene is a useful method. In the case of the position 2, it is possible to start from a commercial product, whereas in the cases of the positions 3 and 4 the amino group is introduced via sulphonyloxy and azido derivatives using S_N2 reactions. The method is potentially useful for the preparation of diisothiocyanato derivatives when an additional enamino group exists (**12**), as this group is a latent NCS group (sequence **20**–**24**).

4. Experimental

4.1. General methods

Melting points are uncorrected. Optical rotations were measured for solutions in dichloromethane. FTIR spectra were recorded for KBr discs or thin film. ^1H NMR spectra (500 or 300 MHz) were obtained for solutions in $CDCl_3$ or MeOH-d_4. Assignments were confirmed by homonuclear 2D COSY correlated experiments. ^{13}C NMR spectra were recorded at 125.7 or 75.4 MHz. Heteronuclear 2D correlated spectra were obtained in order to assist in carbon resonance assignments. Mass spectra (EI and FAB) were recorded with a Kratos MS-80RFA and Micromass AutoSpecQ instruments with a resolution of 1000 or 10 000(10% valley definition). For the FAB spectra, ions were produced by a beam of xenon atoms (6–7 KeV), using 3-nitrobenzyl alcohol and thioglycerol as matrix and NaI as salt. TLC was performed on silica gel HF_{254}, with detection by UV light or charring with H_2SO_4. Silica gel 60 (Merck, 70–230 and 230–400 mesh) was used for preparative chromatography.

4.2. Methyl 2,3-di-O-benzoyl-4,6-O-(4-methoxybenzylidene)-α-D-galactopyranoside **2**

To a stirred solution of methyl 4,6-*O*-(4-methoxybenzylidene)-α-D-galactopyranoside **1**[9] (0.719 g, 2.3 mmol) in pyridine (3.7 ml) at 0°C benzoyl chloride (0.92 ml, 7.1 mmol) in pyridine (3.3. ml) was added dropwise. The mixture was stirred for 12 h at rt and then poured into ice-water (500 ml) and extracted with CH_2Cl_2. The extracts were washed with H_2SO_4 (2N), aq. $NaHCO_3$ (saturated) and water, dried ($MgSO_4$), and concentrated. Column chromatography (2:1 Et_2O:petroleum ether) on silica gel gave **2** (1.140 g, 95%) as an amorphous solid. $[\alpha]_D^{27}$ +209.6 (*c* 1.8); FABMS: *m*/*z* 543 [M+Na]$^+$; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03–6.87 (m, 14H, Ar), 5.78 (m, 2H, H-2, H-3), 5.53 (s, 1H, CH-Ar), 5.29 (d, 1H, $J_{1,2}=1.6$, H-1), 4.64 (d, 1H, $J_{3,4}=1.2$, H-4), 4.34 (dd, 1H, $J_{5,6a}=1.6$, $J_{6a,6b}=12.5$, H-6a), 4.13 (dd, 1H, $J_{5,6b}=1.7$, H-6b), 3.89 (m, 1H, H-5), 3.81 (s, 3H, CH_3O-Ar), and 3.47 (s, 3H, CH_3O) ppm; ^{13}C NMR (125.7 MHz): δ 166.0, 165.8 (2 CO), 159.8–113.3 (18 C, Ar), 100.5 (CH), 97.9 (C-1), 74.1 (C-4), 69.0 (2 C, C-2, C-3), 68.7 (C-6), 62.0 (C-5), 55.5 and 55.1 (2 CH_3O) ppm. Anal. calcd for $C_{29}H_{28}O_9$: C, 66.91; H, 5.42. Found: C, 66.83; H, 5.58.

4.3. Methyl 2,3-di-O-benzoyl-6-O-(4-methoxybenzyl)-α-D-galactopyranoside **3**

To a solution of **2** (0.957 g, 1.84 mmol) and $Na(CN)BH_3$ (0.578 g, 9.2 mmol) in DMF (17 ml) over 4 Å molecular sieves at 0°C, a solution of 0.1% F_3CCOOH in DMF (14 ml) was added dropwise. After 7 h at rt the reaction mixture was filtered through Celite, poured into ice-aq. $NaHCO_3$ (saturated) and extracted with CH_2Cl_2. The organic layer was washed with cool aq. $NaHCO_3$ (saturated), dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (CH_2Cl_2) to yield **3** (0.637 g, 67%) as an amorphous solid. $[\alpha]_D^{27}$ +103.3 (*c* 1.2); FABMS: *m*/*z* 545 [M+Na]$^+$; IR ν_{max} 3300 cm^{-1} (HO); ^{1}H NMR (500 MHz, $CDCl_3$); δ 8.03–6.87 (m, 14H, Ar), 5.72–5.66 (m, 2H, H-2, H-3), 5.22 (d, 1H, $J_{1,2}=3.2$, H-1), 4.57, 4.52 (each d, each 1H, $J_{H,H}=11.6$, CH_2), 4.45 (bs, 1H, H-4), 4.13 (m, 1H, H-5), 3.85–3.78 (m, 2H, H-6a, H-6b), 3.80 (s, 3H, CH_3O-Ar) and 3.43 (s, 3H, CH_3O) ppm; ^{13}C NMR: δ 165.9, 165.7 (2 CO), 159.3–113.8 (18 C, Ar), 97.6 (C-1), 73.4 (CH_2) 71.0 (C-3), 69.7 (C-6), 69.2 (C-4), 69.0 (C-2), 68.1 (C-5), 55.4 and 55.1 (2 CH_3O) ppm. Anal calcd for $C_{29}H_{30}O_9$: C, 66.66; H, 5.79. Found: C, 66.29; H, 6.21.

4.4. Procedure for mesylation of **3** and **8**

To a stirred solution of **3** (0.48 g, 0.92 mmol) or **8** (0.2 g, 0.3 mmol) in pyridine (*x* ml) at 0°C mesyl chloride (*y* ml) was gradually added. The mixture was kept for *t* h at rt, then poured into ice-water and extracted with CH_2Cl_2. The combined organic layers were washed with H_2SO_4 (2N), aq. $NaHCO_3$ (saturated) and water, dried ($MgSO_4$) and concentrated. The residue was purified as described.

4.4.1. Methyl 2,3-di-O-benzoyl-4-O-mesyl-6-O-(4-methoxybenzyl)-α-D-galactopyranoside **4**

$x=27$ ml; $y=0.2$ ml; $t=13$ h. Column chromatography (CH_2Cl_2) gave **4** (0.49 g, 90%) as an amorphous solid. $[\alpha]_D^{27}$ +118.5 (*c* 1.0); FABMS: *m*/*z* 623 [M+Na]$^+$; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03–6.88 (m, 14H, Ar), 5.78 (dd, 1H, $J_{2,3}=10.9$, $J_{3,4}=3.0$, H-3), 5.59 (dd, 1H, $J_{1,2}=3.6$, H-2), 5.45 (d, 1H, H-4), 5.16 (d, 1H, H-1), 4.55, 4.49 (each d, each 1H, $J_{H,H}=11.1$, CH_2), 4.31 (m, 1H, H-5), 3.81 (s, 3H, CH_3O-Ar), 3.70–3.68 (m, 2H, H-6a, H-6b), 3.44 (s, 3H, CH_3O) and 3.02 (s, 3H, Ms) ppm; ^{13}C NMR (125.7 MHz): δ 165.8, 165.5 (2 CO), 159.2–113.7 (18 C, Ar), 97.3 (C-1),

76.6 (C-4), 73.2 (CH_2), 68.4 (C-2), 68.2 (C-3), 67.2 (C-6), 67.0 (C-5), 55.6, 55.1 (2 CH_3O) and 23.6 (Ms) ppm. Anal. calcd for $C_{30}H_{32}O_{11}S$: C, 59.99; H, 5.37; S, 5.34. Found: C, 60.12; H, 5.08; S, 5.10.

4.4.2. 2,3,6-Tri-O-*benzoyl-4*-O-*mesyl*-N-*(2,2-diethoxycarbonylvinyl)-β-D-galactopyranosylamine* ***9***

$x = 5$ ml; $y = 0.07$ ml; $t = 14$ h. Column chromatography (1:1 AcOEt:petroleum ether) gave **9** (0.20 g, 88%) as an amorphous solid. $[\alpha]_D^{26}$ +1.8 (*c* 1.1); FABMS: *m/z* 762 $[M+Na]^+$; IR ν_{max} 1663 cm^{-1} (C=O chelated); ^1H NMR (500 MHz, $CDCl_3$): δ 9.46 (dd, 1H, $J_{NH,HC=} = 13.1$, $J_{NH,1} = 8.9$, NH), 8.07–7.35 (m, 15H, Ar), 7.98 (d, 1H, HC=), 5.78 (dd, 1H, $J_{1,2}$ 8.9, $J_{2,3} = 10.4$, H-2), 5.59 (dd, 1H, $J_{3,4} = 3.1$, H-3), 5.49 (dd, 1H, $J_{4,5} = 0.6$, H-4), 4.82 (t, 1H, H-1), 4.71 (dd, 1H, $J_{5,6a} = 6.0$, $J_{6a,6b} = 11.3$, H-6a), 4.43 (dd, 1H, $J_{5,6b} = 7.5$, H-6b), 4.35 (m, 1H, H-5), 4.28 (m, 2H, CH_2CH_3), 4.15 (q, 2H, $J_{H,H} = 7.1$, CH_2CH_3), 3.14 (s, 3H, Ms), 1.33 and 1.25 (t, 6H, 2 CH_2CH_3) ppm; ^{13}C NMR (125.7 MHz): δ 167.5, 165.8, 165.4, 165.2, 165.1 (5 CO), 157.0 (HC=), 133.6–128.1 (18 C, Ar), 95.0 (C=), 87.5 (C-1), 74.2 (C-4), 72.2 (C-5), 71.0 (C-3), 68.3 (C-2), 61.2 (C-6), 60.2, 59.9 (2 CH_2CH_3), 38.8 (Ms) and 14.1 (2 C, 2 CH_2CH_3) ppm. Anal. calcd for $C_{36}H_{37}O_{14}NS$: C, 58.45; H, 5.04; N, 1.89; S, 4.33. Found: C, 58.49; H, 5.29; N, 1.97; S, 4.46.

*4.5. Procedure for the displacement of MsO group with sodium azide (**5**,**10**)*

To a stirred solution of the corresponding sulphonyloxysugar **4**, **9** (*m* g) in HMPT (*x* ml), sodium azide (*y* g) was added. The mixture was kept for *t* h at *T*°C, then poured into ice-water and extracted with AcOEt. The combined organic layers were washed with water, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography.

4.5.1. Methyl 4-azido-2,3-di-O-*benzoyl-4-deoxy-6*-O-*(4-methoxybenzyl)-α-D-glucopyranoside* ***5***

$m = 0.375$ g, 0.625 mmol; $x = 5.5$ ml; $y = 0.203$ g, 3.12 mmol; $t = 13$ h; $T = 60$°C. Column chromatography (1:4 AcOEt:petroleum ether) gave **5** (0.300 g, 93%) as an amorphous solid. $[\alpha]_D^{26}$ +177.8 (*c* 0.7); FABMS: *m/z* 570 $[M+Na]^+$; IR ν_{max} 2108 cm^{-1} (N_3); ^1H NMR (300 MHz, $CDCl_3$): δ 8.03–6.91 (m, 14H, Ar), 5.91 (m, 1H, H-3), 5.21–5.16 (m, 2H, H-1, H-2), 4.68, 4.55 (each d, each 1H, $J_{H,H} = 11.6$, CH_2), 4.04 (t, 1H, $J_{3,4} = J_{4,5} = 10.0$, H-4), 3.93–3.79 (m, 3H, H-5, H-6a, H-6b), 3.82 (s, 3H, CH_3O-Ar) and 3.41 ppm (s, 3H, CH_3O-C_1); ^{13}C NMR (125.7 MHz): δ 165.7, 165.5 (2 CO), 159.3–113.8 (18 C, Ar), 97.1 (C-1), 73.3 (CH_2), 71.9 (C-2), 70.9 (C-3), 69.2 (C-5), 67.9 (C-6), 60.3 (C-4), 55.5 and 55.2 (2 CH_3O) ppm. Anal calcd for $C_{29}H_{29}O_8N_3$: C, 63.61; H, 5.34; N, 7.67. Found: C, 63.38; H, 5.37; N, 7.40.

4.5.2. 4-Azido-2,3,6-tri-O-*benzoyl-4-deoxy*-N-*(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine* ***10***

$m = 0.1$ g, 0.135 mmol; $x = 1.2$ ml; $y = 0.044$ g, 0.68 mmol; $t = 12$ h; $T = 70$°C. Column chromatography (7:1 toluene:AcOEt) gave **10** (0.086 g, 92%) as an amorphous solid. $[\alpha]_D^{20}$ +6.4 (*c* 0.6); FABMS: *m/z* 709 $[M+Na]^+$; IR ν_{max} 2112 (N_3) and 1660 cm^{-1} (C=O chelated); ^1H NMR (300 MHz, $CDCl_3$): δ 9.31 (dd, 1H, $J_{NH,1} = 9.5$, $J_{NH,CH=} = 13.1$, NH), 8.06–7.19 (m, 15H, Ar), 7.87 (d, 1H, HC=), 5.70 (t, 1H, $J_{2,3} = J_{3,4} = 9.5$, H-3), 5.38 (t, 1H, $J_{1,2} = 9.5$, H-2), 4.70 (t, 1H, H-1), 4.64 (dd, 1H, $J_{5,6a} = 2.3$, $J_{6a,6b} = 12.3$, H-6a), 4.58 (dd, 1H, $J_{5,6b} = 3.8$, H-6b), 4.18, 4.06 (each q, each 2H, $J_{H,H} = 7.1$, 2 CH_2CH_3), 3.89 (t, 1H, $J_{4,5} = 9.5$, H-4), 3.78 (ddd, 1H, H-5), 1.23 and 1.16 (each t, each 3H, 2 CH_2CH_3) ppm; ^{13}C NMR (75.4 MHz): δ 167.4, 166.0, 165.4, 165.2 (5 C, 5 CO), 157.1 (CH=), 133.6–128.1 (18 C, Ar), 95.0 (C=), 87.4 (C-1), 74.4 (C-5), 73.4 (C-3), 71.1 (C-2), 62.9

(C-6), 60.5 (C-4), 60.2, 60.0 (2 CH_2CH_3), 14.2 and 14.1 (2 CH_2CH_3) ppm. Anal. calcd for $C_{35}H_{34}O_{11}N_4$: C, 61.22; H, 4.99; N, 8.16. Found: C, 61.00; H, 4.86; N, 7.86.

4.6. Procedure for the reduction of the azido group **6**,**11**

The corresponding azidosugar **5**, **10** (*m* g) was dissolved in distilled MeOH (*x* ml) and hydrogenated in the presence of palladium-on-charcoal (*y* g) for *t* h at rt and ≈1 atm. The catalyst was filtered off through a Celite pad, and washed with methanol. The filtrate and washings were combined and evaporated to give a syrup which was used without purification in the next step.

4.6.1. Methyl 4-amino-2,3-di-O-benzoyl-4-deoxy-6-O-(4-methoxybenzyl)-α-D-glucopyranoside **6**

$m = 0.224$ g, 0.44 mmol; $x = 5$ ml; $y = 0.022$ g; $t = 6$ h. TLC (1:6) AcOEt:petroleum ether; FABMS: m/z 544 $[M+Na]^+$.

4.6.2. 4-Amino-2,3,6-tri-O-benzoyl-4-deoxy-N-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine **11**

$m = 0.2$ g, 0.29 mmol; $x = 5$ ml; $y = 0.02$ g; $t = 10$ h. TLC (2:1) AcOEt:petroleum ether; FABMS: m/z 683 $[M+Na]^+$.

4.7. General method for isothiocyanato derivatives **7**, **12**

To a heterogeneous mixture of the corresponding glycopyranosylamine (**6**, **11**, *x* g), dichloromethane (*y* ml), calcium carbonate (*z* g), and water (*y* ml), thiophosgene (*k* ml) was added. The mixture was vigorously stirred for *t* h and then filtered. The organic layer was washed with water, dried ($MgSO_4$), concentrated and the residue was purified as indicated. The following compounds were prepared in this manner.

4.7.1. Methyl 2,3-di-O-benzoyl-4-deoxy-4-isothiocyanato-6-O-(4-methoxybenzyl)-α-D-glucopyranoside **7**

$x = 0.213$ g, 0.41 mmol; $y = 6.5$ ml; $z = 0.16$ g, 1.64 mmol; $k = 0.08$ ml, 0.82 mmol; $t = 6$ h. TLC (1:2) AcOEt:petroleum ether (0.121 g, 51% from **6**); $[\alpha]_D^{27}$ +116.8 (*c* 1.0); FABMS: m/z 586 $[M+Na]^+$; IR ν_{max} 2043 cm^{-1} (NCS); ^1H NMR (500 MHz, $CDCl_3$): δ 8.01–6.92 (m, 14H, Ar), 5.98 (t, 1H, $J_{2,3} = J_{3,4} = 10.1$, H-3), 5.17 (d, 1H, $J_{1,2} = 3.6$, H-1), 5.13 (dd, 1H, H-2), 4.65, 4.54 (each d, each 1H, $J_{H,H} = 11.7$, *H*CH, HC*H*), 4.32 (t, 1H, $J_{4,5} = 10.1$, H-4), 4.01 (ddd, 1H, $J_{5,6a} = 3.0$, $J_{5,6b} = 2.0$, H-5), 3.82 (s, 3H, CH_3O-Ar), 3.79 (dd, 1H, $J_{6a,6b} = 11.2$, H-6a), 3.75 (dd, 1H, H-6b) and 3.42 (s, 3H, CH_3O) ppm; ^{13}C NMR (125.7 MHz): δ 165.6, 165.2 (2 CO), 159.3–113.7 (18 C, Ar), 138.1 (NCS), 97.1 (C-1), 73.3 (CH_2), 71.4 (C-2), 70.3 (C-3), 69.3 (C-5), 67.6 (C-6), 56.5 (C-4), 55.5 and 55.1 (2 CH_3O) ppm. Anal. calcd for $C_{30}H_{29}O_8NS$: C, 63.93; H, 5.19; N, 2.48; S, 5.69. Found: C, 63.74; H, 4.96; N, 2.58; S, 6.21.

4.7.2. 2,3,6-Tri-O-benzoyl-4-deoxy-N-(2,2-diethoxycarbonylvinyl)-4-isothiocyanato-β-D-glucopyranosylamine **12**

$x = 0.192$ g, 0.29 mmol; $y = 1.4$ ml; $z = 0.084$ g, 0.848 mmol; $k = 0.042$ ml, 0.424 mmol; $t = 5$ h. TLC (1:1) ether:petroleum ether (0.111 g, 55% from **11**); $[\alpha]_D^{27}$ +6.9 (*c* 0.5); FABMS: m/z 725 $[M+Na]^+$; IR ν_{max} 2041 (NCS), and 1651 cm^{-1} (C=O chelated); ^1H NMR (500 MHz, $CDCl_3$): δ 9.39 (dd, 1H, $J_{NH,1} = 9.0$, $J_{NH,CH=} = 13.0$, NH), 8.12–7.37 (m, 15H, Ar), 7.88 (d, 1H, HC=), 5.87

(t, 1H, $J_{2,3}=J_{3,4}=9.5$, H-3), 5.45 (t, 1H, $J_{1,2}=9.5$, H-2), 4.81 (t, 1H, H-1), 4.73 (dd, 1H, $J_{5,6a}=2.5$, $J_{6a,6b}=12.4$, H-6a), 4.64 (dd, 1H, $J_{5,6b}=4.1$, H-6b), 4.27–4.24 (m, 3H, H-4, CH_2CH$_3$), 4.14 (q, 2H, $J_{H,H}=7.1$, CH_2CH$_3$), 3.99 (ddd, 1H, $J_{4,5}=10.1$, H-5), 1.31 and 1.24 (each t, each 3H, 2 CH$_2$CH_3) ppm; ^{13}C NMR (125.7 MHz): δ 167.5, 166.0, 165.5, 165.4, 165.3 (5 CO), 157.2 (CH=), 141.3 (NCS), 133.7–128.5 (18 C, Ar), 95.1 (C=), 87.2 (C-1), 74.6 (C-5), 72.9 (C-3), 70.9 (C-2), 62.9 (C-6), 60.4, 60.1 (2 CH$_2$CH$_3$), 57.1 (C-4) and 14.4 (2 C, 2 CH$_2$$CH_3$) ppm. Anal. calcd for $C_{36}H_{34}O_{11}N_2S$: C, 61.53; H, 4.88; N, 3.99; S, 4.56. Found: C, 61.42; H, 4.75; N, 4.14; S, 4.84.

4.8. 2,4,6-*Tri*-O-*acetyl*-N-*(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine* **14**

To a stirred solution of *N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine (3 g, 8.55 mmol) in pyridine (15 ml) at –20°C, acetic anhydride (2.5 ml, 26.7 mmol) in pyridine (10 ml) was gradually added. The mixture was kept for 24 h at that temperature, then poured into ice-water and extracted with AcOEt. The combined organic layers were washed with H_2SO_4 (2N), aq. $NaHCO_3$ (saturated) and water, dried ($MgSO_4$) and concentrated. Column chromatography (40:1 CH_2Cl_2:MeOH) of the crude gave 2,3,6- and 2,4,6-tri-*O*-acetylderivatives as a mixture. The treatment of the mixture with Et_2O at reflux gave **14** (2.260 g, 57%) as a solid. Mp 140–142°C; $[\alpha]_D^{28}$ +8.5 (*c* 1.3); FABMS: *m*/*z* 498 [M+Na]$^+$; IR ν_{max} 1670 cm^{-1} (C=O chelated); ^{1}H NMR (500 MHz, $CDCl_3$); δ 9.22 (dd, 1H, $J_{NH,1}=9.0$, $J_{NH,HC=}=13.0$, NH), 7.95 (d, 1H, HC=), 4.96 (t, 1H, $J_{1,2}=J_{2,3}=9.0$, H-2), 4.95 (t, 1H, $J_{3,4}=J_{4,5}=10.0$, H-4), 4.47 (t, 1H, H-1), 4.29–4.19 (m, 5H, H-6a, 2 CH_2CH$_3$), 4.14 (dd, 1H, $J_{5,6b}=2.2$, $J_{6a,6b}=12.4$, H-6b), 3.73 (ddd, 1H, $J_{5,6a}=4.6$, H-5), 3.81 (ddd, 1H, $J_{3,OH}=5.0$, H-3), 2.13, 2.11, 2.10 (each s, each 3H, 3 Ac), 1.33 and 1.29 (each t, each 3H, $J_{H,H}=7.1$, 2 CH$_2$CH_3) ppm; ^{13}C NMR (125.7 MHz): δ 170.5 (2 C, 2 CO), 170.1, 167.5, 165.6 (3 CO), 157.3 (HC=), 94.5 (C=), 86.8 (C-1), 73.6 (C-2), 73.5 (C-5), 72.9 (C-3), 70.2 (C-4), 61.7 (C-6), 60.2, 60.0 (2 CH$_2$CH$_3$), 20.6, (Ac), 20.5 (2 C, 2 Ac), 14.2, and 14.0 (2 CH$_2$$CH_3$) ppm. Anal. calcd for $C_{20}H_{29}O_{12}N$: C, 50.52; H, 6.15; N, 2.95. Found: C, 50.50; H, 6.06; N, 3.04.

4.9. 2,4,6-*Tri*-O-*acetyl*-N-*(2,2-diethoxycarbonylvinyl)-3*-O-*triflyl-β-D-glucopyranosylamine* **15**

Trifluoromethanesulphonic anhydride (0.21 ml, 0.13 mmol) in pyridine (0.1 ml) was added dropwise to a solution of **3** in freshly distilled CH_2Cl_2 (10 ml), and stirred for 2 h at –15°C. Then the reaction mixture was poured into cool aq. $NaHCO_3$ (saturated), extracted with CH_2Cl_2, dried ($MgSO_4$), and concentrated. FABMS: *m*/*z* 630 [M+Na]$^+$. This product was directly used to prepare **16**.

4.10. 2,4,6-*Tri*-O-*acetyl-3-azido-3-deoxy*-N-*(2,2-diethoxycarbonylvinyl)-β-D-allopyranosylamine* **16**

This was prepared using the same procedure described for **5** and **10**. $m=0.639$ g, 1.053 mmol; $x=7.2$ ml; $y=0.34$, 5.2 mmol; $t=1$ h; $T=$ rt. Column chromatography (1:1 ether:petroleum ether) of the residue and crystallisation of the product (0.515 g, 98%) from EtOH gave **16**; mp 139–140°C; $[\alpha]_D^{25}$ +17.0 (*c* 0.8); FABMS: *m*/*z* 523 [M+Na]$^+$; IR ν_{max} 2130 (N_3), and 1659 cm^{-1} (C=O chelated); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.18 (dd, 1 H, $J_{NH,CH=}=13.1$, $J_{NH,1}=9.1$, NH), 7.96 (d, 1H, HC=), 4.96 (dd, 1H, $J_{1,2}=9.1$, $J_{2,3}=3.2$, H-2), 4.93 (dd, 1H, $J_{4,5}=10.0$, $J_{3,4}=3.2$, H-4), 4.82 (t, 1H, H-1), 4.46 (t, 1H, H-3), 4.28–4.19 (m, 5H, H-6a, 2 CH_2CH$_3$), 4.17–4.13 (m, 1H, H-6b), 4.14–4.10 (m, 1H, H-5), 2.14, 2.12, 2.09 (each s, each 3H, 3 Ac) and 1.37–1.26 (m, 6H, 2 CH$_2$CH_3) ppm; ^{13}C NMR (125.7 MHz): δ 170.5, 169.3, 169.2, 167.9, 165.4 (5 C, 5 CO), 157.6 (CH=), 94.3

(C=), 84.1 (C-1), 71.2 (C-5), 69.4 (C-2), 66.9 (C-4), 61.8 (C-6), 60.7 (C-3), 60.2, 60.0 (2 CH_2CH_3), 20.6, 20.4, 20.3 (3 Ac), 14.2, and 14.1 (CH_2CH_3) ppm. Anal. calcd for $C_{20}H_{28}O_{11}N_4$: C, 48.00; H, 5.64; N, 11.20. Found: C, 47.84; H, 5.68; N, 10.70.

4.11. 2,4,6-Tri-O-acetyl-3-amino-3-deoxy-N-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine **17**

A stirred solution of **16** (0.2 g, 0.042 mmol) in (2:3) dioxane:EtOH (10 ml) was hydrogenated in the presence of $Pd(OH)_2$ for 2.5 h at 4 atm. The catalyst was filtered off through a Celite pad, and washed with ethanol. The filtrate and washings were combined, and evaporated to give a syrup which was used without purification in the next step. FABMS: m/z 497 $[M+Na]^+$.

4.12. 2,4,6-Tri-O-acetyl-3-deoxy-N-(2,2-diethoxycarbonylvinyl)-3-isothiocyanato-β-D-allopyranosylamine **18**

This was prepared following the procedure described for **7** and **12**. $x=0.190$ g, 0.4 mmol; $y=6.5$ ml; $z=0.16$ g, 1.6 mmol; $k=0.08$ ml, 0.8 mmol; $t=15$ h. TLC (12:1) ether:petroleum ether (0.090 g, 44% from **16**); $[\alpha]_D^{25}$ –19.7 (c 1.0); FABMS: m/z 539 $[M+Na]^+$; IR ν_{max} 2047 (NCS) and 1663 cm^{-1} (C=O chelated); ^1H NMR (500 MHz, $CDCl_3$): δ 9.24 (dd, 1H, $J_{NH,CH=}=13.0$, $J_{NH,1}=8.9$, NH), 7.98 (d, 1H, HC=), 4.91–4.86 (m, 3H, H-2, H-3, H-4), 4.82 (t, 1H, $J_{1,2}=8.8$, H-1), 4.34–4.19 (m, 6H, H-6a, H-6b, 2 CH_2CH_3), 4.13 (ddd, 1H, $J_{4,5}=9.9$, $J_{5,6a}=2.1$, $J_{5,6b}=4.2$, H-5), 2.15, 2.13, 2.10 (each s, each 3H, 3 Ac), 1.33 and 1.31 (each t, each 3H, $J_{H,H}=7.1$, 2 CH_2CH_3) ppm; ^{13}C NMR (125.7 MHz): δ 170.3, 169.1, 169.0, 167.9, 165.2 (5 CO), 157.4 (CH=), 141.7 (NCS), 94.6 (C=), 84.3 (C-1), 71.6 (C-5), 68.3 (C-2), 66.0 (C-4), 61.6 (C-6), 60.2, 60.0 (2 CH_2CH_3), 58.1 (C-3), 20.5, 20.4, 20.3 (3 Ac), 14.2 and 14.0 (CH_2CH_3) ppm. Anal. calcd for $C_{21}H_{28}O_{11}N_2S$: C, 48.83; H, 5.46; N, 5.42. Found: C, 48.74; H, 5.51; N, 5.75.

4.13. 2-Deoxy-N-(2,2-diethoxycarbonylvinyl)amino-D-mannopyranose **20**

To a stirred solution of D-mannosamine hydrochloride (0.25 g, 1.4 mmol) and sodium carbonate (0.074 g, 0.7 mmol) in water (1.2 ml), diethyl ethoxymethylenemalonate (0.56 ml, 2.8 mmol) was added and the mixture was stirred for 24 h at rt. The water was evaporated under reduced pressure. The residue was purified by column chromatography (6:1 CH_2Cl_2:MeOH) to yield **13** (0.33 g, 68%) as an amorphous solid. FABMS: m/z 372 $[M+Na]^+$; ^{13}C NMR (125.7 MHz, MeOH-d_4): δ 170.0, 166.8 (each 2 C, 4 CO), 162.6 (HC=β), 161.6 (HC=α), 94.6 (C-1β), 94.4 (C-1α), 90.4 (C=α), 90.2 (C=β), 78.8 (C-5β), 74.1 (C-5α), 73.9 (C-3β), 70.6 (C-3α), 69.3 (C-4α), 69.0 (C-4β), 66.1 (C-6β), 65.1 (C-6α), 62.8 (2 C, C-2α, C-2β), 60.9–60.8 (4 C, 4 CH_2CH_3) and 14.8–14.7 (4 C, 4 CH_2CH_3) ppm. Anal. calcd for $C_{14}H_{23}O_9N$: C, 48.13; H, 6.64; N, 4.01. Found: C, 48.19; H, 6.94; N, 3.86.

4.14. 1,3,4,6-Tetra-O-acetyl-2-deoxy-N-(2,2-diethoxycarbonylvinyl)amino-α-D-mannopyranose **21** and 1,3,4,6-tetra-O-acetyl-2-deoxy-N-(2,2-diethoxycarbonylvinyl)amino-β-D-mannopyranose **22**

Compound **20** (0.25 g, 0.716 mmol) was dissolved in (1:1) acetic anhydride: Py (2.5 ml) at 0°C. The mixture was stirred at rt for 18.5 h, then poured into ice-water and extracted with ether. The combined organic layers were washed with H_2SO_4 (2N), aq. $NaHCO_3$ (saturated) and water,

dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (1:1 ether:petroleum ether) to give compounds **21** and **22** as amorphous solids.

Compound **21** (0.154 g, 41%); $[\alpha]_D^{26}$ –97.1 (*c* 1.0); FABMS: *m*/*z* 540 [M+Na]$^+$; IR ν_{max} 1657 cm^{-1} (C=O chelated); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.56 (dd, 1H, $J_{NH,CH=}$ = 13.2, $J_{NH,2}$ = 9.9, NH), 7.83 (d, 1H, HC=), 6.19 (d, 1H, $J_{1,2}$ = 2.0, H-1), 5.34 (dd, 1H, $J_{2,3}$ = 3.7, $J_{3,4}$ = 9.3, H-3), 5.29 (t, 1H, $J_{4,5}$ = 9.3, H-4), 4.25 (q, 2H, $J_{H,H}$ = 7.1, CH_2CH$_3$), 4.21–4.18 (m, 4H, H-6a, H-6b, CH_2CH$_3$), 4.08 (dt, 1H, $J_{5,6a}$ = $J_{5,6b}$ = 3.2 Hz, H-5), 3.86 (ddd, 1H, H-2), 2.20, 2.19, 2.08, 2.06 (each s, each 3H, 4 Ac), 1.35 and 1.28 (each t, each 3H, 2 CH$_2$CH_3) ppm; ^{13}C NMR (125.7 MHz): δ 170.7, 170.1, 169.0, 168.7, 168.0, 165.4 (6 CO), 158.8 (CH=), 92.7 (C=), 91.5 (C-1), 70.6 (C-5), 69.5 (C-3), 65.0 (C-4), 61.1 (C-6), 60.0, 59.8 (2 *C*H$_2$CH$_3$), 58.9 (C-2), 20.7, 20.5, 20.4, 20.3 (4 Ac), 14.3 and 14.2 (2 CH$_2$*C*H$_3$) ppm. Anal. calcd for $C_{22}H_{31}O_{13}N$: C, 51.06; H, 6.04; N, 2.71. Found: C, 50.97; H, 6.20; N, 2.73.

Compound **22** (0.037 g, 11%); $[\alpha]_D^{26}$ –142.8 (*c* 0.6); FABMS: *m*/*z* 540 [M+Na]$^+$; IR ν_{max} 1659 cm^{-1} (C=O chelated); ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.62 (dd, 1H, $J_{NH,CH=}$ = 13.2, $J_{NH,2}$ = 9.6, NH), 7.83 (d, 1H, HC=), 5.88 (d, 1H, $J_{1,2}$ = 1.3, H-1), 5.23 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.8, H-4), 5.09 (dd, 1H, $J_{2,3}$ = 3.8, H-3), 4.29–4.15 (m, 6H, H-6a, H-6b, 2 CH_2CH$_3$), 3.94 (ddd, 1H, H-2), 3.83 (ddd, 1H, $J_{5,6a}$ = 3.6, $J_{5,6b}$ = 2.6, H-5), 2.17, 2.12, 2.08, 2.05 (each s, each 3 H, 4 Ac), 1.35 and 1.28 (each t, each 3H, $J_{H,H}$ = 7.1, 2 CH$_2$CH_3) ppm; ^{13}C NMR (75.4 MHz): δ 170.7, 169.9, 169.1, 168.7, 168.4, 165.8 (6 CO), 159.4 (CH=), 92.3 (C=), 90.3 (C-1), 73.2 (C-5), 71.7 (C-3), 64.8 (C-4), 61.1 (C-6), 59.9, 59.7 (2 *C*H$_2$CH$_3$), 59.4 (C-2), 20.7, 20.5, 20.4 (4 C, 4 Ac), 14.3 and 14.2 (2 CH$_2$*C*H$_3$) ppm. HREIMS calcd for $C_{22}H_{31}O_{13}N$: 517.1795. Found: 517.1825.

4.15. 1,3,4,6-Tetra-O-*acetyl-2-amino-2-deoxy-α-D-mannopyranose* ***23***

Compound **22** (0.05 g, 0.097 mmol) was dissolved in Cl_2/CH_2Cl_2 (1 ml) at 0°C for 30 min. The solvent was evaporated under reduced pressure to give a syrup which was used without purification in the next step. FABMS: *m*/*z* 370 [M+Na]$^+$.

4.16. 1,3,4,6-Tetra-O-*acetyl-2-deoxy-2-isothiocyanato-α-D-mannopyranose* ***24***

This was prepared following the same procedure described for **7**, **12**, and **18**. *x* = 0.034 g, 0.097 mmol; *y* = 2 ml; *z* = 0.050 g, 0.50 mmol; *k* = 0.03 ml, 0.3 mmol; *t* = 6 h. TLC (3:1) ether:petroleum ether (0.028 g, 75% from **21**); $[\alpha]_D^{26}$ –28.8 (*c* 1.7); FABMS: *m*/*z* 412 [M+Na]$^+$; IR ν_{max} 2062 cm^{-1} (NCS); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.18 (d, 1H, $J_{1,2}$ = 2.0, H-1), 5.39 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 10.0, H-4), 5.28 (dd, 1H, $J_{2,3}$ = 4.0, H-3), 4.26 (dd, 1H, H-2), 4.24 (dd, 1H, $J_{5,6b}$ = 4.1, $J_{6a,6b}$ = 12.5, H-6a), 4.15 (dd, 1H, $J_{5,6b}$ = 2.4, H-6b), 4.05 (ddd, 1H, H-5), 2.17, 2.13, 2.12 and 2.07 (each s, each 3H, 4 Ac) ppm; ^{13}C NMR (125.7 MHz): δ 170.6, 170.0, 169.0, 167.9 (4 CO), 140.2 (NCS), 91.0 (C-1), 70.7 (C-5), 69.2 (C-3), 64.9 (C-4), 61.4 (C-6), 57.5 (C-2), 20.7, 20.6 and 20.5 (4 C, 4 Ac) ppm. HREIMS calcd for $C_{13}H_{15}O_7NS$: 329.0569. Found: 329.0562.

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References

1. For leading references, see: (a) Guenther, W.; Kunz, H. *Angew. Chem.* **1990**, *102*, 1068–1069. (b) Fuentes, J.; Molina, J. L.; Olano, D.; Pradera, M. A. *Tetrahedron: Asymmetry* **1996**, *7*, 203–218. For a review, see: (c) García Fernández, J. M.; Ortiz Mellet, C. *Sulfur Reports* **1996**, *19*, 61–169. See also: (d) Fuentes, J.; Molina, J. L.; Pradera, M. A. *Tetrahedron: Asymmetry* **1998**, *9*, 2517–2532. (e) Jiménez-Blanco, J. L.; Saitz Barria, C.; Benito, J. M.; Ortiz Mellet, C.; Fuentes, J.; Santoyo-González, F.; García Fernández, J. M. *Synthesis* **1999**, 1907–1914.
2. Lindhorst, T. K.; Kieburg, Ch. *Synthesis* **1995**, 1228–1230.
3. (a) Marino, C.; Varela, O.; Lederkremer, R. M. *Carbohydr. Res.* **1997**, *304*, 257–260. (b) Marino, C.; Varela, O.; Lederkremer, R. M. *Tetrahedron* **1997**, *53*, 16009–16016.
4. (a) For introduction of the NCS group into the position 3 of glycofuranoses, see: García Fernández, J. M.; Ortiz Mellet, C.; Jiménez-Blanco, J. L.; Fuentes, J. *J. Org. Chem.* **1994**, *59*, 5565–5572. (b) For the position 5 of glycofuranoses, see: Jiménez-Blanco, J. L.; Díaz Pérez, V. M.; Ortiz Mellet, C.; Fuentes, J.; García Fernández, J. M.; Díaz Arribas, J. C.; Cañada, F. J. *Chem. Commun.* **1997**, 1969–1970. (c) For the position 2 of methyl-D-glucopyranoside, see: Fernández-Bolaños, J. G.; Zafra, E.; López, O.; Robina, I.; Fuentes, J. *Tetrahedron: Asymmetry* **1999**, *10*, 3011–3023. (d) For the position 4 of a *O*-benzylated methylglucopyranoside, see: Knapp, S.; Naughton, A. B. J.; Dahr, T. G. M. *Tetrahedron Lett.* **1992**, *33*, 1025–1029. (e) For the primary position of methyl aldopyranosides, see: García Fernández, J. M.; Ortiz Mellet, C.; Fuentes, J. *J. Org. Chem.* **1993**, *58*, 5192–5199. (f) For a disaccharide derivative, see: Pradera, M. A.; Molina, J. L.; Fuentes, J. *Tetrahedron* **1995**, *51*, 923–934.
5. Jeong, J. H.; Murray, B. W.; Takayama, S.; Wong, Ch-H. *J. Am. Chem. Soc.* **1996**, *118*, 4227–4234.
6. Fuentes, J.; Angulo, M.; Pradera, M. A. Communicated at the 10th European Carbohydrate Symposium. Galway, Ireland, July 1999. Communication PA109, Book of Abstracts p. 247.
7. García Fernández, J. M.; Jiménez-Blanco, J. L.; Ortiz Mellet, C.; Fuentes, J. *J. Chem. Soc., Chem. Commun.* **1995**, 57–58.
8. Jiménez-Blanco, J. L.; Ortiz Mellet, C.; Fuentes, J.; García Fernández, J. M. *Chem. Commun.* **1996**, 2077–2078.
9. Johansson, R.; Samuelson, B. *J. Chem Soc., Perkin Trans. 1* **1984**, 2371–2374.
10. Fuentes Mota, J.; García Fernández, J. M.; Ortiz Mellet, C.; Pradera Adrián, M. A.; Babiano Caballero, R. *Carbohydr. Res.* **1989**, *188*, 35–44.
11. Fuentes, J.; Olano, D.; Pradera, M. A. *Tetrahedron: Asymmetry* **1997**, *8*, 3443–3456 and references cited therein.
12. Stevens, J. D. Communicated at the XVIth International Carbohydrate Symposium. Paris, France, July 1992. Communication C-158. Book of Abstracts p. 623.
13. Gómez Sánchez, A.; García Martín, M. G.; Borrachero Moya, P.; Bellanato, J. *J. Chem. Soc., Perkin Trans. 2* **1987**, 301–306.