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Partially Protected D-Glucopyranosyl Isothiocyanates. Synthesis and Transformations into Thiourea and Heterocyclic Derivatives.

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Key Words: Glucosyl isothiocyanates; partially protected sugars; glucosylthioureas; nucleosides; thioureylenedisaccharides.

Abstract: *The syntheses of 2,3,4-tri-O-acetyl(benzoyl)-β-D-glucopyranosyl isothiocyanates (3, 4) from the corresponding acylated N-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine are described. Reactions of 3 and 4 with phenacylamine hydrochloride yielded N-phenacyl-N'-(2,3,4-tri-O-acyl-β-D-glucopyranosyl)thioureas (6, 7) whereas treatments of the same compounds with aminoacetone hydrochloride gave the N-nucleoside analogues 5-methyl-1-(2',3',4'-tri-O-acyl-β-D-glucopyranosyl)-4-imidazoline-2-thiones (8, 9). The partially protected N-(2-thiazolin-2-yl)-β-D-glucopyranosylamine (10) and the thioureylenedisaccharide 11 were prepared from 4 and 2-chloroethylamine hydrochloride under different reaction conditions.*

The isothiocyanates[1] and glycosyl isothiocyanates[2-4] have been the focus of synthetic attention during recent years and they have been transformed into heterocyclic derivatives (nucleosides and glycosylaminoheterocycles), glycosylthioureas, glycosylguanidines and glycosyl derivatives of β-cyclodextrines which have potential pharmacological properties[5-8] (treatment of AIDS, vectorised transport of drugs, etc). The lactosyl and maltosyl isothiocyanates have been studied as hexose-transporter inhibitors[9] and trisaccharide isothiocyanates have been recently prepared and used in the synthesis of model oligosaccharides of biological importance as synthons of *N*-linked glycoproteins[10,11]. On the other hand, partially protected sugar derivatives are of great interest as intermediates in carbohydrate chemistry or as biodegradable surface-active materials. We are currently carrying out a study on isothiocyanate derivatives of carbohydrates. Previously, we have described the preparation of partially protected D-gluco and D-galactopyranosyl isothiocyanates each having one or two free secondary hydroxyl groups[12]. These compounds were prepared through the Schotten-Baumann procedure using a limited amount of acylating reagent, and under these conditions the more reactive primary hydroxyl group is acylated. We now describe the syntheses and certain reactions of 2,3,4-tri-O-acyl-β-D-glucopyranosyl isothiocyanates (**3, 4**) each having a free primary hydroxyl group.

Many biologically important products have two sugar units joined through an atom (oxygen, sulphur, nitrogen or carbon)[13-15] or group of atoms (such as phosphate in dinucleotides, disulphide, hidrazine, carbonate, thiocarbamate, etc)[16-18]. Sugars joined by a thiourea group, non ionic isosteric bridge of phosphates, have been studied to some extent[18-20]; however, as far as we are aware , there are no precedents for partially protected thioureylenedisaccharides . In this paper, we report our first results in this field.

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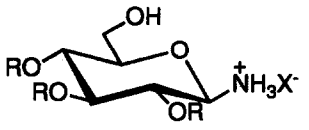

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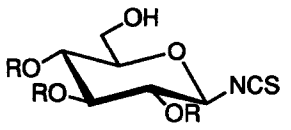
2, R = Bz, X = Cl



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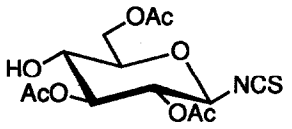

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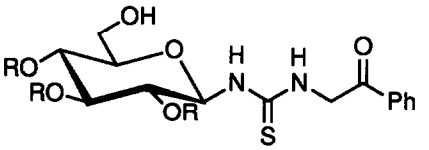

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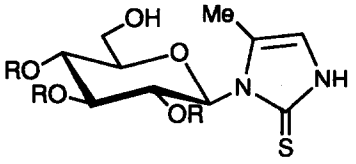
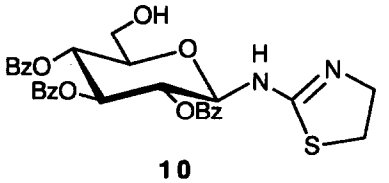


8, R = Ac
9, R = Bz



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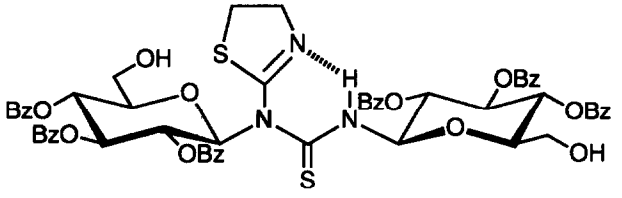

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RESULTS AND DISCUSSION

2,3,4-Tri-*O*-acetyl-β-D-glucopyranosylamine hydrobromide (**1**) and 2,3,4-tri-*O*-benzoyl-β-D-glucopyranosylamine hydrochloride (**2**) were prepared from the corresponding 2,3,4-tri-*O*-acyl-6-*O*-trityl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine[21] by treatment with bromine (chlorine) in dichloromethane. During this reaction the acylvinyl and trityl groups are simultaneously removed, and it is

a new method to remove the trityl group, giving high yield when the target product is not soluble in the reaction medium[22]. Compounds **1** and **2** showed the broad and strong i.r. absorption (3020-2400 cm^{-1}) and the proton resonance at δ 9.17 ppm for the ammonium group.

2,3,4-Tri-*O*-acetyl- (**3**) and 2,3,4-tri-*O*-benzoyl- (**4**) β-D-glucopyranosyl isothiocyanates were obtained from **1** (or **2**) by reaction with thiophosgene in a basic medium[20]. The structures of **3** and **4** were assigned on the basis of i.r., ^1H- (Tables 1 and 2) and ^{13}C- (Table 3) n.m.r. and m.s. data. Both compounds had ν_{NCS} 2020 cm^{-1}, δ 144 ppm for NCS and the mass spectra showed a loss of NCS from M^+ as reported[3] for related glycosyl isothiocyanates.

Table 1

^1H-N.m.r. chemical shifts (δ, ppm) for the sugars rings of compounds **1-11**

Comp.		H-1	H-2	H-3	H-4	H-5	H-6	H-6'
1[a]		5.13d	5.05t	5.47t	5.02t	4.06ddd	3.60dd	3.66dd
2[a]		5.31d	5.49t	6.03t	5.49t	4.31m	<– 3.53 - 3.74m –>	
3[b]		<——— 5.00 - 5.34 m ———>				<——— 3.49 - 3.85m ———>		
4[b]		5.32d	5.62d	5.92t	5.55t	<——— 3.67 - 4.00m ———>		
5[a]		5.55d	4.83d	5.06t	3.53m	3.77m	4.08dd	4.32dd
5[b]		<——— 4.95 - 5.10m ———>				<— 3.50 - 3.62m —>	4.31dd	4.41dd
6[b]		5.84dd	5.06t	5.44t	5.12t	<—3.65 -3.84m—>		3.98ddd
7[b]		6.00m	5.68t	6.45t	5.86t	<—3.90 - 4.25m—>		4.81bdd
8[b]		6.40d	5.40t	5.50t	5.13t	<——— 3.54 - 3.87m ———>		
9[b]		6.76d	5.90t	6.14t	5.60t	<——— 3.64 - 4.08m ———>		
10[b]		5.25d	5.50t	6.03t	5.61t	<——— 3.61 - 4.00m ———>		
11[b]	A[c]	<——— 6.00 - 6.26m ———>			5.66-5.80m	<——— 3.59 - 4.01m ———>		
	B[c]	4.76m[d]	<– 6.00 - 6.26m –>		5.66-5.80m	<——— 3.59-4.01m ———>		

[a] In $(CD_3)SO$. [b] In $CDCl_3$. [c] A and B refers to the sugars residues joined to N and N' respectively. [d] Virtual coupling.

When a solution of **3** in chloroform was left at r.t. for 6 days 2,3,6-tri-O-acetyl-β-D-glucopyranosyl isothiocyanate (**5**) was quantitatively formed. The product **5** was a hygroscopic solid which showed ν_{NCS} 2051 cm^{-1}, δ_{NCS} 143.5, and M^+-NCS. The δ value for the resonance of H-4 was 3.6 ppm corresponding to a C*H*OH proton whereas the same proton in compound **3** resonated at 5.00-5.34 ppm (C*H*OAc). On the contrary an upfield shift was observed when the resonances of the protons H-6 and H-6' in **5** were

compared with the resonances for the same proton in **3**.

The treatment of **3** and **4** with phenacylamine hydrochloride yielded *N*-phenacyl-*N'*-(2,3,4-tri-*O*-acyl-β-D-glucopyranosyl)thioureas (**6**, **7**). The analytical, i.r., ^{1}H- and ^{13}C-n.m.r. and m.s. data of **6** and **7** were consistent with the structures proposed and precluded possible imidazolic or aminothiazolic structures which could result of the cyclodehydration of the *N*-phenacylthioureas[23]. Thus, compounds **6**, **7** had the i.r. band at 1687 cm^{-1} ($\nu_{C=O}$ of phenacyl group), proton resonance of CH_2 at 5.0 ppm and carbon resonances at 52 (CH_2), 183.5 (C=S) and 194 ppm (C=O)[3]. The mass spectra showed a peak corresponding to the loss of the thiourea moiety (M^+-193), and in the case of **6** the losses of AcOH and Ac_2O (see experimental), characteristic of poly-*O*-acetylsugars[24], were observed.

Table 2

^{1}H-N. m.r. measured coupling constants (*J*, Hz) for the sugar rings of compounds **1-10**

Comp.	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
1[a]	9.4	9.4	9.4	9.4	2.3	5.3	10.8
2[a]	8.9	8.9	8.9	8.9	-	-	-
3[b]	-	-	-	-	-	-	-
4[b]	9.3	9.3	9.3	9.3	-	-	-
5[a]	8.5	8.5	8.5	-	2.1	6.2	12.4
5[b]	-	-	-	-	5.2	2.1	12.8
6[b]	9.0	9.2	9.2	9.2	-	-	-
7[b]	9.5	9.5	9.5	9.5	-	3.9	13.0
8[b]	8.7	8.7	8.7	8.7	-	-	-
9[b]	9.6	9.6	9.6	9.6	-	-	-
10[b]	9.4	9.4	9.4	9.4	-	-	-

[a] In $(CD_3)_2SO$. [b] In $CDCl_3$.

The partially protected *N*-nucleoside analogues 5-methyl-1-(2',3',4'-tri-O-acetyl-β-D-glucopyranosyl)-4-imidazoline-2-thiones (**8**, **9**) were prepared by reaction of the corresponding glycosyl isothiocyanate and aminoacetone hydrochloride. Compounds **8** and **9** had λ_{max} 278 nm, ν_{max} 1633 cm^{-1}, δ 6.3 for H-4, δ 11.0 for NH and ^{13}C-n.m.r. signals at 163, 127, 112, and 11 ppm corresponding to C-2, C-5, C-4 and CH_3 respectively. These data are in agreement with those for related nucleosides and ruled out a possible structure of aminothiazole[3,23].

The reaction of β-haloalkylamines with alkyl(aryl)isothiocyanates gives 2-alkyl(aryl)amino-thiazolines[25]. In the carbohydrate field the reaction of per-*O*-acyl-sugar isothiocyanates with

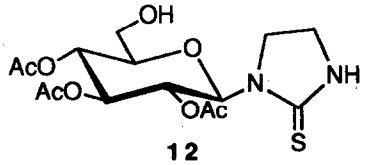
Table 3

Relevant ^{13}C-N m r chemical shifts (δ, ppm) for compounds **1-11**

Comp.		Sugar ring								Heterocycle		
		C-1	C-2	C-3	C-4	C-5	C-6	NCS	C=S	C-2	C-4	C-5
1[a]		78.4	69.9	76.3	67.7	72.3	59.6	-	-	-	-	-
2[a]		78.7	70.9	76.4	68.6	73.6	59.7	-	-	-	-	-
3[b]		83.4	71.9	76.3	67.8	72.2	60.8	144.0	-	-	-	-
4[b]		83.7	72.1	76.8	68.6	72.3	60.8	144.2	-	-	-	-
5[b]		83.3	71.7	76.0	68.1	74.6	62.4	143.5	-	-	-	-
6[b]		82.3	70.7	75.4	68.7	72.6	60.5	-	183.5	-	-	-
7[b]		83.0	71.4	76.1	69.5	72.9	60.9	-	183.5	-	-	-
8[b]		82.9	69.7	76.9	68.2	72.4	60.7	-	-	163.1	112.2	127.1
9[b]		83.2	69.9	77.5	69.0	72.9	60.7	-	-	163.7	112.1	126.9
10[b]		85.6	71.9	76.3	69.4	73.0	61.1	-	-	162.5	57.1	33.9
11[b]	A[c]	90.5	72.8[d]	76.3	69.2[e]	73.6[f]	61.4[g]	-	182.2	165.9	54.4	24.9
	B[c]	82.8	70.6[d]	76.3	69.1[e]	72.9[f]	61.2[g]					

[a] In $(CD_3)_2SO$. [b] In $CDCl_3$. [c] A and B refers to the sugars residues joined to N and N', respectively. [d,e,f,g] These assignments may be interchanged.

β-haloalkylamines has raised a scientific controversy[19] and it has been demonstrated that the reaction yields sugar aminothiazoline or *N*-(2-thiazolin-2-yl)thioureylenedisaccharides according to the reaction conditions. We have carried out this reaction from the partially protected glucosyl isothiocyanate **4** and 2-chloroethylamine hydrochloride. The glucosylaminothiazoline **10** was obtained when an excess of chloroamine was used, and the thioureylenedisaccharide **11** when the chloroamine and **4** were reacted in the 1:2 ratio (see experimental). Compound **10** had ν_{max} at 1628 cm^{-1} indicative of the thiazoline ring[26]. Additionally the two different resonances at δ 57.1 and 33.9 for CH_2-N= and CH_2-S, respectively, are congruent with carbon-heteroatom linkages of different electronegativity, precluding the possible imidazolidine-2-thione structure **12**. The δ values for H-4, and H-5 also confirmed this fact.



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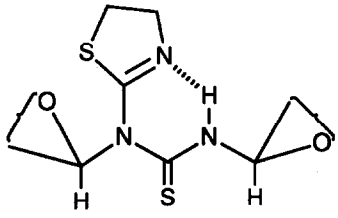
Compound **11** had an i.r. band at 1547 cm^{-1} for the NH group; $\nu_{C=N}$ (1601 cm^{-1}) showed a shift of 27 cm^{-1} toward lower wavenumber compared to **10** indicative of a chelated structure, which is confirmed by the large downfield shift of the NH signal in the ^{1}H-n.m.r. spectrum (13.03 ppm). In the ^{13}C-n.m.r. spectrum, the resonance of C-1' appeared at 82.8 ppm as in other glycosylthioureas[3], but that of C-1 was shifted markedly downfield (90.5 ppm) due to the presence of the 2-aminothiazoline ring. The thiourea bridge was indicated by the thiocarbonyl signal at 182.2 ppm, and the upfield signal at 165.1 ppm was attributed to the C-2 of the thiazoline ring.

The formation of **11** should ocurr *via* addition of **3** to **10**, which proceeds by spontaneous intramolecular cyclization of a *N*-2-chloroethyl-*N'*-glucosylthiourea formed in the first step by reaction of **3** with 2-chloroethylamine.

Each of the compounds described (**1-11**) had the $^4C_1$(D) conformation for the sugar rings as the $^3J_{H,H}$ values (Table 2) were in the appropiate range. Likewise, the large $J_{1,NH}$ value for **11** (8.0 Hz) is consistent with an antiperiplanar arrangement between the corresponding protons. The intramolecular hydrogen bond confers rigidity on the thiourea and anchors the *E, Z* conformation. The upfield chemical shift of the H-1 resonance is similar to that of the *E* conformer in related substituted D-glucopyranose thioureas and thioformamides[19]. Hence, we propose that the *E, Z* conformation (**13**) is the more stable conformer of **11** in solution in chloroform.



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EXPERIMENTAL

General methods.- Melting points are uncorrected. Optical rotations were measured at 22±4°C. F.t.-i.r. spectra were recorded for KBr discs. ^{1}H-n.m.r. spectra were obtained at 200 MHz for solutions in deuteriochloroform or dimethyl sulphoxide. Assigments were confirmed by decoupling and H/D exchange experiments. ^{13}C-n.m.r. spectra were recorded at 50.3 MHz. Proton decoupled APT[27] spectra were obtained to assist in carbon signal assignments. E.i. mass spectra (70 eV) were measured with a Kratos MS-80 RFA instrument, with an ionizing current of 100 μA, and 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). Column chromatography was conducted on Silica Gel 60 (Merck, 70-230 mesh).

2,3,4-Tri-O-acetyl-β-D-*glucopyranosylamine hydrobromide* (**1**).- To a solution of 2,3,4-tri-*O*-acetyl-6-*O*-trityl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine[21] (0.2 g, 0.29 mol) in dichloromethane (4 mL) was added gradually a solution of bromine (0.16 g, 1 mmol) in dichloromethane (4.5 mL) and water (0.05 mL). The mixture was stirred for 4 h at room temperature. The solvent was then removed to leave an orange syrup which was triturated with ether until a white solid (80 mg, 70%) resulted. Crystallised from 1:1 ethanol-ether had m.p. 164-165°C; [α]\S\DO3(21;D)+22.0° (*c* 1.0, methanol); λ_{max}^{MeOH} 209 nm; ν_{max} 3420 (OH), 3020-2400 (NH_3^+), 1750 (CO) and 1235 cm^{-1} (C-O-C). N.m.r. data [$(CD_3)_2SO$]: ^1H, Tables 1, 2 and δ 2.06, 2.11, 2.14 (3s, each 3H, 3 Ac), 3.76 (bs, 1H, OH) and 9.17 (bs, 3H, NH_3^+); ^{13}C, Table 3 and δ 20.4, 20.6, 21.0 (3 CH_3), 169.3, 169.5, and 169.8 (3 CO). *Anal.* Calcd for $C_{12}H_{20}O_8NBr$: C, 37.30; H, 5.18; N, 3.62. Found: C, 37.24; H, 5.21; N, 3.40.

2,3,4-Tri -O-*benzoyl* -β-D-*glucopyranosylamine hydrochloride* (**2**).- Chlorine was passed through a solution of 2,3,4-tri-*O*-benzoyl-6-*O*-trityl-*N*-(2,2-diethoxycarbonylvinyl)-β-D-glucopyranosylamine[21] (1.5 g, 1.74 mmol) in dichloromethane (4.8 mL) until a solid mass resulted. The precipitate was collected and washed with dichloromethane to give **2** (0.6 g, 70%); m.p. 133-135°C, $[\alpha]_D^{18}$+2.1°, $[\alpha]_{546}^{18}$ +5.6° (*c* 1.0, ethanol); λ_{max}^{EtOH} 205, 232, and 276 nm; ν_{max} 3410 (OH), 3020-2300 (NH), 1744 (CO), 1270 (C-O-C), and 710 cm^{-1} (CH aromatic). N.m.r. data [$(CD_3)_2SO$]: ^1H, Tables 1, 2 and δ 3.40 (bs, 1H, OH), 7.30-7.93 (m, 15H, 3 Ph), and 9.17 (bs, 1H, NH_3^+); ^{13}C, Table 3 and δ 126.7-133.9 (18C, 3 Ph), 164.7, 164.8, and 165.2 (3 CO). Mass spectrum: *m/z* 368 (1), 256 (1), 244 (2), 122 (80, $BzOH^+$), 105 (100, Bz^+), and 77 (Ph^+). *Anal.* Calcd for $C_{27}H_{26}O_8NCl$: C, 61.42; H, 4.96: N, 2.65. Found: C, 61.22; H, 4.81; N, 2.20.

2,3,4-Tri-O-*acyl*-β-D-*glucopyranosyl isothiocyanates* (**3**, **4**).- To a heterogeneous mixture of the corresponding 2,3,4-tri-O-acyl-β-D-glucopyranosylamine hydrohalide (**1** or **2**, 1.5 mmol), dichloromethane (8 mL), calcium carbonate (0.4 g, 4.5 mmol), and water (4.5 mL) was added thiophosgene (0.16 mL, 2.25 mmol). The mixture was stirred vigorously for 48 h and then filtered. The organic layer was washed with water (2 x 20 mL), dried ($CaCl_2$), concentrated, and the residue was purified as indicated. The following compounds were prepared in this manner.

2,3,4-Tri-*O*-acetyl-β-D-glucopyranosyl isothiocyanate (**3**); crystallised from 1:1 hexane-ethyl acetate give a hygroscopic solid (0.49 g, 94%); $[\alpha]_D^{26}$ +5.0° (c 1.0, dichloromethane); λ_{max}^{Py} 254 nm; ν_{max} 3455 (OH), 2969 (CH), 2023 (NCS), 1750 (CO), and 1230 cm^{-1} (C-O-C). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2, and δ 2.03, 2.06, 2.11 (3s, each 3H, 3 Ac), and 2.78 (bs, 1H, OH); ^{13}C, Table 3 and δ 21.1 (2C, 2 CH_3), 21.3 (CH_3), 169.0, 169.9, and 170.0 (3 CO). Mass spectrum: *m/z*, 289 (6, M^+ - NCS^-), 229 (7, 289 - AcOH), 196 (5), 169 (30, 289 - 2 AcOH), 127 (40, 169 - CH_2CO), 60 (40, $AcOH^+$), 58 (10, NCS^+), and 43 (100, Ac^+); Found: M^+ - NCS. 289.0914. $C_{12}H_{17}O_8$ requires 289.0923. This compound was analysed as thiourea derivative **6**.

2,3,4-Tri-*O*-benzoyl-β-D-glucopyranosyl isothiocyanate (**4**); column chromatography (ether-hexane 2:1, 1:1) of the residue give a foam (0.508 g, 64%); $[\alpha]_D^{19}$ - 16.2°, $[\alpha]_{546}^{19}$ -18.8° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 235 and 276 nm; ν_{max} 3400 (OH), 3030, 2961 (CH), 2020 (NCS), 1736 (CO), 1270 (C-O-C), and 708 cm^{-1} (CH aromatic). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2, and δ 2.67 (t, 1H, OH), and 7.21-8.10 (m, 15H, 3 Ph); ^{13}C, Table 3 and δ 128.2–133.7 (18C, 3 Ph), 164.6, 165.5, and 165.7 (3 CO). Mass spectrum: *m/z*, 503 (1, M^+ - CH_2O), 475 (1, M^+ - NCS·), 370 (1), 248 (1, 370 - BzOH), 122 (20, $BzOH^+$), 105 (100, Bz^+), 77 (20, Ph^+), 59 (4, $HNCS^+$), and 58 (1, NCS^+); Found: M^+ - NCS· 475.1308. $C_{27}H_{23}O_8$ requires 475.1392. This compound was analysed as thiourea derivative **7**.

*2,3,6-Tri-*O*-acetyl-β-D-glucopyranosyl isothiocyanate* (**5**).- When a solution of **3** in chloroform was left for 6 days at room temperature (n.m.r. tube) **5** was quantitetively formed; $[\alpha]_D^{20}$ - 46.0°, $[\alpha]_D^{20}$ -77 ° (*c* 1.0, dichloromethane); ν_{max} 3300 (OH), 2051 (NCS), 1750 (CO), and 1236 cm^{-1} (C-O-C). N.m.r. data: ^1H [$(CD_3)_2SO$], Tables 1, 2 and δ 2.02 (s, 3H, Ac), 2.07 (s, 6H, 2 Ac), and 5.86 (d, 1H, $J_{H,OH}$ 6.2 Hz, OH); in $CDCl_3$, Tables 1, 2 and δ 2.10, 2.12, 2.15 (3 s, each 3H, 3 Ac), and 3.10 (d, 1 H, $J_{H,OH}$ 5.8 Hz, OH). ^{13}C ($CDCl_3$), Table 3 and δ 20.4, 20.6, 20.7 (3 CH_3), 169.2, 171.0, and 171.7 (3 CO). Mass spectrum: *m/z* 289 (38, M^+ - NCS), 229 (93, 289 - AcOH), 196 (20), 187 (229 - CH_2CO), 169 (30, 289 - 2 AcOH), 154 (20), 139 (18), 127 (90, 169 - CH_2CO), and 60 (15, $AcOH^+$). Found: M^+ - NCS· 289.0934. $C_{12}H_{17}O_8$ requires 289.0923.

N-*Phenacyl*-N'-(*2,3,4-tri-*O*-acyl-β-D-glucopyranosyl)thioureas* (**6**, **7**).- A solution of phenacylamine hydrochloride (0.11 g, 0.63 mmol) in water (2.4 mL) was neutralised with sodium hydrogencarbonate (0.05 g, 0.63 mmol) and added to a solution of the corresponding isothiocyanate (**3** or **4**, 0.58 mmol) in acetone (4 mL) under nitrogen. The resulting solution was kept at room temperature until TLC showed no presence of the isothiocyanate (0.5 h), then concentrated under diminished pressure and the residue was purified as indicated. The following compounds were prepared in this manner.

N-Phenacyl-*N'*-(2,3,4-tri-*O*-acetyl-β-D-glucopyranosyl)thiourea (**6**); crystallised from ethanol (0.19 g, 70%) had m.p. 182-184°C; $[\alpha]_D^{22}$-11.0° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 247 and 254 nm; ν_{max} 3324(OH), 3283 (NH), 2942 (CH), 1748 (CO ester), 1689 (CO ketone), 1227 (C-O-C) and 689 cm^{-1} (CH aromatic). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2 and δ 2.05, 2.07, 2.10 (3s, each 3H, 3 Ac), 3.45 (t, 1 H, $J_{H,OH}$ 5.5 Hz, OH), 4.97 (dd, 1H, $^2J_{H,H}$ 18.1, $J_{H,NH}$ 5.4 Hz, C*H*H'), 5.04 (dd, 1H, CH*H'*), 7.50 (d, 1H, $J_{1,NH}$ 9.2 Hz, N'H), 7.58-7.65, 7.80-8.00 (2m, 5H, Ph), and 7.71 (dd, 1H, NH). ^{13}C, Table 3 and δ 20.5, 20.6, 20.7 (3 CH_3), 51.8 (CH_2), 127.9 (2C, C-2,6 of Ph), 128.7 (2C, C-3,5 of Ph), 134.0 (C-4 of Ph), 134.1 (C-1 of Ph), 169.8, 170.7, 171.1 (3 CO ester), and 193.9 (CO ketone). Mass spectrum: *m/z* 464 (1, M^+ - H_2O), 431 (2, M^+ - SH·), 366 (1, M^+ - CH_2COPh), 289 (18, M^+ -

$NHCSNHCH_2COPh$), 229 (12, 269-AcOH), 194 (1, $PhCOCH_2NHCSNH_2^+$), 169 (30, 229 - AcOH), 127 (25, 229 - Ac_2O), 109 (23, 127 - H_2O), 105 (100, Bz^+), 77 (60, Ph^+), 60 (62, $AcOH^+$), 45 (70), and 43 (90, Ac^+). *Anal.* Calcd for $C_{21}H_{26}O_9N_2S$: C, 52.28; H, 5.43; N, 5.81. Found: C, 52.78; H, 5.43; N, 6.26.

N-Phenacyl-*N'*-(2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)thiourea (**7**); column chromatography (ethyl ether-hexane 3:1) of the residue gives a syrup (0.43 g, 88%), which crystallised from ethanol had m.p. 170-172°C; $[\alpha]_D^{18}$ +17.0°, $[\alpha]_{546}^{18}$ +23.0° (*c* 0.8, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 238 and 282 nm; ν_{max} 3400 (OH), 3312 (NH), 3065, 2945 (CH), 1736 (CO ester), 1686 (CO ketone), 1270 (C-O-C) and 710 cm^{-1} (CH aromatic). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2, and δ 1.92 (bs, 1H, OH), 4.98 (m 2H, CH_2), and 7.10-8.00 (m, 20H, 4 Ph). ^{13}C, Table 3 and δ 52.4 (CH_2), 127.9-133.1 (24C, 4 Ph), 165.6, 166.2, 166.7 (3 CO ester), and 194.1 (CO ketone). Mass spectrum: *m/z* 475 (1, M^+ - $NHCSNHCH_2COPh$), 369 (475 - BzH), 247 (1, 369 - BzOH), 194 (2, $PhCOCH_2NHCSNH_2^+$), 122 (53, $BzOH^+$), 105 (Bz^+), and 77 (Ph^+). *Anal.* Calcd for $C_{36}H_{32}O_9N_2S$: C, 64.67; H, 4.79; N, 4.19. Found: C, 64.42; H, 4.63; N, 4.00.

*5-Methyl-1-(2',3',4'-tri-*O*-acyl-β-D-glucopyranosyl)-4-imidazoline-2-thiones* (**8**, **9**).- A solution of aminoacetone hydrochloride (0.04 g, 0.37 mmol) in water (1.3 mL) was neutralised with sodium hydrogencarbonate (0.03 g, 0.37 mmol) and added to a solution of the corresponding isothiocyanate (**3** or **4**, 0.35 mmol) in acetone (3 mL) under nitrogen. The resulting solution was kept for 30 min at room temperature and then concentrated to dryness. The residue was solved in the minimal amount of methanol (with 0.05 mL of acetic anhydride for **8**) and heated at *t* °C, for *h* hours under *p* pressure with stirring. The mixture was then concentrated to dryness and treated as indicated. The following compounds were prepared in this manner.

5-Methyl-1-(2',3',4'-tri-*O*-acetyl-β-D-glucopyranosyl)-4-imidazoline-2-thione (**8**); *t*, 50°C; h 2h; *p* 1 atm; the residue was evaporated twice from methanol (2 x 5 mL) to give a white foam (0.08 g, 59%); $[\alpha]_D^{18}$ +75.4°, $[\alpha]_{546}^{18}$ +90.2 °(*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 238, and 279 nm; ν_{max} 3376 (OH), 3160 (NH), 2942 (CH), 1753 (CO), 1632 (C=C) and 1223 cm^{-1} (C-O-C). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2, and δ 1.97, 2.04, 2.09 (3s, each 3H, 3 Ac), 2.37 (s, 3H, N-CH_3), 20.2, 20.3, 20.4 (3 CH_3), 169.5, 169.7 and 170.4 (3 CO). Mass spectrum: *m/z* 402 (30, M^+), 384 (8, M^+ - H_2O), 342 (18, M^+ - AcOH), 300 (1, 342 - CH_2CO), 289 (19, glycosyl moiety), 271 (2, 289 - H_2O), 229 (40, 289 - AcOH), 187 (15, 229 - CH_2CO), 169 (78, 229 - AcOH), 127 (60, 169 - CH_2CO and 187 - AcOH), 114 (80, methylimidazoline-thione$^+$), 81 (19, 114 - $SH^·$), 60 (55, $AcOH^+$), and 43 (100, Ac^+). Found: M^+ 402.1122. $C_{16}H_{22}O_8N_2S$ requires 402.1097.

5-Methyl-1-(2',3',4'-tri-*O*-benzoyl-β-D-glucopyranosyl)-4-imidazoline-2-thione (**9**); *t*, 25°C; *h* 24h; *p*, 3 atm; column chromatography (ethyl acetate-hexane 1:1) of the residue gave a white foam (0.19 g,

41%); $[\alpha]_D^{18}$ +57.8°, $[\alpha]_{546}^{18}$+72.0 °(*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 235, and 277 nm; ν_{max} 3422 (OH), 3300 (NH), 1728 (CO), 1634 (C=C), 1262 (C-O-C) and 707 cm^{-1} (CH aromatic). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2, and δ 2.49 (s, 3H, CH_3), 2.88 (bs, 1H, OH), 6.16 (s, 1H, H-4), 7.24-7.80 (m, 15H, 3 Ph), and 11.0 (bs, 1H, NH). ^{13}C, Table 3, and δ 11.1 (CH_3), 128.1-133.8 (18C, 3 Ph), 165.2, 165.3 and 166.2 (3 CO). Mass spectrum: *m/z* 570 (1, M^+ - H_2O), 475 (1, glycosyl moiety), 466 (8, M^+ - BzOH), 449 (1, 570 - BzO·), 327 (1, 449 - BzOH), 122 (62, $BzOH^+$), 114 (5, methylimidazoline-thione$^+$), 105 (100, Bz^+), 81 (4, 114-SH·), and 77 (32, Ph^+). Found: M^+ - H_2O 570.1483. $C_{31}H_{26}O_7N_2S$ requires 570.1461.

2-(2',3', 4'-Tri-O-*benzoyl*-β-D-*glucopyranosyl)amino-2-thiazoline* (**10**).- To a solution of 2-chloroethylamine hydrochloride (0.154 g, 1.33 mmol) in water (2 mL), diethyl ether (3 mL) and M sodium hydroxide (3 mL) were added. The organic layer was decanted and the aqueous solution was extracted with ether (4 x 3 mL). The combined extracts were dried ($MgSO_4$) and then **4** (0.205 g, 0.385 mmol) was added. The mixture was stirred for 12 h at room temperature and the solvent was evaporated. The crude product (**10** hydrochloride, 0.236 g, 100%) was dissolved in water (54 mL) and to this solution dichloromethane (54 mL) and sodium hydrogencarbonate (0.315 g, 3.75 mmol) were added. The mixture was stirred at room temperature for 2h. The organic layer was decanted and then the aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried ($MgSO_4$) and evaporated to dryness. Column chromatography (ethyl acetate) of the residue gave **10** (0.215 g, 97%) as a white foam, which crystallised from ethyl acetate had m.p. 117-119°C; $[\alpha]_D^{18}$+15.7°, $[\alpha]_{546}^{18}$+22° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 235 and 276 nm; 3341 (OH), 3100 (NH), 2944, 2861 (CH), 1734 (CO), 1628 (C=N), 1287 (C-O-C), and 710 cm^{-1} (CH aromatic). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2, and δ 3.22 (t, 2H, $^3J_{H,H}$ 7.2 Hz, S-CH_2), 3.61-4.00 [m, 6H, H-5,6,6' (see Table 1), OH and =N-CH_2] and 7.20-8.03 (m, 16H, 3Ph and NH). ^{13}C, Table 3 and δ 128.1-133.2 (18C, 3Ph), 165.6 (2 CO), and 166.1 (CO). Mass spectrum: *m/z* 558 (1, M^+ - H_2O), 437 (1, 558 - BzO·), 122 (96, $BzOH^+$), 105 (100, Bz^+), 102 (11, Het-NH_2^+), 101 (8, Het-NH^+), and 77 (91,Ph^+). *Anal.* Calcd for $C_{30}H_{28}O_8N_2S$: C, 62.50; H, 4.86; N, 4.86. Found: C, 62.10; H, 5.30; N, 4.62.

N,N'-*Bis(2,3,4-tri*-O-*benzoyl*-β-D-*glucopyranosyl)*-N-*(2-thiazolin-2-yl)thiourea* (**11**).- To a solution of 2-chloroethylamine hydrochloride (0.07 g, 0.61 mmol) in pyridine (1.3 mL) was added **4** (0.65 g, 1.22 mmol). The mixture was kept at room temperature for 2h, and then poured into ice-water. The solid product was filtered and purified by column chromatography (gradient ethyl ether-hexane 2:1, 10:1) gave a white solid (0.561 g, 83%). Crystallised from ethyl ether-hexane 3:1 had m.p. 136-138°C; $[\alpha]_D^{18}$ -45.2°, $[\alpha]_{546}^{18}$ -53.4°(c 1.0, dichloromethene); $\lambda_{max}^{CH_2Cl_2}$ 235 and 280 nm; 3437 (OH), 3200-3000 (NH), 2959, 2878 (CH), 1728 (CO), 1601 (C=N), 547 (NH), 1281 (C-O-C), and 710 cm^{-1} (CH aromatic). N.m.r. data ($CDCl_3$): ^1H, Tables 1, 2 and δ 2.80 (t, 2H, $J_{H,OH}$ 6.1 Hz, 2 OH), 3.06 (t, 2H, $^3J_{H,H}$ 7.3 Hz, S-CH_2), 4.53 (dt, 1H, $^2J_{H,H}$ 11.2 Hz, =NC*H*H'), 4.67 (dt, 1H, =NCH*H'*), 7.28-8.10 (m, 30H, 6Ph), and 13.03

(d, 1H, $J_{N'H,H-1'}$ 8.0 Hz, N'H). ^{13}C, Table 3 and δ 127.9-133.3 (36C, 6 Ph), and 165.4-165.9 (6 CO). Anal. Calcd for $C_{58}H_{51}O_{16}N_3S_2$: C, 62.74; H, 4.63; N, 3.78. Found: C, 62.20; H, 4.70; N, 3.66.

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