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PREPARATION AND PROPERTIES OF 2-DEOXYGLYCOSYL ISOTHIOCYANATES

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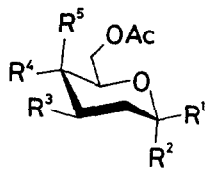
Abstract.- The syntheses of 3,4,6-tri-*O*-acetyl-2- deoxy-α and β-D-*arabino*(D-*lyxo*)hexopyranosyl isothiocyanates (**2**, **3**, **6**, **7**) and 4,6-di-*O*-acetyl-3-bromo-2,3-dideoxy-β-D-*arabino*hexopyranosyl isothiocyanate (**5**) are reported. Treatments of **2**,**3**,**6**, and **7** with phenacylamine hydrochloride and of **2** with aminoacetone hydrochloride gave the corresponding *N*-phenacyl(acetylmethyl)-*N'*-(2-deoxyglycosyl)-thioureas (**8**-**12**). The *N*-nucleoside analogues 5-methyl-1-(3',4',6'-tri-*O*- acetyl-2'-deoxy-α-D-*arabino*hexopyranosyl)-4-imidazoline--2-thione (**13**) was obtained by cyclodehydration of the thiourea **12**.

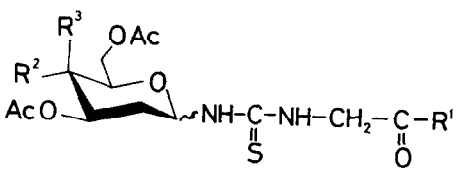
During recent years considerable attention has been directed to the syntheses of heterocyclic derivatives of sugars, such as nucleoside analogues and glycosylaminoheterocycles[1,2], which have potential pharmaceutical properties[3,4] Recently 2-deoxynucleosides, for example 3'-α-azido-3'-deoxythymidine (AZT), have been evaluated for the treatment of AIDS[5] and several efforts[6,7] are being directed to the syntheses of this type of nucleoside. The glycosyl isothiocyanates and glycosylthioureas are valuable and versatile intermediates in the construction of *N*-nucleosides and glycosylaminoheterocycles[8-12]. In addition glycosyl isothiocyanates have been recently transformed into glycosyl isocyanides, 1,5-anhydroalditoles[13] and glycosyl thioformamides[14]. In spite of this interest there are no antecedents for 2-deoxyglycosyl isothiocyanates. In this paper we account the syntheses, spectroscopic properties and certain reactions of 2-deoxy-D-*arabino*- (**2**-**4**) and 2-deoxy-D-*lyxo*hexopyranosyl isothiocyanates (**6**, **7**).

RESULTS AND DISCUSSION

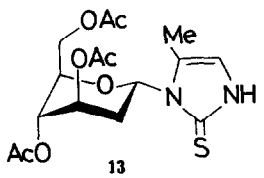
3,4,6-Tri-*O*-acetyl-2-deoxy-α and β-D-*arabino*hexopyranosyl isothiocyanates (**2**, **3**) and 4,6-di-*O*-acetyl-3-bromo-2,3-dideoxy-β-D-*arabino* hexopyranosyl isothiocyanate (**5**) were prepared by reaction of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-*arabino*hexopyranose (**1**)[15] with bromotrimethylsilane (BrTMSi) followed with silver isothiocyanate. These syntheses were tried out under various experimental conditions (table 1) and in all the cases unaltered **1** was partially recovered after reactions.



	R^1	R^2	R^3	R^4	R^5
1	H	OAc	OAc	OAc	H
2	H	NCS	OAc	OAc	H
3	NCS	H	OAc	OAc	H
4	H	NCS	Br	OAc	H
5	NCS	H	Br	OAc	H
6	H	NCS	OAc	H	OAc
7	NCS	H	OAc	H	OAc



	R^1	R^2	R^3	anomeric configuration
8	Ph	OAc	H	α
9	Ph	OAc	H	β
10	Ph	H	OAc	α
11	Ph	H	OAc	β
12	Me	OAc	H	α



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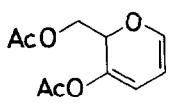

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Table 1. Experimental conditions for preparation of 2-5 from 1.

	A			B		Yield %			
Entry	Temp.	Time	[BrTMSi]/[1] in mol	°C	Time	2	3	4	5
1	r.t.	12 min	2.5:1	{ 60° 80°	1 h 45 min }	33	19	-	-
2	r.t.	35 min	2.5:1	60°	1 h	32	20	-	-
3	45°	4 h	2:1	110°	2 h	40	20	-	-
4	80°	5 h	2:1	110°	2.5 h	4	2	15*	15

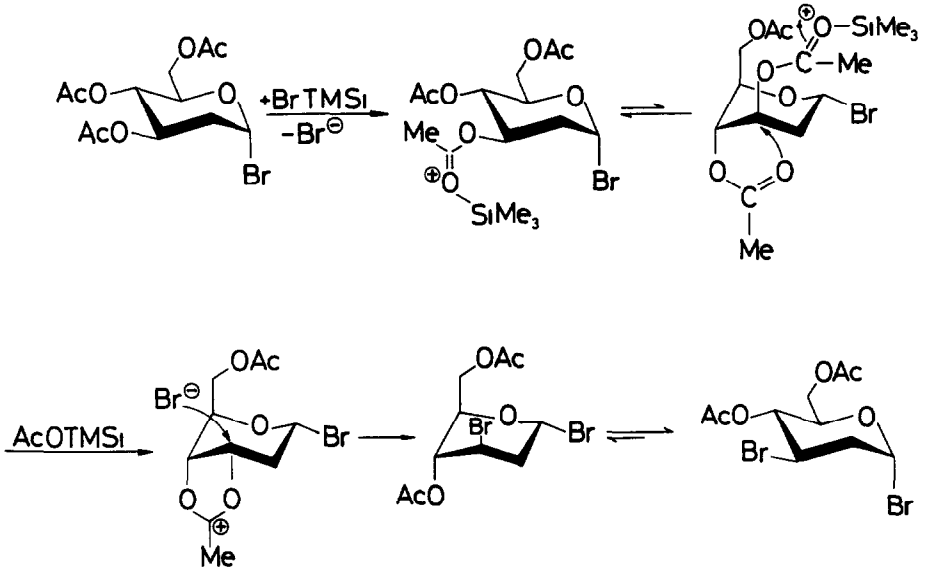
A: First step: reaction of 1 with BrTMSi

B: Second step: reactiom with silver isothiocyanate

* Product 4 was unstable

The first step of the synthesis is the formation of a glycosyl bromide which reacts (second step) with silver isothiocyanate. According to bibliographic data[16] when a 1:1 mixture of 1 and the corresponding β anomer is heated with BrTMSi at 45°C for 4 h, 3,4,6-tri-*O*-acetyl-α-D--*arabino*hexopyranosyl bromide is quantitatively formed. We did not observe, by means of ^{1}H-n.m.r., any anomerization during the treatment of 1 with BrTMSi at r.t. for 4 h, but the transformation is not quantitative. The spectra showed signals for 1 (H-1, 6.25 dd in C_6D_6) and 3,4,6-tri-*O*--acetyl-α-D-*arabino*hexopyranosyl bromide (H-1, 6.02 dd in C_6D_6) but not for β anomers. When the reaction was performed at 50°C a mixture of 1, 3,4,6-tri-*O*-acetyl-α-D-arabinohexopyranosyl bromide and two non-identifiable products, was formed. The second step of the reaction (entries 1 and 2) was performed at 60-80°C and then the anomerization took place yielding 2 and 3. The best yields for 2 and 3 were obtained in the conditions shown in entry 3, but in this case some decomposition was observed (^{1}H-n.m.r.) during the first step.

When the treatment with BrTMSi was carried out at 80°C for 5 h (entry 4) the main products of the synthesis were the 3-bromo-3-deoxyglycosyl isothiocyanates 4 and 5. Compound 4 was an unstable product. Other polybromoderivatives were also detected. The introduction of the bromine atom in the position 3 can be explained through a similar mechanism to that described for the synthesis of 4-*O*-acetyl-3-bromo-2,3,6-trideoxy--α-D-*arabino*hexopyranosyl bromide[17] (scheme 1). This mechanism involves the acetoxonium ion 15, which is formed with participation of the neighbouring 4-acetoxyl group.



15 Scheme 1

The synthesis of 3,4,6-tri-*O*-acetyl-2-deoxy-α and β-D-*lyxo*-hexopyranosyl isothiocyanates (**6** and **7**) was carried out from 2-deoxy-D-galactose by successive treatments with acetic anhydride, BrTMSi at r.t. and silver isothiocyanate. When the reaction with BrTMSi was performed in more vigorous conditions mixtures of non-identifiable polybromoderivatives were obtained.

The structures of **2-7** were assigned on the basis of i.r., ^{1}H- and ^{13}C-n.m.r., analytical and/or high resolution mass spectroscopic data. Compound **4** only could be characterized by i.r., ^{1}H-n.m.r. and m.s. The products **2**, **3**, and **5-7** had the i.r. absorption at ≈ 2040 cm^{-1} and δ ≈ 142 p.p.m. for NCS as reported[8,9,18] for glycosyl isothiocyanates. They also showed a m.s. peak indicative of a loss of 58 (NCS) from M^{+}. Although no mass spectral data for glycosyl isothiocyanates are available, the spectra agree (see experimental) with data reported for acetylated glycosyl derivatives[19].

During the preparation of **6**, **7** a byproduct appeared (see experimental) whose spectroscopic data were indicative of the structure **14**.

N-Phenacyl-*N'*-[3,4,6-tri-*O*-acetyl-2-deoxy-α and β-D-*arabino*(*lyxo*)-hexopyranosyl]thioureas (**8-11**) and *N*-acetylmethyl-*N'*-(3,4,6-tri-*O*-acetyl--2-deoxy-α-D-*arabino*hexopyranosyl)thiourea (**12**) were prepared by reaction of the corresponding 2-deoxyglycosyl isothiocyanate and phenacylamine hydrochloride or aminoacetone hydrochloride. The analytical, i.r., ^{1}H- and ^{13}C-n.m.r. and m.s. data (see experimental) were consistent with the structures proposed and precluded possible aminothiazolic or imidazolic structures. Thus compounds **8-11** showed the i.r. band at 1680-1690 cm^{-1} (C=O group in arylketones) and ^{13}C-n.m.r. signals at ≃ 52 p.p.m. (CH_2) and ≃ 193 p.p.m. (C=O) for phenacyl group. The compound **12** had $\nu_{C=O}$ at 1728 cm^{-1} (methylketone), a singlet for 3H at 2.24 p.p.m. (CH_3CO) and ^{13}C-n.m.r. signals at δ 27.0 (CH_3), 55.2 (CH_2), 182.9 (C=S) and 202.2 (CH_3CO).

The $^{3}J_{H,H}$ values which could be measured for **2**, **3**, **5-12** were indicative that the $^{4}C_{1}$(D) conformation preponderated in solutions in chloroform.

The *N*-nucleoside analogue 5-methyl-1-(3',4',6'-tri-*O*-acetyl-2'--deoxy-α-D-*arabino*hexopyranosyl)-4-imidazoline-2-thione (**13**) was quantitatively prepared by cyclodehydration of **12** with acetic anhydride and its structure was assigned on the basis of spectroscopic data. Compound **13** had λ_{max} 277 nm[9,12,20], ν_{max} 1628 cm^{-1} (C=C)[12] and δ 6.44 for H-4[9,12]. In the ^{13}C-n.m.r. spectrum the acetylmethyl and C=S resonances were replaced by signals at 11.21, 112.4, 126.3, and 160.6 p.p.m. which were assigned to CH_3, C-4, C-5 and C-2 of 5-methyl-4-imidazoline-2-thione ring, respectively. The mass spectrum showed the molecular peak and loss of SH (*m/z* 353). These data ruled out a possible structure of aminothiazole[9].

The $^{3}J_{H,H}$ values of **13** accorded with the $^{1}C_{4}$(D) conformation where the bulky heterocyclic group is equatorial.

EXPERIMENTAL

General methods.- Melting points are uncorrected. Optical rotations were measured at 20-25°C, using 1 cm cells. U.v. spectra were measured with a Philips PU 8720 spectrophotometer. I.r. spectra (KBr discs) were recorded on a Bomen MB-120 f.t.i.r. spectrophotometer ^{1}H- and ^{13}C-n.m.r. spectra were registered in deuteriochloroform at 200 and 50.3 MHz, respectively, on a Varian XL-200 instrument. Assignments of NH were confirmed by H/D exchange experiments, and proton decoupled APT spectra[21] were obtained to assist in carbon signal assignments. The e.i. mass spectra were measured at 70 e.V., with an ion source temperature of 200°C, resolution 1000 or 10000 (10% valley definition), using a MS-80 RFA Kratos instrument. Column chromatography was conducted on Silica Gel 60 (Merck, 70-230 mesh).

3,4,6-Tri-O-acetyl-2-deoxy-α- and *β-*D*-arabinohexopyranosyl isothiocyanates* (2, 3) and *4,6-di-O-acetyl-3-bromo-2,3-dideoxy-α-* and *β-*D*-arabinohexopyranosyl isothiocyanates* (4, 5).- To a stirred solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-*arabino*hexopyranose[15] (0.5 g, 1.5 mmol) in dry toluene (15 mL), BrTMSi (a mL) was added and the mixture was heated at t°C for h hours. Then silver isothiocyanate (b g) was added and the resulting mixture was heated under reflux for 2 h and then filtered through celite and concentrated. Column chromatography (ether-hexane 1:1, 2:1, 3:1) of the residue gave the following compounds.

3,4,6-Tri-*O*-acetyl-2-deoxy-α-D-*arabino*hexopyranosyl isothiocyanate (2); a, 0.38 mL (3.0 mmol; t, 45°C; h, 4 hours; b, 1.0 g (6.0 mmol); crystallised from ether (0.2 g, 40%) had m.p. 70-72°C; $[\alpha]_D^{22}$ +142° (*c* 0.6, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 252, 236 nm; ν_{max} 2029 (NCS), 1742 (CO), and 1235 cm^{-1}(C-O-C). ^{1}H-N.m.r.: δ 1.97 (ddd, 1H, $J_{1,2eq}$= 1.7, $J_{2eq,3}$= 4.7, $J_{2ax,2eq}$= 13.5 Hz, H-2eq), 2.04, 2.07, 2.10 (3s, each 3H, 3Ac), 2.40 (ddd, 1H, $J_{1,2ax}$= 4.1, $J_{2ax,3}$= 11.1 Hz, H-2ax), 4.03-4.13 (m, 2H, H-5, 6'), 4.32 (dd, 1H, $J_{5,6}$= 4.8, $J_{6,6'}$= 12.9 Hz, H-6), 5.03 (t, 1H, $J_{3,4}$= $J_{4,5}$= 9.2 Hz, H-4), 5.28 (ddd, 1H, H-3), and 5.70 (dd, 1H, H-1). ^{13}C, δ 20.4, 20.5, 20.6 ($3CH_3$), 35.5 (C-2), 61.4 (C-6), 68.0 (2C, C-3,4), 70.9 (C-5), 81.7 (C-1), 141.0 (NCS), 169.4, 169.7, and 170.3 (3CO). Mass

spectrum: *m/z* 331 (1, M^+), 273 (2, M^+- NCS$^\bullet$), 213 (20, 273-AcOH), 153 (18), 139 (25), 128 (18), 111 (38), 97 (100), 60 (65), 59 (30), and 58 (5, NCS^+). *Anal.* Calcd for $C_{13}H_{17}O_7NS$: C, 47.12; H, 5.17; N, 4.23. Found: C, 46.88; H, 5.25; N, 4.19.

3,4,6-Tri-*O*-acetyl-2-deoxy-β-D-*arabino*hexopyranosylisothiocyanate (3); a, 0.38 mL (3.0 mmol); t, 45°C; h, 4 hours; b, 1.0 g (6.0 mmol); crystallised from ether (0.1 g, 20%) had m.p. 90-92°C; $[\alpha]_D^{24}$ -26° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 251 nm, ν_{max} 2029 (NCS), 1740 (CO), and 1230 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 1.85 (m, 1H, H-2ax), 2.06 (s, 6H, 2Ac), 2.13 (s, 3H, Ac), 2.55 (ddd, 1H, $J_{1,2}$= 2.1, $J_{2,3}$= 4.8, $J_{2ax,2eq}$= 12.8 Hz, H-2eq), 3.67 (ddd, 1H, $J_{5,6'}$= 2.4, $J_{5,6}$= 4.8, $J_{4,5}$= 9.7 Hz, H-5), 4.13 (dd, 1H, $J_{6,6'}$= 12.0 Hz, H-6'), 4.28 (dd, 1H, H-6), and 4.93-5.14 (m, 3H, H-1, 3, 4). ^{13}C, δ 20.5, 20.6, 20.7 ($3CH_3$), 37.4 (C-2), 61.8 (C-6), 67.9 (C-3), 69.8 (C-4), 74.1 (C-5), 81.3 (C-1), 141.7 (NCS), 169.5, 170.0, and 170.6 (3CO). Mass spectrum: *m/z* 273 (3, M^+- NCS$^\bullet$), 213 (35, 273-AcOH), 153 (25), 139 (28), 111 (55), 97 (100), 60 (15), 59 (10), and 58 (2, NCS^+). *Anal.* Found: C, 47.40; H, 5.31; N, 4.14.

4,6-Di-*O*-acetyl-3-bromo-2,3-dideoxy-α-D-*arabino*hexopyranosyl isothiocyanate (4); a, 0.9 mL (7.0 mmol); t, 80°C; h, 5 hours; b, 0.34 g (2.2 mmol); was an amorphous, hygroscopic and unstable solid (0.075 g, 15%); ν_{max} 2035 (NCS), 1746 (CO), and 1235 (C-O-C). ^{1}H-N.m.r.: δ 2.4-2.6 (m, 2H, $H_{2eq,2ax}$), 4.28 (m, 1H, H-3), 5.15 (t, 1H, $J_{3,4}$= $J_{4,5}$= 9.8 Hz, H-4), 5.58 (dd, 1H, $J_{1,2eq}$= 1.9, $J_{1,2ax}$= 4.0 Hz, H-1). Mass spectrum: *m/z* 353, 351 (1, M^+), 295, 293 (50, M^+-NCS$^\bullet$), 272 (1, M^+-HBr), 251, 249 (7, M^+- AcOH), 235, 233 (15), 213 (28, 295, 293-HBr), 185 (50), 175, 173 (25), 153 (45), 111 (100), 81, 79 (10, Br^+), 60 (40), and 58 (10, NCS^+); Found: M^+ 352.9800, 350.9789. $C_{11}H_{14}O_5NSBr$ requires M, 352.9757, 350.9776.

4,6-Di-*O*-acetyl-3-bromo-2,3-dideoxy-β-D-*arabino*hexopyranosyl isothiocyanate (5); a, 0.9 mL (7.0 mmol); t, 80°C; h, 5 hours; b, 0.34 g (2.2 mmol); was an amorphous and hygroscopic solid (0.075 g, 15%); $[\alpha]_D^{25}$ +34°, $[\alpha]_{546}^{25}$ +46° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 229, 250, and 280 nm; ν_{max} 2035 (NCS), 1746 (CO), and 1235 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 2.11, 2.12

(2s, each 3H, 2Ac), 2.40 (dt, 1H, $J_{1,2ax}$= 10.2, $J_{2ax,2eq}$=$J_{2ax,3}$= 12.7 Hz, H-2ax), 2.74 (ddd, 1H, $J_{1,2eq}$=2.3, $J_{2eq,3}$= 5.1 Hz, H-2eq), 3.62 (ddd, 1H, $J_{5,6'}$= 2.5, $J_{5,6}$= 4.9, $J_{4,5}$= 10.0, H-5), 4.05 (ddd, 1H, $J_{3,4}$= 10.0 Hz, H-3), 4.10 (dd, 1H, $J_{6,6'}$= 12.4 Hz, H-6'), 4.20 (dd, 1H, H-6), 4.93 (dd, 1H, H-1), and 5.10 (t, 1H, H-4). ^{13}C, δ 20.6, 20.7 ($2CH_3$), 42.7 (C-2), 44.9 (C-3), 62.1 (C-6), 70.2 (C-5), 75.8 (C-4), 82.2 (C-1), 142.2 (NCS), 169.2, and 170.6 (2CO). Mass spectrum: *m/z* 353, 351 (1, M^+), 295, 293 (90, M^+-NCS$^\cdot$), 272 (3, M^+-HBr), 251, 249 (7, M^+-AcOH), 235, 233 (18), 213 (28, 295, 293-HBr), 185 (25), 175, 173 (35), 153 (55), 111 (100), 81, 79 (10, Br^+), 60 (40), and 58 (10, NCS^+); Found: M^+ 352.9788, 350.9855.

When **4** and **5** were prepared **2** (4%), **3** (2%) were also isolated and certain polybromoisothiocyanates (m.s.) were detected.

3,4,6-Tri-O-acetyl-2-deoxy-α and *β-*D-*lyxohexopyransyl isothiocyanates* (**6** and **7**).- 2-Deoxy-D-galactose (0.26 g, 0.8 mmol) was conventionally acetylated with acetic anhydride:pyridine 1:1 (2.8 mL) to give a 1:1 mixture of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-α and *β-*D-*lyxo*hexopyranose (0.5 g, 1.5 mmol). This mixture was dissolved in dry toluene (15 mL) and bromotrimethylsilane (0.49 mL, 3.75 mmol) was added. The resulting solution was kept at r.t. for 15 min and then silver isothiocyanate (1.0 g, 6.0 mmol) was added and heated under reflux for 2 hours, filtered trough celite and evaporated to dryness. Column chromatography (ether:hexane 1:2, 1:1) of the residue afforded **6** and **7** as pale yellow hygroscopic syrups, and a colourless syrup whose spectroscopic data were indicative of the structure **14**.

3,4,6-Tri-*O*-acetyl-2-deoxy-α-D-*lyxo*hexopyranosyl isothiocyanate (**6**); yield 0.120 g (23%); $[\alpha]_D^{20}$ +129°, $[\alpha]_{546}^{20}$ +150° (*c* 1,0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 251 nm; ν_{max} 2041 (NCS), 1748 (CO), and 1233 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 2.01 (s, 3H, Ac), 2.06 (m, 1H, H-2eq), 2.07, 2.13 (2s, each 3H, 2Ac), 2.25 (ddd, 1H, $J_{1,2ax}$= 4.2, $J_{2ax,3}$= 11.4, $J_{2ax,2eq}$= 12.7 Hz, H-2ax), 4.08 (dd, 1H, $J_{5,6'}$= 7.1, $J_{6,6'}$= 11.8 Hz, H-6'), 4.12 (dd, 1H, $J_{5,6}$= 5.6 Hz, H-6), 4.28 (ddd, 1H, $J_{4,5}$= 0.7 Hz, H-5), 5.26 (ddd, 1H, $J_{2eq,3}$= 4.9, $J_{3,4}$= 2.9 Hz, H-3), 5.38 (dd, 1H, H-4), and 5.79 (dd, 1H, $J_{1,2eq}$= 1.5 Hz, H-1). ^{13}C, δ 20.5 (1C, CH_3), 20.6 (2C, CH_3), 30.8 (C-2), 61.7 (C-6), 65.4, 65.8 (C-3, 4), 69.8 (C-5), 82.6 (C-1), 141.0 (NCS), 169.7, 169.9, and 170.3 (3CO). Mass spectrum: *m/z* 273 (20, M^+-NCS), 213

(20, 273-AcOH), 153 (22), 139 (30), 128 (5), 111 (60), 97 (100), 60 (20), 59 (19), and 58 (5, NCS^+); Found: M^+-NCS· 273.0969. $C_{12}H_{17}O_7$ requires 273.0974. This compound was analysed as thiourea derivative **10**.

3,4,6-Tri-*O*-acetyl-2-deoxy-β-D-*lyxo*hexopyranosyl isothiocyanate (7); yield 0.130 g (25%); $[\alpha]_D^{20}$ +25°, $[\alpha]_{546}^{20}$ +30° (c 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 254 nm; ν_{max} 2035 (NCS), 1748 (CO), and 1236 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 2.01, 2.07, 2.17 (3s, each 3H, 3Ac), 2.06-2.28 (m, 2H, H-2, 2′), 3.85 (td, 1H, $J_{5,6} = J_{5,6'} = 6.5$, $J_{4,5} = 1.0$ Hz, H-5), 4.10-4.21 (m, 2H, H-6, 6′), 4.96 (m, 1H, H-3), 4.98 (m, 1H, H-1), and 5.26 (dd, 1H, $J_{3,4} = 3.2$ Hz, H-4). ^{13}C, δ 20.5 (3C, $3CH_3$), 33.0 (C-2), 61.6 (C-6), 64.7 (C-3), 67.5 (C-4), 72.9 (C-5), 81.6 (C-1), 141.4 (NCS), 169.6, 169.9, and 170.2 (3CO). Mass spectrum: *m/z* 273 (20, M^+-NCS·), 213 (20, 273-AcOH), 153 (22), 139 (35), 128 (5), 111 (50), 97 (100), 60 (10), 59 (12), and 58 (4, NCS^+); Found: M^+-NCS· 273.0970. $C_{12}H_{17}O_7$ requires 273.0974.

3-Acetoxy-2-acetoxymethyl-2*H*-pyran (**14**); yield 0.03 g (10%); ν_{max} 1748 (CO), 1650 (C=C), and 1240 (C-O-C). ^{1}H-N.m.r.: δ 2.07, 2.10 (2s, each 3H, 2Ac), 4.43 (dd, 1H, $J_{CH',2} = 7.1$, $^2J_{H,H'} = 11.8$ Hz, HCH′-OAc), 4.48 (dd, 1H, $J_{CH,2} = 5.1$ Hz, HCH′-OAc), 6.10 (dd, 1H, H-2), 6.35 (dd, 1H, $J_{5,6} = 1.9$, $J_{4,5} = 3.5$ Hz, H-5), 6.39 (dd, 1H, $J_{4,6} = 0.8$ Hz, H-4), and 7.40 (dd, 1H, H-6). ^{13}C, δ 20.6, 20.8 ($2CH_3$), 63.2 (CH_2Ac), 66.1 (C-2), 109.4, 110.3 (C-4,5), 142.9 (C-6), 149.1 (C-3), 169.9 and 170.4 (2CO). Mass spectrum: *m/z* 211 (1, M^+-1), 185 (5, M^+-1-C_2H_2), 152 (3, M^+-AcOH, 145 (12, Ac_2O^+), 139 (3, M^+-$AcOCH_2$·), 103 (20, Ac_2OH^+), 60 (90, $AcOH^+$), 43 (100, Ac^+). Found: M^+ 212.0696. $C_{10}H_{12}O_5$ requires M, 212.0685.

N-*Phenacyl*-N′-[*3,4,6-tri-O-acetyl-2-deoxy-α* and *β*-D-arabino(lyxo)-*hexopyranosyl*]*thioureas* (**8-11**) and N-*acetylmethyl*-N′-(*3,4,6-tri-O-acetyl-2-deoxy-α*-D-*arabinohexopyranosyl*)*thiourea* (**12**).- Solutions of phenacylamine hydrochloride or aminoacetone hydrochloride (0.43 mmol) in water (2 - 4 mL) were neutralised with sodium hydrogencarbonate (36 mg, 0.43 mmol) and gradually added to a solution of the corresponding isothiocyanate (0.36 mmol for **8-11**, 0.43 mmol for **12**) in acetone (2.5-4.0 mL) under nitrogen. The resulting solutions were stirred at r.t. for 30 min (**8-11**) or 90 min (**12**). The residues obtained after evaporation were

purified by column chromatography (ether-hexane 2:1 for **8**-**11**, ether-hexane 6:1 and ethyl acetate-hexane 2:1 for **12**) to give the following compounds.

N-Phenacyl-*N'*-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*hexopyranosyl)-thiorea (**8**); was an amorphous and hygroscopic solid (140 mg, 83%); $[\alpha]_D^{24}$ +100°, $[\alpha]_{546}^{24}$ +116° (*c* 1.0, dichloromethane), $\lambda_{max}^{CH_2Cl_2}$ 249 and 254 nm; ν_{max} 3320 (NH), 1746 (CO ester), 1692 (CO ketone), and 1235 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 2.04 (s, 3H, Ac), 2.05 (s, 6H, 2Ac), 2.13 (ddd, 1H, $J_{2eq,1}$ = 3.1, $J_{2eq,3}$ = 5.2, $J_{2eq,2ax}$ = 13.0 Hz, H-2eq), 2.38 (dd, 1H, $J_{2ax,3}$ = 7.2 Hz, H-2ax), 4.06-4.25 (m, 2H, H-5,6'), 4.46 (dd, 1H, $J_{5,6}$ = 4.5, $J_{6,6'}$ = 12.5 Hz, H-6), 4.97 (dd, 1H, $^2J_{H,H'}$ = 20.0, $J_{H',NH}$ = 4.0 Hz, CH<u>H</u>'), 5.09 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, H-4), 5.20 (ddd, 1H, H-3), 5.28 (dd, 1H, $J_{H,NH}$ = 5.0 Hz, C<u>H</u>H'), 5.57 (bt, 1H, $J_{1,N'H}$ = 3.1 Hz, H-1), 7.26-8.10 (several m, 5H, Ph), 7.31 (d, 1H, N'H), and 8.15 (dd, 1H, NH). ^{13}C, δ 20.6, 20.7, 20.8 ($3CH_3$), 33.3 (C-2), 52.4 (CH_2), 61.8 (C-6), 68.3, 68.4, 68.6 (C-3,4,5), 79.0 (C-1), 127.9 (2C, C-2,6 of Ph), 128.9 (2C, C-3,5 of Ph), 133.9 (C-1 of Ph), 134.2 (C-4 of Ph), 169.6, 170.1, 170.6 (3CO ester), 183.3 (CS), and 193.2 (CO ketone). Mass spectrum: *m/z* 466 (1, $M^{+\cdot}$), 407 (3, $M^{+\cdot}$-AcO$^\cdot$), 388 (3, $M^{+\cdot}$-C_6H_6), 347 (5, $M^{+\cdot}$-CH_2COPh), 213 (53), 176 (45), 153 (45), 111 (90), 105 (95, $PhCO^+$), 97 (70), 77 (82, Ph^+), 60 (100, $AcOH^+$), and 45 (80). Found: M^+ 466.1299. $C_{21}H_{26}O_8N_2S$ requires M 466.1409.

N-Phenacyl-*N'*-(3,4,6-tri-*O*-acetyl-2-deoxy-β-D-*arabino*hexopyranosyl)-thiourea (**9**); was an amorphous and hygroscopic solid (141 mg, 83%); $[\alpha]_D^{24}$ -115°, $[\alpha]_{546}^{24}$ -91° (*c* 0.8, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 250 nm; ν_{max} 3335 (NH), 1746 (CO ester), 1694 (CO ketone), and 1233 (C-O-C). ^{1}H-N.m.r.: δ 1.85-2.20 (m, 2H, H-2ax,2eq), 2.06, 2.09, 2.12 (3s, each 3H, 3Ac), 3.88 (m, 1H, H-5), 4.24 (dd, 1H, $J_{5,6'}$ = 2.2, $J_{6,6'}$ = 12.6 Hz, H-6'), 4.37 (dd, 1H, $J_{5,6}$ = 4.7 Hz, H-6), 4.86-5.56 (m, 5H, H-1,3,4 and CH_2), 6.84 (d, 1H, $J_{1,NH}$ = 6.3 Hz), 7.46-8.00 (m, 5H, Ph), and 8.03 (m, 1H, NH). ^{13}C, δ 21.1 (2C, $2CH_3$), 21.3 (CH_3), 35.5 (C-2), 52.3 (CH_2), 62.5 (C-6), 66.4, 71.0, 73.8 (C-3,4,5), 80.7 (C-1), 128.4 (2C, C-2,6 of Ph), 129.3 (2C, C-3,5 of Ph), 134.4 (C-1 of Ph), 134.7 (C-4 of Ph), 170.4, 170.6, 171.3 (3CO ester), 183.1 (CS), and 193.2 (CO ketone). Mass spectrum: *m/z* 388 (1, $M^{+\cdot}$-C_6H_6), 213 (2), 153 (30), 111 (90), 105 (18, $PhCO^+$), 97 (35), 77 (10, Ph^+), 60 (100, $AcOH^+$), and 45 (90). Found: $M^{+\cdot}$-C_6H_6 388.0930. $C_{15}H_{20}O_8N_2S$ requires 388.0941.

N-Phenacyl-*N'*-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*lyxo*hexopyranosyl)-thiourea (10); crystallised from ethanol (103 mg, 61%) had m.p. 148-150°C; $[\alpha]_D^{25}$ +133°, $[\alpha]_{546}^{25}$ +142° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 248 nm; ν_{max} 3304 (NH), 1744 (CO, ester), 1690 (CO ketone), and 1239 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 1.94, 1.98 (2s, each 3H, 2Ac), 1.99 (m, 1H, H-2eq), 2.05 (s, 3H, Ac), 2.34 (dt, 1H, $J_{2ax,3} = J_{2ax,2eq} = 11.5$, $J_{1,2ax} = 6.3$ Hz, H-2ax), 4.17-4.36 (m, 3H, H-5,6,6'), 5.01 (dd, 1H, $J_{H',NH} = 4.0$, $J_{H,H'} = 20.0$ Hz, CHH'), 5.22 (dd, 1H, $J_{H,NH} = 4.2$ Hz, CHH'), 5.24-5.39 (m, 2H, H-3,4), 5.62 (dd, $J_{1,N'H} = 3.2$), 7.23 (d, 1H, N'H), 7.46-8.05 (m, 5H, Ph), and 8.24 (dd, 1H, NH). ^{13}C δ 20.5, 20.6, 20.7 ($3CH_3$), 28.6 (C-2), 52.5 (CH_2), 62.0 (C-6), 67.5 (C-5), 65.4, 65.9 (C-3,4), 79.6 (C-1), 127.9 (2C, C-2,6 of Ph), 128.9 (2C, C-3,5 of Ph), 133.9 (C-1 of Ph), 134.2 (C-4 of Ph), 169.8, 170.0, 170.4 (3CO ester), 183.4 (CS) and 193.2 (CO ketone). Mass spectrum *m/z* 388 (15, M^+-C_6H_6), 347 (1, M^+-CH_2COPh), 213 (10), 176 (10), 153 (22), 111 (32), 105 (85, $PhCO^+$), 97 (80), 77 (55, Ph^+), 60 (100, $AcOH^+$), and 45 (95). *Anal* Calcd for $C_{21}H_{26}O_8N_2S$: C, 54.07; H, 5.57; N, 6.00. Found: C, 53.77; H, 5.79; N, 6.29.

N-Phenacyl-*N'*-(3,4,6-tri-*O*-acetyl-2-deoxy-β-D-*lyxo*hexopyranosyl)-thiourea (11); was an amorphous and hygroscopic solid (90 mg, 53%); $[\alpha]_D^{24}$ +24°; $[\alpha]_{546}^{24}$ +28° (*c* 0.9, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 247 and 254 nm; ν_{max} 3355 (NH), 1744 (CO ester), 1694 (CO ketone) and 1235 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 1.88-2.23 (m, 2H, H-2ax,2eq), 2.02, 2.08, 2.16 (3s, each 3H, 3Ac), 4.02-4.32 (m, 3H, H-5,6,6'), 5.03 (dd, 1H, $J_{H',NH} = 5.1$, $^2J_{H,H'} = 20.5$ Hz, CHH'), 5.09 (m, 1H, H-3), 5.15 (dd, 1H, $J_{H,NH} = 4.8$ Hz, CHH'), 5.29 (m, 1H, H-1), 5.36 (dd, $J_{3,4} = 2.5$, $J_{4,5} = 0.5$ Hz, H-4), 6.97 (d, 1H, $J_{1,N'H} = 6.4$ Hz, N'H), 7.45-8.04 (several m, 5H, Ph), and 7.70 (m, 1H, NH). ^{13}C δ 20.5, 20.6, 20.7 ($3CH_3$), 29.6 (C-2), 52.1 (CH_2), 62.0 (C-6), 65.2 (C-4), 68.2 (C-3), 72.5 (C-5), 80.4 (C-1), 127.9 (2C, C-2,6 of Ph), 128.9 (2C, C-3,5 of Ph), 133.8 (C-1 of Ph), 134.3 (C-4 of Ph), 169.8, 170.1, 170.6 (3CO ester), 182.3 (CS), and 193.4 (CO ketone). Mass spectrum: *m/z* 466 (1, M^+), 407 (1, M^+-AcO·), 388 (15, M^+-C_6H_6), 347 (1, M^+-CH_2COPh), 213 (15), 176 (17), 153 (20), 111 (45), 105 (60, $PhCO^+$), 97 (100), 77 (37, Ph^+), 60 (90, $AcOH^+$), and 45 (82). Found: M^+ 466.1450. $C_{21}H_{26}O_8N_2S$ requires M 466.1410.

N-Acetylmethyl-*N'*-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-

hexopyranosyl)thiourea (**12**); was a colourless syrup (79 mg, 46%); $[\alpha]_D^{24}$ +105°, $[\alpha]_{546}^{24}$ +127° (*c* 0.8, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 244, 258, and 266 nm; ν_{max} 3338 (NH), 1743 (CO ester), 1728 (CO ketone), and 1233 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 2.04, 2.05, 2.06 (3s, each 3H, 3Ac), 2.24 (s, 3H, CH_3 ketone), 2.08 (ddd, 1H, $J_{1,2eq}$ = 0.8, $J_{2eq,3}$ = 4.6, $J_{2eq,2ax}$ = 13.4 Hz, H-2eq), 2.33 (ddd, 1H, $J_{1,2ax}$ = 3.4, $J_{2ax,3}$ = 9.1 Hz, H-2ax), 4.00-4.18 (m, 2H, H-5,6'), 4.40-4.48 (m, 2H, H-6',CHH'), 4.70 (dd, 1H, $J_{H,NH}$ = 4.5, $^2J_{H,H'}$ = 20.0 Hz, CHH'), 5.07 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, H-4), 5.29 (ddd, 1H, H-3), 5.53 (m, 1H, H-1), 7.05 (bs, 1H, N'H), and 7.80 (t, 1H, $J_{H',NH}$ = 4.5 Hz, NH). ^{13}C, δ 20.4 (2C, $2CH_3$), 20.7 (CH_3), 27.0 (CH_3 ketone), 33.0 (C-2), 55.2 (CH_2), 61.5 (C-6), 68.2, 68.3, and 68.4 (C-3,4,5), 78.6 (C-1), 169.5, 170.0, 170.4 (3CO ester), 182.9 (CS), and 202.2 (CO ketone). Mass spectrum: *m/z* 404 (2, M^+), 386 (M^+-H_2O), 371 (1), 326 (8), 213 (13), 153 (20), 139 (12), 114 (45), 111 (60), 97 (50), 81 (18), 73 (20), and 60 (100). Found: M^+ 404.1154. $C_{16}H_{24}O_8N_2S$ requires M 404.1253.

*5-Methyl-1-(3',4',6'-tri-O-acetyl-2'-deoxy-α-*D*-arabinohexopyranosyl)-4-imidazoline-2-thione* (**13**).- To a solution of **12** (75 mg, 0.19 mmol) in dry methanol (5 mL) a catalytic amount of acetic anhydride was added. The resulting solution was heated at 50°C for 2 hours and then concentrated to dryness. Ethanol (5 mL) was evaporated several times from the residue until the acetic anhydride was removed. Compound **13** (71 mg, 100%) was a colourless syrup; $[\alpha]_D^{20}$ +21°, $[\alpha]_{546}^{20}$ +25° (*c* 1.0, dichloromethane); $\lambda_{max}^{CH_2Cl_2}$ 277 nm; ν_{max} 3318 (NH), 1746 (CO ester), 1628 (C=C imidazoline), and 1240 cm^{-1} (C-O-C). ^{1}H-N.m.r.: δ 2.10, 2.14, 2.21 (3s, each 3H, 3 Ac), 2.15 (m, 1H, H-2'eq), 2.34 (d, 3H, $J_{4,CH}$ = 1.2 Hz, Het-C$\underline{H}_3$), 2.48 (ddd, 1H, $J_{2'ax,3}$ = 3.9, $J_{1',2'ax}$ = 10.9, $J_{2'ax,2'eq}$ = 3.9 Hz, H-2'ax), 4.34-4.66 (m, 3H, H-5',6',6"), 4.88 (dd, 1H, $J_{4',5'}$ = 0.5, $J_{3',4'}$ = 3.8 Hz, H-4'), 5.22 (m, 1H, H-3'), 6.44 (q, 1H, H-4), 6.68 (dd, 1H, $J_{1',2'eq}$ = 2.8 Hz, H-1'), and 11.27 (bs, 1H, NH). ^{13}C, δ 11.21 (Het-$\underline{C}H_3$), 20.6, 20.7, 20.8 ($3CH_3$), 28.9 (C-2'), 60.5 (C-6'), 65.3, 67.2 (C-3',4'), 74.8 (C-5'), 75.9 (C-1'), 112.4 (C-4), 126.3 (C-5), 160.6 (C-2), 169.1 (2C, 2CO), and 170.5 (CO). Mass spectrum: *m/z* 386 (5, M^+), 353 (3, M^+-SH), 326 (18, M^+-AcOH), 28 (2), 266 (2), 213 (10), 153 (20), 139 (18), 111 (62), 97 (58), 81 (15) and 60 (18). Found: 386.1134. $C_{16}H_{22}O_7N_2S$ requires M, 386.1147.

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