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Condensation of 2-Amino-2-deoxysugars with Isothiocyanates. Synthesis of *cis*-1,2-Fused Glycopyrano Heterocycles.

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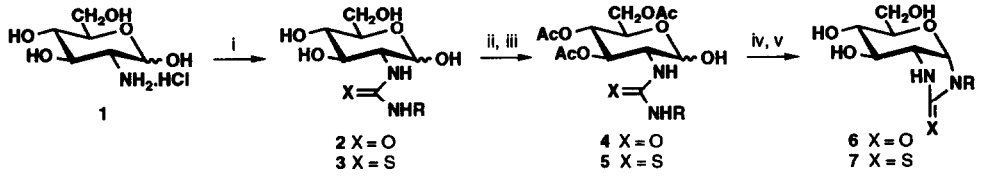
Abstract: The reactions of 2-amino- and 2-alkylamino-2-deoxyglycopyranoses with isothiocyanates gave thioureas and heterocyclic derivatives. Moreover, *cis*-fused glycopyrano[2,1-*d*]imidazolidin-2-thiones, which have a close structural analogy with some naturally-occurring glycosidase inhibitors, were synthesised for the first time. The mechanism of formation of glycofurano and glycopyrano[2,1-*d*]imidazolidin-2-thiones occurs *via* the intermediacy of monocyclic 5-hydroxyimidazolidin-2-thiones. These substances are generated by intramolecular nucleophilic addition of an NH group to the aldehyde function of the sugar. The monocyclic intermediates have been isolated and their participation in the formation of bicyclic imidazolidin-2-thiones and/or monocyclic imidazolin-2-thiones proved. In stark contrast, *cis*-fused glycopyranothiazolidines were prepared by nucleophilic displacements.

INTRODUCTION

The preparation of *cis*-1,2-fused glycopyrano heterocycles constitutes an important synthetic target, since many naturally-occurring compounds and related substances have that structural arrangement.[1] Recently, we have reported[2] the synthesis of *cis* fused glycopyrano[2,1-*d*]imidazolidin-2-ones (**6**) using the five-step sequence outlined in Scheme 1. The key step involves the intramolecular cyclisation of the anomerically deprotected ureido derivatives (**4**). The latter was prepared by regioselective deacetylation[3] of the per-*O*-acyl ureas, which are readily available from **1** by reaction with isocyanates and further conventional acetylation.



Scheme 1. *Reagents*: i, RNCX; ii, Ac_2O, C_5H_5N; iii, silica gel, MeOH; iv, AcOH; v, NH_3/MeOH.

The transformation of the ureas **2** into bicyclic imidazolidin-2-ones[2,4] has been the subject of a puzzling controversy for decades, and only now the mechanism has become visible, evidencing the participation of monocyclic structures of 5-hydroxyimidazolidin-2-ones as intermediates.[2,5] In this paper, we extend these strategies to the preparation of D-glucopyrano[2,1-*d*]imidazolidin-2-thiones (**7**) and D-glucopyrano[2,1-*d*]-2-iminothiazolidines, and novel alternative routes for the preparation of intermediates are described.

Although a similar behaviour to oxoanalogues can be expected, it is known that replacement of oxygen

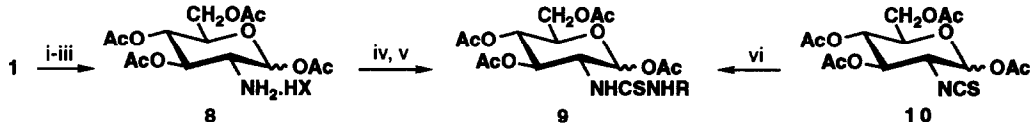
by sulphur in urea and related compounds often leads to significant changes in product type and reaction pathway, and so we decided to conduct a parallel investigation into the reactions of aminosugars with isothiocyanates.

RESULTS

Reaction of 2-amino-2-deoxyglycopyranoses with isothiocyanates.

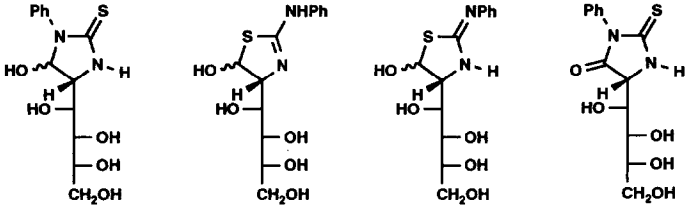
Similarly to isocyanates, numerous structures were assigned to the condensation products of **1** with aryl(alkyl) isothiocyanates in acidic media.[6-11] However, it has been demonstrated[12] that a *cis*-fused D-glucofurano[2,1-*d*]imidazolidin-2-thione was the correct structure in all cases.

The first and general synthesis described in the literature[11,13] of unprotected 2-deoxy-2-thioureido derivatives (**3**) involves deacetylation of the corresponding per-*O*-acetyl thioureas (**9**), which are accessible either by reaction of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride (**8**)[14] with isothiocyanates,[11,13,15] or by reaction of the isothiocyanate **10**[16] with alkyl(aryl)amines (Scheme 2).[17]

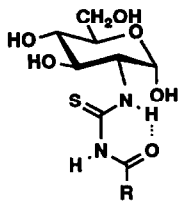


Scheme 2. *Reagents:* i, 4-$CH_3OC_6H_4CHO$, aq. NaOH; ii, Ac_2O, C_5H_5N; iii, aq. HCl, acetone; iv, aq. $NaHCO_3$, $CHCl_3$; v, RNCS; vi, RNH_2.

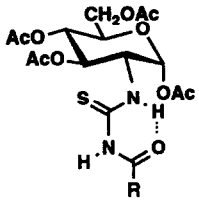
Likewise, several authors reported the preparation of thioureas **3** by direct condensation of **1** with alkyl,[8] aryl,[8,21] and acyl isothiocyanates.[22] No structural data, however, supporting unequivocally the structure **3** were given.[23] Remarkably, Scott[24a] proposed in 1962 a structure of thiolimidazole for the condensation product of **1** with phenyl isothiocyanate. Later, he retracted[24b,24c] this assignment and, based on spectroscopic data and electrophoretic analysis, proposed the 5-hydroxy-1-phenyl-4-(D-*arabino*-tetritol-1-yl)imidazolidin-2-thione **11**, ruling out a structure of 2-aminothiazoline **12** or its imino tautomer **13**. In addition, the reduction product of the phenylthiohydantoine **14**, presumably **11**, showed the same electrophoretic behaviour than that of **1** with phenyl isothiocyanate.[24b,25] Recently, a X-ray diffraction study[26] has confirmed the structure **11** assigned by Scott[24c] to the reaction product of **1** with phenyl isothiocyanate.



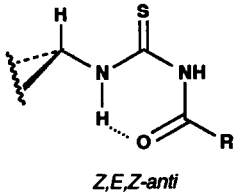
We have reinvestigated the reaction of 2-amino-2-deoxyaldoses with isothiocyanates searching for a shorter synthesis of per-*O*-acetyl glycopyranothioureas. Thus, the condensation of **1** with benzoyl or ethoxycarbonyl isothiocyanates gave the *N*-acylthioureas **15** and **16**, respectively. Their per-*O*-acetyl derivatives **17** and **18** were obtained by conventional acetylation.



15 R = Ph
16 R = OEt



17 R = Ph
18 R = OEt



Z,E,Z-anti

19

Although spectroscopic data (Tables 1-3) quite agree with structures proposed by Krüger and Rudy,[22] two salient features should be mentioned. Firstly, acylthioureas **15-18** having α-anomeric configuration are exclusively obtained, as evidenced by the small $J_{1,2}$ values (~3.6 Hz) for **17** and **18** and $^1J_{C\text{-}1,H\text{-}1}$ values (~168 Hz for **15-16** and ~178 Hz for **17-18**). Similar couplings constants have been found for other derivatives of **1** with the same anomeric configuration.[27] Secondly, the downfield shift of the NH group at C-2 (δ_{NH}~11 ppm) suggests the presence of a strong intramolecular hydrogen bonding between that group and the carbonyl,[28] anchoring a (*Z,E,Z*)-conformation (**19**) for the acylthiourea moiety.

Table 1. ^{13}C-NMR chemical shifts[a] (ppm) for **15-18**, **26**, and **27**.

Comp	C-1	C-2	C-3	C-4	C-5	C-6	C=S	C=O[g]	Alkyl	Aromatic
15[b,e]	89.14	59.95	70.86[c]	70.76[c]	72.37	60.90	180.58	168.54		133.18, 132.2, 128.57
16[b,f]	89.42	59.76	71.01[c]	70.86[c]	72.49	61.11	179.91	153.87	62.13, 14.40	
17[d]	89.38	56.29	67.40	69.69	70.50	61.36	181.39	166.76		133.67, 131.22, 128.97, 127.58
18[d]	89.54	56.06	67.36	69.70	70.50	61.37	180.53	152.41	62.96, 14.02	
26[d]	89.99	55.65	70.43	66.91	69.40	61.20	180.57			135.40, 129.80, 127.49, 125.27
27[d]	92.32	57.54	72.44[c]	67.70	72.34[c]	61.58	181.40			135.70, 129.78, 127.22, 125.01

[a] At 50.33 MHz. [b] In DMSO-d_6. [c] These signals could be interchanged. [d] In $CDCl_3$. [e] $^1J_{C1,H1}$167.6 Hz; $^1J_{C2,H2}$139.2 Hz; $^1J_{C3,H3}$146.5 Hz; $^1J_{C4,H4}$137.9 Hz; $^1J_{C5,H5}$137.9 Hz; $^1J_{C6,H6}$139.8 Hz. [f] $^1J_{C1,H1}$178.5 Hz; [g] Signals for acetoxy groups have been omitted.

Table 2. ^{1}H-NMR chemical shifts[a] (ppm) for **17**, **18**, **26**, and **27**.

Comp	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	C_2NH	RNH	Alkyl	Aryl
17	6.42d	5.16m	5.51t	5.27t	4.09m	4.33dd	4.09m	10.92d	9.19s		7.87-7.47m
18	6.35d	5.12m	5.44t	5.26t	4.08m	4.32dd	4.08m	9.82d	8.29s	4.23q, 1.31t	
26	6.31d	—— 5.25-5.13m ——			3.96m	4.25dd	4.05dd	6.04d	8.84s		7.49-7.16m
27	5.74d	—— 5.28-5.09m ——			3.81m	4.23dd	4.10dd	6.38d	8.66s		7.44-7.13m

[a] At 200.13 MHz in $CDCl_3$.

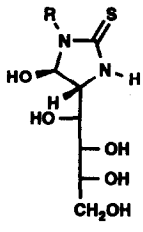
Table 3. ^{1}H-NMR coupling constants[a] (Hz) for **17**, **18**, **26**, and **27**.

Comp	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{2,NH}$	J_{Et}
17	3.6	10.1	10.1	10.1	3.7	b	12.5	8.8	
18	3.6	9.9	10.0	9.8	4.0	b	12.6	8.8	7.0
26	3.2	b	b	9.5[c]	4.0	2.2	12.5	8.3	
27	7.8	b	b	b	4.2	2.0	12.4	8.3	

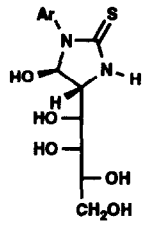
[a] At 200.13 MHz in $CDCl_3$. [b] Not observed. [c] After addition of $Eu(fod)_3$.

By contrast, the reaction of **1** with several aryl isothiocyanates in aqueous medium led invariably to the corresponding 1-aryl-5-hydroxy-4-(D-*arabino*-tetritol-1-yl)imidazolidin-2-thiones (**20-23**). Analogously, reactions of 2-amino-2-deoxy-D-galactopyranose and 2-amino-2-deoxy-β-D-*glycero*-L-*gluco*-heptopyranose[28] with 1-naphthyl isothiocyanate gave **24** and **25**, respectively.

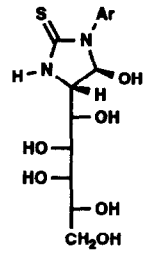
The deacetylation of **9** for the preparation of unprotected thioureido derivatives **3**, using ammonia in methanol as described by Morel[11] and Geigy[13] was unpractical. In this polar and basic medium **3** was initially formed, but it is not stable and rapidly cyclises to the corresponding 5-hydroxyimidazolidin-2-thione. Thus, monocycle **20** was obtained from **26** and **27** and monocycles **21** and **30** were isolated from **28**[18] and **29**,[19] respectively. Compounds **20-25** and **30** are *N*-substituted thioanalogues of the antibiotic CV-1,[29] which are easily available by these two synthetic routes. Thiourea **26** was prepared following the procedure described[18] for analogous thioureas and **27** according to Scheme 2.



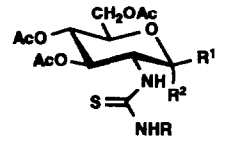
20 R = Ph
21 R = 4-MeOC$_6$H$_4$
22 R = 4-BrC$_6$H$_4$
23 R = 1-C$_{10}$H$_7$
30 R = CH$_3$



24 Ar = 1-C$_{10}$H$_7$

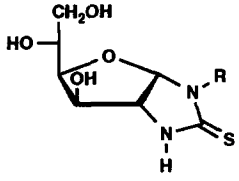


25 Ar = 1-C$_{10}$H$_7$

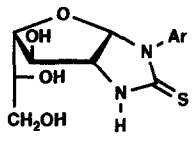


26 R = Ph, R^1 = H, R^2 = OAc
27 R = Ph, R^1 = OAc, R^2 = H
28 R = 4-MeOC$_6$H$_4$, R^1 = H, R^2 = OAc
29 R = CH$_3$, R^1 = H, R^2 = OAc

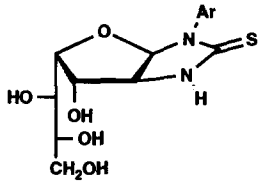
1-Aryl-(1,2-dideoxy-glycofurano)[2,1-*d*]imidazolidin-2-thiones **31-36** were prepared in high yields by treating the corresponding monocyclic imidazolidin-2-thiones **20-25** with dilute acetic acid. The analogous cyclisation of **30** afforded a mixture of **37** and **38**. Interestingly, compound **16** could not be transformed into a monocyclic imidazolidin-2-thione in basic medium, or into a bicyclic imidazolidin-2-thione in acid medium. No intermediates were detected during the transformation of **20-25** and **30** into bicycles **31-37** as revealed their conversion in DMSO-d_6 by NMR monitoring.



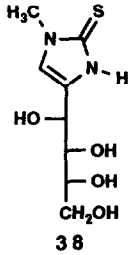
31 R = Ph
32 R = 4-MeOC$_6$H$_4$
33 R = 4-BrC$_6$H$_4$
34 R = 1-C$_{10}$H$_7$
37 R = CH$_3$



35 Ar = 1-C$_{10}$H$_7$



36 Ar = 1-C$_{10}$H$_7$



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Analogous furanoid bicyclic structures were also formed in the reaction of 2-alkylamino-2-deoxyaldoses with isothiocyanates.[30] The small $J_{2,3}$ values (~0 Hz) discard a pyranoid structure for **31-37**. Structures of

compounds **31**,[12e,12f] **33**,[12d] and **37**[12c] have been determined by X-ray diffraction crystallography.[31]

Spectroscopic characterisation of isothiocyanate-aminosugar adducts.

Unlike compounds **15-18**, **26** and **27**, derivatives **20-25** and **30-37** do not display in their IR spectra the characteristic NH absorption at ~1530 cm^{-1}, which is absent from cyclic systems.[2] The C-1* configuration assigned to **20-22** and **30** is in accord with the small $J_{1,2}$ values (<2 Hz).[2,5] In these cases, the disposition between H-1 and H-2 is *trans*. In some cases, the *cis* isomer could be detected in the ^1H NMR spectra in very low concentration. However, the chemical shift of C-1 (~90 ppm) for **20-22** is within the range showed for the C-1 of a 2-deoxy-2-thioureidoglycopyranose as **15-18**, **26** and **27**, and therefore that assignment does not diagnose a monocyclic structure, contrarily to the oxygen counterparts.[2,5] The almost identical shifts of C-3, C-4, and C-5 (and C-6 for **25**) are in accord with the presence of an open polihydroxyalkyl chain[2,5] (Table 4). The signal at ~180 ppm, attributable to the C=S group, rules out an isomeric structure of 2-iminothiazolidine as **13**.

Table 4. ^{13}C-NMR chemical shifts[a] (ppm) for **20-25** and **30-38**.

Comp	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C=S	Alkyl
20	87.53	65.31	69.22	71.44	70.39	63.36		179.98	
21	87.69	65.30	69.24	71.47	70.42	63.38		180.45	55.41
22	87.34	65.36	69.25	71.48	70.39	63.37		179.79	
23a[b]	87.73	66.41	70.63	71.61	71.51	63.42		181.98	
23b[c]	89.89	65.89	69.46	71.25	70.22	e		181.50	
24a[b,f]	87.96	64.86	69.83	70.17	70.11	63.23		182.25	
24b[c]	90.72	64.37	e	e	e	62.85		e	
25a[b]	87.73	66.49	69.75	70.64	70.45	69.75	63.12	182.51	
25b[c]	89.92	65.93	e	70.11	e	e	63.12	181.93	
30	86.30	64.54	69.24	71.31	70.45	63.34		180.72	30.12
31	94.77	65.34	68.35	74.05	79.51	63.91		181.17	
32	94.68	65.18	68.19	74.02	79.22	63.83		181.52	55.33
33	94.39	65.26	68.16	73.76	79.50	63.73		180.77	
34a[b]	93.81	66.01	68.06	74.19	79.16	63.81		182.61	
34b[c]	96.82	66.01	68.36	73.76	80.14	63.90		182.61	
35a[b]	94.63	67.10	70.77	76.14	88.51	63.64		181.72	
35b[c]	97.05	67.88	70.46	76.14	86.42	63.01		181.72	
36a[b]	93.94	66.12[d]	66.29[d]	74.43	78.82	71.15	62.77	182.69	
36b[c]	96.90	66.12[d]	66.29[d]	73.97	79.39	71.15	62.50	182.98	
37	93.39	64.48	68.36	74.16	79.32	63.77		181.68	30.66
38	116.44	130.54	73.48	71.43	64.59	63.59		160.49	33.80

[a] At 50.33 MHz in DMSO-d_6. [b] Major conformer. [c] Minor conformer. [d] These signals could be interchanged. [e] Not observed. [f] $^1J_{C1,H1}$ 163.0; $^1J_{C2,H2}$ 153.6; $^1J_{C3,H3} = {}^1J_{C4,H4}$ 141.7; $^1J_{C5,H5}$ 144.0; $^1J_{C6,H6}$ 141.2 (^1J in Hz).

Compounds **23-25** show signal duplicity in their ^1H- and ^{13}C NMR spectra, indicating the presence of two products. Doublets attributed to H-1 (~5.60 and ~5.30 ppm, respectively, and $J_{1,2}$~ 0 Hz in both cases) were transformed in singlets by D_2O-exchange. This rules out an α,β anomeric mixture of 2-deoxy-2-(1-naphthylamino)-glycopyranose, or a mixture of epimers at C-1 having a structure of monocyclic imidazolidin-2-

*The original numbering of 2-[3-acyl(aryl)thioureido]-2-deoxysugars is maintained in the related monocyclic and bicyclic imidazolidin-2-thiones to clarify the exposition. The correct nomenclature is given in the Experimental.

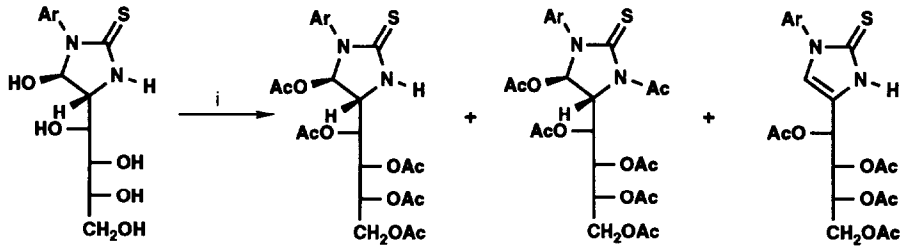
thione. The first case would be consistent[2] with coupling constants of ~3.5 (α-anomer) and ~8 Hz (β-anomer), and the second one[2,5] with ~0 (*trans*) and ~6 Hz (*cis*), which are quite different from experimental values. Furthermore, the chemical shifts for C-1 signals (~91 and ~87 ppm) agree with those expected for α-anomers, but not for β-anomers. The close resemblance in chemical shifts for duplicated absorptions in both ^{1}H- and ^{13}C-NMR spectra, along with their analogy with those of **20-22** suggest monocyclic structures of 5-hydroxyimidazolidin-2-thione with the same configuration (*R*) at C-1 ($J_{1,2}$~0 Hz).

A possible explanation could be encountered in a C-2 epimerisation.[2] However, the duplicity of signals might be also attributed to the presence of a pair of atropisomers, originated by the restricted rotation around the C(naphthyl)-N bond.[32] This latter hypothesis was further confirmed by preparing compounds **34-36** that also display signal duplicity in their NMR spectra.

Chemical characterisation of aminosugar-isothiocyanate adducts.

As previously noted the structure proposed by Scott[24c] for **20**, **23**, and **24**, has been recently confirmed[26] for **20** by X-ray diffraction analysis. However, spectroscopic data are insufficient to do unambiguous assignments. For this reason, we have studied their transformation into the corresponding per-*O*-acetyl derivatives in which the original structural arrangement can be preserved.

Thus, acetylation of **20** afforded a mixture of acetylated compounds **39-41**, whose ratio depends on the reaction temperature. At -35°, **39** is almost exclusively formed but at higher temperatures the ratio of **40** and **41** increases. All of them maintain the monocyclic structure and, **39** and **40** the stereochemistry (*R*, $J_{1,2}$ 0 Hz) of the heterocycle as well (Tables 5-7). Analogously, **42-44** were formed from **21**. Controlled acetylation of **23** at -15° mainly afforded **45**. On heating a solution of this compound in DMSO-d_6, a mild, fast, and complete transformation into **46** was observed by ^{1}H NMR monitoring.



20 Ar = Ph
21 Ar = 4-MeOC$_6$H$_4$
23 Ar = 1-C$_{10}$H$_7$

39 Ar = Ph
42 Ar = 4-MeOC$_6$H$_4$
45 Ar = 1-C$_{10}$H$_7$

40 Ar = Ph
43 Ar = 4-MeOC$_6$H$_4$

41 Ar = Ph
44 Ar = 4-MeOC$_6$H$_4$
46 Ar = 1-C$_{10}$H$_7$

Scheme 3. *Reagents*: i, Ac_2O, C_5H_5N.

The structure of imidazolin-2-thione in **41** was confirmed by unequivocal synthesis from **48**, that was prepared[8] by acid isomerisation of **31**. Similarly, **44** was obtained from **49**, which was synthesised[33] by condensation of fructosamine **47** with thiocyanate ion. Conventional acetylation of **48** with acetic anhydride in pyridine between -20° to +80° led almost exclusively to **41**. Nevertheless, acetylation of **49** gave a mixture of **44**[7] and **51** whose ratio changed with the temperature. At room temperature, equimolar amounts were obtained (**51/44** = 1.1), whereas at 80° **44** was prevalent. Recrystallisation from ethanol of the crude mixture of **44** and

Table 5. ^{1}H-NMR chemical shifts[a] (ppm) for **39-46** and **51**.

Comp	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	NH	Alkyl	Aryl	NAc
39	6.51s	3.96dd	5.50t	5.42dd	5.17m	4.28dd	4.13dd	7.14s		7.52-7.35m	
40	6.44s	4.93d	5.62dd	5.42dd	5.34m	4.32dd	4.11dd			7.51-7.33m	2.86s (3H)
41	6.90s		6.01d	5.55dd	5.23m	4.28dd	4.13dd	11.34s		7.59-7.40m	
42	6.45s	3.94d	5.47t	5.41dd	5.16m	4.27dd	4.13dd		3.81s	7.24d,6.92d	
43	6.39s	4.90d	5.60dd	5.42dd	5.36m	4.32dd	4.11dd		3.83s	7.24d,6.96d	2.85s (3H)
44	6.77s		6.05d	5.54dd	5.23m	4.26dd	4.14dd	11.22bs	3.81s	7.44d,7.04d	2.85s (3H)
45a[b]	6.42s	4.06d	5.63dd	5.34dd	5.09m	4.26dd	4.16dd	8.04bs		7.97-7.41m	
45b[c]	6.62d	4.08m	5.55dd	5.43dd	5.17m	e	4.14dd	7.29bs			
46[d]	7.16s		6.02d	5.56dd	5.25m	4.34dd	4.19dd	e		8.07-7.35m	
51	6.63d		6.58dd	5.62dd	5.29m	4.30dd	4.20dd		3.81s	7.49-7.02m	3.11s (3H)

[a] In $CDCl_3$ at 200.13 MHz and 293K unless otherwise indicated. [b] Major conformer. [c] Minor conformer. [d] In DMSO-d_6 at 350K. [e] Not observed.

Table 6. ^{1}H-NMR coupling constants[a] (Hz) for **39-46** and **51**.

Comp	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{1,3}$
39	0.0	3.4	3.4	7.8	3.1	4.7	12.5	
40	0.0	6.0	3.6	6.9	3.0	5.3	12.4	
41			4.1	7.8	2.9	4.9	12.5	
42	0.0	3.4	3.4	7.8	2.9	4.6	12.6	
43	0.0	6.1	3.7	6.9	3.0	5.4	12.3	
44			4.0	8.1	3.0	4.9	12.5	
45a[b]	0.0	7.4	3.2	7.9	2.9	4.2	12.6	
45b[c]	1.5	4.4	2.9	8.4	3.1	4.1	12.7	
46[d]			4.1	7.2	3.1	5.6	12.3	
51			2.2	9.3	2.5	4.9	12.5	1.1

[a] In $CDCl_3$ at 200.13 MHz and 293K unless otherwise indicated. [b] Major conformer. [c] Minor conformer. [d] In DMSO-d_6 at 350K.

Table 7. ^{13}C-NMR chemical shifts[a,b] (ppm) for **39-46**, **48**, and **51**.

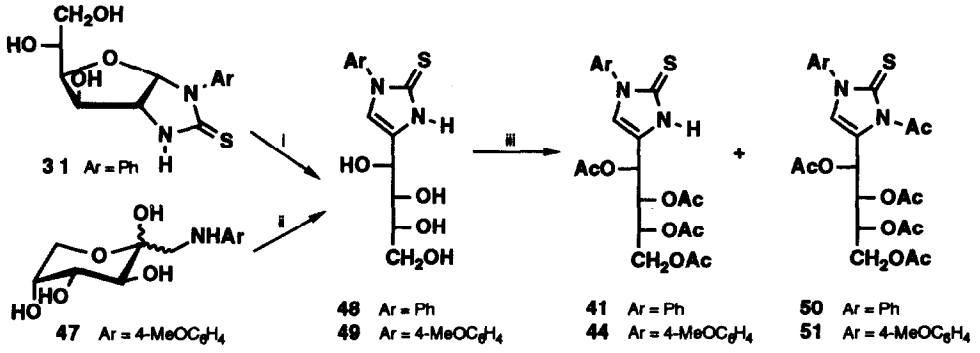
									Acetamide	
Comp	C-1	C-2	C-3	C-4	C-5	C-6	C=S	Alkyl	C=O	CH_3
39	89.45	61.71	69.86	69.32	68.44	61.27	184.20			
40	80.15	61.42	68.98	68.69	68.59	61.76	180.13		171.68	26.62
41	117.66	123.68	64.39	70.30	68.58	61.50	163.17			
42	88.78	61.40[c]	69.58	69.24	68.31	61.19[c]	184.46	55.24		
43	84.29	61.25	69.02[c]	68.68[c]	68.68[c]	61.76	180.49	55.41	171.70	26.61
44	118.46	123.05	64.49	70.11	68.37	61.47	163.36	55.68		
45a[d]	85.95	60.88	69.43	68.30	67.86	60.93	184.11			
45b[e]	89.39	61.50	68.96	68.30	68.14	61.15	184.25			
46a[d,f]	119.00	124.43	69.48	68.01	64.99	61.71	163.79			
46b[e,f]	119.20	124.07	70.13	68.19	64.99	61.71	164.13			
48[f]	115.96	131.60	73.11	71.18	64.40	63.49	160.99			
51	120.70	125.56	68.44	67.91	66.48	61.95	167.44	55.74	172.85	27.92

[a] At 50.33 MHz and 293K. [b] In $CDCl_3$ unless otherwise indicated. [c] These signals could be interchanged. [d] Major conformer. [e] Minor conformer. [f] In DMSO-d_6.

51 gave only **44**, probably by *N*-deacetylation of **51**.

Imidazolin-2-thiones **41**, **44**, and **51** were characterised by the olefinic resonances of C-1 and C-2 and the upfield shift of the C=S signal (~163 ppm) with respect to **39**, **40**, **42**, and **43**. The *N*-acetyl group in **40** and **43** induces a remarkable downfield shift of H-2 ($\Delta\delta$~1.0 ppm) and upfield shifts of C-1 ($\Delta\delta$~-5 to -9 ppm) and C=S ($\Delta\delta$~-4 ppm) when compared with **39** and **42**. An unusual deshielding of methyl signal of the acetamido group ($\Delta\delta$~0.8 ppm) is observed in **40**, **43**, and **51**, caused by its proximity to the heterocyclic C=S in the more stable *s-trans*-conformation. In this disposition the dipole-dipole repulsion between C=O and C=S groups is minimised. This suggestion is in agreement with the results obtained by theoretical calculations.[34]

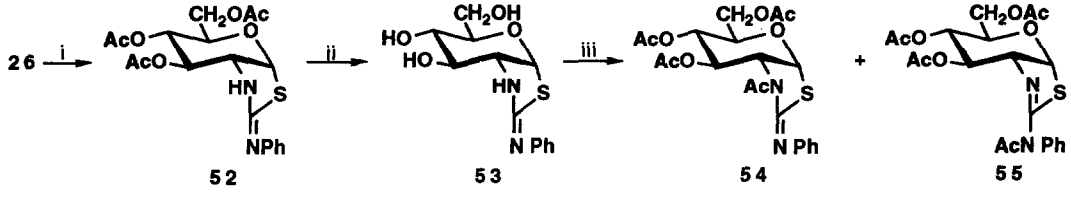
In conclusion, per-*O*-acetyl derivatives **39**, **42**, and **45** are ideal derivatives for the structural characterisation of monocycles **20-25** and **30**.



Scheme 4. *Reagents*: i, AcOH; ii, KSCN; iii, Ac_2O, C_5H_5N.

Synthesis of *cis*-1,2-fused glycopyrano heterocycles

Because of the direct condensation of isothiocyanates with 2-aminosugars is not a suitable way of access to per-*O*-acetyl thioureas, we have utilised the classical route depicted in Scheme 2. The treatment of these acetylated thioureas with tin(IV) chloride in dichloromethane leads to per-*O*-acetyl-D-glucopyrano[2,1-*d*]-2-iminothiazolidines, which can be deprotected with ammonia/methanol. Following this protocol **52** and **53** were prepared from **26**. These compounds lacked ^{13}C NMR signal for C=S (~180 ppm) but showed the characteristic[18] resonance of the 2-iminothiazolidine group at ~157 ppm (Table 10). The structure of **53** was confirmed by preparing its acetyl derivatives **54** and **55**, in which contraction of pyranoid ring did not take place (Scheme 5).

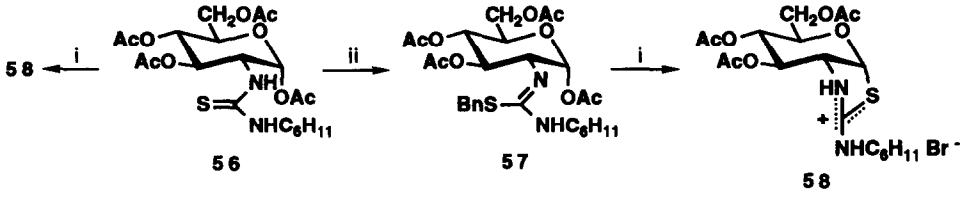


Scheme 5. *Reagents*: i, $SnCl_4$, CH_2Cl_2; ii, NH_3, MeOH; iii, Ac_2O, C_5H_5N.

^1H NMR spectra of **54** and **55** showed four signals for acetyl groups. Chemical shift of *N*-acetyl group

of **55** is indistinguishable from the acetate groups; however, in **54** it appears shifted to downfield (δ_{NAc}~2.5 ppm) with respect to the acetates. This difference could be explained analogously as in compounds **40**, **43**, and **51**. Furthermore, the differences in the *J* values of **54** and **55** are indicative of a large conformational change in the pyranoid rings due to the *exo* or *endo* localization of the *N*-acetyl group.

Likewise, the reaction of per-*O*-acetyl thioureas (*e.g.* **56**) with HBr/AcOH gave bicyclic iminothiazolidines as hydrobromides (*e.g.* **58**).[18] In order to avoid the participation of the sulphur atom in the cyclisation step, **56** was converted into benzylisothiourea **57**, but its further treatment with HBr/AcOH led again to **58** (Scheme 6).



Scheme 6. *Reagents*: i, HBr/AcOH; ii, $PhCH_2Cl$, $NaHCO_3$.

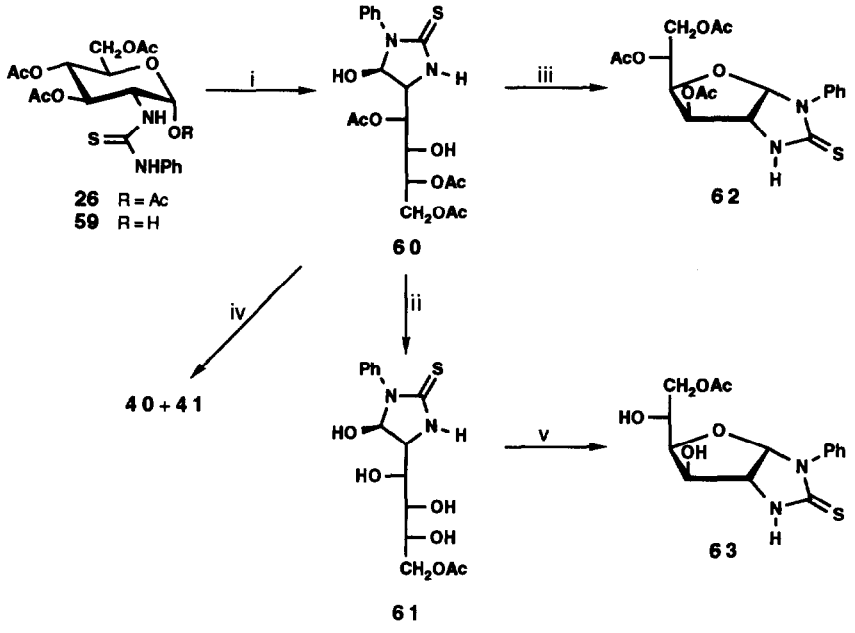
Our next target was the preparation of thioureas **5**, generated from **9** by selective deacetylation at the anomeric centre, as starting materials in the synthesis of D-glucopyrano[2,1-*d*]imidazolidin-2-thiones **7**. Anomeric deacetylation of **26** or **27** with sodium methoxide in methanol, according to the protocol of Micheel and Lengsfeld[35] for ureas, gave a complex mixture. The treatment with silica gel in methanol, reported by us,[3] was also unsuccessful. Compound **59** should be initially formed, but it rapidly decomposes. Silica gel-mediated deacetylation for one day led to the monocyclic imidazolidin-2-thione **60** in good yield; however, the prolonged reaction with silica gel for three days gave a very low yield of the monoacetyl derivative **61**.

Table 8. ^{1}H-NMR chemical shifts[a] (ppm) for **52**, **54**, **55**, **57**, **59-63**, and **66-69**.

Comp	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	C_2NH	Aryl	NAc	OH
52	6.21d	4.39m	5.46dd	4.97m	3.99m	—4.17m—		7.35s	7.33-7.00m		
54	6.13d	5.21dd	5.50dd	5.21t	4.23m	4.32dd	4.07dd		7.40-6.95m	2.54s (3H)	
55	6.06d	4.21m	5.30dd	4.84m	3.72m	4.14m			7.48-7.20m	1.98s (3H)	
57[b]	6.01bs	4.04m	5.33t	5.13t	4.04m	4.36dd	4.25dd	c	7.35-7.16m		
59[d]	6.46dd	4.94m	5.29t	5.17t	—4.20-4.10m—			6.37d	7.47-7.17m		3.97m
60	5.57bs	4.11m	5.25bs	4.09m	5.01d	4.39dd	4.28dd	7.54s	7.40-7.30m		
61[e]	5.47dd	—3.75-3.67m—		3.35m 3.45d[d]	3.71m	4.25dd	3.99dd	8.45s	7.49-7.24m		6.81d[f] 4.94d[g] 4.71d[h]
62	6.01d	4.37d	5.34d	4.42dd	5.28m	4.60dd	4.14dd	7.69s	7.45-7.34m		
63[e,i]	6.08d	4.36d	4.25d	3.83dd	c	—4.05d—		c	7.45-7.31m		c
66[c]	5.41dd	3.45m	5.25t	4.89t	—4.16m—		4.01m	8.46bs			7.79d
67	5.83d	4.19m	5.07t	4.99m	4.04m	—4.22-4.17m—		6.91bs	7.53-7.35m		
68	6.87s		6.18d	5.40dd	3.99m	—4.20-4.06m—		11.67bs	7.56-7.36m		c
						4.18dd[i]	4.10dd[i]				
69	6.95s		5.87d	4.16m	5.12m	4.45dd	4.36dd	11.07bs	7.57-7.37m		4.59d

[a] At 200.13 MHz in $CDCl_3$ unless otherwise indicated. [b] Alkyl group gave the following signals: 3.98s (2H) and 2.00-1.10m (11H). [c] Not observed. [d] The ArNH proton appeared at 8.24 ppm as singlet. [e] In DMSO-d_6. [f] C_1-OH. [g] C_3-OH and C_5-OH. [h] C_4-OH. [i] After addition of D_2O.

^1H and ^{13}C NMR spectra of **60** and **61** showed three and one acetate signals, respectively. The small values (≤2 Hz) of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ in **60** rule out the isomeric structure **59**. The absence of acetate group in C-4 of **60** is in accord with the chemical shift of H-4, which appears shifted to upfield ($\Delta\delta$~-1 ppm)[36] with respect to H-3 and H-5 signals of **60** and H-3, H-4, and H-5 signals of **39**. In addition, $\delta_{H\text{-}5}$ of **60** is similar to that of **39**.



Scheme 7. *Reagents*: i, silica gel, MeOH, 1 day; ii, silica gel, MeOH, 3 days; iii, Δ, *aq*. EtOH; iv, Ac_2O, C_5H_5N; v, AcOH, DMSO-d_6.

The monocyclic structure of **60** was confirmed by acetylation, which gave a mixture of **40** and **41**, and by cyclisation to **62** by heating in neutral or acid medium. The latter had identical physical and spectroscopic properties to those of an authentical sample.[12] The acetate location in **61** is in agreement with the presence of doublets for the three secondary hydroxyl groups. This compound was transformed into **63**, slowly in DMSO-d_6 and rapidly in the presence of acetic acid.

Anomerically deacetylated thioureido derivatives (*e.g.* **59**) could be prepared using the synthetic route outlined in Scheme 8. The key step was the condensation of isothiocyanates with the aminosugar **66**. This compound was synthesised by controlled *N*-deprotection of the enamine **65**, which was readily obtained in a one step from **64**[37] by acetylation with acetyl chloride and further hydrolysis of the glycosyl chloride formed,[38] or by anomeric deacetylation[3] of the per-*O*-acetyl derivative[37] of **64**.

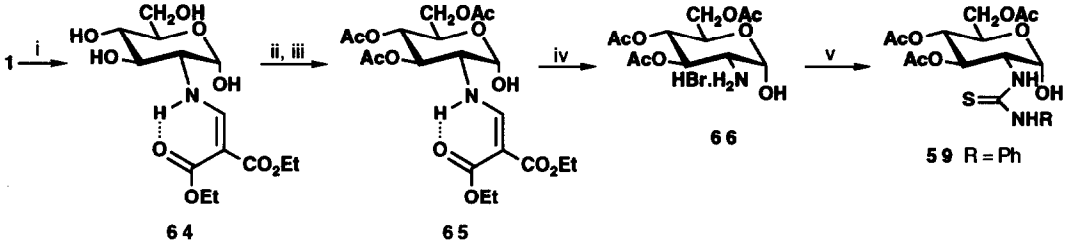
Compound **59** was transformed into **60** with silica gel-methanol for one day, thus confirming the intermediacy of the former in the direct synthesis of **60** from **26** (*vide supra*).

The α-anomeric configuration of compounds **59** and **66** is evidenced by the small $J_{1,2}$ values (~3.5 Hz) and the high rotatory powers.

Table 9. ^{1}H-NMR coupling constants[a] (Hz) for **52**, **54**, **55**, **57**, **59-63**, and **66-69**.

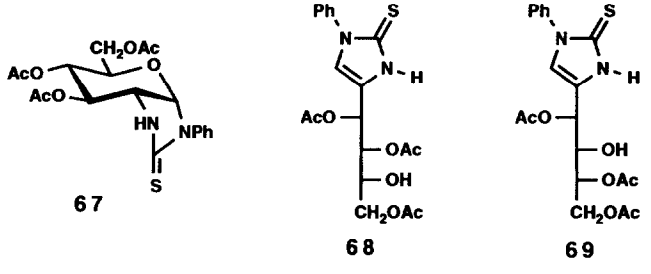
Comp	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{2,NH}$	$J_{2,4}$	$J_{H,OH}$
52	6.5	4.3	3.2	9.4	5.1	3.0			0.8	
54	6.4	8.7	9.8	9.8	4.6	1.7	12.2			
55	7.1	3.9	2.1	9.3	4.8	4.2	b		1.3	
57	b	10.5	10.5	10.5	3.4	3.8	12.3	b		
59	3.2	9.7	9.7	9.7	b	b	b	9.0		3.2
60	<1.0	<1.0	<1.0	8.6	2.1	4.3	12.0			
61[c]	1.6	b	b	8.5[d]	2.0	6.5	11.2			8.6[e], 8, 6.4[f]
62	6.5	0.0	2.9	9.5	2.2	4.8	12.4			
63[c,d]	6.5	0.0	2.0	8.0	b	b	b			b
66[c]	~3.0	9.7	9.7	9.7	b	3.7	13.5			4.3
67	7.9	3.1	3.1	9.1	6.2	3.0	b		0.8	
68			4.2	7.5	3.3[d]	4.6[d]	11.6[d]			b
69			1.9	9.2	2.4	4.2	12.8			7.7

[a]At 200.13 MHz in $CDCl_3$ unless otherwise indicated. [b]Not observed. [c]In DMSO-d_6. [d]After addition of D_2O. [e]C1-OH and C4-OH. [f]C3-OH and C5-OH.



Scheme 8. *Reagents*: i, $EtOCH=C(CO_2Et)_2$, Et_3N, MeOH; ii, CH_3COCl; iii, H_2O; iv, Br_2, H_2O, Cl_3CH; v, RNCS, C_5H_5N.

Finally, treatment of **59** with acetic acid gave the desired pyranoid bicycle **67** and the tri-*O*-acetylated imidazolin-2-thione **68**. NMR analyses of the crude mixture showed that the ratio of these compounds was largely dependent on the reaction medium. While in glacial acetic acid **68** was predominant, reaction in 50% aqueous acetic acid afforded **67** as the major product. Further separation of **68** by preparative TLC resulted in the acetate migration at C-4, and a mixture of **68** and **69** was isolated. This silica gel-mediated migration is analogous to that observed in **60** (Scheme 7). Isomeric structures **52** and **62** could not be detected.



These structures are in accord with their spectroscopic data. The *cis* fusion between the sugar ring and

the heterocycle in **67** was confirmed by the small $J_{2,3}$ and $J_{3,4}$ values (Table 9). Larger coupling constans (~9 Hz) should be expected for a *trans* fusion.[39,40] Compounds **68** and **69** were characterised by the chemical shifts of C=S group ($\delta_{C=S}$ ~160 ppm) and the olefinic carbons. The localisation of the free OH groups at C-5 of **68** and at C-4 of **69** is consistent with the chemical shift of their H-5 and H-4 protons, which showed upfield shifts ($|\Delta\delta|>1$ ppm) with respect to the corresponding protons in **41**.

Table 10. ^{13}C-NMR chemical shifts[a] (ppm) for **52-55**, **57**, **59-63**, and **66-69**.

									Acetamide	
Comp	C-1	C-2	C-3	C-4	C-5	C-6	C=S	C=N	C=O	CH_3
52	87.40	68.20	69.30[c]	71.70[c]	68.60[c]	63.30		157.30		
53[b]	87.40[d]	48.73	75.76[c]	74.12[c]	69.49[c]	61.41		154.76		
54	81.76	59.13	71.68	66.40	70.15	61.37		150.80[c]	170.55	25.52
55	86.61	70.18[c]	68.65[c]	68.33[c]	67.94[c]	63.22		158.81	171.01	24.31
57[e]	92.20	50.20	73.10	70.40	68.60	62.20		162.20		
59	90.90	57.44	70.79[c]	67.91[c]	67.49[c]	61.94	180.40			
60	88.96	62.69	70.18	69.83	69.52	64.63	181.56			
61[b]	87.34	66.54	70.20	68.69	68.53	65.16	179.92			
62	95.69	63.76	75.79	76.51	67.62	63.19	183.17			
63[b]	95.99	66.19[c]	75.03	79.86	66.36[c]	67.63	182.42			
66[b]	88.93	51.80	69.04	66.48	68.41	61.97				
67	87.71	54.15	70.80	68.01	67.79	63.15	183.67			
68	117.84	124.35	72.41[c]	67.57[c]	65.26[c]	64.50	162.17			
69	118.72	125.27	70.28[c]	69.75[c]	64.40[c]	62.53	161.72			

[a] At 50.33 MHz in $CDCl_3$ unless otherwise indicated. [b] In DMSO-d_6. [c] These signals could be interchanged. [d] Broad signals. [e] Alkyl group resonated at 37.30, 32.40, 25.70 and 24.60 ppm.

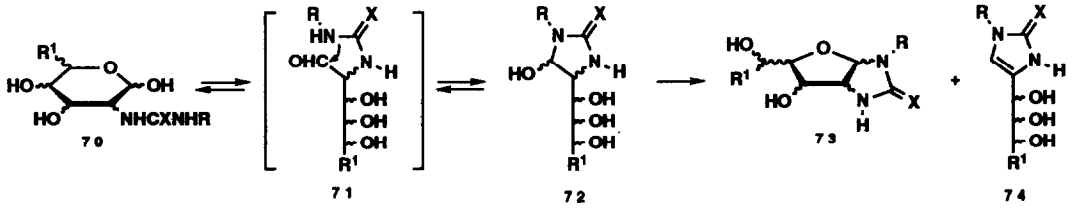
DISCUSSION.

The initial compounds formed in the reaction of 2-amino- and 2-alkylamino-2-deoxysugars with isothiocyanates at pH~7 are 2-deoxy-2-thioureido-glycopyranoses. However, these substances have only been isolated from acyl isothiocyanates, and thus thioureas **15** and **16** can be easily prepared. In contrast, aryl and alkyl isothiocyanates give more reactive thioureas that cyclise invariably to 5-hydroxyimidazolidin-2-thiones (**20-25** and **30**). The thiocarbonyl group has a higher single-bond character than the corresponding carbonyl group, and this fact reflects the greater nucleophilicity of NH group in thioureido derivatives. In stark contrast, *N*-acyl thioureas exhibit a diminished nucleophilicity owing to the electron-withdrawing acyl groups and acid or basic catalysis failed to transform these compounds into monocyclic or bicyclic derivatives.

Evidences supporting the intermediacy of thioureas in the formation of the aforementioned heterocycles was obtained by deacetylation of per-*O*-acetyl thioureas with ammonia in methanol. The transient aryl(alkyl)thioureas were too reactive and cyclised to heterocyclic derivatives (**20**, **21**, and **30**), which were the only products isolated. Consequently, the products described hitherto as thioureas[11,13] following that deacetylation procedure are indeed heterocyclic compounds.

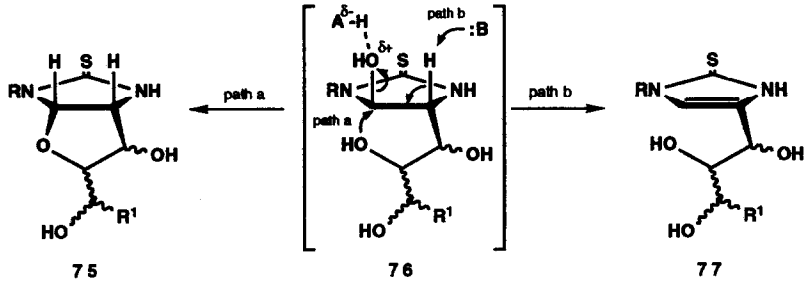
When aryl(alkyl) isothiocyanates were condensed with 2-amino-2-deoxysugars at pH<7, or monocycles (as **20-25** and **30**) treated with acids, glycofurano[2,1-*d*]imidazolidin-2-thiones (as **31-37**) and occasionally polyhydroxyalkyl imidazolin-2-thiones (as **38**) were formed. Similarly, 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-selones have been prepared[41] in good yield by reaction of **1** with aryl isoselenocyanates in acid medium, and their structure established by X-ray crystallography.[41,42]

These findings suggest that the mechanism follows a similar pathway to that of oxoanalogues;[2,5] that is, nucleophilic addition of NH in the thiourea or selenourea to the acyclic aldehyde **71**. The resulting monocycle **72** is converted, in acidic medium, into **73** and/or **74** (Scheme 9, X=S or Se).



Scheme 9

The formation of unsaturated monocycles such as **74** may be interpreted in terms of an alternative reaction in acid medium from monocycles **72**. These substances can undergo either an intramolecular cyclisation (path a) giving furanoid bicycles **75**, or an elimination (path b) affording imidazolin-2-thione derivatives **77** (Scheme 10). Compounds **75** can also be isomerised to **77**, though under more drastic conditions.[8,21,43] Compounds with both structures **75** and **77** have been isolated in reactions of 2-aminoaldoses with potassium cyanate,[44,45] potassium thiocyanate,[46] and cyanamide.[47]

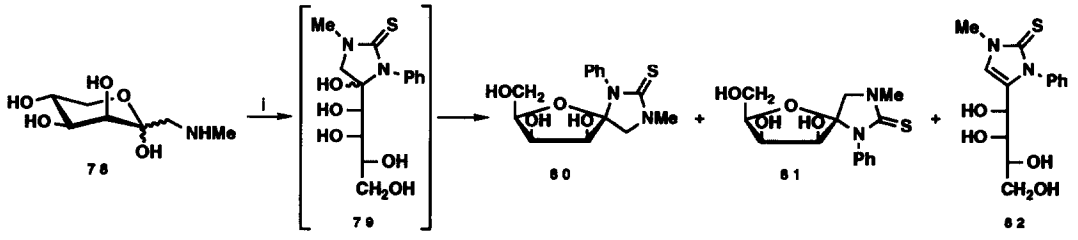


Scheme 10

Reaction of 2-ketoses and 1-amino-1-deoxy-2-ketoses with heterocumulenes likely involves a similar mechanism. Recently, spiranic compounds **80** and **81**, epimers at C-5, have been prepared by reaction of 1-deoxy-1-methylamino-D-*lyxo*-hexulose (**78**) with phenyl isothiocyanate[48] (Scheme 11). Their formation must proceed *via* the monocycle **79** that, under acid catalysis, undergoes an entropically favoured 5-*exo-tetragonal* cyclisation (kinetic control),[49] although the pyranoid isomers arising from a 6-*exo-tetragonal* cyclisation should be more stable compounds (thermodynamic control).

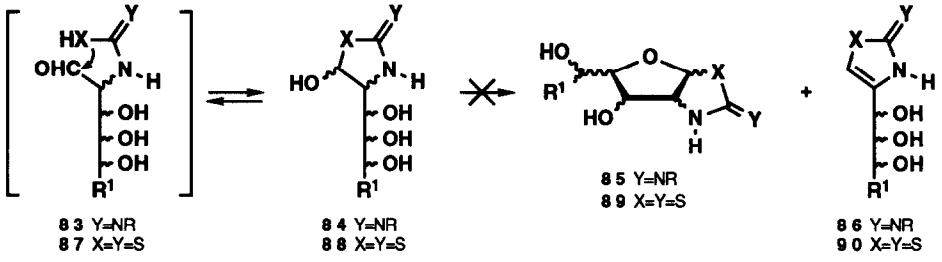
It is to be noted that reactions of 1-amino-1-deoxy-2-ketoses yield rarely spiranic products, but rather unsaturated monocycles as **82**. Typical examples are reactions of 1-amino-1-deoxy-2-ketoses with isocyanates,[33,50] isothiocyanates,[7, 33,51] or cyanamide.[52,53] Transition state **91** outlines the possible pathways leading to both structures, and explains the distinct behaviour of 2-amino-2-deoxyaldoses which produce preferably furanoid bicycles (**75**), opposite to 1-amino-1-deoxy-2-ketoses that give unsaturated monocycles (**77**) almost exclusively. Steric hindrance would disfavour the cyclisation to spirocompounds (as **80** or **81**) rather than the alternative elimination pathway. The former would be favoured if the reaction follows a S_N1

mechanism; but the mechanism S_N2 (path a), which has been suggested[2,5] for this type of reactions, would be very much reduced at a tetrasubstituted carbon. On the contrary, the elimination (path b) could always take place regardless of the stereochemistry of that carbon atom bearing the hydroxyl leaving group.



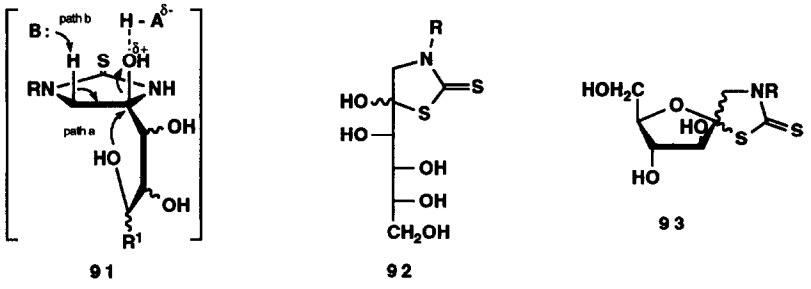
Scheme 11. *Reagents*: i, PhNCS, EtOH, 70°C.

Nevertheless, Butler *et al.*[54] have demonstrated that reactions of thioureas with carbonyl compounds are more complex than the corresponding processes with ureas, due to the nucleophilic participation of sulphur atom. Therefore, it is virtually impossible to rule out monocyclic or bicyclic structures **84-86** (X=S or Se), which may be generated from the isothiourea **83** (X=S) or the isoselenourea **83** (X=Se). Analogous nucleophilic additions of SH group to the aldehyde function of 2-aminoaldoses take place when these react with carbon disulphide,[55] giving monocyclic thiazolidin-2-thiones **88** (Scheme 12).

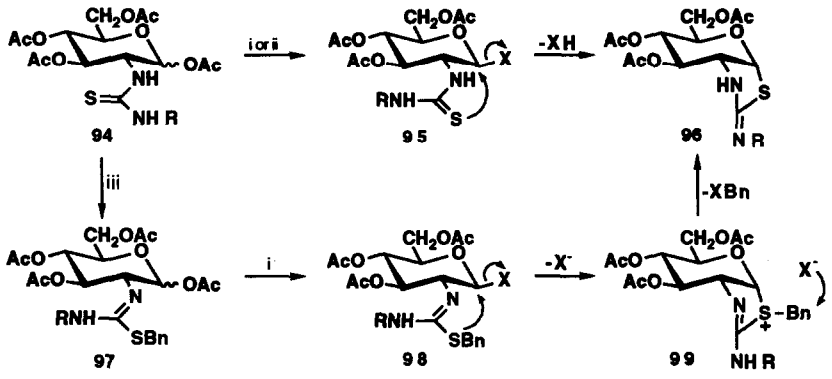


Scheme 12

A similar behaviour has been found in 1-amino-1-deoxyketoses. Thus, 1-amino-1-deoxy-D-fructose[55,56] and its *N*-alkylderivatives[57] react with S_2C providing the monocycles **92**. These compounds can be easily prepared[57] by treatment of *N*-alkylglycosylamines with carbon disulphide *via* an Amadori rearrangement.[58]



Compounds **88** and **92** have never been transformed into furanoid thiazolidin-2-thiones having either a 1,2-fusion (**89**) or a spiranic linkage (**93**), respectively.[59] It would appear from this result that structures such as **85** (X=S) cannot be formed by cyclisation of monocycles **84**. Furthermore, compounds having structures **84** and **86** have never been isolated or detected in the reactions of aminosugars with isothiocyanates under acid conditions, or by deacetylation of per-*O*-acyl thioureas. Also, electrophoretic analyses[24b] have discarded the presence of a structure as **84**. In addition, these results rule out the mechanism depicted in Scheme 12 as well as a direct displacement at the anomeric centre, which would lead exclusively to **85** (X=S). This latter strategy can be appropiately exploited in the synthesis of glycopyrano[2,1-*d*]-2-iminothiazolidines from per-*O*-acetyl thioureido derivatives **94**. Cyclisation was attempted by means of HBr/AcOH[18] or with tin(IV) chloride in dichloromethane, but in both cases cyclisation occurs invariably by sulphur attack (**96**), presumably *via* the intermediacy of the corresponding glycosyl halide **95**. Still, further protection of the sulphur atom by converting **94** into the isothiourea **97** gave the same type of cyclisation (Scheme 13). There are similar displacement reactions at non-anomeric positions of thioureido sugars, but imidazolidin-2-thiones could not be obtained.[60] The foregoing route might also be employed in the synthesis of glycopyrano[2,1-*d*]-2-iminoselenazolidines.[61]

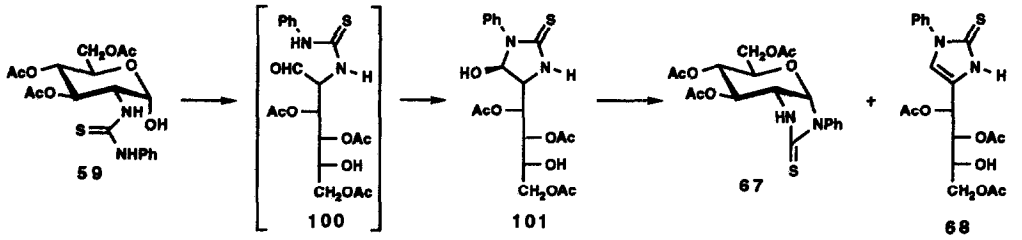


Scheme 13. *Reagents*: i, HBr, AcOH; ii, $SnCl_4$, CH_2Cl_2; iii, BnCl, $NaHCO_3$, MeOH, Δ.

Similarly to their oxoanalogues,[2] the synthesis of glycopyrano[2,1-*d*]imidazolidin-2-thiones could be envisaged *via* the cyclisation of an anomerically deprotected thioureidosugar. The experimental findings of Scheme 14 for partially protected substrates agree well with the mechanism portrayed in Scheme 9. The isolation of monocycles **60** and **68** evidences the participation of **101** as intermediate. This latter can lead either to **67** and **68** in acid medium or can undergo acetate migration from C-4 to C-5 yielding **60**. A similar behaviour was encountered for **68** that was converted into a mixture of **68** and **69** in the presence of silica gel. Again, structures resulting from the nucleophilic participation of sulphur atom (*e.g.* **52**) were not detected.

Remarkably, it should be noted the acid-dependent transformation of **59** (indeed **101**) into the bicycle **67** and the unsaturated monocycle **68**. Table 11 summarises the experimental results of such a cyclisation and those of **20** and **21**. The ratio of unsaturated monocycle increases as acetic acid concentration does it.

These results are in total agreement with the mechanism showed in Scheme 10 involving a bifunctional catalysis. The latter is more important in nonaqueous solvents,[62] and this fact explains why the proportion of unsaturated monocycles increases in glacial acetic acid.



Scheme 14

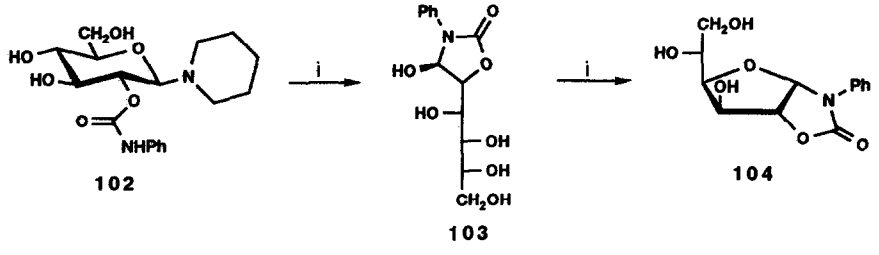
Table 11. Acid treatment of **20**[a], **21**[a], and **101**[b].

Starting material	**20**		**21**		**101**[c]	
Medium \ Products[d]	**31**	**48**	**32**	**49**	**67**	**68**
Aqueous AcOH[e]	100%	0%	100%	0%	85%	15%
Glacial AcOH	85%	15%	80%	20%	31%	69%

[a] 100°, 30 min.; [b] 60°, 4 h.; [c] Actually **59**; [d] Determined by ^{1}H NMR integration; [e] 30% for **20** and **21** and 50% for **101**.

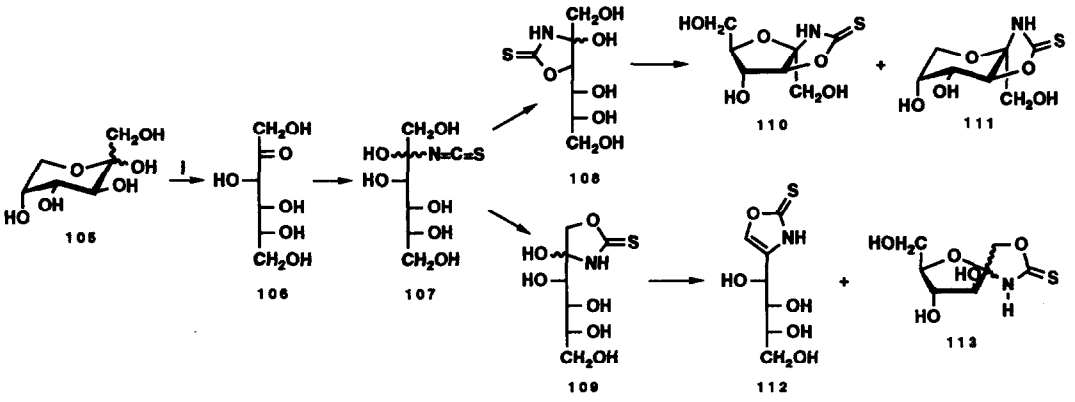
Since the spectroscopic characterisation of monocycles **20-25** and **30** is not completely unambiguous, the best characterisation can be achieved by preparing their acetyl derivatives (as **40**, **43**, and **45**, see Results). This transformation, however, should be performed at low temperatures for preserving the stereochemical arrangement of the starting monocycles. Upon heating, acetylated monocycles (as **39**) undergo a smooth conversion into unsaturated systems (as **41**) whose ratio increases as temperature increases. The *trans* configuration of acetylated monocycles enables an easy pyrolytic *syn*-elimination of acetic acid through a six-membered pericyclic process.

In summary, the reactivity of aminosugars toward isothiocyanates is analogous to that of isocyanates.[2,5] Scheme 10 constitutes an unifying approach for this type of reactions, and rationalises a wide variety of experimental results in the reactions of sugars and aminosugars with heterocumulenes that started over 100 years ago. It is expected that other processes follow a similar mechanism as well, and an illustration of this assessment is depicted in Scheme 15. The monocyclic oxazolidin-2-one **103**, generated by controlled hydrolysis of *N*-[2-*O*-(*N*-phenylcarbamoyl)-β-D-glucopyranosyl]pyperidine (**102**), could be isolated and then converted into bicycle **104** under acid catalysis.[63] The formation of other bicyclic oxazolidin-2-ones can be explained in this way.[64]



Scheme 15. *Reagents*: i, aqueous HCl.

Assuming a similar mechanism to that outlined in Scheme 9, more complex reactions can also be explained. Thus, it has been recently described[65] the formation of four products at least (**110-113**) in the reaction of D-fructose with potassium thiocyanate in acid medium.



Scheme 16. *Reagents*: i, KNCS, aqueous HCl.

The product formation can be elegantly rationalised invoking the participation of monocycles **108** and **109** as intermediates (Scheme 16). These compounds are formed by intramolecular cyclisation of the isothiocyanate **107** with the neighbouring hydroxyl groups.

ACKNOWLEDGEMENT. We gratefully acknowledge the financial support from DGICYT (PB93-0525-C02-01).

EXPERIMENTAL

General methods have been previously described.[2] Benzoyl and ethoxycarbonyl isothiocyanates were obtained from Aldrich and used without further purification.

2-(3-Benzoylthioureido)-2-deoxy-α-D-glucopyranose (15).- A solution of 2-amino-2-deoxy-α-D-glucopyranose hydrochloride, **1**, (1.1 g., 5.0 mmol) in water (2.0 mL) was treated with sodium hydrogencarbonate (0.42 g, 5.0 mmol). After 15 min., acetone (3.0 mL) and benzoyl isothiocyanate (0.7 mL, 5.0 mmol) were added with stirring and the homogeneous mixture was kept at room temperature overnight. The solvent was evaporated and the resulting syrup was washed repeatedly with ether and left in the refrigerator for 12 h. Then, the resulting solid was filtered off and washed with cold 96% ethanol, acetone, and ether to give **15** (0.9 g, 53%), m.p. 193-194°C, $[\alpha]_D$ +65° (*c* 1.0, pyridine), [lit.[22] m.p. 185°C, $[\alpha]_D$ +83° (*c* 2.0, pyridine)]. ν_{max} 3540-3000 (OH, NH), 1640 (C=O), 1525 (NH), 1270 (C=S), 1600, 760, and 715 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 11.37 (1H, s, CONH), 11.07 (1H, d, $J_{2,NH}$ 7.8, NH), 7.94-7.52 (5H, m, Ar), 6.79 (1H, bs, OH-1), 5.28 (3H, m, H-1, OH-3, OH-4), 4.55 (1H, bs, OH-6), 4.32 (1H, m, H-2), 3.69-3.40 (4H, m, H-3,5,6,6'), 3.26 (1H, t, $J_{3,4}$ =$J_{4,5}$ 8.2, H-4).

2-Deoxy-2-(3-ethoxycarbonylthioureido)-α-D-glucopyranose (16).- To a solution of **1** (0.65 g, 3.0 mmol) in water (7.0 mL) was added sodium carbonate (0.17 g, 1.6 mmol). After 15 min., acetone (15.0 mL) and ethoxycarbonyl isothiocyanate (0.35 mL, 3.0 mmol) were added with stirring and the homogeneous mixture was kept at room temperature for 6 h. The yellowish solution was concentrated until the appearance of white crystals, and then left in the refrigerator for 12 h. Crystals were filtered off and successively washed with cold water, acetone, and ether to give **16** (0.5 g, 55%), m.p. 120-122°C, $[\alpha]_D$ +79° (*c* 0.5, pyridine), [lit.[22] m.p. 168°C, $[\alpha]_D$ +83° (*c* 1.0, pyridine)]. ν_{max} 3560, 3500-3000 (OH, NH), 1730 (C=O, ester), 1535 (NH), 1245 cm^{-1} (C=S), δ_H (200 MHz, DMSO-d_6) 10.98 (1H, bs, CONH), 9.96 (1H, d, $J_{2,NH}$ 8.3, NH), 6.71 (1H, d, $J_{1,OH}$ 4.4, OH-1), 5.18 (1H, t, $J_{1,2}$ 3.7, H-1), 5.12 (1H, d, $J_{3,OH}$ 5.4, OH-3), 5.08 (1H, d, $J_{4,OH}$ 9.9, OH-4), 4.53 (1H, t, $J_{6,OH}$ 5.5, OH-6), 4.25 (1H, m, $J_{2,3}$ 10.5, H-2), 4.17 (3H, q, $J_{CH,CH}$ 7.0, Et), 3.62 (4H, m, H-3, 5, 6, 6'), 3.22 (1H, m, $J_{3,4}$ ~$J_{4,5}$ 9.0, H-4), 1.23 (2H, t, Et).

1,3,4,6-Tetra-*O*-acetyl-2-(3-benzoylthioureido)-2-deoxy-α-D-glucopyranose (17).- To a solution of **15** (0.23 g, 0.7 mmol) in pyridine (2.5 mL) was added acetic anhydride (1.5 mL), and the reaction mixture was left at room temperature for 15 h. Then, it was poured into ice-water, and the resulting solid was filtered off and washed with cold water (0.22 g, 65%). Recrystallised

from 80% ethanol had m.p. 94-96°C, $[\alpha]_D$ +61° (*c* 0.5, chloroform), [lit.[22] m.p. 132°C, $[\alpha]_D$ +46° (*c* 2.0, chloroform)], ν_{max} 3500-3000 (NH), 1750 (C=O, ester), 1670 (C=O), 1530 (NH), 1235 (C=S), 1230 (C-O-C), 1605, 1495, 780, and 710 cm^{-1} (aromatic).

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3-ethoxycarbonylthioureido)-α-D-glucopyranose (18).- Compound **18** (97%) was obtained from **16** as described for **17**, m.p. 83-85°C (96% ethanol), $[\alpha]_D$ +51° (*c* 0.5, chloroform), ν_{max} 3280, 3230 (NH), 1750 (C=O, ester), 1725 (C=O, carbamate), 1535 (NH), 1250 (C=S), and 1220 cm^{-1} (C-O-C). Anal. found: C, 45.00; H, 5.49; N, 5.79. Calcd. for $C_{18}H_{26}N_2O_{11}S$: C, 45.19; H, 5.48; N, 5.85.

Preparation of 1-aryl-4-(D-alditol-1-yl)-5-hydroxyimidazolidin-2-thiones.

Procedure A.- To a solution of 2-amino-2-deoxy-D-aldopyranose hydrochloride (23.2 mmol) in water (54.0 mL) was added sodium carbonate (12.3 mmol). After 15 min, aryl isothiocyanate (23.2 mmol) and acetone (108 mL) were added with stirring and the mixture was kept at room temperature for 30 min., and then it was heated at 80°C (external bath) for 15 min. The yellowish solution was filtered off, and the filtrate evaporated. The resulting solid was filtered off and successively washed with cold ethanol and ether.

Procedure B.- To a solution of the corresponding 1,3,4,6-tetra-*O*-acetyl-2-[3-aryl(alkyl)thioureido]-2-deoxy-α or β-D-glucopyranose (1.2 mmol) in absolute methanol (18.0 mL), was added a saturated methanolic solution of ammonia (18.0 mL) cooled previously at -20°C. The reaction mixture was stirred at room temperature for 2 h, and then it was evaporated to dryness, and the residue crystallised from ethanol.

(4*R*, 5*R*)-1-Phenyl-4-(D-*arabino*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (20).- From **1** and phenyl isothiocyanate and following the procedure A, compound **20** (60%) was obtained, m.p. 152-154°C (ethanol), $[\alpha]_D$ +31° (*c* 1.0, pyridine), [lit.[8] m.p. 154°C, $[\alpha]_D$ +47° (*c* 2.0, pyridine)], ν_{max} 3500-2900 (OH, NH), 1450 (NH), 1250 (C=S), 1600, 1495, and 700 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 8.43 (1H, s, NH), 7.49-7.21 (5H, m, Ar), 6.78 (1H, d, $J_{1,OH}$ 8.6, OH-1), 5.47 (1H, dd, $J_{1,2}$ 2.0, H-1), 4.84 (1H, d, $J_{3,OH}$ 5.9, OH-3), 4.55 (1H, d, $J_{4,OH}$ 6.4, OH-4), 4.51 (1H, d, $J_{5,OH}$ 7.6, OH-5), 4.37 (1H, t, $J_{6,OH}$ 5.0, OH-6), 3.77-3.35 (6H, m, H-2 to H-6'). Anal. found: C, 49.54; H, 5.85; N, 8.87. Calcd. for $C_{13}H_{18}N_2O_5S$: C, 49.67; H, 5.77; N, 8.91.

Following the procedure B, compound **20** was obtained either from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(3-phenylthioureido)-α or β-D-glucopyranose, **26** (92%) or **27** (74%).

Procedure C.- Compound **20** was also obtained following the method by Krüger and Rudy.[8] A suspension of 2-amino-2-deoxy-D-glucopyranose[66] (6.0 g, 33.5 mmol) and phenyl isothiocyanate (4.1 mL, 34.0 mmol) in absolute ethanol (34.0 mL) was heated at 100°C (external bath) for 10 min. The yellowish solution was filtered and, after cooling, a solid was obtained which was filtered off and washed with methanol, ethanol, and ether (7.9 g, 75%). Recrystallisation from ethanol gave pure **20**.

(4*R*, 5*R*)-1-(4-Methoxyphenyl)-4-(D-*arabino*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (21).- From **1** and 4-methoxyphenyl isothiocyanate and following the procedure A, compound **21** (73%) was obtained, m.p. 170-172°C (ethanol), $[\alpha]_D$ +19° (*c* 0.5, pyridine), ν_{max} 3500-2900 (OH, NH), 2940, 2880, and 1250 (OCH_3), 1445 (NH), 1600, 1580, 1510, and 830 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 8.30 (1H, s, NH), 7.29 (2H, d, *J* 9.0, Ar), 6.93 (2H, d, Ar), 6.73 (1H, d, $J_{1,OH}$ 8.4, OH-1), 5.38 (1H, dd, $J_{1,2}$ 1.9, H-1), 4.85 (1H, d, $J_{3,OH}$ 6.2, OH-3), 4.60 (1H, d, $J_{4,OH}$ 5.5, OH-4), 4.55 (1H, d, $J_{5,OH}$ 7.42, OH-5), 4.48 (1H, d, $J_{6,OH}$ 5.1, OH-6), 3.75-3.35 (6H, m, H-2 to H-6'). Anal. found: C, 48.82; H, 5.84; N, 8.06. Calcd. for $C_{14}H_{20}N_2O_6S$: C, 48.83; H, 5.85; N, 8.13.

Following the procedure B, compound **21** was prepared from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-[3-(4-methoxyphenyl)thioureido]-α-D-glucopyranose,[18] **28**, (99%).

(4*R*, 5*R*)-1-(4-Bromophenyl)-4-(D-*arabino*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (22).- From **1** and 4-bromophenyl isothiocyanate and following the procedure A, compound **22** (86%) was obtained, m.p. 157-159°C (dec.), $[\alpha]_D$ +26° (*c* 0.5, pyridine), ν_{max} 3500-3000 (OH, NH), 1455 (NH), 1230, 1210 (C=S), 1580, 1490, and 820 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 8.55 (1H, s, NH), 7.59-7.46 (4H, m, Ar), 6.87 (1H, d, $J_{1,OH}$ 8.0, OH-1), 5.53 (1H, d, $J_{1,2}$<1.0, H-1), 4.92 (1H, d, $J_{3,OH}$ 4.6, OH-3), 4.62-4.58 (2H, m, OH-4 and 5), 4.51 (1H, m, OH-6), 3.75-3.47 (6H, m, H-2 to H-6'). Anal. found: C, 40.14; H, 4.22; N, 7.29. Calcd. for $C_{13}H_{17}BrN_2O_5S$: C, 39.71; H, 4.36; N, 7.12.

(4*R*, 5*R*)-1-(1-Naphthyl)-4-(D-*arabino*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (23).- From **1** and 1-naphthyl isothiocyanate and following the procedure A, compound **23** as monohydrate (82%) was obtained, m.p. 157-158°C (1:1 ethanol-water), $[\alpha]_D$ +37° (*c* 1.0, pyridine), [lit.[24c] m.p. 154-155°C], ν_{max} 3500-3100 (OH, NH), 1615 (H_2O),[67] 1460 (NH), 1250 (C=S), 1600, and 770 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6), **23a** (major isomer), 8.35 (1H, s, NH), 8.07-7.43 (4H, m, Ar), 6.88 (1H, d, $J_{1,OH}$ 8.0, OH-1), 5.32 (1H, d, $J_{1,2}$<1, H-1), 5.04 (1H, d, $J_{3,OH}$ 6.0, OH-3), 4.73 (1H, d, $J_{4,OH}$ 6.4, OH-4), 4.65 (1H, m, OH-5), 4.49 (1H, m, OH-6), 3.91-3.49 (6H, m, H-2 to H-6'); **23b** (minor isomer), 8.42 (1H, s, NH), 8.07-7.43 (4H, m, Ar), 6.71 (1H, d, $J_{1,OH}$ 7.5, OH-1), 5.60 (1H, d, $J_{1,2}$<1, H-1), 4.95 (1H, m, OH-3), 3.90-3.40 (6H, m, H-2 to H-6').

Procedure C.- To a solution of **1** (0.5 g, 2.3 mmol) in water (5.0 mL) was added a solution of 1-naphthyl isothiocyanate (0.5 g, 2.7 mmol) in pyridine (5 mL), and the reaction mixture was heated at 80°C (external bath) for 15 min. After cooling, additional water (5.0 mL) was added and the aqueous phase was washed with benzene (3 x 20 mL). Compound **23** crystallised from the aqueous layer, it was collected by filtration, and washed with cold water (0.4 g, 47%).

(4*R*, 5*R*)-1-(1-Naphthyl)-4-(D-*lyxo*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (24).- From 2-amino-2-deoxy-α-D-galactopyranose hydrochloride and 1-naphthyl isothiocyanate and following the procedure A, compound **24** (71%) was obtained,

m.p. 183-185°C, $[\alpha]_D$ -6° (*c* 0.5, pyridine), ν_{max} 3500-3100 (OH, NH), 1480 (NH), 1270 (C=S), 1600, 1525, and 770 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6), **24a** (major isomer), 8.60 (1H, s, NH), 8.11 (1H, d, Ar), 7.96 (2H, m, Ar), 7.52 (4H, m, Ar), 6.85 (1H, d, $J_{1,OH}$ 8.1, OH-1), 5.47 (1H, d, $J_{3,OH}$ 8.2, OH-3), 5.43 (1H, d, $J_{1,2}$ <1, H-1), 4.65 (1H, bt~s, OH-6), 4.47 (1H, d, $J_{4,OH}$ 5.2, OH-4), 4.37 (1H, d, $J_{5,OH}$ 6.0, OH-5), 4.10 (1H, bs, H-2), 3.92-3.25 (5H, m, H-3 to H-6'); **24b** (minor isomer), 6.71 (1H, d, $J_{1,OH}$ 8.0, OH-1), 5.58 (1H, d, $J_{1,2}$ <1, H-1), 5.32 (1H, d, $J_{3,OH}$ 5.0, OH-3). Anal. found: C, 55.96; H, 5.42; N, 7.64. Calcd. for $C_{17}H_{20}N_2O_5S$: C, 56.03; H, 5.53; N, 7.69.

(4*S*, 5*S*)-1-(1-Naphthyl)-4-(D-*galacto*-pentitol-1-yl)-5-hydroxyimidazolidin-2-thione (25).- From 2-amino-2-deoxy-β-D-*glycero*-L-*gluco*-heptopyranose[28] and 1-naphthyl isothiocyanate and following the procedure A, compound **25** (75%) was obtained, m.p. 172-174°C (ethanol-water), $[\alpha]_D$ -3.5° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3600-3000 (OH, NH), 1635 (H_2O),[67] 1480 (NH), 1260 (C=S), 1590, 1500, and 765 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6), **25a** (major isomer), 8.40 (1H, s, NH), 8.20-7.35 (7H, m, Ar), 6.91 (1H, d, $J_{1,OH}$ 7.9, OH-1), 5.36 (1H, d, $J_{1,2}$ 0.0, H-1), 5.20-4.10 (4H, m, OH-3 to OH-6), 4.00-3.31 (6H, m, H-2 to H-6'); **25b** (minor isomer), 6.75 (1H, d, $J_{1,OH}$ 8.0, OH-1), 5.64 (1H, d, $J_{1,2}$ 0.0, H-1). Anal. found: C, 53.78; H, 5.99; N, 7.20. Calcd. for $C_{18}H_{22}N_2O_6S.1/2H_2O$: C, 53.59; H, 5.75; N, 6.94.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3-phenylthioureido)-α-D-glucopyranose (26).- To a solution of calcium carbonate (1.3 g., 13.0 mmol) in water (130 mL) was added a solution of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrochloride[68] (10.0 g., 26.1 mmol) in dichloromethane (130 mL), and the reaction mixture was vigorously stirred at room temperature for 30 min. The organic layer was separated, washed with water, dried ($MgSO_4$) and concentrated until 50 mL. Then, phenyl isothiocyanate (3.5 g., 26.1 mmol) was added and the mixture was kept at room temperature for 24 h. The solvent was evaporated to dryness and the resulting oil was crystallised from ethyl acetate-light petroleum to give **26** (7.6 g, 60%), m.p. 89-90°C, $[\alpha]_D$ +85° (*c* 1.2, chloroform), λ_{max}(EtOH) 244 and 268 nm (ε_{mM} 16.5 and 15.3), ν_{max} 3340 and 3210 (NH), 1750 (C=O, ester), 1530 (NH), 1225 (C-O-C), 1595, 750, and 700 cm^{-1} (aromatic). Anal. found: C, 52.04; H, 5.45; N, 5.69. Calcd. for $C_{21}H_{26}N_2O_9S$: C, 52.28; H, 5.43; N, 5.80.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3-phenylthioureido)-β-D-glucopyranose (27).- Compound **27** (59 %) was prepared from 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride[14] as described for **26**. Crystallised from ether had m.p. 105-107°C, $[\alpha]_D$ +16° (*c* 1.0, chloroform), ν_{max} 3320 and 3270 (NH), 1750 (C=O, ester), 1545 (NH), 1220 (C-O-C), 1595, 1510, 750, and 690 cm^{-1} (aromatic). Anal. found: C, 52.36; H, 5.32; N, 5.81. Calcd. for $C_{21}H_{26}N_2O_9S$: C, 52.28; H, 5.43; N, 5.80.

(4*R*, 5*R*)-1-Methyl-4-(D-*arabino*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (30).- From 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(3-methylthioureido)-α-D-glucopyranose[19] (**29**), and following the procedure B, compound **30** (99%) was obtained, m.p. 144-145°C (ethanol), $[\alpha]_D$ +75° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1490, 1450 (NH), and 1270 cm^{-1} (C=S), δ_H (200 MHz, DMSO-d_6) 7.85 (1H, s, NH), 6.53 (1H, d, $J_{1,OH}$ 7.2, OH-1), 5.02 (1H, dd, $J_{1,2}$ 2.8, H-1), 4.64 (1H, d, $J_{3,OH}$ 6.2, OH-3), 4.53 (1H, d, $J_{4,OH}$ 5.1, OH-4), 4.47 (1H, d, $J_{5,OH}$ 7.7, OH-5), 4.41 (1H, d, $J_{6,OH}$ 5.0, OH-6), 3.60-3.28 (6H, m, H-2 to 6'). Anal. found: C, 37.96; H, 6.53; N, 11.06. Calcd. for $C_8H_{16}N_2O_5S$: C, 38.09; H, 6.39; N, 11.10.

Reaction of 16 in basic medium.- To a solution of **16** (0.02 g, 0.06 mmol) in water (1.0 mL) was added pyridine until pH 8. The reaction mixture was heated at 50°C (external bath) for 16 h. Transformation into a monocyclic imidazolidin-2-thione was not detected by t.l.c. (chloroform-methanol 3:1) or NMR spectroscopy.

Preparation of 1-aryl(alkyl)-(1,2-dideoxyglycofurano)[2,1-*d*]imidazolidin-2-thiones.

A suspension of 1-aryl(alkyl)-4-(D-alditol-1-yl)-5-hydroxyimidazolidin-2-thione (0.7 mmol) in 30% aqueous acetic acid (10.0 mL) was heated at 100°C (external bath) for 30 min. The hot solution was filtered off and, after cooling, the title compound crystallised.

1-Phenyl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-thione (31).- a) From **20**, compound **31** (83%) was obtained, m.p. 209-211°C, $[\alpha]_D$ +61° (*c* 0.5, pyridine), [lit.[8] m.p. 208°C, $[\alpha]_D$ +58° (*c* 2.0, pyridine)], ν_{max} 3420, 3380, 3300-3000 (OH, NH), 1475 (NH), 1240, 1230 (C=S), 1595, 1585, 1490, 1450, 760, and 695 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 9.16 (1H, s, NH), 7.50-7.23 (5H, m, Ar), 5.97 (1H, d, $J_{1,2}$ 6.3, H-1), 5.39 (1H, d, $J_{3,OH}$ 5.0, OH-3), 4.79 (1H, d, $J_{5,OH}$ 4.7, OH-5), 4.55 (1H, t, $J_{6,OH}$ 5.3, OH-6), 4.18 (1H, d, $J_{2,3}$ 0.0, H-2), 4.13 (1H, dd, $J_{3,4}$ 1.8, H-3), 3.73 (1H, m, H-5), 3.67 (1H, dd, $J_{4,5}$ 8.6, H-4), 3.59 (1H, m, $J_{5,6}$ 2.3, $J_{6,6'}$ 11.0, H-6), 3.41 (1H, m, $J_{5,6'}$ 5.4, H-6').

b) A solution of **20** (0.3 mmol) in glacial acetic acid (3.0 mL) was heated at 100°C (external bath) for 30 min. Solvent evaporation and NMR analysis of the crude product revealed a mixture 85:15 of **31** and **48**.

1-(4-Methoxyphenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-thione (32).- a) From **21**, compound **32** (81%) was obtained, m.p. 218-220°C, $[\alpha]_D$ +67° (*c* 1.0, pyridine), [lit.[7] m.p. 225°C, $[\alpha]_D$ +74° (*c* 2.1, pyridine); lit.[11] m.p. 235-236°C, $[\alpha]_D$ +79.6° (*c* 2.1, *N,N*-dimethylformamide)], ν_{max} 3440, 3369, 3300-3000 (OH, NH), 1475 (NH), 1250, 1245 (C=S), 1605, 1580, 1515, and 835 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 9.05 (1H, s, NH), 7.29 (2H, d, *J* 9.0, Ar), 6.93 (2H, d, Ar), 5.88 (1H, d, $J_{1,2}$ 6.4, H-1), 5.36 (1H, d, $J_{3,OH}$ 5.0, OH-3), 4.78 (1H, d, $J_{5,OH}$ 5.7, OH-5), 4.55 (1H, t, $J_{6,OH}$ 5.6, OH-6), 4.15 (1H, d, $J_{2,3}$ 0.0, H-2), 4.11 (1H, dd, $J_{3,4}$ 2.0, H-3), 3.76 (3H, s, OMe), 3.65 (1H, dd, $J_{4,5}$ 8.6, H-4), 3.73-3.44 (3H, m, H- 5, H-6, and H-6').

b) A solution of **21** (0.3 mmol) in glacial acetic acid (3.0 mL) was heated at 100°C (external bath) for 30 min. Solvent evaporation

and NMR analysis of the crude product revealed a mixture 80:20 of **32** and **49**.

1-(4-Bromophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-thione (33).- From **22**, compound **33** (83%) was obtained, m.p. 235-237°C, $[\alpha]_D$ +60° (*c* 1.0, pyridine), [lit.[15] m.p. 232-234°C], ν_{max} 3440, 3350, 3300-3000 (OH, NH), 1480 (NH), 1230 (C=S), 1590, 1580, 1495, and 825 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 9.27 (1H, s, NH), 7.58 (2H, d, *J* 8.8, Ar), 7.47 (2H, d, Ar), 6.00 (1H, d, $J_{1,2}$ 6.3, H-1), 5.41 (1H, d, $J_{3,OH}$ 4.9, OH-3), 4.79 (1H, d, $J_{5,OH}$ 5.6, OH-5), 4.55 (1H, t, $J_{6,OH}$ 5.0, OH-6), 4.19 (1H, d, $J_{2,3}$ 0.0, H-2), 4.14 (1H, dd, $J_{3,4}$ 1.9, H-3), 3.67 (1H, dd, $J_{4,5}$ 8.7, H-4), 3.74 (1H, m, $J_{5,6}$ 3.4, $J_{5,6'}$ 5.1, H-5), 3.57 (1H, m, $J_{6,6'}$ 11.1, H-6), 3.43 (1H, m, H-6').

1-(1-Naphthyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-thione (34).- From **23**, compound **34** (92%) was obtained, m.p. 192-194°C (80% ethanol), $[\alpha]_D$ +97° (*c* 0.5, pyridine), [lit.[21] m.p. 237-239°C, $[\alpha]_D$ +123° (*c* 2.0, pyridine)], ν_{max} 3500-3000 (OH, NH), 1460, 1440 (NH), 1270, 1230 (C=S), 1585, and 760 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6), **34a** (major isomer), 9.23 (1H, s, NH), 7.97-7.37 (7H, m, Ar), 5.87 (1H, d, $J_{3,OH}$ 6.2, OH-3), 5.40 (1H, bs, H-1); **34b** (minor isomer), 6.03 (1H, d, $J_{3,OH}$ 6.4, OH-3).

1-(1-Naphthyl)-(1,2-dideoxy-α-D-galactofurano)[2,1-*d*]imidazolidin-2-thione (35).- From **24**, compound **35** (41%) was obtained, m.p. 168-170°C (dec., ethanol-water), $[\alpha]_D$ +19° (*c* 0.25, *N,N*-dimethylformamide), ν_{max} 3500-3000 (OH, NH), 1670 (H_2O),[67] 1470 (NH), 1265 (C=S), 1600, 1510, 1455, and 780 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6), **35a** (major isomer), 9.27 (1H, s, NH), 8.02-7.50 (7H, m, Ar), 5.87 (1H, d, $J_{1,2}$ 6.7, H-1), 5.57 (1H, d, $J_{3,OH}$ 4.7, OH-3), 4.81 (1H, d, $J_{5,OH}$ 4.7, OH-5), 4.72 (1H, t, $J_{6,OH}$ 4.8, OH-6), 4.44 (1H, d, $J_{2,3}$ 0.0, H-2), 4.35 (1H, m, $J_{3,4}$<2, H-3), 3.93 (1H, dd, $J_{4,5}$ 5.4, H-4), 3.60-3.40 (3H, m, H-5, H-6, and H-6'); **35b** (minor isomer), 5.95 (1H, d, $J_{3,2}$ 6.5, H-1), 4.62 (1H, t, $J_{6,OH}$ 4.8, OH-6). Anal. found: C, 57.51; H, 5.43; N, 7.87. Calcd. for $C_{17}H_{18}N_2O_4S.1/2H_2O$: C, 57.45; H, 5.39; N, 7.88.

1-(1-Naphthyl)-(1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]imidazolidin-2-thione (36).- From **25**, compound **36** (72%) was obtained, m.p. 176-178°C (50% ethanol), $[\alpha]_D$ -53.5° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3520, 3500-3000 (OH, NH), 1445 (NH), 1265, 1245 (C=S), 1600, 1470, and 780 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6), **36a** (major isomer), 9.25 (1H, s, NH), 8.10-7.50 (7H, m, Ar), 5.88 (1H, d, $J_{1,2}$ 6.0, H-1), 5.41 (1H, bs, OH-3), 4.69-3.42 (3H, m, OH-5, OH-6, and OH-7), 4.48 (1H, d, $J_{2,3}$ 0.0, H-2), 4.69-3.42 (6H, m, H-3 to H-7'); **36b** (minor isomer), 6.02 (1H, d, $J_{1,2}$ 6.4, H-1). Anal. found: C, 56.88; H, 5.31; N, 7.34. Calcd. for $C_{18}H_{20}N_2O_5S$: C, 57.43; H, 5.36; N, 7.44.

1-Methyl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-thione (37).- From **30**, a mixture of compounds **37** and **38** in proportion 9:1 was obtained. Recrystallisation from ethanol gave pure **37**, m.p. 170-172°C, $[\alpha]_D$ -8° (*c* 1.0, pyridine), [lit.[8] m.p. 189°C, $[\alpha]_D$ -5° (*c* 2, pyridine)], ν_{max} 3500-3000 (OH, NH), 1485 (NH), δ_H (200 MHz, DMSO-d_6) 8.67 (1H, s, NH), 5.69 (1H, d, $J_{1,2}$ 6.0, H-1), 5.29 (1H, d, $J_{3,OH}$ 4.5, OH-3), 4.72 (1H, d, $J_{5,OH}$ 5.6, OH-5), 4.50 (1H, t, $J_{6,OH}$ 5.3, OH-6), 3.99 (2H, d, $J_{2,3}$ 0.0, H-2, 3), 3.72 (1H, m, H-5), 3.58 (1H, m, $J_{5,6}$ 3.7, $J_{6,6'}$ 10.6, H-6), 3.44-3.32 (2H, m, H-4, H-6'), 2.95 (3H, s, Me).

Reaction of 16 in acid medium.- Following the general procedure for the preparation of 1-aryl(alkyl)-(1,2-dideoxy-α-D-glycofurano)[2,1-*d*]imidazolidin-2-thiones, **16** could not be transformed into a bicyclic compound.

Reaction of 20 and 21 in glacial acetic acid.- A solution de **20** or **21** (0.3 mmol) in glacial acetic acid (3.0 mL) was heated at 100°C (external bath) for 30 min. Then, it was concentrated to dryness and the residual mixture was analysed by t.l.c. and NMR spectroscopy.

Acetylation of 20.- To a solution of **20** (0.1 g., 0.3 mmol) in pyridine (0.5 mL) was added acetic anhydride (0.7 mL), and the reaction mixture was kept at different temperatures for two days. After being poured into ice-water, the resulting solid was filtered off, washed with cold water, dried and analysed by NMR spectroscopy. At -35°C **20** gave a mixture of **39** and **41** (0.07g.); at -15°C **41** and **39** (0.11 g., ratio **41/39**=1.4); at 0°C **39**, **40**, and **41** (0.14 g., ratio **39/40**=1.5); at 80°C **41** (0.05 g). (4*R*, 5*R*)-5-Acetoxy-*N*-acetyl-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-phenylimidazolidin-2-thione (**40**) was separated (17%) by preparative t.l.c. (benzene-acetone 3:1). Recrystallised from 96% ethanol had m.p. 49-50°C, $[\alpha]_D$ -14° (*c* 0.5, chloroform), ν_{max} 1745 (C=O, ester), 1690 (C=O amide), 1230 (C=S), 1220 (C-O-C), 1590, 1585, 1495, 1450, 730, and 690 cm^{-1} (aromatic)(neat). Anal. found: C, 53.08; H, 5.48; N, 4.88. Calcd. for $C_{25}H_{30}N_2O_{11}S$: C, 53.00; H, 5.30; N, 4.95.

Acetylation of 21.- Acetylation of **21** was carried as described for **20**. At -35°C **21** gave a mixture of **42** and **44**[7] (0.06 g., ratio **44/42**=2.0); at -15°C **42** and **44** (0.09 g., ratio **42/44**=0.7); at 0°C **42** and **43** (0.13 g., ratio **42/43**=9.5); at room temperature **43** and **44** (0.15 g., ratio **43/44**=2.1); at 80°C **43** and **44** (0.05 g., ratio **44/43**=4.1). Solid obtained at room temperature was recrystallised from ethanol-water to give pure (4*R*, 5*R*)-5-acetoxy-*N*-acetyl-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-(4-methoxyphenyl)imidazolidin-2-thione, **43**, (51%), m.p. 99-100°C; $[\alpha]_D$ -8.0° (*c* 0.5 chloroform), ν_{max} 2840 and 1240 (OCH_3), 1740 (C=O ester), 1690 (C=O amide), 1200 (C-O-C), 1600, 1580, 1510, and 720 cm^{-1} (aromatic). Anal. found: C, 52.30; H, 5.42; N, 4.67. Calcd. for $C_{26}H_{32}N_2O_{12}S$: C, 52.35; H, 5.41; N, 4.69.

(4*R*, 5*R*)-5-Acetoxy-1-(1-naphthyl)-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazolidin-2-thione (45).- To a solution of **23** (1.0 g, 2.7 mmol) in pyridine (5.5 mL) was added acetic anhydride (6.8 mL), and the reaction mixture was kept at -15°C for 24 h. After being poured into ice-water, the resulting white solid was filtered off and washed with cold water (1.5 g, 94%), m.p. 151-152°C (96% ethanol), $[\alpha]_D$ +43.5° (*c* 1.0, chloroform), ν_{max} 3180 (NH), 1750 (C=O, ester), 1425 (NH), 1240 (C=S), 1210 (C-O-C), 1595, 1505, and 770 cm^{-1} (aromatic). Anal. found: C, 56.65; H, 5.52; N, 4.87. Calcd. for $C_{27}H_{30}N_2O_{10}S$: C, 56.44; H, 5.26; N, 4.86.

Transformation of 45 into 46.- A solution of **45** (0.08 g) in DMSO-d_6 (0.5 ml) was heated and its transformation monitored by NMR. A total conversion into 1-(1-naphthyl)-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazolin-2-thione (**46**) was observed.

Acetylation of 48.- To a solution of **48**[8] (0.3 mmol) in pyridine (1.2 ml) was added acetic anhydride (1.2 ml), and the reaction mixture was kept at different temperatures for two days. After being poured into ice-water, the resulting solid was filtered off and washed with cold water to give almost exclusively 1-phenyl-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazolin-2-thione (**41**). At -35°C, 66%; at -15°C, 86%; at 0°C, 77%; at room temperature, 48%; at 45°C, 33%; at 80°C, 86%. Recrystallised from 96% ethanol had m.p. 108-109°C, $[\alpha]_D$ -65° (*c* 0.5, chloroform), ν_{max} 1755, 1740 (C=O, ester), 1250 (C=S), 1215 (C-O-C), 1600, 1500, 760, and 690 (aromatic). Anal. found: C, 53.66; H, 5.22; N, 5.77. Calcd. for $C_{21}H_{24}N_2O_8S$: C, 54.30; H, 5.21; N, 6.03.

Acetylation of 49.- To a solution of **49** (0.1 g., 0.3 mmol) in pyridine (1.1 mL) was added acetic anhydride (1.1 mL), and the reaction mixture was kept at different temperatures for two days. After being poured into ice-water, the resulting solid was filtered off, washed with cold water and dried to give a mixture of **44**[7] and **51**. At room temperature, 0.062 g., (ratio **44/51**=1.1); at 45°C, 0.08 g., (ratio **51/44**=1.6); at 80°C, **44** was only obtained (0.12 g., 80%).

2-Phenylamino-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-d]-2-thiazoline (52).- To a solution of **26** (4.0 g, 8.3 mmol) in dichloromethane (200 mL) was added tin(IV) chloride (4.0 mL), and the reaction mixture was stirred at room temperature for 24 h. Then, it was filtered and the organic phase was washed with saturated aqueous solution of sodium hydrogencarbonate, water, dried ($MgSO_4$), and evaporated to dryness. The residue was crystallised from ether (3.1 g, 89%), m.p. 110-111°C (ethyl acetate-ether), $[\alpha]_D$ -5° (*c* 0.5, chloroform), ν_{max} 3320 (NH), 1760, 1740, 1720 (C=O, ester), 1635 (C=N), 1535 (NH), 1600, 1510, 1460, 760, and 695 cm^{-1} (aromatic). Anal. found: C, 54.26; H, 5.37; N, 6.60. Calcd. for $C_{19}H_{22}N_2O_7S$: C, 54.02; H, 5.25; N, 6.63.

2-Phenylamino-(1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-thiazoline (53).- Deacetylation of **52** (0.7 g, 1.7 mmol) following the general procedure with ammonia in methanol (see above) gave **53** (0.42 g, 86%), m.p. 193-197°C (dec.), $[\alpha]_D$ +137° (*c* 0.5, pyridine), ν_{max} 3500-2300 (NH, OH), 1570 (NH), 1590, 1490, 730, and 685 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6,) 9.0 (1H, bs, NH), 7.38 (2H, m, Ar), 7.23 (2H, t, Ar), 6.93 (1H, t, Ar), 6.25 (1H, d, $J_{1,2}$ 6.2, H-1), 5.21 (1H, d, $J_{3,OH}$ 4.6, OH-3), 5.02 (1H, d, $J_{4,OH}$ 5.2, OH-4), 4.96 (1H, t, $J_{6,OH}$ 4.7, OH-6), 3.97 (1H, bt, $J_{2,3}$ ~5, H-2), 3.80 (1H, m, $J_{3,4}$ ~5, H-3), 3.64 (1H, m, $J_{4,5}$ 9.4, H-4), 3.46 (2H, m, H-6, H-6'), 3.34 (1H, m, H-5). Anal. found: C, 52.90; H, 5.60; N, 9.45. Calcd. for $C_{13}H_{16}N_2O_4S$: C, 52.69; H, 5.44; N, 9.45.

3-Acetyl-2-phenylimino-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]thiazolidine (54) and 2-*N*-phenylacetamido-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-thiazoline (55).- Conventional treat-ment of **53** (0.4 g, 1.4 mmol) with acetic anhydride (3.2 mL) in pyridine (4.0 mL) at 0°C for 12 h., gave a mixture of **54** and **55** (0.44 g), which was separated and purified by preparative t.l.c. (benzene-acetone 3:1). Compound **54** (0.05 g, 7%), syrup, had $[\alpha]_D$ -81.5 (*c* 0.8, chloroform), ν_{max} 1745 (C=O ester), 1690 (CO amide), 1650 (C=N), 1240 (C-O-C ester), 1595, 1490, 770, and 700 (aromatic). Mass spectrum: m/z 464.1250. Calcd. for M^+ of $C_{21}H_{24}N_2O_8S$: 464.1253.

Compound **55** (0.3 g, 48%), syrup, had $[\alpha]_D$-53.0 (*c* 1.0, chloroform), ν_{max} 1750, 1740, and 1730 (C=O ester), 1700 (C=O amide), 1630 (C=N), 1240 (C-O-C ester), 1600, 1590, 1490, 760, and 700 cm^{-1} (aromatic). Mass spectrum: m/z 464.1238. Calcd. for M^+ of $C_{21}H_{24}N_2O_8S$: 464.1253.

1,3,4,6-Tetra-*O*-acetyl-2-(2-benzylthio)cyclohexyliminomethylamino-2-deoxy-α-D-glucopyranose (57).- To a solution of 1,3,4,6-tetra-*O*-acetyl-2-(3-cyclohexylthioureido)-2-deoxy-α-D-glucopyranose,[18] **56**, (1.5 g, 3.1 mmol) in ethanol (10.0 mL) was added benzyl chloride (6.0 mL, 52.1 mmol) and sodium hydrogencarbonate (5.0 g, 59.5 mmol). The reaction mixture was heated at reflux for six hours. The inorganic salts were filtered and the resulting solution evaporated until the formation of crystals (0.3 g, 17%). Recrystallised from ethanol had m.p. 98-99°C, $[\alpha]_D$ +28° (*c* 1.0, chloroform), λ_{max}(EtOH) 270 nm (ε_{mM} 4.70), ν_{max} 3450 (NH), 1745 (C=O, ester), 1610 (C=N), 1500 (aromatic), and 1240 (C-O-C). Anal. found: C, 58.01; H, 6.70; N, 4.80 Calcd. for $C_{28}H_{38}N_2O_9S$: C, 58.10; H, 6.61; N, 4.84

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(3-phenylthioureido)-α-D-glucopyranose (59).- To a solution of **66** (3.0 g, 7.8 mmol) in pyridine (30.0 mL) was added, with stirring, phenyl isothiocyanate (1.0 mL, 8.3 mmol). After 24 h. at room temperature, the reaction mixture was poured into ice, and the resulting oil was extracted with chloroform. The organic solution was successively washed with *N* hydrochloric acid, saturated aqueous solution of sodium hydrogencarbonate, and water, and dried over anhydrous magnesium sulphate. The solution was evaporated and the amorphous residue was crystallised from ether to give **59** (2.4 g, 71%), m.p. 156-158°C (ethanol-water), $[\alpha]_D$ +111° (*c* 0.5, chloroform), ν_{max} 3400-3100 (NH, OH), 1740, 1710 (C=O, ester), 1540 (NH), 1270 (C=S), 1240, 1220 (C-O-C), 1600, 1495, 1450, 760, and 700 (aromatic). Anal. found: C, 52.11; H, 5.56; N, 6.32. Calcd. for $C_{19}H_{24}N_2O_8S$: C, 51.81; H, 5.49; N, 6.36.

(4*R*, 5*R*)-1-Phenyl-4-(1,3,4-tri-*O*-acetyl-D-*arabino*-tetritol-1-yl)-5-hydroxyimidazolidin-2-thione (60).- a) A suspension of **26** (1.0 g, 2.1 mmol) and silica gel (1.0 g) in absolute methanol (100 mL) was stirred vigorously at room temperature for 24 h. Silica gel was filtered off and washed with acetone (3 x 40 mL). The combined extracts were evaporated to give a white foam (1.0 g), which was purified by flash chromatography (benzene-acetone, 3:1) giving **60** as an hygroscopic amorphous solid (0.6 g, 63%), m.p. 47-49°C, $[\alpha]_D$ +10° (*c* 0.5, chloroform), ν_{max} 3700-3000 (NH, OH), 1760 (C=O, ester), 1240 (C-O-C), 1610, 1515, 775, and 710 cm^{-1} (aromatic). Anal. found: C, 52.43; H, 5.69; N, 5.88. Calcd. for $C_{19}H_{24}N_2O_8S$: C, 51.81; H, 5.49;

N. 6.36.

b) A suspension of **59** (0.1 g, 0.2 mmol) and silica gel (0.1 g) in absolute methanol (10.6 mL) was stirred vigorously at room temperature for 24 h. Silica gel was filtered off and washed with acetone (3 x 10 mL). The combined extracts were evaporated to give a white foam (0.1 g), which was purified by preparative t.l.c (benzene-acetone, 3:1) giving **60** as amorphous solid (0.07 g, 65%).

Acetylation of 60.- To a solution of **60** (0.2 g, 0.45 mmol) in pyridine (1.0 mL), was added acetic anhydride (0.7 mL). The reaction mixture was kept at 0°C for 12 h, and then it was poured into ice. The resulting solid (0.14 g) was purified by preparative t.l.c. (benzene-acetone, 3:1) to give **40** (0.04 g, 16%) and **41** (0.06 g, 21%).

(4*R*, 5*R*)-4-(4-*O*-Acetyl-D-*arabino*-tetritol-1-yl)-1-phenyl-5-hydroxyimidazolidin-2-thione (61).- A suspension of **26** (1.0 g, 2.1 mmol) and silica gel (1.0 g) in absolute methanol (100 mL) was stirred vigorously at room temperature for 3 days. Work-up as described above for **60** and purification by flash chromatography (chloroform-methanol, 15:1) afforded **61** (0.02 g, 2%), m.p. 146-148°C, ν_{max} 3500-2900 (NH, OH), 1725 (C=O, ester), 1460 (NH), 1260 (C=S), 1220 (C-O-C), 1600, 1500, 745, and 690 (aromatic). Mass spectrum: m/z 338 ($M^+ - H_2O$). Calcd. for M^+ of $C_{15}H_{20}N_2O_6S$: 356.

1-Phenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-thione (62).- A suspension of **60** (0.4 g, 1.0 mmol) in ethanol-water (10 mL) was heated at 80°C for 10 min. After cooling, **62** crystallised (0.1 g, 26%), m.p. 155-158°C, $[\alpha]_D$ +87° (*c* 0.5, chloroform), [lit.[12a] m.p. 152-154°C, $[\alpha]_D$ +87° (*c* 0.5, chloroform)], ν_{max} 3300 (NH), 1745, 1735, 1710 (C=O ester), 1425 (NH), 1250 (C=S), 1235, 1220 (C-O-C), 1595, 1495, 770, 760 and 690 cm^{-1} (aromatic).

Transformation of 61 into 63.- This transformation was monitored by NMR in a sample prepared as follows: to a solution of **61** (0.01 g, 0.03 mmol) in DMSO-d_6 (0.5 ml) a drop of acetic acid was added and the reaction mixture was keep at room temperature. After several days, NMR spectra showed a total conversion into 1-phenyl-(6-*O*-acetyl-1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazoli-din-2-thione (**63**).

3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose hydrobromide (66).- To a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-[(2,2-diethoxycarbonylvinyl)amino]-α-D-glucopyranose,[37,38] **65**, (12.0 g, 25.3 mmol) in chloroform (90 mL) was added dropwise a solution of bromine (1.1 mL, 21.9 mmol) in chloroform (73 mL) and water (0.4 mL). The reaction mixture was kept at room temperature, and after ~30 min., crystallisation took place. The flask was kept at 0°C for 4 h, and then the product was filtered off and washed with ether (6.1 g, 62%), m.p. 193-197°C (methanol-ether), $[\alpha]_D$ +88° (*c* 0.5, pyridine), ν_{max} 3500-2800 (NH, OH), 1740 (C=O, ester), 1590, 1560 (NH), and 1210 cm^{-1} (C-O-C). Anal. found: C, 37.49; H, 5.29; N, 3.58. Calcd. for $C_{12}H_{20}BrNO_8$: C, 37.32; H, 5.22; N, 3.63.

1-Phenyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]imidazolidin-2-thione (67).- a) A solution of **59** (0.08 g., 0.18 mmol) in 50% aqueous acetic acid (2.0 mL) was heated at 60°C (external bath) for 4 hours. The reaction mixture was concentrated until dryness and the residue, a mixture 85:15 of **67** and 1-phenyl-4-(1,2,4-tri-*O*-acetyl-D-*arabino*-tetritol-1-yl)imidazolin-2-thione, **68**, was crystallised from ether-light petroleum to give **67** (0.06 g., 75%), m.p. 77-80°C, $[\alpha]_D$+53° (*c* 0.5, chloroform), ν_{max} 3500-3100 (NH), 1750 (C=O, ester), 1435 (NH), 1240 (C-O-C, ester), 1600, 1505, 1460, 765, and 700 cm^{-1} (aromatic) (neat). Mass spectrum: m/z 422.1145. Calcd. for M^+ of $C_{19}H_{22}N_2O_7S$: 422.11476. Anal. found: C, 53.65; H, 5.21; N, 6.45. Calcd. for $C_{19}H_{22}N_2O_7S$: C, 54.02; H, 5.25; N, 6.63.

b) A solution of **59** (0.15 g., 0.3 mmol) in glacial acetic acid (2.0 mL) was heated at 60°C (external bath) for 2 h. Solvent evaporation and NMR analysis of the crude product revealed a mixture 3:7 of **67** and **68**, which was separated and purified by preparative t.l.c. (benzene-acetone 3:1) to give **67** (0.034 g., 24%) and a mixture of **68** and **69** (0.095 g., 68%). This mixture of isomers had mass spectrum: m/z 422.1155. Calcd. for M^+ of $C_{19}H_{22}N_2O_7S$: 422.1155.

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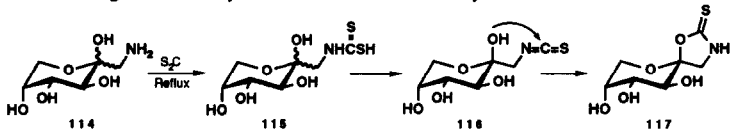

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