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ON THE MECHANISM OF FORMATION OF GLYCOFURANO[2,1-*d*]-IMIDAZOLIDIN-2-ONES. REACTION OF 2-AMINO-2-DEOXYHEPTOPYRANOSES WITH ISOCYANATES.

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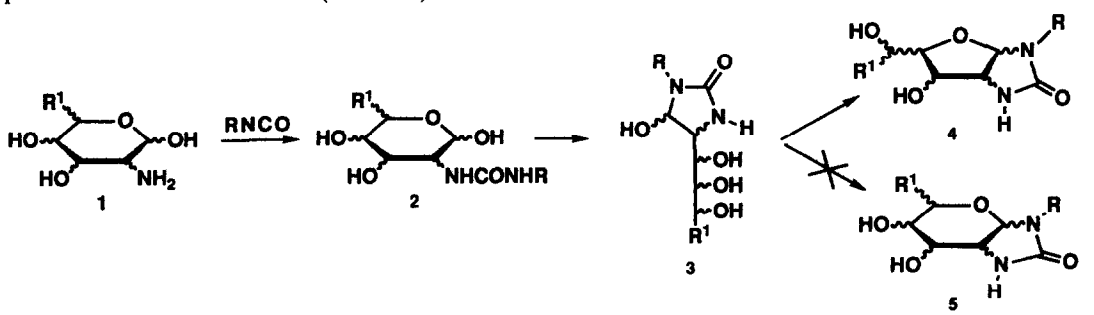
Abstract: Reaction of 2-aminosugars with isocyanates has been extended to other higher-carbon sugars. Ureido derivatives or, in most cases, monocyclic structures can be easily isolated. Importantly, the last substances display a relative *trans* disposition between the substituents at C-4 and C-5 of the heterocyclic ring, as a consequence of a rapid *cis-trans* isomerisation in acidic media. This stereochemical feature ensures the stereocontrolled ring closure to give exclusively *cis*-fused glycofuranose systems. In the light of these results, some related reactions have been revised.

Introduction

In the preceding paper[1], we have reported the first and general synthesis of acetylderivatives of *cis*-fused glycopyrano[2,1-*d*]imidazolidin-2-ones **5** and have reinvestigated the reaction of 2-amino-2-deoxysugars with isocyanates. The latter constitutes a useful and old transformation in carbohydrate chemistry, which has been the subject of controversy for long time with continuous clarifications. In the light of our results, however, the mechanism of formation as well as the true intermediates of the process appear now visible. Several salient features can be therefore concluded: 2-deoxy-2-ureidosugars (**2**) are the initial products of this reaction; they are transformed into monocyclic structures (**3**) at basic pH values while, under acid conditions are invariably converted to *cis*-fused furanoid bicycles (**4**). Furthermore, we have showed that monocyclic structures are not only the intermediates leading to both furanoid and pyranoid bicycles, but also other cyclisation reactions can proceed *via* a similar mechanism (Scheme 1).

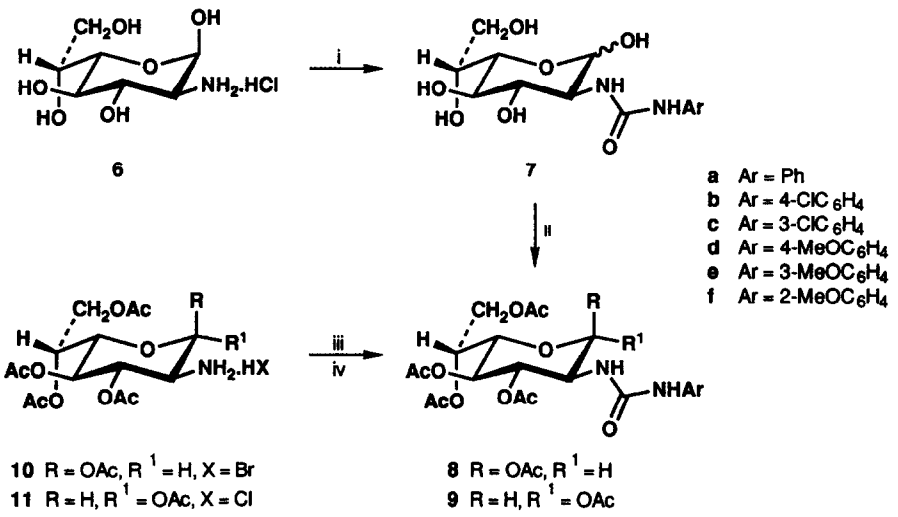


Scheme 1

Herein, we extend our results to 2-amino- and 2-alkylamino-2-deoxyheptoses, and report some stereochemical evidences which support completely the mechanism proposed.

Results

Reaction of 2-amino-2-deoxy-β-D-*glycero*-L-*gluco*-heptopyranose hydrochloride (**6**)[2] with aryl isocyanates in aqueous $NaHCO_3$-dioxane at room temperature, gives 2-(3-arylureido)-2-deoxy-D-*glycero*-L-*gluco*-heptopyranoses (**7**) in high yields (Scheme 2). *N,N'*-Diarylureas were unavoidable by-products of the process and in some cases, satisfactory analysis could not be obtained.



Scheme 2. *Reagents* i, ArNCO, aq. $NaHCO_3$; ii, Ac_2O, C_5H_5N; iii, aq. $NaHCO_3/CHCl_3$; iv, ArNCO

Spectroscopic data of **7** are in agreement with the assigned structures (Table 1). Thus, the glycosidic signals were very similar to those of **6** in $(CD_3)_2SO$-d_6, and anomeric mixtures were found in some cases. As 2-(3-arylureido)-2-deoxyhexopyranoses[1], the isomer having the axial hydroxyl group at C-1 was predominant.

Table 1. ^{13}C-NMR chemical shifts[a] (ppm) for **6** and **7**.

Comp	Anomer	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C=O
6	β	89 05	54.61	69.62	70 11	70 22	68 57	62.64	
	α	93 42	57 59	72 69	69.31	74 65	68 14	62.11	
7a	β	91.46	54.35	70 38	70 38	71 90	69 17	63 17	155 32
7b	β	91 42	54 39	70 33	70 33	71 84	69 13	63 15	155 18
7c	β	91 27	54.28	70 21	70 21	71.70	69 01	63.03	154 94
7d	β	91 53	54.41	70.31	70.42	71 94	69.17	63 18	155 63
	α	96 75	58 30	74.37	69.96	75 06	68 74	62.55	156.89
7e	β	91.48	54.34	70.32	70 32	71 90	69.15	63.16	159.85
7f	β	91 41	54.36	70 14	70 49	71.61	69.05	63.08	155.40

[a] In DMSO-d_6 at 50 33 MHz

Pyranoid structures of **7** were established by conventional acetylation (acetic anhydride in pyridine) yielding anomeric mixtures of the per-*O*-acetylated derivatives (**8** and **9**), that in the most cases could be separated by crystallisation (Tables 2-4).

Table 2. ^{13}C-NMR chemical shifts[a,b] (ppm) for 8 and 9.

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C=O
8a	91.05	51.53	71.12	66.70	69.90	66.60	62.09	154.95
9a	92.94	54.10	72.73	67 26	72.73	66.66	62 50	155.35
8b	90.85	51.69	71.09	66.60	69.91	66.60	62.04	154.87
9b	93 01	54.18	72.91	67 16	72.70	66.60	62.53	155 11
8c	91.00	51 74	71.16	66 58	69.94	66.58	62.12	154 24
8d	90 92	51.51	71 03	66.53	69.87	66.53	62 43	156.72
9d	93.11	53.43	72.68	66.53	67.03	66.53	62.44	156.05
8e	91.03	51.74	71.15	66.63	70 00	66 63	62.18	160.42
9e	92.91	54.14	72.78	72 70	67.18	66.63	62 51	160 32
8f	91 08	51.32	71.19	66 70	69.73	66 54	62 05	154 50

[a] In $CDCl_3$ at 50 33 MHz. [b] Signal for acetoxy groups have been omitted

Table 3. ^{1}H-NMR chemical shifts[a,b] (ppm) for 8 and 9.

Comp.	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-7'	ArNH	S-NH[c]	CH_3	Ar
8a	6.25d	4.45m	—5.21m—		4.05m	5.21m	4.25dd	4.13dd	7.05s	5.21m		7.35-7.05m
9a	5.85d	4.02m	5.35t	5.10t	3.92dd	5.27m	4.36dd	4.15dd	7.37s	5 59d		7.31-7.05m
8b	6.25d	4.41m	—5.20m—		4.06m	5.20m	4.25dd	4.14dd	7.31s	5.39d		7.23m
9b	5.78d	4.02m	5.27t	5 09t	3.90dd	5.28m	4.36dd	4.16dd	7.40s	5 57d		7.27s
8c	6.25d	4.41m	—5.20m—		4.07m	5.20m	4.26dd	4.14dd	7.17s	5.31m		7.35-7 02m
8d	6.24d	4.40m	—5.19m—		4.05m	5.19m	4.27dd	4.16dd	7.22-7.08m	5.32d	3.77s	7.13d, 6.84d
8e	6.23d	4.42m	—5.20m—		4.04m	5.20m	4.25dd	4.12dd	7.33s	5.07d	3.79s	7.21-6.63m
9e	5.86d	4.01q	5.35t	5.11t	3.94dd	5.27m	4.37dd	4.16dd	7.33s	5.53d	3.77s	7.22-6.62m
8f	6.23d	4.50m	—5.25m—		4.11m	5.25m	4.26dd	4.14dd	7.31s	5.58d	3.69s	8.00-6.76m

[a] In $CDCl_3$ at 200 MHz. [b] Signal for acetoxy groups have been omitted [c] S = sugar moiety

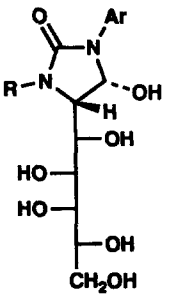
Table 4. ^{1}H-NMR coupling constants[a] (Hz) for 8 and 9.

Comp.	$J_{1,2}$	$J_{2,3}$	$J_{2,NH}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$
8a	3.7	9.4	9.4				5.1	7.3	11.5
9a	8.8	9.7	9.1	9.7	9.7	2.0	4.6	8.0	11.7
8b	3.6	9.4	9.4				5.2	7.3	11.6
9b	8.8	9.7	9.1	9.7	9.7	2 0	4.5	8.0	11.7
8c	3.7	8.9	9.3		8.7		5.1	7.3	11.6
8d	6.4	9.8	9.3				5.0	4.3	11.6
8e	3.6	9.0	9.0		8.2		5.0	7.5	11.7
9e	8.8	9.8	9.2	9.8	9.8	2.2	4.7	8.1	11.7
8f	3.6	9.8	9.5		7.9		5.3	7.3	11.8

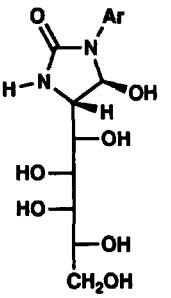
[a] In $CDCl_3$ at 200 MHz

Compounds **8** and **9** display a $^{1}C_4$(L) conformation in solution. The β-anomeric configuration of **8** was attributed on the basis of the small $J_{1,2}$ value (~3.6 Hz), and that of **9** (α-anomer) was consistent with a large $J_{1,2}$ value (~8.8 Hz). Structures of **8a**, **8b**, **9a**, and **9b** were confirmed by synthesis from **10**[3] or **11**[4] with the corresponding aryl isocyanates.

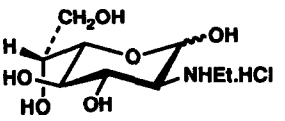
Solubility affects markedly the formation of products, because in solution ureas **7** are transformed into monocycles. Thus, the reaction of **6** with 4-nitrophenyl isocyanate gave, under the same conditions described above, a mixture of the C-1* epimers **12** and **14**. Similarly, condensation of phenyl isocyanate with 2-deoxy-2-ethylamino-D-*glycero*-L-*gluco*-heptopyranose hydrochloride[5] (**17**) affords the monocyclic imidazolidin-2-one (**13**) in low yield. Compounds **15** and **16** were quantitatively formed by cyclisation of **7a** and **7d** in basic media.



1 2 Ar = 4-NO $_2$C$_6$H$_4$, R = H
1 3 Ar = Ph, R = Et



1 4 Ar = 4-NO $_2$C$_6$H$_4$
1 5 Ar = Ph
1 6 Ar = 4-MeOC $_6$H$_4$



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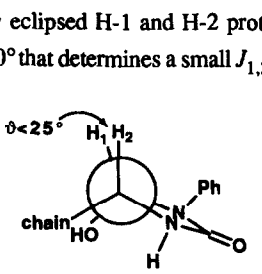
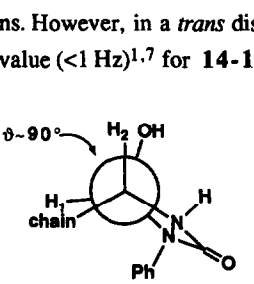
The C-1 of *cis* and *trans* monocyclic imidazolidin-2-ones resonates at similar chemical shifts to those measured for the C-1 carbon of other monocycles[1]. An open polyhydroxyalkyl chain is also evidenced[6] by the almost coincidental chemical shifts of C-3, C-4, C-5, and C-6 for **12-16** (Table 5).

The C-1 configuration was assigned by $J_{1,2}$ values. In a *cis* disposition between H-1 and H-2 (**12** and **13**), $J_{1,2}$ coupling constant showed large values (>5 Hz) as occurs for similar structures[7] with a small dihedral angle (<25°) between closely eclipsed H-1 and H-2 protons. However, in a *trans* disposition, the conformation shows a dihedral angle of ~90° that determines a small $J_{1,2}$ value (<1 Hz)[1,7] for **14-16.**



***cis* isomer**



***trans* isomer**

Compound **13** showed an unexpected behaviour. The ^{13}C-NMR spectrum of a just dissolved sample in DMSO-d_6 is assignable to a monocyclic structure. However, its slow conversion into another compound having similar chemical shifts for all carbons was detected when the spectrum was registered every so often (Fig. 1). This is indicative of a slow and total epimerisation at C-1. The C-1 configuration of the first compound **13** must be *R* (H-1 and H-2 protons in *cis* disposition, $J_{1,2}$ 6.0 Hz) because the epimerization at this carbon leads to the more stable (*S*)-diastereomer **18** (H-1 and H-2 protons in *trans* disposition, $J_{1,2}$ 0 Hz).

*As in the previous paper[1], the original numbering of 2-(3-arylureido)-2-deoxysugars is maintained in the related monocyclic and bicyclic imidazolidin-2-ones to clarify the exposition. The correct numeration and nomenclature are given in the Experimental.

Table 5. ^{13}C-NMR chemical shifts[a] (ppm) for 12-16, 18, 19, 22-27, 31, 33, and 34.

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C=O	Ar	Et
12[a]	81.75	60.95	69.83	69.71	69.52	69.52	63.14	156.52	146.01, 141.05 124.66, 117.56	
13[a,b]	77.97	58.82	70.10	69.67	69.54	69.38	63.18	157.28	139.09, 128.08 122.31, 119.41	12.24 37.10
14[a]	79.53	56.29	70.13	69.14	68.41	69.52	63.31	157.01	146.25, 141.38 125.31, 117.65	
15[a]	82.32	61.16	69.80	69.80	69.69	69.46	63.25	157.42	139.54, 128.54 122.55, 119.50	
16[a,c]	82.67	61.09	69.61	69.61	69.61	69.37	63.09	157.40	155.14, 132.41 122.00, 113.63	
18[a,b]	79.36	63.29	69.67	69.54	68.86	68.16	63.18	155.46	139.64, 128.08 121.96, 119.00	12.55 37.11
19[d]	78.93	54.69	68.70	67.99	67.60	67.53	62.89	158.34	136.04, 128.97 125.62, 123.01	11.88 39.03
22[d]	79.00	53.39	67.33	67.33	67.33	67.33	62.52	157.76	143.83, 142.13 124.57, 120.24	
23[d,e]	77.84	57.44	67.74	67.22	66.83	66.04	61.64	151.11	144.38, 141.70 124.97, 119.24	
24[d]	108.15	119.31	69.09	67.94	67.49	64.84	62.04	152.56	144.87, 141.74 125.70, 120.70	
25[d]	88.01	55.78	69.54	68.64	67.73	67.35	61.96	156.93	143.77, 143.39 124.84, 118.66	14.99 59.63
26[d]	83.27	59.14	69.31	67.62	67.42	67.24	62.07	158.15	137.54, 128.82 124.41, 120.61	18.21[f] 58.21[f]
27[c,d]	84.06	59.36	69.39	67.64	67.64	67.64	62.16	158.19	157.15, 130.06 123.91, 114.22	
31[a]	90.16	60.89	74.35	78.63	66.31	70.92	62.63	155.67	157.67, 132.29 122.31, 113.84	
33[a]	87.36	64.22	71.62	78.86	66.19	70.63	62.46	155.82	139.38, 128.58 122.91, 119.13	
34[d]	88.09	62.66	73.32	75.14	67.20	69.22	61.72	155.74	138.20, 128.85 124.06, 119.49	

[a]In DMSO-d_6 at 50.33MHz. [b] At 20.15 MHz. [c] Methoxy group of **16**, **27**, and **31** resonated at 55 21, 55 45, and 55.28 ppm, respectively. [d]In $CDCl_3$. [e]Methyl group of NAc resonated at 24.14 ppm. [f]Ethanol of crystallisation (1:1)

Further calculations[8] by means of molecular mechanics [MMP2(86)][9] demonstrated that the *trans*-isomer **18** is enthalpically favoured by >1Kcal/mol over the *cis*-isomer **13**. This situation indicates a great preference (>85%) of the former at room temperature.

Conventional acetylation of **13** gave the hexa-*O*-acetyl derivative **19**. The isomeric structures **20** and **21** were discarded on the basis of: a) the chemical shift of C-1 of **20** and **21** would be higher (> 87 p.p.m.) than that of **13** and **19** (Table 5), b) the lack of a signal assignable to the N-Ac methyl group[10] for **21** (~2.6 p.p.m. and ~40 p.p.m. in ^{1}H- and ^{13}C NMR spectra, respectively), c) the presence of coupling constants inconsistent with the more stable $^1C_4$ conformation for the pyranoid ring possessing a L-*gluco* configuration, and d) the presence in the mass spectra of some peaks attributable to the characteristic (B+30) and (B+30 - H_2O) or (B+30 - AcOH) fragments (B=heterocyclic moiety)[11]. The $J_{1,2}$ coupling constant (5.9 Hz) is indicative of a *R* configuration at C-1 of **19**, which confirms the stereochemical assignment of **13**.

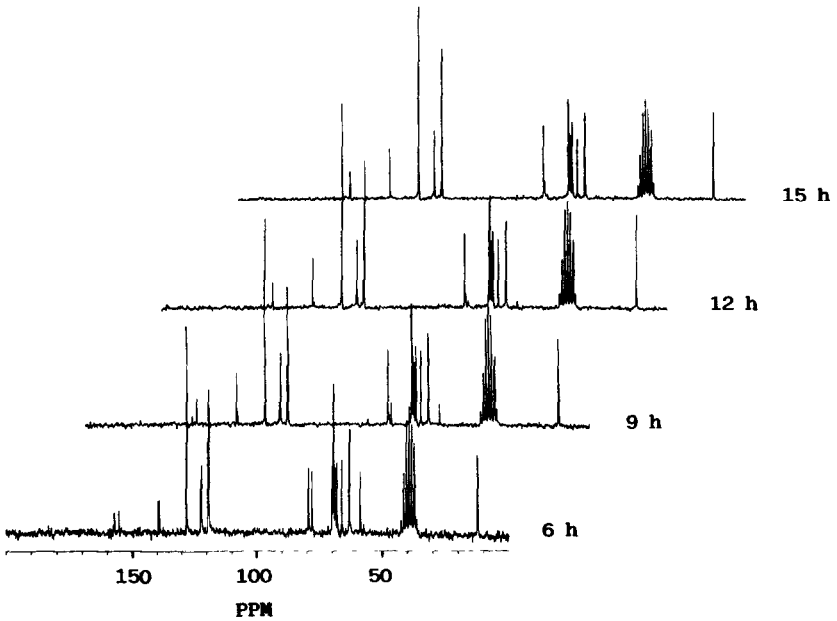


Figure 1. ^{13}C NMR spectra (20.15 MHz) taken at intervals during the transformation of **13** into **18** in DMSO-d_6 at 30°.

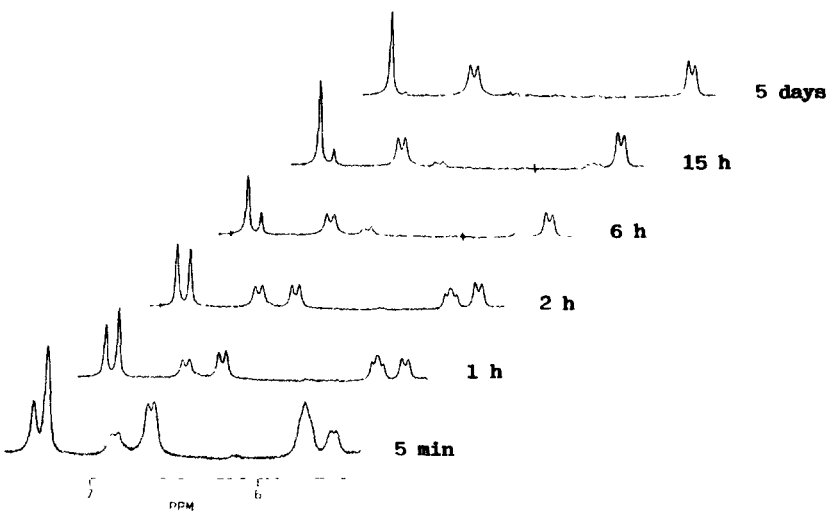


Figure 2. ^{1}H NMR spectra (200 MHz) taken at intervals during the transformation of **12** (from a mixture of **12** and **14**) into **14** in DMSO-d_6 at 25°.

Table 6. ^{1}H-NMR chemical shifts[a] (ppm) for 19, 22-27, 31, 33, and 34.

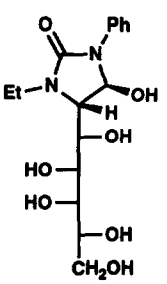
Comp.	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-7'	NH	CH_3	CH_2	OH	Ar	N-Ac
19[b]	7.17d	3.80dd	5.69d	5.09d	5.04dd	5.29ddd	4.33dd	3.77d		1.11t	3.69m		7.46-7.21m	
22	7.24d	3.97dd	5.56d	4.99d	5.14dd	5.34m	4.31dd	3.82dd	7.39s				8.20d 7.72d	
23	6.78s	4.61d	5.56dd	5.26dd	5.38dd	5.13m	4.21dd	3.84dd					8.27d 7.76d	2.64s
24	6.72s		5.85d	5.51dd	5.44dd	5.34m	4.30dd	3.86dd	9.54s				8.30d 7.84d	
25	5.56s	3.78d	5.22dd	5.34dd	5.50dd	5.24m	4.28dd	3.83dd	7.39s	1.18t	3.46q		8.23d 7.79d	
26	5.38d	3.60d	5.10dd	5.43dd	5.30dd	5.22m	4.27dd	3.80dd	6.23s	1.23t[c]	3.70q[c]	4.56d	7.50-7.11m	
27	5.33d	3.59dd	5.16dd	5.52dd	5.35dd	5.24m	4.28dd	3.82dd	5.71s	3.79s		3.98d	7.36dd 6.85dd	
31[d]	5.81d	3.97d	———		4.10-3.30m		———		7.34s	3.71s		5.43-4.00m	7.44d 6.87d	
33[d]	5.95d	4.06d	———		3.90-3.41m		———			1.11t	3.14q	5.26d 4.44-4.24m	7.63-7.05m	
34	5.95d	4.09d	5.22d	4.18dd	5.50dd	5.46m	4.32dd	3.93dd		1.24t	3.76m 3.27m		7.65-7.08m	

[a] In $CDCl_3$ at 200 MHz. [b] At 360 MHz [c] Ethanol of crystallisation (1 1) [d] In DMSO-d_6.

Table 7. ^{1}H-NMR coupling constants[a] (Hz) for 19, 22-27, 31, 33, and 34.

Comp.	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$	$J_{1,OH}$	$J_{2,NH}$
19[b]	5.9	9.8	0.0	10.2	1.5	4.1	8.3	11.9		
22	5.7	9.9	0.0	10.3	1.4	4.3	8.2	11.8		
23	0.0	7.1	1.6	9.0	2.0	5.3	6.9	11.6		
24			2.8	9.2	1.9	4.9	7.4	11.7		
25	0.0	3.5	2.2	9.5	2.7	5.0	7.3	11.8		
26	0.0	7.0	1.9	9.6	1.9	4.7	7.4	11.7		
27	<1.0	6.3	2.2	9.6	2.3	4 7	7.5	11.9	8.1	
31[c]	6.1	0.0								0.0
33[c]	6.3	0.0								
34	6.6	0.0	2.9	9.1	2.7	5.3	6.7	11.5		

[a] In $CDCl_3$ at 200 MHz [b] At 360 MHz. [c] In DMSO-d_6



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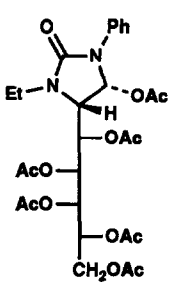

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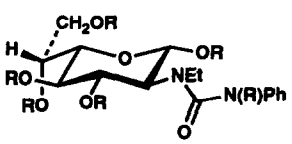
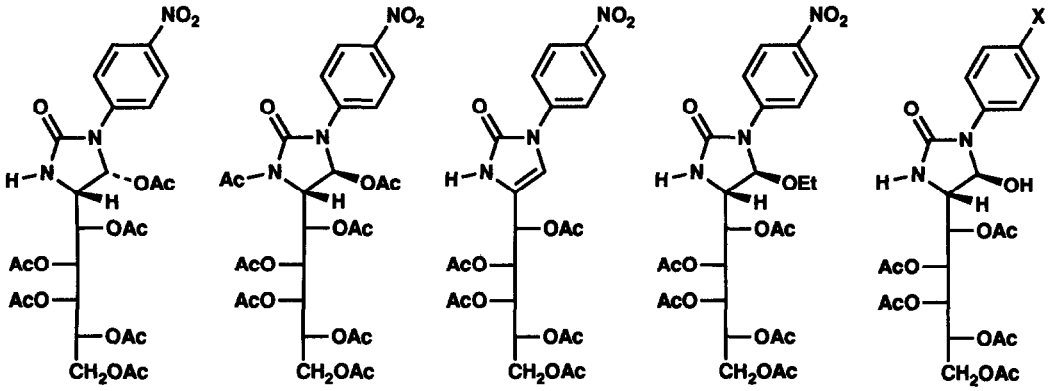


20 R = H
21 R = Ac

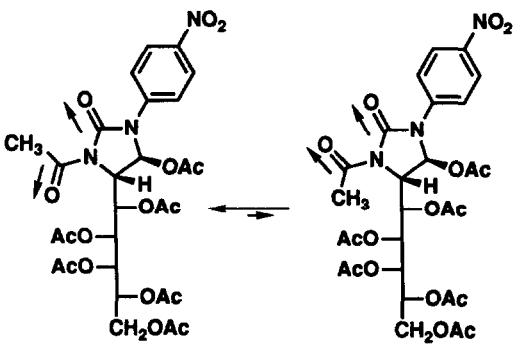
Likewise, the transformation of **12** into **14** from a mixture of both compounds, was almost complete and in the equilibrium a conversion of ~90% was observed. Figure 2 depicts the conversion of H-1 triplet of compound **12** ($J_{1,2} = J_{1,NH}$ 7.0 Hz) to one doublet for **14** ($J_{1,2}$ 0, $J_{1,NH}$ 7.5 Hz).

Acetylation of the mixture of **12** and **14** leads to a complex mixture of acetylated derivatives, from which compounds **22-25** were isolated by crystallisation or preparative TLC. Compound **25** was formed in the presence of ethanol during the work-up. Compounds **26** and **27** were obtained from **15** and **16**, respectively.



22 **23** **24** **25** **26** X=H, **27** X=MeO

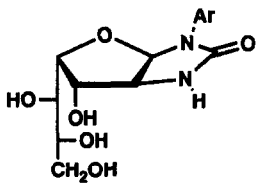
Important differences were found in the chemical shifts of some protons of compounds **19**, **22**, and **23** when compared with **26** and **27**. This effect may be attributed to the presence of the heterocyclic acetate in the first ones, were H-1 for instance, resonated at lower field ($\Delta\delta$ >1.5 p.p.m.) (Table 6). On the other hand, the unusual deshielding of methyl signal of NAc (2.64 ppm) group of **23** is caused by the heterocyclic C=O bond in the more-stable conformation (**28**) of the acetamido group. The alternative conformation **29** is destabilised by the dipole-dipole repulsion of C=O bonds[12,13,14].



28 **29**

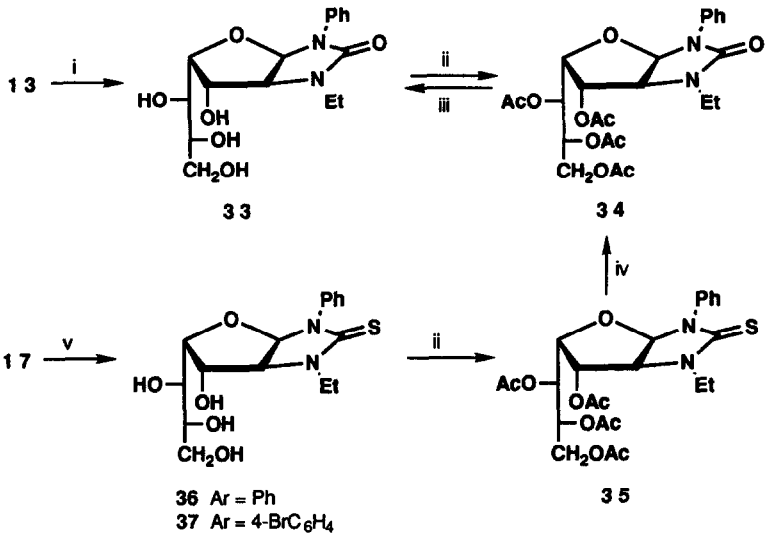
Treatment of **15**, **16**, and **13** with hot dilute acetic acid gave 1-aryl-(1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]imidazolidin-2-ones **30**, **31**, and **33**, respectively, in high yield. Compounds **30** and **32** have been also obtained from the corresponding 2-(3-arylureido)-2-deoxy-heptopyranoses **7a** and **7b** in the same way[10]. Conventional acetylation of **33** gives its tetra-*O*-acetyl derivative **34**.

Furanoid structures of **30-34** were established on the basis of the small $J_{2,3}$ values (~0 Hz) if H-2 and H-3 protons are in *trans* orientation (*cis* arrangement gives a $J_{2,3}$ of 5-7 Hz)[1,10].



30 Ar = Ph
31 Ar = 4-MeOC$_6$H$_4$
32 Ar = 4-ClC$_6$H$_4$

Compounds **33** and **34** were unequivocally prepared by transformation of **35** into **34** using nitrous acid[15]. Zemplen deacetylation of **34** gave **33**.



33 **34**

36 Ar = Ph
37 Ar = 4-BrC$_6$H$_4$

35

Scheme 3. *Reagents*: i, aq. AcOH, Δ; ii, Ac_2O, C_5H_5N; iii, MeO^-/MeOH; iv, $NaNO_2$/ aq. HCl/$CHCl_3$; v, ArNCS, aq. $NaHCO_3$.

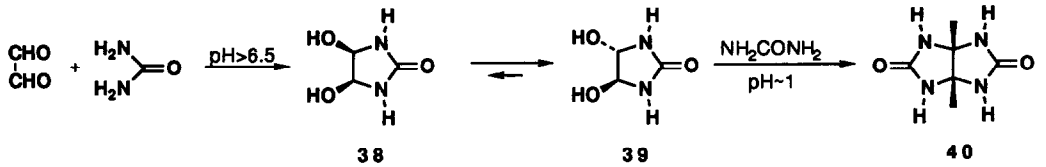
Compound **35** was prepared by acetylation of **36**, that was previously obtained by condensation of **17** with phenyl isothiocyanate[8]. The spectroscopic data of **36** were coincident with those of their 4-bromophenyl analogue **37**[5], whose structure has been confirmed by X-ray crystallography[16].

Discussion

As previously indicated[1] for 2-amino-2-deoxyhexoses, reaction of 2-amino- and 2-alkylamino-2-deoxyheptoses with aryl isocyanates at neutral pH values provides initially 2-(3-arylureido)-2-deoxy-glycopyranoses. These substances are rapidly converted to polyhydroxyalkyl 5-hydroxyimidazolidin-2-one derivatives (**12-16**) at basic pH values. However, at pH<7 only (1,2-dideoxy-β-D-*glycero*-L-*gluco*-hepto-furano)[2,1-*d*]imidazolidin-2-ones (**30-33**) are formed and Scheme 1 shows the mechanism proposed[1] for their formation.

Monocycles **14-16** display a relative *trans* disposition between the substituents at C-4 and C-5 of the

heterocyclic moiety. Curiously, monocycles **12** and **13** are obtained having a *cis*-configuration, but they are slowly transformed into the more stable *trans*-isomers **14** and **18**, respectively (see Figs.1 and 2). Similar observations have been already reported by Vail, Barker, and Mennit[17] for the reaction of glyoxal with urea.

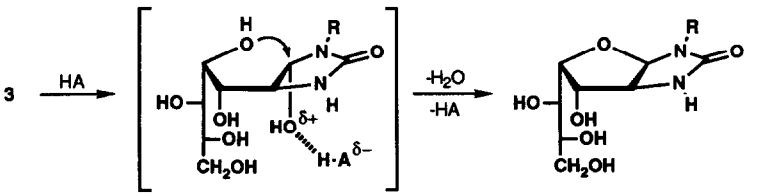


38 **39** **40**

Scheme 4

Addition of urea to glyoxal under basic conditions affords initially equimolar amounts of the *cis*- and *trans*-isomers (**38**, **39**), but the less stable *cis*-isomer (**38**) is rapidly converted to *trans*-**39** which predominates in the resulting equilibrium mixture. At acidic pH, the concentration of *cis* isomer remains at a low level, whereas the concentration of the *trans* isomer increases rapidly. Importantly, *cis-trans* isomerization is catalysed by acids. At a pH~2.0, the equilibrium was reached in only 4-5 min., but at pH values >7 the conversion to the equilibrium mixture requires 24 h. Finally, at pH~1, glycoluril (**40**)[18] was formed.

These results are similar to those found for **12** and **13** and provide a reasonable explanation for the formation of monocycles (**12-16** and **18**) and bicycles (**30-33**) by cyclisation of the corresponding ureidoderivatives. The rapid *cis-trans* isomerization of monocycles at acidic pH values ensures the exclusive formation of *cis*-fused glycofuranose derivatives **42** by S_N2 substitution.

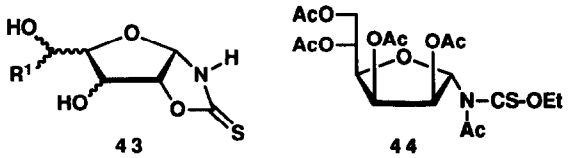


41 **42**

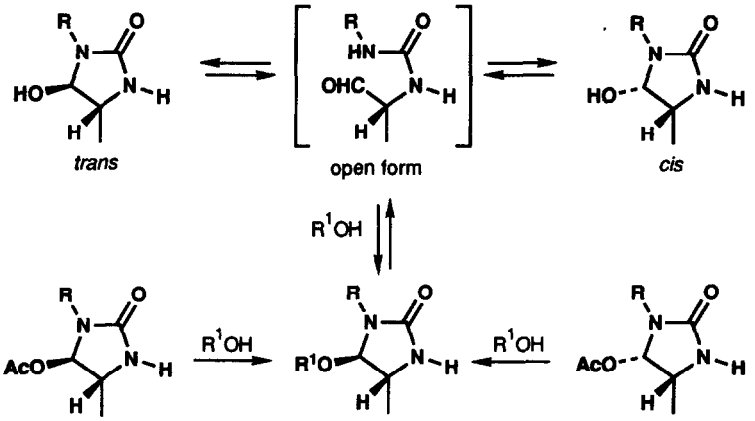
Scheme 5

The *cis-trans* isomerization of 5-hydroxyimidazolidin-2-ones should occur *via* an open chain aldehydic intermediate. This compound might also mediate the formation of compound **25** having an alkoxy substituent, although acetate substitution in C-1 is also possible (Scheme 6).

A similar behaviour has been reported on this matter, but erroneously interpreted. It is known[19,20] that the reaction of aldoses with thiocyanic acid at acidic pH values leads to furanoid bicyclic oxazolidin-2-thiones **43**. However, Jochims *et al.*[21] assigned structure **44** to a compound obtained in low yield (4%) from the reaction of D-mannose (**45**) with thiocyanic acid and further acetylation and treatment with ethanol.

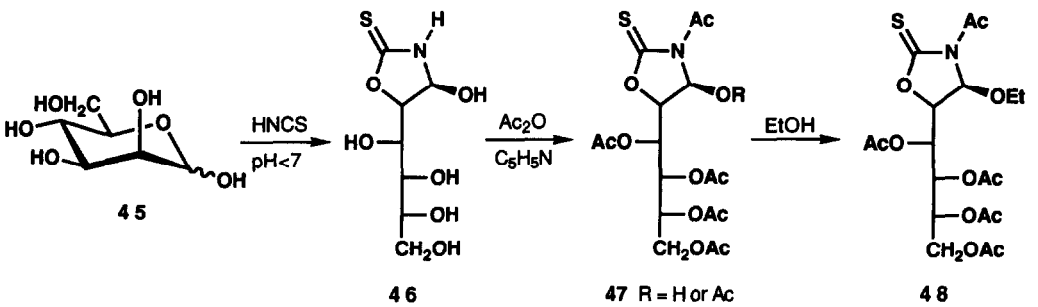


43 **44**



Scheme 6

Nevertheless, spectroscopic data of **44** are quite different to those reported[22] for α-*lixo*furanoid compounds, and suggest presumably a monocyclic structure (as **25**) of (4*S*,5*S*)-*N*-acetyl-5-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-4-ethoxyoxazolidin-2-thione (**48**). The (4*S*) configuration is consistent with the small $J_{1,2}$ value (1.3 Hz). Its formation, *via* intermediates **46** and **47**, is outlined in Scheme 6 and proves again the participation of monocyclic structure in the formation of bicycles **43**.



Scheme 7

In summary, we have found that reactions of 2-(alkyl)amino-2-deoxyheptoses with aryl isocyanates produce ureidoderivatives in high yields, which cyclise at pH>6 to a mixture of *cis* and *trans* monocycles. Acid-catalysed isomerisation proceeds quickly in solution to give the termodynamically more stable *trans*-isomers. At pH<6 both ureas and monocycles are converted to furanoid bicycles.

The intermediacy of monocyclic structures constitutes an unifying approach for numerous cyclisation reactions of sugars and aminosugars, and solves other structural, stereochemical, and mechanistic problems largely discussed in the past.

Acknowledgement.

Financial support of DGICYT (PB89-0492) is gratefully acknowledged. We also thank Dr. J. A. Galbis for recording NMR spectra of compound **13**.

Experimental

The ^{1}H- (360, 200, and 80 MHz) and ^{13}C-NMR (50.33 and 20.15 MHz) spectra were recorded with Brucker 360, Brucker AC 200-E, or Brucker WP-80-SY spectrometres. The rest of general methods have been previously described[1].

General procedure for the preparation of 2-(3-arylureido)-2-deoxy-D-*glycero*-L-*gluco*-heptopyranoses (7).- To a solution of **6** (30 mmol) in water (33 mL), sodium hydrogencarbonate (30 mmol) and aryl isocyanate (36 mmol) in dioxane (7.5 mL), were added. After a few minutes a white solid precipitated from the solution. The resulting suspension was stirred for 30 min, and the ureido derivative was filtered off and successively washed with cold water, acetone-ethanol and ether.

2-Deoxy-2-(3-phenylureido)-D-*glycero*-L-*gluco*-heptopyranose (7a).- From phenyl isocyanate, compound **7a** (75%) was obtained, m.p. 165-167°C (96% ethanol), $[\alpha]_D$ -57° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1645 (C=O), 1567 (NH), 1600, 1500, 736, and 687 cm^{-1} (aromatic). Anal. found: C, 48.97; H, 6.26; N, 7.94. Calcd. for $C_{14}H_{20}N_2O_7.H_2O$: C, 48.55; H, 6.40; N, 8.09.

2-[3-(4-Chlorophenylureido)]-2-deoxy-D-*glycero*-L-*gluco*-heptopyranose (7b).- From 4-chlorophenyl isocyanate, compound **7b** (60%) was prepared, m.p. 173-175°C (96% ethanol), $[\alpha]_D$ -31° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1560 (NH), 1591, 1490, and 826 cm^{-1} (aromatic). Anal. found: C, 43.82; H, 5.16; N, 7.20. Calcd. for $C_{14}H_{19}N_2O_7Cl.H_2O$: C, 44.16; H, 5.56; N, 7.36.

2-[3-(3-Chlorophenylureido)]-2-deoxy-D-*glycero*-L-*gluco*-heptopyranose (7c).- From 3-chlorophenyl isocyanate, compound **7c** (74%) was obtained, m.p. 164-166°C (96% ethanol), $[\alpha]_D$ -51° (*c* 1.0, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1650 (C=O), 1580 (NH), 1600, 1490, and 780 cm^{-1} (aromatic). Anal. found: C, 44.06; H, 5.74; N, 7.53. Calcd. for $C_{14}H_{19}N_2O_7Cl.H_2O$: C, 44.16; H, 5.56; N, 7.36.

2-Deoxy-2-[3-(4-methoxyphenylureido)]-D-*glycero*-L-*gluco*-heptopyranose (7d).- From 4-methoxyphenyl isocyanate, compound **7d** (93%) was obtained, m.p. 178-180°C, $[\alpha]_D$ -52° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1575 (NH), 1243 (OCH_3), 1606, 1513, and 834 cm^{-1} (aromatic). Anal. found: C, 49.09; H, 6.28; N, 7.48. Calcd. for $C_{15}H_{22}N_2O_8.1/2H_2O$: C, 49.04; H, 6.31; N, 7.62.

2-Deoxy-2-[3-(3-methoxyphenylureido)]-D-*glycero*-L-*gluco*-heptopyranose (7e).- From 3-methoxyphenyl isocyanate, compound **7e** (68%) was obtained, m.p. 170-172°C, $[\alpha]_D$ -54° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1645 (C=O), 1575 (NH), 1297 (OCH_3), 1614, 1490, 779, and 764 cm^{-1} (aromatic). Anal. found: C, 47.53; H, 6.16; N, 7.33. Calcd. for $C_{15}H_{22}N_2O_8.H_2O$: C, 47.87; H, 6.42; N, 7.44.

2-Deoxy-2-[3-(2-methoxyphenylureido)]-D-*glycero*-L-*gluco*-heptopyranose (7f).- From 2-methoxyphenyl isocyanate, compound **7f** (64%) was obtained, m.p. 159-160°C, $[\alpha]_D$ -54° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1621 (C=O), 1575 (NH), 1259 (OCH_3), 1490, and 749 cm^{-1} (aromatic). This compound was analysed as its acetyl derivative **8f**.

Preparation of 1,3,4,6,7-penta-*O*-acetyl-2-(3-arylureido)-2-deoxy-D-*glycero*-L-*gluco*-heptopyranoses.

Procedure A: To a solution of 2-(3-arylureido)-2-deoxy-D-*glycero*-L-*gluco*-heptopyranose (20.0 mmol) in pyridine (18 mL) acetic anhydride (30 mL) was added. After 24 h at room temperature, the reaction mixture was poured into ice-water to give a mixture of α– and β–anomers as a solid that was filtered and washed with cold water. From this anomeric mixture the α-anomer was generally isolated by fractional crystallisation. In some cases, the β-anomer could be obtained from the mother liquors by crystallisation.

Procedure B: To a suspension of per-*O*-acetyl-2-amino-2-deoxy-β or α-D-*glycero*-L-*gluco*-heptopyranose hydrohalide (3.0 mmol) in water (15 mL) and benzene (25 mL), calcium carbonate (2.0 mmol) was added. The mixture was stirred for 1h, the solid filtered off, and the organic phase was separated, dried (Na_2SO_4), and evaporated. The resulting residue was dissolved in chloroform (25 mL) and aryl isocyanate (3.0 mmol) was added. After 2 h at room temperature, the reaction mixture was evaporated and the residue crystallised from ethanol.

1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-2-(3-phenylureido)-β and α-D-*glycero*-L-*gluco*-heptopyranoses (8a and 9a).- Following the procedure A, **7a** afforded a mixture of **8a** and **9a** (81%). Recrystallisation from ethanol-ether gives the pure β-anomer **8a** (53%), m.p. 127-129°C, $[\alpha]_D$ -62° (*c* 1.0, chloroform), ν_{max} 3380 and 1550 (NH, H_2O), 3600 and 1650 (H_2O)[23], 1740, 1240, and 1220 (ester), 1700 (C=O urea), 1600, 1500, 755, and 690 cm^{-1} (aromatic). Anal. found: C, 51.88; H, 5.70; N, 5.07. Calcd. for $C_{24}H_{30}N_2O_{12}.H_2O$; C, 51.80; H, 5.80; N, 5.03.

Fractional crystallisation from the mother liquors afforded **9a** that was recrystallised from ethanol-ether (7%), m.p. 213-215°C, $[\alpha]_D$ +13° (*c* 1.3, chloroform), ν_{max} 3350 and 1545 (NH), 1750 and 1235 (ester), 1675 (C=O urea), 1600, 1500, and 745 cm^{-1} (aromatic). Anal. found: C, 53.43; H, 5.68; N, 4.97. Calcd. for $C_{24}H_{30}N_2O_{12}$: C, 53.53; H, 5.62; N, 5.20.

Following the procedure B, the reaction of **10**[3] and phenyl isocyanate afforded **8a** (42%). In the same way, compound **9a** (26%) could be obtained from **11**[3].

1,3,4,6,7-Penta-*O*-acetyl-2-[3-(4-chlorophenylureido)]-2-deoxy-β and α-D-*glycero*-L-*gluco*-heptopyranoses (8b and 9b).- Following the procedure A, **7b** afforded a mixture of **8b** and **9b** (89%). Recrystallisation from ethyl ether-light petroleum gives the pure β-anomer **8b** (51%), m.p. 95-97°C, $[\alpha]_D$ -41° (*c* 1.0, chloroform), ν_{max} 3360 and 1540 (NH), 1745, and 1220 (ester), 1700 (C=O urea), 1590, 1490, and 820 cm^{-1} (aromatic). Anal. found: C, 50.21; H, 5.38; N, 4.56. Calcd. for $C_{24}H_{29}ClN_2O_{12}$: C, 50.31; H, 5.10; N, 4.89. The α-anomer **9b** could not be isolated, although was detected by TLC.

Following the procedure B, the reaction of **10**[3] and 4-chlorophenyl isocyanate afforded **8b** (44%). In the same way, compound **9b** could be obtained (53%) from **11**[4], m.p. 220-222°C (ethyl ether-light petroleum), $[\alpha]_D$ +18° (*c* 1.3, chloroform), ν_{max} 3360 and 1540 (NH), 1740, 1240, 1230, and 1210 (ester), 1670 (C=O urea), 1590, 1490, and 820 cm^{-1} (aromatic). Anal. found: C, 50.20; H, 5.16; N, 4.90. Calcd. for $C_{24}H_{29}ClN_2O_{12}$: C, 50.31; H, 5.10; N, 4.89.

1,3,4,6,7-Penta-*O*-acetyl-2-[3-(3-chlorophenylureido)]-2-deoxy-β-D-*glycero*-L-*gluco*-heptopyranose (8c and 9c).- Following the procedure A, **7c** afforded a mixture of **8c** and **9c** (65%). Recrystallisation from 96% ethanol gives the pure β-anomer **8c** (39%), m.p. 138-140°C, $[\alpha]_D$ -60° (*c* 0.5, chloroform), ν_{max} 3390 and 1544 (NH), 1753 and 1228 (ester), 1706 (C=O urea), 1598, 1483, 788, and 687 cm^{-1} (aromatic). Anal. found: C, 50.33; H, 5.02; N, 5.25. Calcd. for $C_{24}H_{29}ClN_2O_{12}$: C, 50.31; H, 5.10; N, 4.89. The α-anomer **9c** could not be isolated, although was detected by TLC.

1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-2-[3-(4-methoxyphenylureido)]-β and α-D-*glycero*-L-*gluco*-heptopyranose (8d and 9d).- Following the procedure A, **7d** afforded a mixture of **8d** and **9d** (87%), which could not be separated.

1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-2-[3-(3-methoxyphenylureido)]-β and α-D-*glycero*-L-*gluco*-heptopyranose (8e and 9e).- Following the procedure A, **7e** afforded a mixture of **8e** and **9e** (84%). Recrystallisation from 96% ethanol gives the pure β-anomer **8e** (56%), m.p. 128-131°C, $[\alpha]_D$ -62° (*c* 0.5, chloroform), ν_{max} 3390 and 1552 (NH), 1753, 1240, and 1220 (ester), 1699 (C=O urea), 1606, 1374, 780, and 695 cm^{-1} (aromatic). Anal. found: C, 52.72; H, 5.62; N, 4.80. Calcd. for $C_{25}H_{32}N_2O_{13}$: C, 52.82; H, 5.67; N, 4.93.

Fractional crystallisation from the mother liquors afforded **9e** that was recrystallised from 96% ethanol (6%), m.p. 209-210°C, $[\alpha]_D$ +8° (*c* 1.0, chloroform), ν_{max} 3356 and 1547 (NH), 1746 and 1236 (ester), 1672 (C=O urea), 1611, 1508, 775, 754, and 604 cm^{-1} (aromatic). Anal. found: C, 52.84; H, 5.71; N, 4.96. Calcd. for $C_{25}H_{32}N_2O_{13}$: C, 52.82; H, 5.67; N, 4.93.

1,3,4,6,7-Penta-*O*-acetyl-2-deoxy-2-[3-(2-methoxyphenylureido)]-β-D-*glycero*-L-*gluco*-heptopyranose (8f and 9f).- Following the procedure A, **7f** afforded a mixture of **8f** and **9f** (75%). Recrystallisation from 96% ethanol gives the pure β-anomer **8f** (32%), m.p. 120-122°C, $[\alpha]_D$ -55° (*c* 1.0, chloroform), ν_{max} 3350 and 1555 (NH), 1760 and 1230 (ester), 1670 (C=O urea), 1610, 1490, 760, and 610 cm^{-1} (aromatic). Anal. found: C, 52.88; H, 5.62; N, 5.07. Calcd. for $C_{25}H_{32}N_2O_{13}$: C, 52.82; H, 5.67; N, 4.93.

(4*S*,5*S*)- and (4*S*,5*R*)-4-(D-*Galacto*-pentitol-1-yl)-5-hydroxy-1-(4-nitrophenyl)imidazolidin-2-one (12 and 14).- To a solution of **6** (1.6 g, 6.5 mmol) in water (7 ml), were added sodium hydrogencarbonate (0.6 g, 6.5 mmol), and 4-nitrophenyl isocyanate (1.27 g, 7.7 mmol) in dioxane (6 ml). After a few minutes a yellow solid precipitated. The resulting suspension was stirred (3 h) at room temperature and, after kept 12 h in the refrigerator, was filtered and successively washed with acetone and ether to give a mixture of **12** and **14** (2.2 g, 92%, ratio 3:7), δ_H (200 MHz, DMSO-d_6): for **12**, 8.33-7.68 (4H, m, Ar), 7.25 (1H, s, NH), 6.62 (1H, d, $J_{1,OH}$ 7.0, OH-1), 5.71 (1H, t, $J_{1,2}$ 7.0, H-1); for **14**, 8.33-7.68 (4H, m, Ar), 7.33 (1H, s, NH), 6.84 (1H, d, $J_{1,OH}$ 7.5, OH-1), 5.55 (1H, d, $J_{1,2}$ 0.0, H-1).

(4*R*,5*S*)- and (4*S*,5*S*)-1-Ethyl-5-(D-*galacto*-pentitol-1-yl)-4-hydroxy-3-phenylimidazolidin-2-one (13 and 18).- To a stirred solution of 2-deoxy-2-ethylamino-D-*glycero*-L-*gluco*-heptopyranose hydrochloride[5] (5.2 g, 19.0 mmol) in water (25 ml) were added sodium hydrogencarbonate (1.6 g, 19.0 mmol), and phenyl isocyanate (2.7 ml, 19.0 mmol) in dioxane (10 ml). The reaction mixture was stirred for 12 h at room temperature, and then was stored in the refrigerator for 48 h. After removal of crystals of *N,N'*-diphenylurea by filtration, a few drops of ether were added to the solution. The needles of **13** were filtered off and successively washed with cold water, acetone, and ether (0.3 g, 4%), m.p. 150-151°C, $[\alpha]_D$ -15.5° (*c* 1.0, pyridine), ν_{max} 3500-3200 (OH, NH), 1650 (C=O), 1595, 1500, 760, and 700 cm^{-1} (aromatic), δ_H (80 MHz, DMSO-d_6) 7.68-6.92 (5H, m, Ar), 6.18 (1H, d, $J_{1,OH}$ 7.6, OH-1), 5.55 (1H, dd, $J_{1,2}$ 6.0, H-2), 1.07 (3H, t, CH_2CH_3). Anal. found: C, 54.18; H, 7.00; N, 7.62. Calcd. for $C_{16}H_{24}N_2O_7$: C, 53.92; H, 6.79; N, 7.86.

The transformation of **13** into **18** was observed when a sample of **13**, in DMSO-d_6, was kept at room temperature for 24 h and successive ^{1}H-N.M.R. spectra were then recorded. The most important signals of the ^{1}H-N.M.R spectrum of **18** (δ_H, 80 MHz, DMSO-d_6) are: 7.72-6.87 (5H, m, Ar), 6.37 (1H, d, $J_{1,OH}$ 8.6, OH-1), 5.48 (1H, d, $J_{1,2}$ 0.0, H-1), 1.13 (3H, t, CH_2CH_3).

(4*S*,5*S*)-4-(D-*Galacto*-pentitol-1-yl)-5-hydroxy-1-phenylimidazolidin-2-one (15).- To a suspension of **7a** (0.25 g, 0.76 mmol) in water (25 ml), some drops of pyridine were added to maintain pH~8 and was stirred at 50-55°C for 6 h. The progress of the reaction was monitored by t.l.c. with $CHCl_3$-MeOH (3:1). The undissolved material was filtered, the solution evaporated and dried by successive evaporations from ethanol to give a white solid that was filtered and recrystallised from ethanol (0.17 g, 68%), m.p.198-199°C, $[\alpha]_D$ -25.5° (*c* 0.5, pyridine), ν_{max} 3600-3100 (OH, NH), 1695 (C=O), 1595, 1500, 760, and 690 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.64-6.99 (5H, m, Ar), 6.75 (1H, s, NH), 6.53 (1H, d, $J_{1,OH}$ 8.3, OH-1), 5.40 (1H, d, $J_{1,2}$ 0.0, H-1). Anal. found: C, 51.32; H, 6.21; N, 8.54. Calcd. for $C_{14}H_{22}N_2O_7$: C, 51.22; H, 6.14; N, 8.53.

(4*S*,5*S*)-4-(D-*Galacto*-pentitol-1-yl)-5-hydroxy-1-(4-methoxyphenyl)imidazolidin-2-one (16).- Compound **16** was prepared from **7d** (0.43 g, 1.2 mmol) as described for **15** (reaction time 7h). The white solid obtained was suspended in ethanol, filtered, and washed which cold ethanol and ether (0.33 g, 77%), m.p. 159-161°C, $[\alpha]_D$ -20.5° (*c* 0.5, pyridine), ν_{max} 3600-3100 (OH, NH), 1706 (C=O), 1610, 1521, 1452, and 840 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.46-6.88 (4H, m, Ar), 6.55 (1H, s, NH),

6.38 (1H, d, $J_{1,OH}$ 8.6, OH-1), 5.30 (1H, d, $J_{1,2}$ 0.0, H-1), 3.72 (3H, s, OCH_3). Anal. found: C, 50.40; H, 6.33; N, 7.83. Calcd. for $C_{15}H_{22}N_2O_8$: C, 50.28; H, 6.19; N, 7.82.

(4*S*,5*R*)-5-Acetoxy-4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-3-ethyl-1-phenylimidazolidin-2-one (19).- To a solution of **13** (0.1 g, 0.3 mmol) in pyridine (0.9 mL) acetic anhydride (0.7 mL) was added. The reaction mixture was stored for 48 h in the refrigerator and then poured into ice-water to give **19** (0.12g, 71%), m.p. 140-141°C, $[\alpha]_D$ +41.5° (*c* 0.7, chloroform), ν_{max} 1740, 1715, and 1220 (ester), 1700 (C=O urea), 1595, 1500, 770, and 700 cm^{-1} (aromatic). Anal. found: C, 55.23; H, 6.06; N,4.49. Calcd. for $C_{28}H_{36}N_2O_{13}$: C, 55.26; H, 5.96; N, 4.60.

Acetylation of 12 and 14.- To a solution of a mixture of **12** and **14** (0.5 g, 1.3 mmol) in pyridine (2.5 mL) acetic anhydride (3.0 mL) was added. The reaction mixture was stored at room temperature for 4 days and then poured into ice-water to give a white solid (0.5 g). Crystallised from 96% ethanol gave (4*S*,5*R*)-5-acetoxy-4-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(4-nitrophenyl)imidazolidin-2-one (**22**) (0.23 g, 28%), m.p. 205-206°C, $[\alpha]_D$ +52.5° (*c* 0.5, chloroform), ν_{max} 3340 (NH), 1760 and 1220 (ester), 1740 (C=O urea), 1530, 1350, and 880 (NO_2), 1605, 1510, and 800 cm^{-1} (aromatic). Anal. found: C, 49.88; H, 4.96; N, 6.56. Calcd. for $C_{26}H_{31}N_3O_{15}$: C, 49.92; H, 4.99; N, 6.71.

From the mother liquors of **22** three new compounds were separated by preparative t.l.c. (benzene-acetone, 3:1):

(4*S*,5*S*)-4-acetoxy-1-acetyl-5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-3-(4-nitrophenyl)imidazolidin-2-one (**23**) (0.053 g, 6%), m.p. 155-157°C (99% ethanol), $[\alpha]_D$ +46° (*c* 0.5, chloroform), ν_{max} 1750 and 1705 (C=O), 1520 and 1380 (NO_2), 1600, 1500, and 850 cm^{-1} (aromatic). Anal. found: C, 50.78; H, 5.12; N, 6.28. Calcd. for $C_{28}H_{33}N_3O_{16}$: C, 50.38; H, 4.98; N, 6.29.

4-(1,2,3,4,5-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(4-nitrophenyl)imidazolin-2-one (**24**) (0.032 g, 4.3%), colourless oil, $[\alpha]_D$ +21° (*c* 0.4, chloroform), ν_{max} 3340 (NH), 1750 and 1235 (ester), 1710 (C=O urea), 1520, 1370, and 855 (NO_2), 1600, 1500, and 820 cm^{-1} (aromatic).

(4*S*,5*S*)-4-(1,2,3,4,5-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-5-ethoxy-1-(4-nitrophenyl)imidazolidin-2-one (**25**) (0.022 g, 2.5%), m.p. 193-195°C (99% ethanol), $[\alpha]_D$ +12° (*c* 0.4, chloroform), ν_{max} 3370 (NH), 1750 and 1230 (ester), 1725 (C=O urea), 1520, 1340, and 860 (NO_2), 1600, 1505, and 820 cm^{-1} (aromatic). Mass espectrum: *m/z* 611.1957. Calcd. for M^+ of $C_{26}H_{33}N_3O_{14}$: 611.1962.

(4*S*,5*S*)-4-(1,2,3,4,5-Penta-*O*-acetyl-D-*galacto*-pentytol-1-yl)-5-hydroxy-1-phenylimidazolidin-2-one (26).- (a) To a solution of **15** (0.5 g, 1.6 mmol) in pyridine (4 mL) at 0°C acetic anhydride (5 ml) was added. The reaction mixture was kept for 12 h in the refrigerator and 24 h at room temperature, then poured into ice-water to give **26** (0.6 g, 73%), that was recrystallised from 96% ethanol, m.p. 108-111°C, $[\alpha]_D$ +16.5° (*c* 0.5, chloroform), ν_{max} 3500-3200 (OH, NH), 1740, 1225, and 1200 (ester), 1700 (C=O urea), 1595, 1500, 750, and 690 cm^{-1} (aromatic). Anal. found: C, 53.14; H, 5.46; N, 5.14. Calcd. for $C_{26}H_{32}N_2O_{13}$: C, 53.52; H, 5.57; N, 5.20.

(b) When the reaction was carried out as in (a), but at -20°C, **26** (33%) was also isolated.

(c) To a solution of freshly fused zinc chloride (0.19 g) in acetic anhydride (5 ml), **15** (0.5 g, 1.6 mmol) was added. The reaction mixture was stored 12 h in the refrigerator and then poured into ice-water to give **26** (0.14 g, 14%).

(4*S*,5*S*)-4-(1,2,3,4,5-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-5-hydroxy-1-(4-methoxyphenyl)imidazolidin-2-one (27).- Compound **27** (47%) was obtained from **16** as described for **26** (method a), m.p. 119-120°C (96% ethanol), $[\alpha]_D$ -7° (*c* 0.5, chloroform), ν_{max} 3600-3300 (OH, NH), 1750, 1735, 1700, 1235, and 1205 (ester), 1680 (C=O urea), 1515 and 835 cm^{-1} (aromatic). Anal. found: C, 51.49; H, 5.90; N, 4.71. Calcd. for $C_{25}H_{32}N_2O_{13}.H_2O$: C, 51.19; H, 5.84; N, 4.78.

1-Phenyl-(1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]imidazolidin-2-one (30).- A solution of **15** (0.2 g, 0.64 mmol) in 30% aqueous acetic acid (0.7 mL) was heated at 100°C for 30 min. Then ethanol was added and the reaction mixture was concentrated until crystallisation of **30** (0.13 g, 65%), m.p. 206-209°C, $[\alpha]_D$ -110.5° (*c* 0.5, pyridine), [lit.[10], m.p. 211-212°C, $[\alpha]_D$ -114.5° (*c* 0.5, pyridine)].

1-(4-Methoxyphenyl)-(1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]imidazolidin-2-one (31).- Compound **31** (95%) was obtained from **16** as described for **30**, m.p. 172-174°C, $[\alpha]_D$ -103.5° (*c* 0.5, pyridine), ν_{max} 3600-3000 (OH, NH), 1710 (C=O urea), 1590, 1520, and 835 cm^{-1} (aromatic). Anal. found: C, 52.29; H, 5 98; N, 8.17. Calcd. for $C_{15}H_{20}N_2O_7$: C, 52.94; H, 5.92; N, 8.23.

3-Ethyl-1-phenyl-(1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]imidazolidin-2-one (33).- (a) Compound **33** (93%) was obtained from **13** as described for **30**. The oily residue was solidified by addition of ether, m.p. 71-72°C, $[\alpha]_D$ -76.5° (*c* 0.5, pyridine), ν_{max} 3600-3100 (OH, NH), 1690 (C=O urea), 1605, 1505, 760, and 700 cm^{-1} (aromatic). Anal. found: C, 55.85; H, 6.80; N, 8.05. Calcd. for $C_{16}H_{22}N_2O_6.1/2H_2O$: C, 55.32; H, 6.67; N, 8.06.

(b) To a solution of **34** (0.17 g, 0.34 mmol) in methanol (2 mL), *N* sodium methoxide was added dropwise until the reaction was completed (TLC, benzene-acetonitrile, 3:1), and then Amberlite IR-120 was added until pH~7. The solution was filtered and evaporated to dryness. By addition of ether compound **33** precipitated (0.07 g, 60%).

3-Ethyl-1-phenyl-(3,5,6,7-tetra-*O*-acetyl-1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]-imidazolidin-2-one (34).- (a) Conventional acetylation of **33** gave **34** (93%). Recrystallised from 99% ethanol had, m.p. 126-127°C, $[\alpha]_D$ -48.5° (*c* 0.5, chloroform), ν_{max} 1745 and 1230 (ester), 1700 (C=O urea), 1600, 1505, 750, and 690 cm^{-1} (aromatic). Anal. found: C, 56.76;

H, 5.91; N, 5.40. Calcd. for $C_{24}H_{30}N_2O_{10}$: C, 56.91; H, 5.97; N, 5.53.

(b) To a solution vigorously stirred of 3-ethyl-1-phenyl-(3,5,6,7-tetra-*O*-acetyl-1,2-dideoxy-β-D-*glycero*-L-*gluco*-heptofurano)[2,1-*d*]imidazolidin-2-thione (**35**)[8] (1.3 g, 2.5 mmmol) in chloroform (33 mL) and 4*N* HCl (33 mL), $NaNO_2$ (6.6 g, 96 mmol) was slowly added in several portions. The reaction mixture was stirred for 1 h and then the organic layer separated, washed with water and dried. The solution was evaporated to dryness and the residue treated with ethanol to give **34** (0.2 g, 16%).

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