Tetrahedron Vol. 49, No. 13, pp. 2655-2675, 1993
Printed in Great Britain

0040-4020/93 $6.00+00

THE REACTION OF 2-AMINO-2-DEOXYHEXOPYRANOSES WITH ISOCYANATES. SYNTHESIS OF UREAS AND THEIR TRANSFORMATION INTO HETEROCYCLIC DERIVATIVES.

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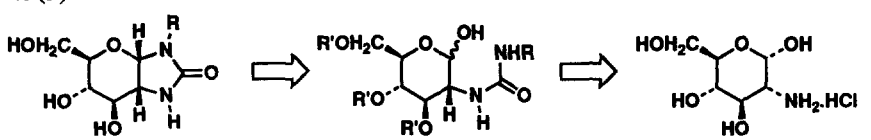
(*Received in UK 9 December* 1992)

Abstract: The reactions of 2-amino-2-deoxyglycopyranoses with aryl isocyanates have been investigated in detail and ureas and heterocyclic derivatives are obtained. The mechanism of formation of glycofurano[2,1-*d*]imidazolidin-2-ones **62** has now become visible, while previous reports and the classical literature dealing with the subject in question proposed alternative structures for the reaction products. The reactions are pH-dependent and only furanoid bicycles are smoothly obtained at acidic pH values, whereas in neutral or basic media 5-hydroxyimidazolidin-2-one derivatives **66** can be isolated. These monocyclic structures appear to be the true intermediates of the reaction and, under appropriate conditions, can be converted exclusively into the corresponding *cis*-fused five-membered ring systems. Likewise, the first *cis*-fused glycopyrano[2,1-*d*]imidazolidin-2-ones **75** have been also prepared.

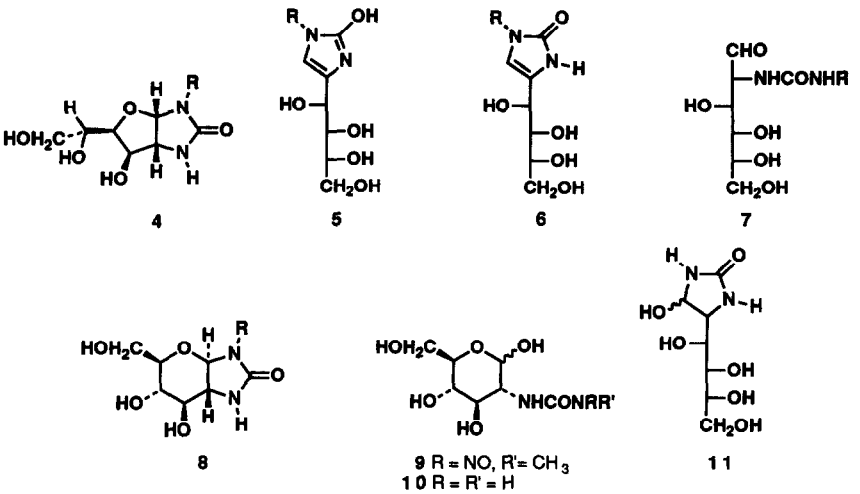
Introduction

In recent years, a number of polyhydroxylated bicyclic nitrogen heterocycles have attracted considerable attention. These include castanospermine[1,2] and kifunensine[3,4], which are potent inhibitors of glycosidase enzymes, as well as other structurally related substances such as ezomicines[5,6], octosilic acids[6,7], and glycocinnamoylspermidines and some of their degradation products[8]. Carbohydrate-based syntheses represent feasible and convenient approaches for the stereocontrolled construction of these molecules. As part of our continuing work on the utilisation of 2-aminosugars in synthesis, we investigated the preparation of analogous bicycles. By looking at the compound **1** as the target molecule, a facile preparative route can be envisaged by disconnection of one cocyclic bond in the fused-ring system[9]. This disconnective strategy results in a selectively deprotected aminosugar at the anomeric centre (**2**), which could then be available from the 2-amino-2-deoxy-D-glucopyranose (**3**).



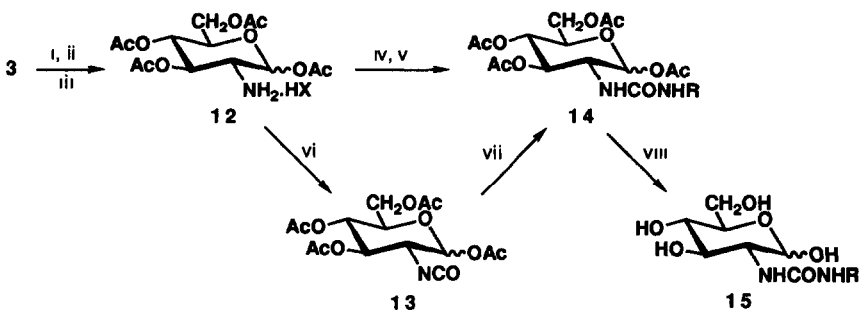
1 **2** **3**

However, the direct reaction of 2-amino-2-deoxysugars with isocyanates does not lead to the pyranoid bicycles **1**[10-12]. This reaction was reported as early as the beginning of this century. Compounds having monocyclic (**5**,**6**)[10,13-15], acyclic (**7**)[16], pyranoid bicyclic (**1**,**8**)[17-21], and furanoid bicyclic (**4**)[10-12,22] structures have been assigned for the products isolated from the direct reaction of (**3**) with isocyanates.



It is notheworthy that some of these structures, **1** (R=H) and **8** (R=H) were initially proposed for two degradation products of the antitumoral antibiotic streptozotocin (**9**)[23,24], and **1** (R=H) and **4** (R=H) for the antibiotics SF-1993 (**10**)[25] and CV-1 (**11**)[26], respectively. Nevertheless, further studies demonstrated the structures **1**, **5**, **8**, and, in some cases, **6** were erroneously assigned[27].

Since the direct coupling between **3** and isocyanates fails, two different routes have been used for preparing per-*O*-acetyl-2-[3-alkyl(aryl)ureido]-2-deoxy-D-glucopyranoses (**14**), as precursors of **15**. The first one is the reaction of 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-α or β-D-glucopyranose hydrohalides (**12**) with silver cyanate[17,29] or alkyl(aryl) isocyanates[17-21,23,30,31]. The second route to **14** involves the treatment of isocyanate **13** with alkyl(aryl)amines[24,32]. Finally, the deacetylation of **14** gave the corresponding unprotected ureas (**15**)[17,19,24,33] or bicyclic structures as **4**[31], although other research groups have erroneously proposed[17] the structure **1** for some of these compounds (Scheme 1).



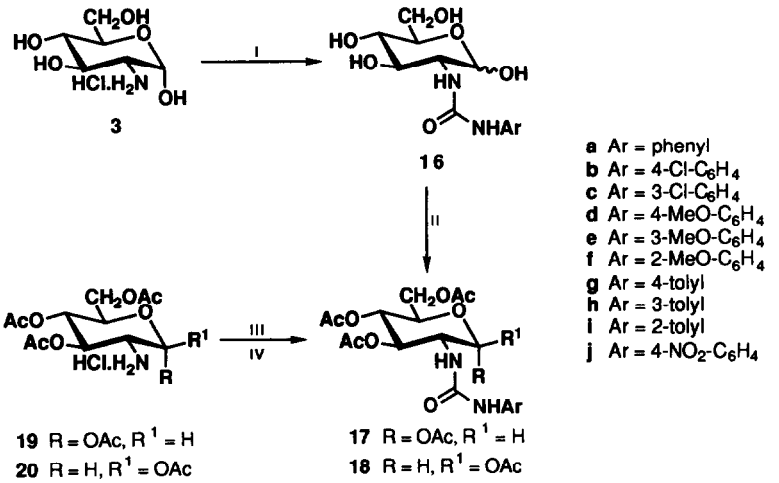
Scheme 1 *Reagents* i, NH protection; ii, Ac_2O, C_5H_5N; iii, NH deprotection; iv, aq. $NaHCO_3$; v, RNCO; vi, Cl_2CO; vii, RNH_2; viii, NH_3, MeOH

Owing to the low yield of these linear syntheses, in five or six steps, and the structural ambiguity[33] of compounds formed, we have reinvestigated the direct reaction of 2-amino-2-deoxysugars with aryl isocyanates and now report a multigram one-step synthesis of unprotected 2-(3-arylureido)-2-deoxy-glycopyranoses and

their per-*O*-acetyl derivatives as well as of *N*-substituted derivatives of the antibiotic CV-1 (**11**). These compounds, under acid catalysis, are invariably converted into furanoid bicycles **4**. Neither the exclusive preponderance of **4** nor a plausible mechanism for its formation have been previously explained. Interestingly, we were also able to prepare pyranoid bicycles possesing the structure **1**, following another synthetic route.

Results

The reaction of **3** with aryl isocyanates in aq. $NaHCO_3$-dioxane proceeded quickly at room temperature to afford precipitates of the corresponding 2-(3-arylureido)-2-deoxy-D-glucopyranoses (**16**).



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

Unfortunately, this procedure resulted in small amounts of symmetric *N,N'*-diarylureas, presumably caused by partial hydrolysis of aryl isocyanates. Their presence in the crude products was readily detected by NMR spectroscopy. In some cases, however, recrystallisation of **16** failed to remove the contaminants and promoted their transformation into 1-aryl-4,5-(1,2-dideoxy-D-glucofurano)[2,1-*d*]imidazolidin-2-ones (**4**)[12]. In these cases, elemental analyses of **16** were not satisfactory.

Their structure were assigned on the basis of their IR and ^{13}C NMR spectroscopic data. IR spectra showed characteristic absorption bands of C=O (~1630 cm^{-1}) and NH (~1560 cm^{-1}) groups. In some cases, all signals appeared duplicated in the ^{13}C NMR spectra (Table 1). The glycosidic regions were very similar to those of **3** in $(CD_3)_2SO$-d_6, and confirmed the presence of anomeric mixtures for **16**. The α-isomer was always predominant. Assignments were made for comparison with the published data[34,35] for **3** and some of its derivatives[36].

Conventional treatment of **16** with acetic anhydride and pyridine gave high yields of the anomeric mixtures of the *O*-acetylated derivatives **17** and **18**, that could be fractionated by crystallisation. ^1H and ^{13}C NMR spectra of **17** and **18** showed some analogies with those thioureas already described[37-39] although the presence of the C=O instead of the C=S group causes a significative difference in the chemical shift of H-2 (Δδ ~0.6-0.8 p.p.m.) (Tables 2-4). As expected, all compounds described showed a $^4C_1$(D) conformation. The

Table 1. ^{13}C-NMR chemical shifts[a] (ppm) for 3, 16, 22 and 25.

Comp.	Anomer	C-1	C-2	C-3	C-4	C-5	C-6	C=O
3	α	88 75	54 62	69.69	70 23	72.11	60 60	
	β	92 92	57 56	72 28	70.23	76.84	60.60	
16a	α	91.17	54.45	71.29	71.57	72.01	61.27	155.22
	β	96 07	58 26	74.58		76.45	61 27	156.45
16b	α	91.23	54.46	71 12	71.51	72.33	61.22	155.09
16c	α	91.23	54 49	71.12	71.55	72 31	61.22	155.06
16d	α	91.36	54.50	71.23	71.66	72.31	61 27	155.57
	β	96.29	58 24	74.81	71 04	76.81	61 27	156.72
16e	α	91.34	54.47	71.24	71.64	72.35	61 31	155.25
	β	96 14	58 14	74.77	71 24	76.84	61 31	156.14
16f	α	91 37	54.58	71.04	71 44	72 23	61 30	155 51
16g	α	91 53	54 56	71.34	71 87	72 35	61 38	155 69
	β	96 46	58 18	74.91	71.33	76.83	61 38	156.78
16h	α	91 54	54.63	71 36	71.86	72 40	61 43	155 63
	β	96.39	58 26	74.91	71 35	76 89	61 43	156 65
16i	α	91.59	54 78	71.47	71 87	72.40	61 46	155 90
	β	96.55	58 44	75 03	71 17	76 91	62 28	157 09
16j	α	91.01	54 51	70 98	71 37	72 35	61 11	154.37
22	α	93 05	54.21	72 71	68.30	67 67	61 35	157 60
25	α	91 58	50.34	70 57	68.61	68 50	60 72	155 56

[a] In DMSO-d_6 at 50 33 MHz

Table 2. ^{13}C-NMR chemical shifts[a,b] (ppm) for 17, 18, 26, and 27.

Comp	C-1	C-2	C-3	C-4	C-5	C-6	C=O
17a	91.19	51 70	70.98	67.52	69 76	61 59	154.79
18a	92.70	53 81	72.59	68 24	72 46	61 84	155 45
17b	91 12	51 85	70.98	67.44	69.78	61 57	154 43
18b	92.85	54 07	72 71	68.02	72.71	61 74	154 98
17c	90 99	51 48	70 59	67.51	69.62	61 69	154 89
17d	91 07	51 59	70 86	67 56	69.73	61 61	156 81
18d	92 82	53 55	72.67	67 99	72 47	61.61	156 17
17e	91 16	51 47	70 85	67 53	69 71	61 61	154 92
17f	91.14	51.25	70 90	67 63	69 46	61.63	154 35
17g	91 17	51.59	70.88	67.56	69 74	61 62	155 30
18g	92.64	53 75	72 56	68 27	72.39	61.86	155 75
17h	91.11	51.45	70 75	67 57	69.72	61 68	155 34
18h	92 77	53 96	72 67	68 13	72 57	61 78	155 26
17i	90.95	51.44	70 73	67 41	69 61	61 50	155 69
18i	92 50	53 89	72 47	68 21	72 33	61 80	155 98
17j	90 15	50 70	70 18	67 63	69 22	61.38	153 96
26	91.77	47 62	68.61	68.11	66 83	61 32	155.41
27	93 25	50 43	71 45	70 43	66 54	61 32	155.22

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

anomeric configurations of **17** were assigned on the basis of the small $J_{1,2}$ value (~3.4 Hz) and those of **18** were consistent with a large $J_{1,2}$ value (~8.6 Hz). Also, $[\alpha]_D$ values support completely the anomeric configurations of these compounds. These assignments are consistent with the structures of **17a, 17b, 18a, 18b,** and **18g-18i** that were unequivocally synthesised by treatment of **19**[40] or **20**[41] with the corresponding aryl isocyanates.

The chemical shift of H-2 proton, similar to that of the corresponding proton of the *Z* isomer in sug formamides[42], and the large couplings $J_{2,NH}$ observed are indicative of a (*Z*)-*anti*-disposition for the urea framework. In the *syn*-conformation the ArNHCO group causes 1,3-diaxial interactions and would induce remarkable variations in the chemical shifts of the H-2 proton[43].

Table 3. ^{1}H-NMR chemical shifts[a,b] (ppm) for 17 and 18.

Comp.	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	ArNH	S-NH[c]	CH_3	Ar
17a	6.25d	4.43m	—5.21m—		3.98m	4.26dd	4.06dd	6.97s	5.21m		7.35-7.06m
18a	5.85d	4.15m	5.34t	5.14t	3.88m	4.29dd	4.14dd	7.53s	5.78d		7.27m
17b	6.25d	4.40m	—5.25m—		3.98m	4.27dd	4.06dd	6.98s	5.25m		7.23m
18b	5.80d	4.10m	5.26t	5.13t	3.85m	4.30dd	4.14dd	7.25s	5.46s		7.25s
17c	6.32d	4.50m	—5.29m—		4.08m	4.28dd	4.08dd	7.75s	5.77d		7.25-6.93m
17d	6.25d	4.45m	—5.18m—		——4.30-4.02m——			7.36s	5.34d	3.76s	7.24-6.80m
18d	5.69d	4.02m	5.25t	5.11t	——4.30-4.02m——			7.29s	5.61d	3.76s	7.24-6.80m
17e	6.26d	4.46td	—5.26m—		4.04m	4.27dd	4.11dd	7.38s	5.51d	3.75s	7.20-6.40m
17f	6.24d	4.51m	—5.29m—		4.06m	4.26dd	4.11dd	7.31s	5.72d	3.67s	6.97-6.73m
17g	6.25d	4.46m	—5.23m—		3.98m	4.26dd	4.05dd	7.10s	5.30d	2.28s	7.17-7.05m
18g	5.80d	4.03m	5.30t	5.12t	3.84m	4.29dd	4.13dd	7.51s	5.79d	2.26s	7.16-7.03m
17h	6.25d	4.49m	—5.26m—		4.04m	4.27dd	4.07dd	7.48s	5.68d	2.25s	7.17-6.84m
18h	5.86d	4.09m	5.33t	5.15t	3.88m	4.30dd	4.14dd	7.25s	5.53d	2.29s	7.22-6.87m
17i	6.25d	4.44m	—5.21m—		4.01m	4.27dd	4.07dd	7.03s	5.27d	2.22s	7.39-7.10m
18i	5.87d	3.99m	5.34t	5 10t	3.88m	4.26dd	4.10dd	7.07s	5.72d	2.14s	7.36-6.98m
17j[d]	6.07d	4.20m	5.23t	5.10t	4.03m	—4.20m—		9.25s	6.61d		8.16d, 7.61d

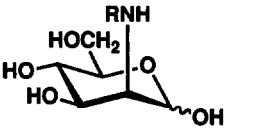
[a] In $CDCl_3$ at 200 MHz. [b] Signals for acetoxy groups have been omitted. [c] S = sugar moiety. [d] In DMSO-d_6.

Table 4. ^{1}H-NMR coupling constants[a] (Hz) for 17 and 18.

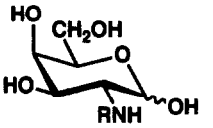
Comp.	$J_{1,2}$	$J_{2,3}$	$J_{2,NH}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
17a	3.6					4.0	2.3	12.4
18a	8.7	9.5	9.3	9.5	9.5	4.7	3.1	12.3
17b	3.6					4.0	3.1	12.4
18b	8.7	9.5	9.4	9.5	9.5	4.5	3.0	12.4
17c	3.3		9.4			3.9		12.3
17d	3.5		9.3					
18d	8.5	9.5	9.3	9.5	9.5			
17e	3.6	9.4	9.4			4.3	2.3	12.6
17f	3.6	9.5	9.4			4.1	2.3	12.4
17g	3.6		9.5			4.1	2.3	12.4
18g	8.6	9.8	8.9	9.6	9.6	4.7	2.5	12.6
17h	3.6	9.4	9.4			4.3		12.6
18h	8.7	9 5	9 3	9.5	9 5	4.7	2.2	12.4
17i	3.6	9.5				3.9	<1.0	12.4
18i	8.7	9.6	9.1	9.5	9.5	4.6	<1.0	12.5
17j[b]	3.5	9.8	9.1	9.6	9.6			

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

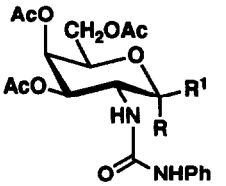
Reactions of 2-amino-2-deoxy-D-mannopyranose (**21**) and 2-amino-2-deoxy-D-galactopyranose (**24**) with phenyl and 4-chlorophenyl isocyanates originated the ureido derivatives **22**, **23**, and **25**. These compounds showed analogous spectral data to those previously reported for **16**. On the other hand, conventional acetylation of **25** gave a mixture of **26** and **27**.



21 R = H
22 R = PhNHCO
23 R = 4-ClC$_6$H$_4$NHCO

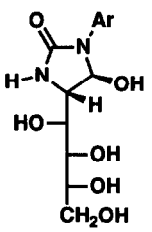


24 R = H
25 R = PhNHCO

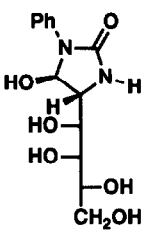


26 R = OAc, R^1 = H
27 R = H, R^1 = OAc

When the 2-(3-arylureido)-2-deoxysugars do not precipitate immediately from the reaction mixture of the aminosugar and aryl isocyanate, due to their larger solubility, new products can be obtained. Thus, when the crude compounds **22**, **23**, and **25** were dissolved in water at room temperature they transformed into the monocyclic imidazolidin-2-ones **28-30**. This behaviour is shared by other 2-deoxy-2-ureidosugars in weakly basic aqueous solutions (pH<10) at room temperature. In these conditions **16a** and **16b** were converted quantitatively to **31**and **32**, respectively. In more basic media epimerisation at C-2 occurs. Thus when **16b** was dissolved in a solution of sodium carbonate (pH>10), an almost equimolar mixture of monocycles **29** and **32** was isolated. Analogous epimerisation processes have been observed in other 2-acylamino-2-deoxysugars[44].



28 Ar = Ph
29 Ar = 4-ClC$_6$H$_4$



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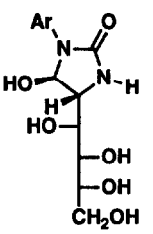
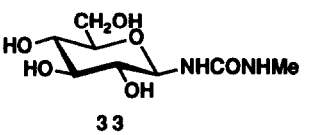


31 Ar = Ph
32 Ar = 4-ClC$_6$H$_4$



33

The classical deacetylation procedure of **17b** using ammonia in ethanol as described by Morel[19] (see Scheme 1), led to a mixture of **16b** together with the monocycle **32**. NMR analyses of crude reaction mixture revealed a urea/monocycle ratio ~1:4. A similar behaviour[45] was found in other per-*O*-acetyl ureidoderivatives. Thus, this method of deacetylation for the preparation of unprotected ureidoderivatives appears to be uneffective.

The isomerization of ureidoderivatives into monocyclic imidazolidin-2-one was also observed in other solvents. For example, **16b** was slowly (several days) transformed into **32** when was dissolved in $(CD_3)_2SO$-d_6 as observed by NMR spectroscopy.

IR spectra of **28-32** showed the characteristic absorption of urea group (1700-1650 cm^{-1}) and the lack of the NH band at 1550 cm^{-1} that is present in the 2-(3-arylureido)-2-deoxysugars. The C-1 of monocyclic

imidazolidin-2-ones* resonates at 78-83 p.p.m. and agrees well with the chemical shift measured for the C-1 carbon[8] of **33** (81.9 p.p.m.) and other glycosylureas[46]. However, these values are different to those of C-1 of starting ureas or bicyclic imidazolidin-2-ones (≥ 90 p.p.m.). Moreover, the almost identical chemical shifts of C-3, C-4, and C-5 for **28-32** are in accordance with the presence of an open polyhydroxyalkyl chain[34] (Table 5).

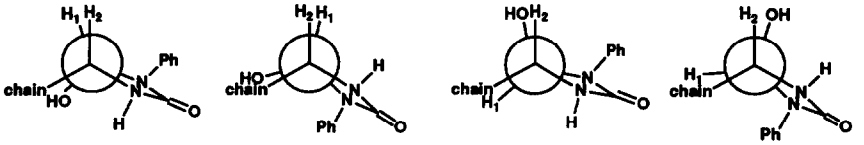
Table 5. ^{13}C-NMR chemical shifts (ppm) for 28-32, 38-40, 42 and 46-48.

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	C=O	Ar
28[a]	82.67	59.34	71.03	69.86	69.80	63.89	156.75	139.75, 128.46 122.20, 118.95
29[a]	82.51	59.38	71.07	69.96	69.79	63.90	156.59	138.73, 128.40 125.95, 120.24
30[a]	83.05	59.42	69 95	69.95	69.95	63.33	157.83	139.83, 128.47 122.27, 119.21
31[a]	82.20	60.99	71.40	70.69	69.58	63.37	157.24	139.53, 128.40 122.34, 119.28
31[b]	83.80	61.07	70.67	70.39	69.52	62.73	160.03	135.99, 129.33 126 67, 124.88
32[a]	82.01	60.90	71.37	70.58	69.51	63.31	156.95	138.51, 128.23 125.94, 120 38
38[c]	83.20	59.16	69.85	68.32	67.92	61 51	158 23	137.53, 128.76 124.28, 120.34
39[d]	79.11	57.66	68.66	67.69	67.57	61.72	151.58	134.41, 131.47 129.44, 121.87
40[c]	109.64	117.73	70 10	68.80	65.24	61.53	153.07	136.55, 129.13 126.13, 121.89
42[d]	78.11	59.30	69.48	68.51	68.11	61.33	151.84	133.79, 132.42 129.45, 124.35
46[a]	88.92	55 67	70.81	79.60	69.76	63.47	157.33	139.52, 128.63 122.68, 118 45
47[c]	90.15	55.47	72 17	76.55	68.28	62.91	157.41	137.95, 128 87 124.36, 119.87
48[a]	89.65	61 54	76.42	86.08	70.66	63.10	156.54	139.37, 128 47 122.68, 119.05

[a]In DMSO-d_6 at 50 33MHz [b]In D_2O [c]In $CDCl_3$ [d]Methyl group of NAc resonated at 24 06 and 23 82 ppm for **39** and **42**, respectively.

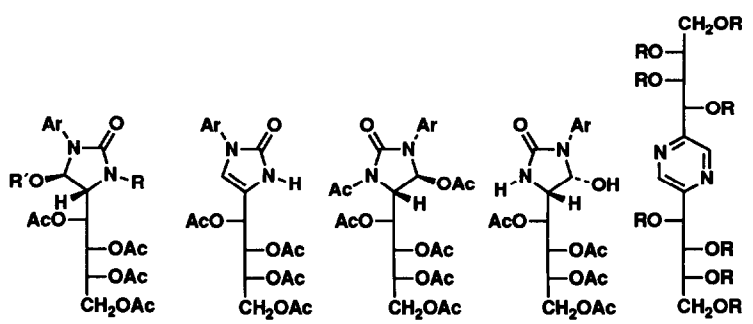
The C-1 configuration can be assigned on the basis of the $J_{1,2}$ values. In the case of the *cis* disposition between H-1 and H-2, the small dihedral angle (<25°) in both possible conformations (**34** and **35**) determinates large values (>5 Hz) for $J_{1,2}$ coupling constant as it has been described for similar structures[47]. When the relative disposition is *trans* (**36** and **37**), the more stable conformation (**37**) shows a dihedral angle of ~90° that agrees with a small $J_{1,2}$ value (<1 Hz)[47]. For that, the lack of coupling constant between H-1 and H-2 in **28-32** confirms a *trans* disposition between these protons.

*In the Results and Discussion paragraphs, 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.



34 35 36 37

The acetylations of monocyclic imidazolidin-2-ones gave complex mixtures in which only some products could be isolated. From **31**, compounds **38** and **40** were obtained, and **39** from **32**. Finally, acetylation of **29** gave a mixture of **41-43**. Compound **42** was also isolated when the mixture of **29** and **32**, obtained by cyclisation and epimerisation of **16b**, was acetylated. Compounds with structure of imidazolin-2-one such as **40-41**, have been synthesised by acetylation of adducts formed in the reaction of 1-alkyl(aryl)amino-1-deoxy-D-fructose with alkaline or ammonium cyanates[49]. Occassionally, **29** was contaminated with 2,5-bis(D-*arabino*-tetritol-1-yl)pyrazine (**44**)[48], formed by self-condensation of **21** in the alkaline medium, and characterised as its octa-*O*-acetyl derivative **45**.



38 Ar = Ph, R = R' = H
39 Ar = 4-ClC$_6$H$_4$, R = R' = Ac
40 Ar = Ph **41** Ar = 4-ClC$_6$H$_4$
42 Ar = 4-ClC$_6$H$_4$ **43** Ar = 4-ClC$_6$H$_4$ **44** R = H **45** R = Ac

Table 6. ^{1}**H-NMR chemical shifts**[a] **(ppm) for 38-40, 42 and 46-48.**

Comp.	H-1	H-2	H-3	H-4	H-5	H-6	H-6'	NH	CH_3	CH_2	OH	Ar	N-Ac
38	5.33d	3.71d	5.19dd	5.47dd	5.10m	4.22dd	4.06dd	6.69s			5.02d	7.34d 7.24t 7.08t	
39	6.67s	4.61dd	5.72dd	5.30dd	5.25m	4.23dd	4.02dd					7.50-7.32m	2.61s
40	6.65s		5.96d	5.59dd	5.22m	4.29dd	4.13dd	10.19s				7.57d 7.42t 7.27t	
42	6.76s	4.60s	5.66d	5.58dd	5.17ddd	4.28dd	4.19dd					7.42-7.35m	2.54s
46[b]	5.72d	4.13dd	4.28m	—3.69m—		3.50dd	3 31dd	7.14s			5.14d 4.68d 4.43t	7.66-7.00m 7.30t 7.02t	
47	5.79d	4.44dd	5.37m	4.24dd	5.37m	4.54dd	4.14dd	6.10s				7.63-7.13m	
48[b]	5.89d	3.95d	4.10d	3.79t	——3.49-3.28——			7.61s			5.48d	7.64-7.04m	

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

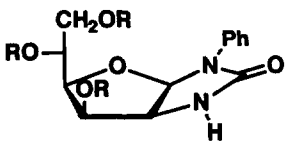
Table 7. ^{1}H-NMR coupling constants[a] (Hz) for 38-40, 42, and 46-48.

Comp.	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{1,OH}$	$J_{1,3}$	$J_{2,NH}$
38	0.0	6.8	2.7	8.1	2.9	5.1	12.5	10.3		
39	0.5	6.0	2.6	7.2	2.9	5.1	12.4			
40			4.5	7.2	3.0	5.5	12.4		1.7	
42	0.0	0.0	4.0	7.7	2.7	4.9	12.4			
46[b]	7.3	6.5	3.7		2.2	4.9	11.1			0.7
47	7.3	6.5	4.2	8.9	2.5	4.9	12.3			
48[b]	6.6	0.0	3.7	3.7						

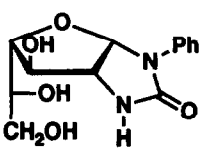
[a] In $CDCl_3$ at 200 MHz. [b] In DMSO-d_6

The presence of the heterocyclic acetate in **39** and **42** induces important differences in the chemical shifts of some protons respect to the unsubstituted **38**. Thus, H-1 of the first ones resonated at lower field ($\Delta\delta$~1.4 p.p.m.) than H-1 of the second ones (Tables 6 and 7).

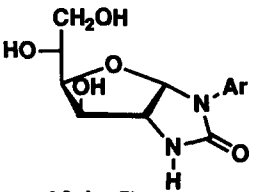
Solutions of monocyclic imidazolidin-2-ones **28**, **30-32** in hot dilute acetic acid gave the corresponding 1-aryl-(1,2-dideoxy-glycofurano)[2,1-*d*]imidazolidin-2-ones **46**, **48-50** in high yield. Compounds **49** and **50** have been also obtained from the corresponding 2-(3-arylureido)-2-deoxy-glycopyranoses **16a** and **16b** in the same way[12].



46 R = H
47 R = Ac



48

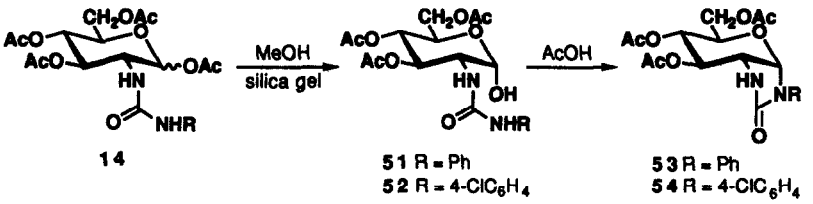


49 Ar = Ph
50 Ar = 4-ClC$_6$H$_4$

In the ^{13}C NMR spectra of these compounds (Table 5) the signal of C-4 is more deshielded than C-5, which indicates the sugar ring to be furanoid[12]. The furanoid nature of **48-50** is also evidenced by the small $J_{2,3}$ values (~0 Hz) if H-2 and H-3 are in *trans* orientation (Tables 6 and 7), whereas the *cis* arrangement of **46** and its tri-*O*-acetyl derivative **47** gives medium values of $J_{2,3}$ (5-7 Hz)[12]. In addition, the structure **49** was confirmed unequivocally by X-ray crystallographic analysis[22].

Until now, we have showed that furanoid bicycles are exclusively obtained by cyclisation of unprotected adducts derived from the reaction of 2-amino-2-deoxysugars with isocyanates. In view of these results, we explored the selected strategy depicted in Scheme 3. First, the per-*O*-acetyl-2-(3-alkyl or aryl)ureido-2-deoxy-D-glucopyranoses (**14**) were regioselectively deacetylated at the anomeric position by using silica gel in methanol[50]. Particularly noteworthy is that this deacetylation proceeded with complete stereoselectivity to afford α-anomers **51** and **52** ($J_{1,2}$ ~ 3.5 Hz) (Table 8).

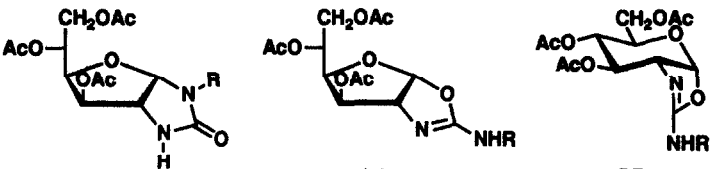
Subsequent acid catalysed-cyclisation gave the desired pyranoid bicycles **53** and **54**. Spectroscopic data support completely the structure of the latter (Tables 8-10).



14 51 R = Ph; 52 R = 4-ClC6H4 53 R = Ph; 54 R = 4-ClC6H4

Scheme 3

The alternative isomeric structures **55** ($\delta_{C\text{-}1}$~91 p.p.m.)[12] and **56-57** ($\delta_{C\text{-}1}$~99 p.p.m.)[51] should be ruled out on the basis of their spectroscopic data, which are quite different to those of **53** and **54** ($\delta_{C\text{-}1}$~83 p.p.m.). Also, the $J_{2,3}$ values (3.2 Hz) are in disagreement with those expected for furanoid rings of **55** and **56** (~0 Hz). Likewise, the small $J_{2,3}$ and $J_{3,4}$ values (Table 10) are consistent with a *cis* fusion between both rings. A *trans* fusion (as in **8**) provides larger coupling constants (~9 Hz).



55 56 57

Table 8. ^{13}C-NMR chemical shifts[a] (ppm) for 51-54.

Comp.	C-1	C-2	C-3	C-4	C-5	C-6	C=O	Ar
51[b]	91.13	52.04	70.89	68.68	66.62	62.32	154.57	140.12, 128.78 121.31, 117.48
52[b]	91.09	52.09	70.88	68.67	66.64	62.33	154.44	139.13, 128.59 124.79, 118.95
53	83.35	50.39	71.40	67.87	67.31	63.19	157.88	137.26, 128.92 125.07, 121.42
54	83.08	50.12	70.90	67.77	67.35	63.15	157.72	135.97, 130.05 128.82, 122.18

[a] In $CDCl_3$ at 50.33 MHz. [b] In DMSO-d_6.

Table 9. ^{1}H-NMR chemical shifts[a] (ppm) for 51-54.

Comp.	H-1	H-2	H-3	H-4	H-5	H-6	H-6	NH	Ar	OH
51[b]	5.14dd	3.98td	5.22t	4.97t	——4.24-4.02m——			8.74s 6.12d	7.43-6.92m	7.39d
52[b]	5.07dd	3.91td	5.20t	4.91t	——4.17-3.97m——			8.83s 6.10d	7.37d, 7.26d	7.35d
53	5.85d	4.02m	5.06t	4.98m	4.03m	4.23dd	4.12dd	5.64s	7.63-7.14m	
54	5.81d	4.00m	5.08t	4.96dd	4.00m	4.22dd	4.12dd	6.06s	7.59d, 7.32d	

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

Table 10. ^{1}H-NMR coupling constants[a] (Hz) for 51-54.

Comp.	$J_{1,2}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	$J_{2,NH}$
51[b]	3.4	9.7		9.7	9.7				9.7
52[b]	3.7	9.5		9.5	9.5				9.5
53	7.5	3.2	0.6	3.2	9.1	6.7	2.6	12.0	
54	7.6	3.2		2.8	9.1	6.6	2.9	12.0	

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

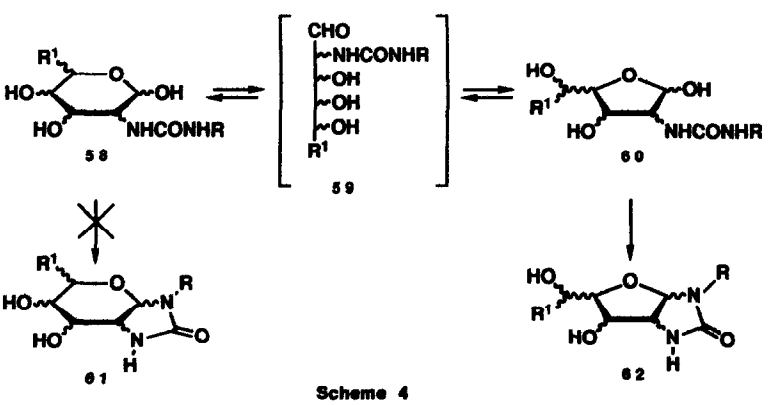
Discussion

The reaction of 2-amino-2-deoxysugars with aryl isocyanates at pH~7 gave 2-(3-arylureido)-2-deoxy-glycopyranoses as initial compounds. In this neutral medium, these compounds are slowly converted into 5-hydroxyimidazolidin-2-one derivatives (**28-32**) and this transformation proceeds rapidly at pH > 7. At acidic pH values, the final product is invariably a glycofurano[2,1-*d*]imidazolidin-2-one (**46-50**).

As consequence of our experimental results and literature data[12,27], it is now well-established that the reaction of 2-amino-2-deoxy-aldopyranoses with isocyanates under acid catalysis yields always furanoid bicycles. Since a ring transformation takes place from pyranoid to furanoid structures, the intermediacy of an acyclic compound seems to be involved in such a transformation. At first sight, a mechanistic possibility involves the formation of the furanoid ring and then the heterocyclic moiety of imidazolidine (Scheme 4).

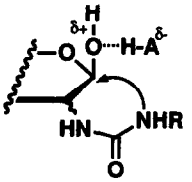
Pyranoid **58** and furanoid **60** structures are equilibrated through the corresponding acyclic aldehyde **59**. Interestingly, this equilibrium should be pH-dependent and thus with D-glucose, hemiacetalic forms predominate at pH<7, whereas the acyclic intermediate is favoured at basic pH values[52].

The formation of **61** or **62** would plausibly be accomplished under acid catalysis, *via* an intramolecular deplacement (S_Ni) of a protonated or associated anomeric hydroxyl (**63**) or an oxocarbonium ion (**64**). However, cyclopentannelation of NHCO-groups of ureas using intramolecular S_N2 reactions leads exclusively to oxazolines under acid or weakly basic conditions[51,53-55]. In strongly basic media, ureas produce imidazolidin-2-ones[55-57]. In addition, ethyl glycosides **65**[51] were not detected when cyclisation of **16a** to **49** was conducted in ethanolic media. This result is in disagreement with an oxocarbonium ion as intermediate.



Scheme 4

In view of this mechanism, it is otherwise quite surprising that pyranoid structures such as **61** cannot be isolated, although structures **62** could be more stable for D-*gluco* or D-*galacto*, but not for D-*manno* configurations[58].



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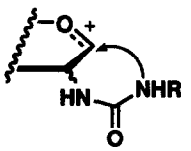

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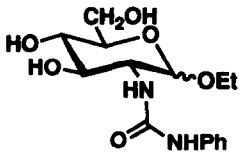
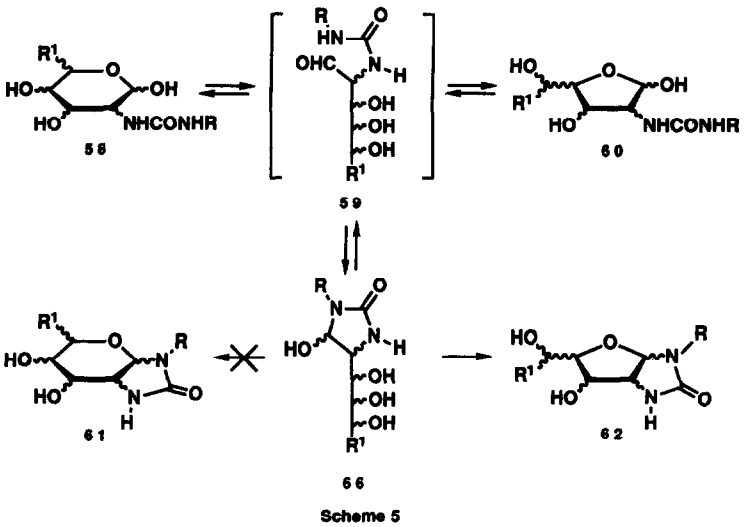


65

A second mechanistic hypothesis is the generation of the imidazolidin-2-one prior to the sugar ring formation. This possibility must involve the formation of monocyclic 5-hydroxyimidazolidines (**66**) as intermediates, which is outlined in Scheme 5.

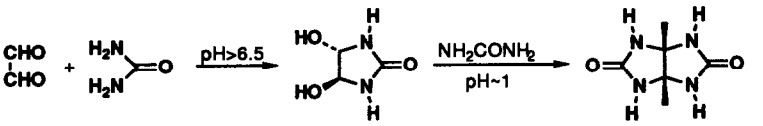


Scheme 5

Herein we have reported the isolation of such monocyclic structures, which constitutes a strong experimental evidence for that assumption[59]. Furthermore, ^{1}H NMR monitoring in D_2O solutions of several ureas (**58**) at pH>7 demonstrated a rapid and complete transformation into monocycles **66**. The cyclization step (**59**→**66**) must occur by nucleophilic addition of an amidic NH to an aldehyde group to give rise to an *N*-(1-hydroxyalkyl)urea derivative. This behavior is general and has been widely described[27d,60-62].

The addition of ureas to aldehydes involves a multistep mechanism. Kinetic studies demonstrated[63] that the formation of the *N*-(1-hydroxyalkyl)ureas, the rate-determining step, is controlled by general acid and base catalysis, whereas the further dehydration of the *N*-(1-hydroxyalkyl)ureas needs an acid catalysis. Reaction can be therefore stopped in the first step by simple pH control. Thus, the reaction of glyoxal with urea at pH>6.5 gave only *trans*-dihydroxy-2-imidazolidine (**67**)[64]. By using 1,3-disubstituted ureas, the heterocycles can be easily isolated. Under acidic conditions (pH~1), the monocycle is not stable and adds more urea to afford the corresponding glycoluril (**68**)[65].

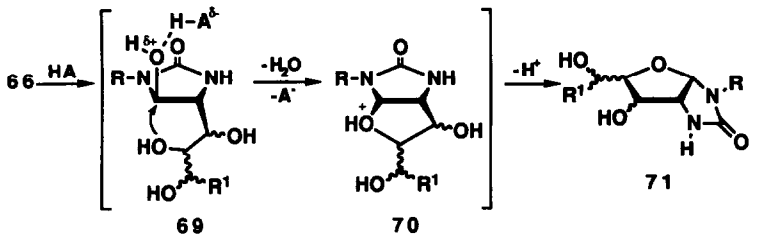
These results allow us to provide a reasonable explanation for the cyclization of ureidoderivatives of 2-amino-2-deoxyaldoses to 5-hydroxyimidazolidin-2-ones (**66**). As **67**, these monocycles display a relative *trans* disposition between the substituents at C-4 and C-5 of the heterocyclic moiety.



67 **68**

Moreover, both 2-deoxy-2-ureidoaldoses and their corresponding monocycles **66** are smoothly transformed into glycofurano derivatives (**62**). The ring closure proceeds under mild conditions (30% aqueous acetic acid) and it is consistent with an intramolecular deplacement of the heterocyclic 5-hydroxy group (5-*exo-tetragonal* cyclisation)[66], associated by hydrogen bonding with the catalyst (**69**). Another important experimental feature is that in compounds **62** the two five-membered rings have always a *cis*-fusion (**71**), which is facilitated by the relative *trans* disposition between the heterocyclic hydroxyl group and the sugar chain (Scheme 6).

We have therefore showed that this mechanism would be in complete accordance with these experimental findings described. Also, the participation of 5-hydroxyimidazolidin-2-ones (**66**) as intermediates explains satisfactorily the exclusive formation of glycofuranose derivatives **71** because of 5-*exo-tetragonal* cyclisation is entropically favoured over 6-*exo-tetragonal* cyclisation[66].

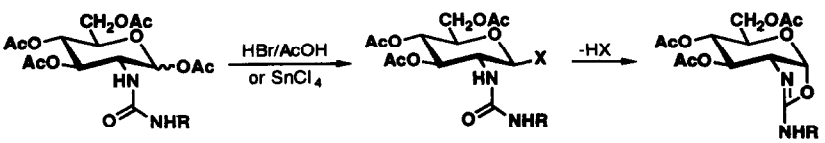


69 **70** **71**

Scheme 6

For that, compounds with structure as **71** were formed when 2-deoxy-2-ureidoaldoses are generated, as occurs in the chemical degradation of the antibiotics glycocinamoylspermidines[8] and streptozotocine[27e].

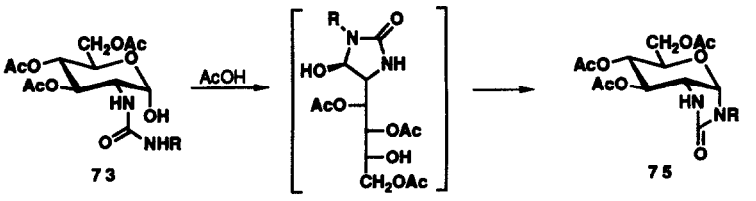
In orden to avoid the sugar ring contraction to a five-membered ring system, the next logical aspect we examined was the preparation of the corresponding protected compounds, such as the per-*O*-acyl-2-ureido derivatives. However, the cyclisation promoted by hydrogen bromide-glacial acetic acid or tin(IV) chloride gave no per-*O*-acetyl-D-glucopyrano[2,1-*d*]imidazolidin-2-ones (as **53** and **54**), but per-*O*-acetyl-D-glucopyrano[2,1-*d*]-2-oxazolines (**57**)[51] (Scheme 7). These reactions occur through the corresponding glycosyl halide (**72**).



14 **72** X = Br or Cl **57**

Scheme 7

Analogously to the formation of glycofurano[2,1-*d*]imidazolidin-2-ones (Scheme 5) the key transformation in the synthesis of D-glucopyrano[2,1-*d*]imidazolidin-2-ones (**75**) should be the intramolecular nucleophilic addition of the ureido NH group of **73** to the aldehyde group *masked* as hemiacetal. The reaction must proceed *via* the monocyclic intermediate **74** which cyclises by the 5-OH group, the only unprotected hydroxy group of the sugar chain, to give pyranoid bicycles (Scheme 8).



Scheme 8

Conclusions

a) The reaction of 2-amino-2-deoxy-D-glucopyranose with arylisocyanates gives ureido derivatives in high yields.

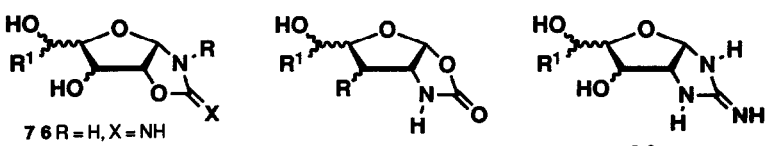
b) In solution at pH>6 ureidoderivatives cyclise to monocyclic imidazolidin-2-ones, whereas at pH<6 both ureas and monocycles are transformed into furanoid bicyclic imidazolidin-2-ones.

c) Deacetylation of per-*O*-acetyl-2-deoxy-2-ureido-D-glucopyranoses with ammonia in methanol, according to Morel protocol[19], affords mainly monocycles and it cannot be considered a useful method for the preparation of ureas.

d) Pyranoid bycicles can be obtained by selective deprotection of the anomeric centre of per-*O*-acyl-2-deoxy-2-ureidosugars and further cyclisation.

e) The formation of bicycles (both furanoid and pyranoid) proceeds *via* monocyclic structures. These are generated by nucleophilic addition of ureido-NH groups to the sugar carbonyl, and then acid-catalysed cyclisation.

f) In addition, it is plausible that the formation of similar *cis*-fused furanoid bicycles can proceed *via* monocyclic intermediates like **66**. Thus, compounds **76** are generated by reaction of aldoses or glycosylamines with cyanamide[67,68], compounds **77** from aldoses with thiocyanic acid[29,69], and **78** from aldoses with urea[70,71] or cyanic acid[72]. Compounds **78** are also formed in the alkaline degradation of some *N*-nucleosides such as Zebularine and related analogues[73], and **80** in the alkaline degradation of streptozotocin (**9**)[23,24]. Furthermore, cyclisation of sugar carbamates produces structures such as **79**[58] or **81**[74]. Finally, compounds **82** result by condensation of 2-aminosugars with cyanamide[75].



76 R = H, X = NH
77 R = H, X = S
78 R = H, X = O
79 R = alkyl, X = O

80 R = OH
81 R = H

82

Consecuently, the mechanism proposed in the formation of these compounds, e.g. **76** from glycosylamines with cyanamide[68], should be revised.

Acknowledgement. This work was made possible by the financial support of DGICYT (PB89-0492).

EXPERIMENTAL

The ^{1}H- (200.13 MHz) and ^{13}C-n.m.r. (50.33 MHz) spectra were recorded with a Bruker AC 200-E spectrometer. Assignments were confirmed by homo- and heteronuclear double-resonance experiments, and DEPT. Optical rotations were measured at 22±5° with a Perkin-Elmer 141 polarimeter. Infrared spectra (KBr discs) were recorded in the range 4000-600 cm^{-1} using a Perkin-Elmer 399 or Midac (FT) spectrophotometers. Electron impact (EI) mass spectra (35 and 70 eV) were obtained with a Kratos MS-80 RFA instrument, with a ionizing current of 100 μA, and accelerating voltage of 4 KV, and a resolution of 1000 (10% valley definition). The elemental composition of the ions was determined with a resolution of 10000 (10% valley definition). T.l.c. was conducted on silica gel GF_{254} (Merck) with benzene-ether (3:2), chloroform-methanol (3:1), benzene-acetone (3:1), or benzene-methanol (9:1), and detection with u.v. light or iodine vapour. Melting points were determined on a Gallenkamp apparatus and are uncorrected. Microanalyses were carried out with a Perkin-Elmer 240C analyser.

General procedure for the preparation of 2-deoxy-2-(3-arylureido)aldopyranoses.- To an appropriate 2-amino-2-deoxyaldopyranose hydrochloride (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-glucopyranose (16a).- From **3** and phenyl isocyanate, compound **16a** (86%) was obtained, m.p. 184-185°C (1:1, ethanol-water), $[\alpha]_D$ +50° (*c* 1.0, *N,N*-dimethylformamide), ν_{max} 3500-3200 (OH, NH), 1637 (C=O), 1567 (NH), 1590, 1506, 734, and 687 cm^{-1} (aromatic). Anal. found: C, 51.83; H, 6.13; N, 9.16. Calcd. for $C_{13}H_{18}N_2O_6$: C, 52.34; H, 6.08; N, 9.39.

2-[3-(4-Chlorophenylureido)]-2-deoxy-D-glucopyranose (16b).- From **3** and 4-chlorophenyl isocyanate, compound **16b** (99%) was obtained, m.p. 177-179°C (1:1, ethanol-water), $[\alpha]_D$ +44° (*c* 1.0, *N,N*-dimethylformamide) [lit.[19] m.p. 171-173°C (ethanol), $[\alpha]_D$ +88° (*c* 0.97, *N,N*-dimethylformamide)], ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1567 (NH), 1590, 1490, and 826 cm^{-1} (aromatic).

2-[3-(3-Chlorophenylureido)]-2-deoxy-D-glucopyranose (16c).- From **3** and 3-chlorophenyl isocyanate, compound **16c** (69%) was obtained, m.p. 172-174°C (1:1, ethanol-water), $[\alpha]_D$ +47° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1567 (NH), 1595, 1475, 865, and 687 cm^{-1} (aromatic). Anal. found: C, 46.62; H, 5.20; N, 8.25. Calcd. for $C_{13}H_{17}N_2O_6Cl$: C, 46.93; H, 5.15; N, 8.42.

2-Deoxy-2-[3-(4-methoxyphenylureido)]-D-glucopyranose (16d).- From **3** and 4-methoxyphenyl isocyanate, compound **16d** (98%) was obtained, m.p. 186-188°C (1:1, ethanol-water), $[\alpha]_D$ +39° (*c* 1.0, *N,N*-dimethylformamide), [lit.[19] m.p. 135-138° (ethanol-ether), $[\alpha]_D$ +13° (*c* 1.0, *N,N*-dimethylformamide)], ν_{max} 3500-3200 (OH, NH), 1637 (C=O), 1575 (NH), 1243 (OCH_3), 1606, 1513, and 820 cm^{-1} (aromatic).

2-Deoxy-2-[3-(3-methoxyphenylureido)]-D-glucopyranose (16e).- From **3** and 3-methoxyphenyl isocyanate, compound **16e** (52%) was obtained, m.p. 171-172°C, $[\alpha]_D$ +38° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1567 (NH), 1282 (OCH_3), 1606, 1490, 857, and 687 cm^{-1} (aromatic). This compound was analysed as per-*O*-acetyl derivative.

2-Deoxy-2-[3-(2-methoxyphenylureido)]-D-glucopyranose (16f).- From **3** and 2-methoxyphenyl isocyanate, compound **16f** (67%) was obtained, m.p. 173-175°C, $[\alpha]_D$ +53° (*c* 1.0, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1645 (C=O), 1567 (NH), 1259 (OCH_3), 1606, 1490, and 741 cm^{-1} (aromatic). Anal. found: C, 50.63; H, 6.22; N, 8.39. Calcd. for $C_{14}H_{20}N_2O_7$: C, 51.22; H, 6.14; N, 8.53.

2-Deoxy-2-[3-(4-tolylureido)]-D-glucopyranose (16g).- From **3** and 4-tolyl isocyanate, compound **16g** (90%) was obtained, m.p. 182-184°C (1:1, ethanol-water), $[\alpha]_D$ +43° (*c* 1.0, *N,N*-dimethylformamide) [lit.[19] mp 180-181°, $[\alpha]_D$ +45° (*c* 1.0, *N,N*-dimethylformamide)], ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1567 (NH), 1521, and 788 cm^{-1} (aromatic).

2-Deoxy-2-[3-(3-tolylureido)]-D-glucopyranose (16h).- From **3** and 3-tolyl isocyanate, compound **16h** (90%) was obtained, m.p. 174-176°C (ethanol-water), $[\alpha]_D$ +43° (*c* 1.0, *N,N*-dimethylformamide), ν_{max} 3500-3100 (OH, NH), 1637 (C=O), 1567 (NH), 1483, 757, and 687 cm^{-1} (aromatic). Anal. found: C, 54 26; H, 6 48; N, 8.93 Calcd. for $C_{14}H_{20}N_2O_7$: C, 53.84; H, 6.45; N, 8 97.

2-Deoxy-2-[3-(2-tolylureido)]-D-glucopyranose (16i).- From **3** and 2-tolyl isocyanate, compound **16i** (85%) was obtained, m.p. 192-194°C (ethanol-water), $[\alpha]_D$ +41° (*c* 1.0, *N,N*-dimethylformamide), ν_{max} 3500-3200 (OH, NH), 1637 (C=O), 1583 (NH), 1459, and 749 cm^{-1} (aromatic). This compound was analysed as per-*O*-acetyl derivative **17i**.

2-Deoxy-2-[3-(4-nitrophenylureido)]-D-glucopyranose (16j).- From **3** and 4-nitrophenyl isocyanate, compound **16j** (67%) was obtained, m.p. 169-171°C, $[\alpha]_D$ +22° (*c* 0.5, *N,N*-dimethylformamide-water 9:1), [lit.[19] m.p 153-155°C, $[\alpha]_D$+18° (*c*

1.0, *N,N*-dimethylformamide-water 9:1)], ν_{max} 3500-3200 (OH, NH), 1650 (C=O), 1570 (NH), 1520, 1345 (NO_2), 1610, 1510, 870 and 860 cm^{-1} (aromatic).

Preparation of per-*O*-acetyl-2-(3-arylureido)-2-deoxyaldopyranoses.

Procedure A: To a solution of 2-(3-arylureido)-2-deoxyaldopyranose (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 crystallization. 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-D-glucopyranose hydrochloride (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-Tetra-*O*-acetyl-2-deoxy-2-(3-phenylureido)-α and β-D-glucopyranoses (17a and 18a).- From **16a** and following the procedure A, a mixture of **17a** and **18a** (91%) was obtained. The pure α-anomer **17a** (68%) was isolated by recrystallisation from 96% ethanol, m.p. 211-213°C, $[\alpha]_D$ +101° (*c* 1.1, chloroform), ν_{max} 3390, 3340, and 1550 (NH), 1745, 1720, and 1230 (ester), 1690 (C=O urea), 1600, 1500, 770, and 700 cm^{-1} (aromatic), [lit.[17], m.p. 215°C, $[\alpha]_D$ +77° (*c* 1.0, ethanol)].

Pure **18a** (9%) was crystallised from the mother liquors of **17a**, m.p. 203-205°C, $[\alpha]_D$ +25° (*c* 1.0, chloroform), ν_{max} 3380, 3340, and 1540 (NH), 1755, 1740, 1730 and 1230 (ester), 1685 (C=O urea), 1590, 1500, 750, and 690 cm^{-1} (aromatic), [lit.[17], m.p. 204°C, $[\alpha]_D$ +22° (*c* 1.0, ethanol)].

Following the procedure B, the reaction of **19**[40] and phenyl isocyanate afforded **17a** (24%). In the same way, compound **18a** could be obtained (61%) from **20**[41].

1,3,4,6-Tetra-*O*-acetyl-2-[3-(4-chlorophenylureido)]-2-deoxy-α and β-D-glucopyranoses (17b and 18b).- From **16b** and following the procedure A, a mixture of **17b** and **18b** (87%) was obtained. The pure α-anomer **17b** (77%) was isolated by recrystallisation from 96% ethanol, m.p. 210-212°C, $[\alpha]_D$ +87° (*c* 1.0, chloroform), ν_{max} 3400, 3320, and 1550 (NH), 1750, 1720, and 1225 (ester), 1695 (C=O urea), 1590, 1490, and 830 cm^{-1} (aromatic). Anal. found: C, 50.08; H, 5.06; N, 5.46. Calcd. for $C_{21}H_{25}ClN_2O_{10}$: C, 50.36; H, 5.03; N, 5.59.

Pure **18b** (5%) was crystallised from the mother liquors of **17b**, m.p. 210-212°C, $[\alpha]_D$+17° (*c* 1.0, chloroform), ν_{max} 3390, 3360, and 1540 (NH), 1755, 1730, and 1220 (ester), 1685 (C=O urea), 1590, 1490, and 840 cm^{-1} (aromatic), [lit.[19], m.p. 209-210°C, $[\alpha]_D$ +38° (*c* 1.0, *N,N*-dimethylformamide)].

Following the procedure B, the reaction of **19**[40] and 4-chlorophenyl isocyanate afforded **17b** (58%). In the same way, compound **18b** could be obtained (86%) from **20**[41].

1,3,4,6-Tetra-*O*-acetyl-2-[3-(3-chlorophenylureido)]-2-deoxy-α-D-glucopyranose (17c).- From **16c** and following the procedure A, a mixture of **17c** and **18c** (90%) was obtained. The pure α-anomer **17c** (65%) was isolated by recrystallisation from 96% ethanol, m.p. 167-168°C, $[\alpha]_D$ +65° (*c* 0.5, chloroform), ν_{max} 3382, 3297, and 1544 (NH), 1753, 1714, and 1228 (ester), 1709 (C=O urea), 1598, 1483, and 780 cm^{-1} (aromatic). Anal. found: C, 50.49; H, 4.95; N 5.74. Calcd. for $C_{21}H_{25}N_2O_{10}Cl$: C, 50.36; H, 5.03; N, 5.59.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(4-methoxyphenylureido)]-α-D-glucopyranose (17d).- From **16d** and following the procedure A, a mixture of **17d** and **18d** (84%) was obtained. In this case, the mixture of both anomers could not be resolved. Anal. found: C, 53.62; H, 5.73; N, 5.69. Calcd. for $C_{22}H_{28}N_2O_{11}$: C, 53.22; H, 5.68; N, 5.64.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(3-methoxyphenylureido)]-α-D-glucopyranose (17e).- From **16e** and following the procedure A, a mixture of **17e** and **18e** (84%) was obtained. The pure α-anomer **17e** (63%) was isolated by recrystallisation from 96% ethanol, m.p. 128-130°C, $[\alpha]_D$ +77° (*c* 1.0, chloroform), ν_{max} 3410, 3380, and 1550 (NH), 1755, 1730, and 1230 (ester), 1700 (C=O urea), 1615, 1605, 1495, 785, and 695 cm^{-1} (aromatic). Anal. found: C, 53.22; H, 6.07; N 5.35. Calcd. for $C_{22}H_{28}N_2O_{11}$: C, 53.22; H, 5.68; N, 5.64.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(2-methoxyphenylureido)]-α-D-glucopyranose (17f).-From **16f** and following the procedure A, a mixture of **17f** and **18f** (70%) was obtained. The pure α-anomer **17f** (56%) was isolated by recrystallisation from 96% ethanol, m.p. 183-185°C, $[\alpha]_D$ +91° (*c* 1.0, chloroform), ν_{max} 3390, and 1540 (NH), 1760, and 1230 (ester), 1718 (C=O urea), 1610, 1495, and 770 cm^{-1} (aromatic). Anal. found: C, 53.19; H, 5.75; N 5.57. Calcd. for $C_{22}H_{28}N_2O_{11}$: C, 53.22; H, 5.68; N, 5.64.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(4-tolylureido)]-α and β-D-glucopyranoses (17g and 18g).- From **16g** and following the procedure A, a mixture of **17g** and **18g** (81%) was obtained. The pure α-anomer **17g** (40%) was isolated by recrystallization from 96% ethanol, m.p. 204-205°C, $[\alpha]_D$ +105° (*c* 1.0, chloroform), ν_{max} 3413, 3343, and 1552 (NH), 1753, 1735, 1720, and 1228 (ester), 1699 (C=O urea), 1606, 1520, and 825 cm^{-1} (aromatic). Anal. found. C, 55.15; H, 5.90; N, 5.89. Calcd. for $C_{22}H_{28}N_2O_{10}$: C, 55.00; H, 5.87; N, 5.83.

Following the procedure B, the reaction of **20**[41] and 4-tolyl isocianate afforded **18g** (64%), m.p. 202-204°C, $[\alpha]_D$+37° (*c* 1.0, *N,N*-dimethylformamide), ν_{max} 3390, 3360, and 1550 (NH), 1755, 1740, and 1240 (ester), 1690 (C=O urea), 1605, 1520, and 825 cm^{-1} (aromatic), [lit.[19], m.p. 200-201°C, $[\alpha]_D$ +38° (*c* 1.0, *N,N*-dimethylformamide)]

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(3-tolylureido)]-α and β-D-glucopyranoses (17h and 18h).- From **16h** and following the procedure A, a mixture of **17h** and **18h** (93%) was obtained. The pure α-anomer **17h** (57%) was isolated by recrystallization from 96% ethanol, m.p. 176-179°C, $[\alpha]_D$ +83° (*c* 1.0, chloroform), ν_{max} 3399, 3310, and 1560 (NH), 1760, 1740, and 1230 (ester), 1710 (C=O urea), 1606, 1490, 790 and 760 cm^{-1} (aromatic). Anal. found: C, 55.69; H, 5.95; N, 6.05. Calcd. for $C_{22}H_{28}N_2O_{10}$: C, 55.00; H, 5.87; N, 5.83.

Following the procedure B, the reaction of **20**[41] and 3-tolyl isocianate afforded **18h** (64%), m.p. 210-211°C, $[\alpha]_D$+23° (*c* 1.0, chloroform), ν_{max} 3390 and 1560 (NH), 1755 and 1240 (ester), 1685 (C=O urea), 1600, 1500, 790, and 700 cm^{-1} (aromatic). Anal. found: C, 54.85; H, 5.87; N 5.98. Calcd. for $C_{22}H_{28}N_2O_{10}$: C, 55.00; H, 5.87; N, 5.83.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(2-tolylureido)]-α and β-D-glucopyranoses (17i and 18i) .- From **16i** and following the procedure A, a mixture of **17i** and **18i** (81%) was obtained. The pure α-anomer **17i** (49%) was isolated by recrystallization from 96% ethanol, m.p. 154-156°C, $[\alpha]_D$ +82° (*c* 0.5, chloroform), ν_{max} 3320 and 1560 (NH), 1745 and 1240 (ester), 1660 (C=O urea), 1590, 1490, and 750 cm^{-1} (aromatic). Anal. found: C, 54.99; H, 5.90; N, 5.96. Calcd. for $C_{22}H_{28}N_2O_{10}$: C, 55.00; H, 5.87; N, 5.83.

Following the procedure B, the reaction of **20**[41] and 2-tolyl isocianate afforded **18i** (64%), m.p. 210-212°C, $[\alpha]_D$+20° (*c* 1.0, chloroform), ν_{max} 3320 and 1560 (NH), 1755 and 1230 (ester), 1650 (C=O urea), 1610, 1590, 765, and 750 cm^{-1} (aromatic). Anal. found: C, 54.57; H, 5.90; N 5.88. Calcd. for $C_{22}H_{28}N_2O_{10}$: C, 55.00; H, 5.87; N, 5.83.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-[3-(4-nitrophenylureido)]-α-D-glucopyranose (17j).- From **16j** and following the procedure A, **17j** (90%) was obtained, m.p. 207-209°C, $[\alpha]_D$ +66° (*c* 0.5, chloroform), ν_{max} 3367, 3343, and 1560 (NH), 1745 and 1220 (ester), 1630 (C=O urea), 1336 (NO_2), 1606, 1498, 849, and 730 cm^{-1} (aromatic). Anal. found: C, 49.62; H,4.89; N, 8.23. Calcd. for $C_{21}H_{25}N_3O_{12}$: C, 49.32; H, 4.93; N, 8.23.

(4*S*,5*S*)-4-(D-*Arabino*-tetrytol-1-yl)-5-hydroxy-1-phenylimidazolidin-2-one (28).- To a stirred solution of **21**.HCl (0.5 g, 2.3 mmol) in water (3.0 mL) were added sodium carbonate (0.2 g, 1.9 mmol), and phenyl isocyanate (0.3 mL, 2.5 mmol) in dioxane (0.6 mL). The reaction mixture was stirred for 12 h at room temperature. After removal of *N,N'*-diphenylurea by filtration, the solution was evaporated and 96% ethanol was added. After several days in the refrigerator compound **28** was filtered off and successively washed with cold ethanol and ether (0.35 g, 51%). Recrystallised from 99% ethanol had m.p. 149-151°C, $[\alpha]_D$ +9.5° (*c* 0.5, *N,N*-dimethylformamide), ν_{max} 3500-3000 (OH, NH), 1690 (C=O), 1606, 1510, 750, and 690 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.62-7.00 (5H, m, Ar), 7.24 (1H, s, NH), 6.47 (1H, d, $J_{1,OH}$ 7.8, OH-1), 5.51 (1H, d, $J_{1,2}$ 0.0, H-1). Anal. found: C, 52.15; H, 6.09; N, 9.35. Calcd. for $C_{13}H_{18}N_2O_6$: C, 52.34; H, 6.08; N, 9.39.

(4*S*,5*S*)-4-(D-*Arabino*-tetrytol-1-yl)-1-(4-chlorophenyl)-5-hydroxyimidazolidin-2-one (29).- Compound **29** (0.30 g, 40%) was obtained from **21**.HCl (0.5 g, 2.3 mmol) and 4-chlorophenyl isocyanate (0.4 g, 2.6 mmol) as described for **28**, m.p. 205-207°C, $[\alpha]_D$ +25° (*c* 0.5, pyridine), ν_{max} 3500-3000 (OH, NH), 1690 (C=O), 1600, 1505, and 818 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.67-7.34 (4H, m, Ar), 7.36 (1H, s, NH), 6.53 (1H, d, $J_{1,OH}$ 8.2, OH-1), 5.54 (1H, d, $J_{1,2}$ 0, H-1). Anal. found: C, 46.66; H, 5.22; N, 8.33. Calcd. for $C_{13}H_{17}ClN_2O_6$: C, 46.93; H, 5.15; N, 8.42.

In some cases, 2,5-bis(D-*arabino*-tetrytol-1-yl)pyrazine (**44**) was isolated and characterised as its acetyl derivative **45**, m.p. 180-181°C, $[\alpha]_D$ -7.2° (*c* 0.5, chloroform), [lit.[48], m.p. 174°C, $[\alpha]_D$ -7.2° (*c* 1.0, chloroform)], δ_C (50.33 MHz, $CDCl_3$) 170.58 (2C, C=O), 169.81 (2C, C=O), 169.65 (2C, C=O), 168.85 (2C, C=O), 151.17 (C-2 and C-5), 141.45 (C-3 and C-6), 72 00 (2C, C-1'), 70.03 (2C, C-2'), 68.10 (2C, C-3'), 61.84 (2C, C-4'), 20.78 (2C, CH_3), 20.66 (4C, CH_3), and 20.03 (2C, CH_3).

2-Deoxy-2-(3-phenylureido)-D-galactopyranose (25) and (4*R*,5*R*)-5-hydroxy-4-(D-*lyxo*-tetrytol-1-yl)-1-phenylimidazolidin-2-one (30).- To a stirred solution of **24**.HCl (1.0 g, 4.6 mmol) in water (5.0 mL) were added sodium hydrogencarbonate (0.4 g, 4.8 mmol), and phenyl isocyanate (0.6 mL, 5.0 mmol) in dioxane (1.2 mL). After a few minutes a white solid precipitate. Filtration and washing with water, acetone, and ether gave **25** (31%). When **25** was not immediately filtered, the reaction mixture was kept at room temperature for 1 h, and then water (40 mL) and sodium carbonate (until pH~8) were added. The suspension was heated (50-55°C) and vigorously stirred for 6 h. After removal of *N,N'*-diphenylurea by filtration, the solution was evaporated and 96% ethanol was added. After several days in the refrigerator compound **30** was filtered off and successively washed with cold ethanol and ether (1.08 g, 78%). Recrystallised from 99% ethanol had m.p. 171-172°C, $[\alpha]_D$ +24.5° (*c* 0.5, pyridine), ν_{max} 3500-3000 (OH, NH), 1690 (C=O), 1610, 1510, 760, and 700 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.74-7.08 (5H, m, Ar), 6.93 (1H, s, NH), 6.47 (1H, d, $J_{1,OH}$ 8.8, OH-1), 5.50 (1H, dd, $J_{1,2}$ 1.9, H-1). Anal. found: C, 52.18; H, 6.17; N, 9.42. Calcd. for $C_{13}H_{18}N_2O_6$: C, 52.34; H, 6.08; N, 9.39.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3-phenylureido)-α and β-D-galactopyranoses (26 and 27).- Conventional acetylation of **25** gave a mixture of **26** and **27** (53%). In this case, the mixture of both anomers could not be resolved; δ_H (200 MHz, $CDCl_3$): for **26**, 7.37-7.00 (6H, m, Ar-NH), 6.32 (1H, d, $J_{1,2}$ 3.6, H-1), 5.41 (1H, d, $J_{3,4}$ 3.0, H-4), 5.28 (1H, d, $J_{2,NH}$ 9.6, S-NH), 5.222 (1H, dd, $J_{2,3}$ 11.3, H-3), 4.64 (1H, ddd, H-2); for **27**, 7.37-7.00 (6H, m, Ar-NH), 5.73 (1H, d, $J_{1,2}$ 8.5, H-1), 5.48 (1H, d, $J_{2,NH}$ 9.3, S-NH), 5.33 (1H, d, $J_{3,4}$ 3.6, H-4), 5.13 (1H, dd, $J_{2,3}$ 11.3, H-3), 4.27 (1H, m, H-2).

(4*R*,5*R*)-4-(D-*Arabino*-tetritol-1-yl)-5-hydroxy-1-phenylimidazolidin-2-one (31).- To a suspension of **16a** (0.5 g, 1.7 mmol) in water (10 mL) a few drops of pyridine (to maintain the pH~8) were added and then heated (50-55°C) and vigorously stirred for 8 h. The solution was filtered off, evaporated and 96% ethanol was added. After several days in the refrigerator compound

31 was filtered off and successively washed with cold ethanol and ether (0.40 g, 80%). Recrystallised from 99% ethanol had m.p. 167-169°C, $[\alpha]_D$ +18° (*c* 0.5, pyridine), ν_{max} 3600-3100 (OH, NH), 1670 (C=O), 1600, 1510, 760, and 700 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.63-7.01 (5H, m, Ar), 6.75 (1H, s, NH), 6.48 (1H, d, $J_{1,OH}$ 8.6, OH-1), 5.40 (1H, d, $J_{1,2}$ 0.0, H-1). Anal. found: C, 52.32; H, 6.26; N, 9.32. Calcd. for $C_{13}H_{18}N_2O_6$: C, 52.34; H, 6.08; N, 9.39.

This transformation was monitored by NMR in a sample prepared as follows: to a solution of **16a** (0.09 g, 0.3 mmol) in deuterium oxide (1 mL) sodium carbonate (until pH~8) was added and the reaction mixture was heated at 50-55° for 6 h. After filtration, ^1H- and ^{13}C NMR spectra showed a total conversion into **49**.

(4*R*,5*R*)-4-(D-*Arabino*-tetrytol-1-yl)-1-(4-chlorophenyl)-5-hydroxyimidazolidin-2-one (32).- Compound **32** (70%) was obtained from **16b** as described for **31**, m.p. 169-171°C, $[\alpha]_D$ +8° (*c* 1.0, pyridine), ν_{max} 3600-3000 (OH, NH), 1700 (C=O), 1600, 1500, and 745 cm^{-1} (aromatic), δ_H (200 MHz, DMSO-d_6) 7.67-7.33 (4H, m, Ar), 6.88 (1H, s, NH), 6.54 (1H, d, $J_{1,OH}$ 8.3, OH-1), 5.39 (1H, d, $J_{1,2}$ 0.0, H-1). Anal. found: C, 46.99; H, 5.31; N, 8.36. Calcd. for $C_{13}H_{17}ClN_2O_6$: C, 46.93; H, 5.15; N, 8.42.

Deacetylation of 17b.- To a solution of **17b** (0.5 g, 1.0 mmol) in methanol, a solution of methanol saturated with ammonia (14 mL) was added. The reaction mixture was kept for 2 h at 0° and 4 h at room temperature and then evaporated to an oily residue (0.30 g of a mixture of **32** and **16b** in a ratio 4:1 determined by NMR). The residue was treated with 99% ethanol and **16b** (0.06 g, 18%) crystallised. From the mother liquors **32** (0.23 g, 70%) was obtained by crystallisation.

(4*R*,5*R*)-4-(1,2,3,4-Tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-5-hydroxy-1-phenylimidazolidin-2-one (38) and 4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-1-phenylimidazolin-2-one (40).- To a solution of **31** (1.0 g, 3.4 mmol) in pyridine (10 mL), acetic anhydride (8 mL) was added. The reaction mixture was kept at 0°C for 24 h. Then was poured into ice-water to give **38** (0.72 g, 47%) as a white solid. Recrystallised from 96% ethanol had, m.p. 159-160°C, $[\alpha]_D$ +26° (*c* 0.5, chloroform), ν_{max} 3530, 3420, 3360, 3270, and 3150 (OH, NH), 1755, 1740, and 1230 (ester), 1720 (C=O urea), 1605, 1505, 765 and 700 cm^{-1} (aromatic). Anal. found: C, 54.02; H, 5.71; N, 5.95. Calcd. for $C_{21}H_{26}N_2O_{10}$: C, 54.07; H, 5.62; N, 6.01.

The aqueous layer was extracted with chloroform and the organic solution was washed successively with *N* hydrochloric acid, saturated aqueous solution of sodium hydrogencarbonate, and water. The solution was evaporated and the residue was crystallised from 96% ethanol to give **40** (0.32 g, 21%), m.p. 120-121°C, $[\alpha]_D$ -45° (*c* 0.5, chloroform), ν_{max} 3300-3100 (NH), 1760, 1750, and 1230 (ester), 1700 (C=O urea), 1600, 1510, 765 and 710 cm^{-1} (aromatic). Anal. found: C, 56.18; H, 5.51; N, 6.25. Calcd. for $C_{21}H_{24}N_2O_9$: C, 56.25; H, 5.39; N, 6.25.

(4*R*,5*R*)-1-Acetyl-4-acetoxy-5-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-chlorophenyl)-imidazolidin-2-one (39).- Acetylation of **32** (0.17 g, 0.5 mmol) as described for **31** yielded a mixture of products (0.21 g.) from which **39** (0.02 g, 7%) was separated by preparative t.l.c. (benzene-methanol, 9:1). Colourless oil, $[\alpha]_D$ -11.5° (*c* 0.9, chloroform), ν_{max} 1760, 1266, and 1212 (ester), 1705 (C=O urea), 1600, 1500, and 830 cm^{-1} (aromatic). Mass espectrum: *m/z* 584.1402. Calcd. for M^+ of $C_{25}H_{29}ClN_2O_{12}$: 584.1409.

Acetylation of 29.- To a solution of **29** (0.24 g, 0.7 mmol) in pyridine (2.4 mL) acetic anhydride (2.0 mL) was added. The reaction mixture was kept for 17 h at room temperature and then poured into ice-water to give a solid mixture (0.3 g) of **41-43**. From this mixture (4*S*,5*S*)-1-acetyl-4-acetoxy-5-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)-3-(4-chlorophenyl)imidazolidin-2-one (**42**, 0.15 g, 36%) was separated by preparative t.l.c. as a colourless oil, $[\alpha]_D$ +2° (*c* 0.5, chloroform), ν_{max} 1760 and 1251, (ester), 1700 (C=O, urea and acetamido), 1600, 1500, and 834 cm^{-1} (aromatic). Mass espectrum: *m/z* 584.1418. Calcd. for M^+ of $C_{25}H_{29}ClN_2O_{12}$: 584.1409.

Compounds **41** and **43** could not be separated although were identified by NMR data.

Transformation of 16b into 29 and 32.- To a solution of **16b** (1.0 g, 3.3 mmol) in 50% ethanol (400 mL) sodium carbonate (until pH~10) was added. The reaction mixture was heated (30-40°C) and vigorously stirred for 3 h and then for 2 days at room temperature. After evaporation to dryness, the residue was solidified (0.85 g) by addition of ether. ^1H- and ^{13}C NMR spectra showed a mixture of **29** and **32** (in almost equal ratio) and traces of **16b**. Conventional acetylation of the crude mixture give a white solid (0.32 g). Compound **42** was isolated (0.03 g, 6%) by preparative t.l.c. (benzene-methanol 9:1).

1-Phenyl-(1,2-dideoxy-β-D-*manno*-hexofurano)[2,1-*d*]imidazolidin-2-one (46).- To a solution of **21**.HCl (0.5 g, 2.3 mmol) in water (2.5 mL) sodium hydrogencarbonate (0.2 g, 1.2 mmol) and phenyl isocyanate (0.32 mL, 2.8 mmol) in dioxane (0.6 mL) were added. The reaction mixture was kept 12 h at room temperature and then evaporated to dryness. The solid residue was extracted with water and the solution was concentrated to give **46** (0.3 g, 46%), m.p. 201-203°C, $[\alpha]_D$ -187.5° (*c* 0.5, pyridine), ν_{max} 3500 and 3450-3100 (OH, NH), 1660 (C=O urea), 1590, 1490, 750, and 680 cm^{-1} (aromatic). Anal. found: C, 55.57; H, 5.80; N, 9.84. Calcd. for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.75; N, 9.99.

1-Phenyl-(3,5,6-tri-*O*-acetyl-1,2-dideoxy-β-D-mannofurano)[2,1-*d*]imidazolidin-2-one (47).- Conventional acetylation at 0°C of **46** gave **47** (95%). Recrystallised from 96% ethanol had, m.p. 200-202°C, $[\alpha]_D$ -180° (*c* 0.5, chloroform), ν_{max} 3260 and 3140 (NH), 1760, 1740, 1725, and 1240 (ester), 1690 (C=O urea), 1600, 1500, 765, and 695 cm^{-1} (aromatic) Anal. found: C, 56.06; H, 5.46; N, 6.82. Calcd. for $C_{19}H_{22}N_2O_8$: C, 56.16; H, 5.46; N, 6.89.

1-Phenyl-(1,2-dideoxy-α-D-galactofurano)[2,1-*d*]imidazolidin-2-one (48).- A solution of **30** (0.12 g, 0.4 mmol) in 30% aqueous acetic acid (2 mL) was heated at 100°C for 30 min. The reaction mixture was concentrated to dryness and the residue

crystallised from 99% ethanol (0.054 g, 49%), m.p. 113-115°C, $[\alpha]_D$ +76° (*c* 0.5, pyridine), ν_{max} 3600-3000 (OH, NH), 1710 (C=O urea), 1605, 1510, 760, and 700 cm^{-1} (aromatic). Anal. found: C, 54.77; H, 5.94; N, 9.47. Calcd. for $C_{13}H_{16}N_2O_5$. 1/2CH_3CH_2OH: C, 55.43; H, 6.31; N, 9.24.

1-Phenyl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-one (49).- a) Compound **49** (85%) was obtained from **31** as described for **48**, m.p. 214-216°C, $[\alpha]_D$ +91° (*c* 0.6, pyridine) [lit.[12], m.p. 214-216°C, $[\alpha]_D$ +93° (*c* 0.5, pyridine)].

b) A suspension of **16a** (0.33 g, 1.1 mmol) in 50% ethanol (10 mL) and acetic acid (2 mL) was heated at 80° for 2 h. The reaction mixture was concentrated to dryness and the residue crystallised from 99% ethanol to give **49** (0.22 g, 71%). Other compounds were not isolated or detected in the mother liquors.

1-(4-Chlorophenyl)-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidin-2-one (50).- Compound **50** (92%) was obtained from **32** as described for **48**, m.p. 218-220°C, $[\alpha]_D$ +115° (*c* 0.6, pyridine) [lit.[12], m.p. 217-218°C, $[\alpha]_D$ +116.5° (*c* 0.5, pyridine)].

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(3-phenylureido)-α-D-glucopyranose (51).- A suspension of **17a** (1.0 g, 2.1 mmol) and silica gel (Merck GF_{254}, 1.0 g) in dry methanol (100 mL) was vigorously stirred at room temperature for 2 days. The silica gel was filtered and washed with methanol (2x40 mL). Evaporation of organic extracts gave a white foam (0.99 g). Crystallised from aqueous ethanol gave **51** (0.6 g, 66%), m.p. 170-173°C [lit.[17,76], m.p. 170°C].

3,4,6-Tri-*O*-acetyl-2-deoxy-2-[3-(4-chlorophenylureido)]-α-D-glucopyranose (52).-Compound **52** (71%) was obtained from **17b** as described for **51**, m.p. 170-172°C, $[\alpha]_D$ +70° (*c* 1, chloroform), ν_{max} 3485 and 3340 (NH, OH), 1740 and 1225 (ester), 1685 (C=O urea), 1540 and 1520 (NH), 1590, 1490, and 820 cm^{-1} (aromatic). Anal. found: C, 50.00; H, 5.11; N, 6.03. Calcd. for $C_{19}H_{23}ClN_2O_9$: C, 49.74; H, 5.05; N, 6.10.

1-Phenyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]imidazolidin-2-one (53).- A solution of **51** (0.4 g, 0.9 mmol) in glacial acetic acid (4 mL) was heated at 50°C for 2 days, and then evaporated to dryness. Compound **53** (0.22 g, 58%) was obtained from the oily residue by preparative t.l.c. (benzene-methanol, 9.1). Crystallised from ether-light petroleum had, m.p. 127-128°C, $[\alpha]_D$ +70° (*c* 0.5, chloroform), ν_{max} 3240 and 3140 (NH), 1760, 1750, 1740, and 1240 (ester), 1690 (C=O urea), 1605, 1505, 770, and 700 cm^{-1} (aromatic). Anal. found. C, 56.16; H, 5.44; N, 6.85. Calcd. for $C_{19}H_{22}N_2O_8$: C, 56.16; H, 5.46; N, 6.89.

1-(4-Chlorophenyl)-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]imidazolidin-2-one (54).- Compound **54** (52%) was obtained from **52** as described for **53**, m.p. 165-166°C, $[\alpha]_D$ +29° (*c* 0.5, chloroform), ν_{max} 3240 and 3140 (NH), 1760, 1740, 1725, 1250, 1240 and 1220 (ester), 1685 (C=O urea), 1595, 1500, and 835 cm^{-1} (aromatic). Anal. found: C, 51.78; H, 4.84; N, 6.23. Calcd. for $C_{19}H_{21}ClN_2O_8$: C, 51.77; H, 4.80; N, 6.35.

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