Pergamon

Tetrahedron, Vol. 53, No. 40, pp. 13783-13796, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00898-3

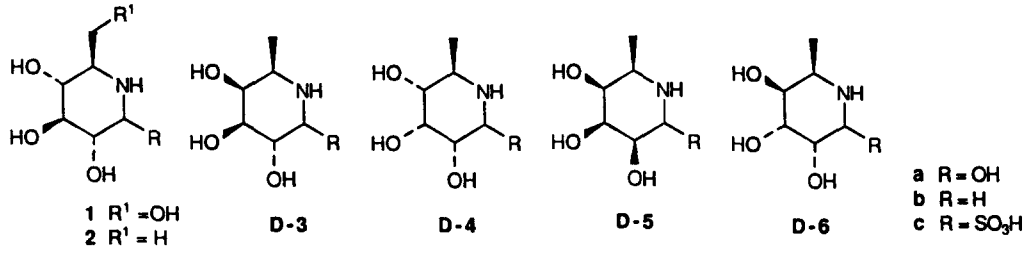
6-Deoxy-Nojirimycin and 6-Deoxy-*gulo*-Nojirimycin in the racemic and D-Series, D-*Fuco*-Nojirimycin and their 1-Deoxyderivatives *via* Hetero-*Diels-Alder* Cycloadditions.

Albert Defoin*, Hervé Sarazin, Jacques Streith

École Nationale Supérieure de Chimie de Mulhouse, Université de Haute Alsace, 3, rue Alfred Werner, F-68093 Mulhouse Cédex[†].

Abstract. Nucleophilic ring opening of the cyclic sulfates (±)-**9c** and **D-9c** and of the epoxide (±)-**13**, or double substitution of the bis-triflate **D-10** (derived from the Diels-Alder adduct of hexadienal dimethylacetal to achiral or enantiomerically pure nitroso-derivatives) led to 6-deoxy-nojirimycin and 6-deoxy-*gulo*-nojirimycin in the racemic and D-series, to D-*fuco*-nojirimycin and to their 1-deoxyderivatives *via* their crystalline 1-deoxy-1-sulfonic acid derivatives (sulfite adducts). 6-Deoxy-nojirimycin and its isomers are mixtures of α- and β-anomers and of the corresponding imine.

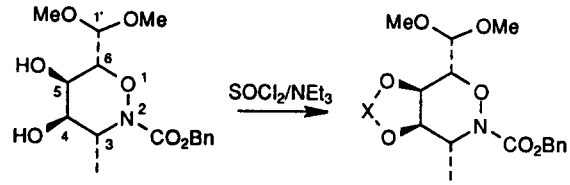
Introduction. - Some 5-Amino-5-deoxy-hexoses are natural aminosugars with potent glycosidase inhibitory properties [1]. Nojirimycin **1a** [2,3], *manno*-nojirimycin (nojirimycin B) [4,5] and galactostatine [6], which have the D-*gluco*- , D-*manno*- and D-*galacto*-configurations, respectively, are potent inhibitors of the corresponding glycosidases [1]. *Allo*-nojirimycin, albeit not a natural product, had also been synthesised [7]. All true aminosugars are rather unstable compounds, which lead to crystalline and stable adducts with SO_2 [2,4,8]. They can easily be reduced or oxidised to the corresponding 1-deoxy derivates or δ-lactams [4,8,9] which possess similar inhibitory properties when compared with the above cited true amino-sugars [1,2,10], but are more stable and therefore more easy to prepare.



Scheme 1

Some 1,6-dideoxy-derivatives have already been synthesised and do show some inhibitory properties [11-18] (*Scheme 1*) : 1-deoxy-L-*fuco*-nojirimycin **L-3b** [11] is a potent α-L-fucosidase inhibitor whereas its D-*rhamno* and L-*rhamno* isomers are poor inhibitors of D-rhamnosidase [12]. 1,6-Dideoxy-nojirimycin **2b** inhibits α- and β-glucosidases [13], to a lesser degree though as 1-deoxy-nojirimycin **1b**. 6-Deoxy-amino-sugars analogous to 6-deoxy-nojirimycin **2a** are unknown compounds. In the preceding publication, we described the

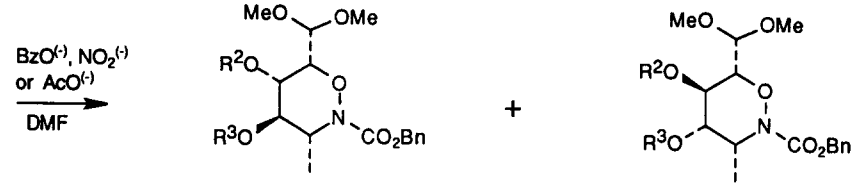
† *E-Mail : J.Streith @univ-mulhouse.fr ; fax: (0033) (0)3 89 43 77 90*



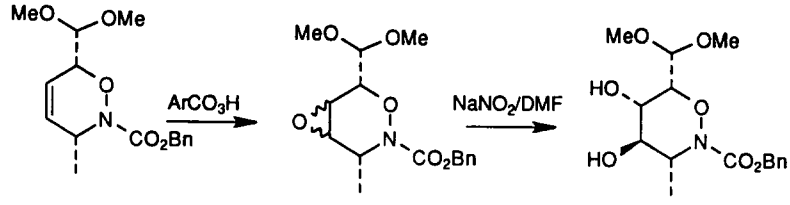
(±),D-8

$Ru^{VIII}/NaIO_4$

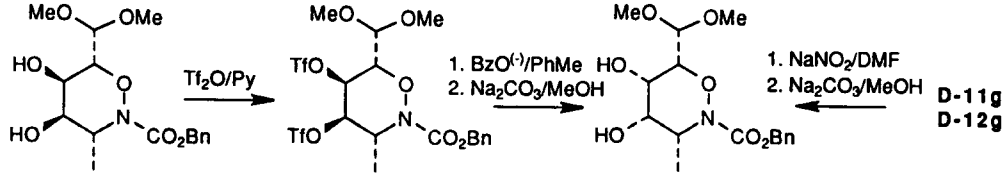
(±),D-9a X = S–O
(±),D-9b X = S–O
(±),D-9c X = SO_2



H_2SO_4 / Na_2CO_3/MeOH	(±)-11a	R^2 = Bz	R^3 = SO_3H		(±)-12a	R^2 = SO_3H	R^3 = Bz
	(±)-11b	R^2 = H	R^3 = Bz		(±)-12b	R^2 = H	R^3 = Bz
	(±)-11c	R^2 = H	R^3 = H		(±)-12c	R^2 = H	R^3 = H
H_2SO_4	D-11c	R^2 = H	R^3 = H		D-12c	R^2 = H	R^3 = H
	D-11d	R^2 = H	R^3 = SO_3H		D-12d	R^2 = SO_3H	R^3 = H
H_2SO_4	D-11e	R^2 = Ac	R^3 = SO_3H		D-12e	R^2 = SO_3H	R^3 = Ac
Tf_2O/Py	D-11f	R^2 = Ac	R^3 = H		D-12f	R^2 = H	R^3 = Ac
	D-11g	R^2 = Ac	R^3 = Tf		D-12g	R^2 = Tf	R^3 = Ac



(±)-7 (±)-13 (±)-11c



D-8 D-10 D-14

Scheme 2

five step synthesis of 6-deoxy-*allo*-nojirimycin, both in the racemic (±)-**4a** and chiral **D-4a** forms, and of the racemic 6-deoxy *talo*-nojirimycin (±)-**5a**, starting from sorbaldehyde dimethylacetal [14].

We describe herein the synthesis of enantiomerically pure 6-deoxy-nojirimycin **D-2a**, D-*fuco*-nojirimycin **D-3a**, 6-deoxy-D-*gulo*-nojirimycin **D-6a**, as well as of racemic (±)-**2a** and (±)-**6a**. These compounds were reduced into the corresponding 1-deoxy-derivatives (±)-**2b**, **D-2b**, **D-3b**, (±)-**6a**, **D-6a**. Deoxy-amino-sugars **D-2b**[13a], **D-3b** [13b], **L-3b** [11,17,18a] and **D-6b** [18b] in the D-glucose, D- and L-fucose and D-gulose series had already been obtained using chemio-enzymatic [13] or chemical syntheses [11,17,18]. The work described herein has been disclosed partially by us in preliminary communications [19].

Results.-

1) Single and double inversion of diol 10a. - Crystalline racemic cyclic sulfates (±)-**9c** and oily chiral **D-9c** were prepared in two steps in 86 and 80 % yields respectively, according to the *Sharpless* procedure [20] by reaction of the corresponding diols (±)-**8** and **D-8**. The diols were treated with $SOCl_2/NEt_3$ followed by oxidation (catalytic amounts of Ru^{VIII}/ $NaIO_4$) of the resulting intermediate diastereoisomeric cyclic sulfite mixtures (±)-**9a,b** and **D-9a,b** (*Scheme 2*).

The *Sharpless* opening procedure (ammonium benzoate/DMF) was used with (±)-**9c** and gave the two expected benzoate-sulfate monoester regioisomers (±)-**11a**, (±)-**12a**. No reaction occurred in acetone. Mild hydrolysis of the sulfate monoester moieties with catalytic amounts of H_2SO_4 in dioxane gave monobenzoates (±)-**11b**, (±)-**12b**. The migration of the benzoyl group toward the 4-position was observed for the major isomer (±)-**11b**. Methanolysis of the monoester mixture with Na_2CO_3/MeOH gave the two isomeric *trans*-diols (±)-**11c**, (±)-**12c** (75:25) which were separated by chromatography in 91 % overall yield from (±)-**9c**.

A shorter methodology was applied in the chiral series using sodium nitrite in DMF ; **D-9c** led to the two sulfate monoester regioisomers **D-11d**, **D-12d**, which, after hydrolysis with catalytic amounts of sulfuric acid as above, led to the two isomeric *trans*-diols **D-11c**, **D-12c** (70:30) in 76 % overall yield after chromatography.

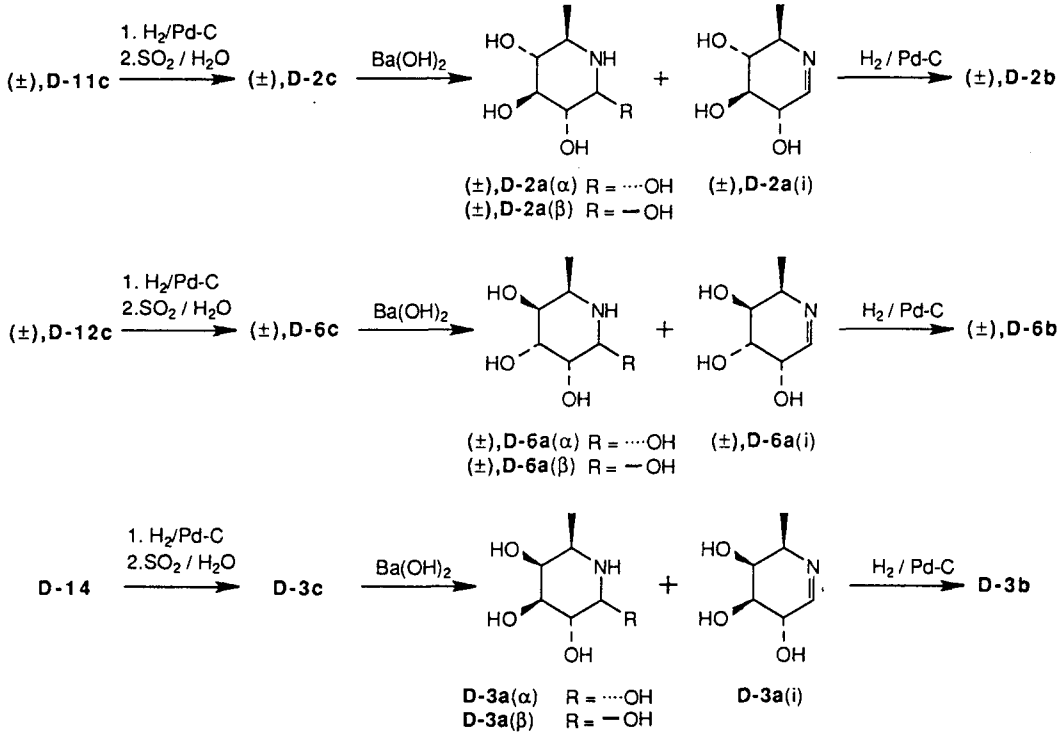
When cyclic sulfate was opened with acetate anion, the acetyl group did not migrate after hydrolysis, as compared to the benzoyl group (see above). Furthermore, inversion of the second alcohol function could be achieved *via* its triflic ester. Opening chiral cyclic sulfate **D-9c** with ammonium acetate in DMF gave the acetate regioisomers **D-11e**, **D-12e** (75:25). Hydrolysis of the sulfuric mono-esters to **D-11f**, **D-12f** followed by esterification with triflic anhydride gave the isomeric triflates **D-11g**, **D-12g** ; treatment of these triflates with sodium nitrite in DMF according to the *Dax* procedure [21], followed by methanolysis of the acetate group (Na_2CO_3/MeOH), gave the inverted *cis* diol **D-14** as the only reaction product (73 % from **D-9c**).

In all instances, the opening of the cyclic sulfate occurred predominantly in the equatorial 5-position by axial attack of the benzoate, nitrite or acetate anion to give derivatives of the *trans*-diaxial diol **D-11c**, a result which we had already observed previously [15]. The various intermediate esters were characterised only by ^{1}H-NMR and have not been purified.

2) Epoxide opening by nitrite anion. - Epoxidation of the racemic adduct (±)-**7** with *m*-chloroperbenzoic acid in CH_2Cl_2 proceeded slowly to give (±)-**13** (85%) as a diastereoisomeric mixture (*ca.* 70:30) (*Scheme 2*). Epoxides are usually cleaved in acidic medium [22], but in this case the action of formic acid led only to unclear reaction, presumably because of aldehyde deprotection. Nucleophilic reaction with nitrite anion in DMF at 100°C was slow and gave directly the *trans*-diol (±)-**11c** in moderate yield (52%). Both epoxides (±)-**13** led also to the same final *trans*-diaxial diol (±)-**11c** by axial attack of the nitrite anion.

3) Double inversion of bis-triflate D-10. -Esterification of diol **D-8** with triflic anhydride in pyridine/CH_2Cl_2 led in 95 % yield to the moderately stable bistriflate **D-10**. Treatment of this latter compound with benzoate anion using *Binkley's* conditions [23] gave a complex mixture of products which were formed both *via* inversion and elimination of the triflate groups, the expected diol **D-14** was obtained after methanolysis (Na_2CO_3/MeOH) in 58 % yield (*Scheme 2*). Using other nucleophiles (tetrabutylammonium nitrite in toluene [23], ammonium benzoate [20] or sodium nitrite in DMF [21]) led to intractable mixtures.

4) Amino-sugar synthesis (Scheme 3). - The reaction scheme we describe herein is identical to the one we followed in the allose and talose series [14]. Hydrogenolysis (H_2-Pd/C in EtOH) of the oxazane-diols (±)-**11c**, **D-11c**, (±)-**12c**, **D-12c**, **D-14**, followed by hydrolysis of the resulting acyclic aminosugar dimethylacetals with aqueous sulfurous acid (50°C, 5 days), gave the crystalline sulfite adducts of aminosugars (±)-**2c**, **D-2c** (66 % and 67 %) in the racemic and D-glucose series. Similarly (±)-**6c** (70 %) and **D-6c** (55 %) were obtained in the racemic and D-gulose series, as well as **D-3c** (42 %) in the D-fucose series.



Scheme 3

The corresponding aminosugars (±)-**2a** (6-deoxy-D,L-nojirimycin), **D-2a** (6-deoxy-nojirimycin), (±)-**6a**, **D-6a** (6-deoxy-D,L- and D-*gulo*-nojirimycin) and **D-3a** (D-*fuco*-nojirimycin) were obtained by removal of the sulfonic group with $Ba(OH)_2$ (1 eq.) which precipitated as $BaSO_3$ salt. In all cases, these free aminosugars appeared as mixtures of both α- and β-anomers, and of the corresponding imine form (i) : (±)- and **D-2a**(α), **2a**(β), **2a**(i), (±)- and **D-6a**(α), **6a**(β), **6a**(i), and **D-3a**(α), **3a**(β), **3a**(i). Hydrogenolysis of each mixture over Pd/C gave in essentially quantitative yield the 1-deoxy-derivatives (±) **2b** **D-2b**, (±)-**6b**, **D-6b**, **D-3b**, respectively. Enantiomerically pure 1-deoxy-aminosugars **D-2b** and **D-6b** have already been synthesised previously by us [15]. 1,6-Dideoxy-nojirimycin **D-2b** is a known compound [13a], as well as **D-3b** [13b] and **D-6b** [18b]. **D-3b** is the enantiomer of the known 1-deoxy-L-*fuco*-nojirimycin [11,17,18] (all physical data, but opposite values of rotatory power, were in good agreement). Racemic compounds (±)-**2b** and (±)-**6b** were characterised as their crystalline tetra-acetate derivatives.

Structural analyses [24].-

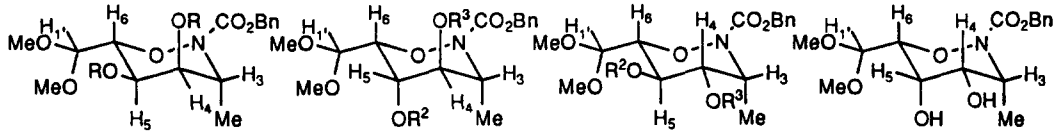
1) Absolute configuration. - Adduct **D-7** has been obtained with excellent enantiomeric excess (> 99 %) and has the (3*R*,6*R*) configuration [14]. Chiral aminosugars also appear in the D-series, in good agreement with their $[\alpha]_D$ values [11,13a,17].

Table 1 [24]. ^{1}H-NMR Spectra ($CDCl_3$, 300 K) of oxazanes **8**, **9c**, **10**, **11a-c,f**, **12a-c,f**, **13**, **14**, δ in ppm, J in Hz, internal standard TMS.

	H-C(1')	H-C(3)	H-C(4)	H-C(5)	H-C(6)	MeC(3)	CH_2[a]		OMe		J(1',6)	J(3,Me)	J(3,4)	J(4,5)	J(5,6)	J(3,5)
8[bc]	4.53	4.54	3.85	4.06	4.16	1.31	5.17	5.24	3.44	3.50	4.8	7.1	2.2	3.2	9.7	
9c[d]	4.49	4.77	4.90	5.17	4.44	1.38	5.19	5.26	3.41	3.45	1.5	7.3	1.6	5.0	8.7	
10[d]	4.48	4.69	5.13	5.40	4.47	1.44	5.12	5.31	3.41	3.46	3.0	6.9	4.3	2.7	6.2	
11a[ef]	4.50	4.65	4.52	5.53	4.44	1.40	5.16	5.22	3.16	3.29	7.1	7.2	1.7	3.0	1.7	0.8
11b[cf]	4.55	4.37	5.16	3.94	4.49	1.43	5.20	5.26	3.21	3.35	7.3	7.2	1.4	4.5	1.8	1.4
11c	4.62	4.29	3.80	3.90	4.23	1.49	5.18	5.24	3.42	3.48	4.6	7.1	1.8	3.3	1.7	1.2
11f[dg]	4.42	4.31	3.79	4.88	4.37	1.38	5.18	5.24	3.30	3.35	7.4	7.3	1.8	3.1	1.9	1.0
12a[ef]	4.75	4.70	5.51	4.95	4.13	1.35	5.16	5.22	3.33	3.40	3.1	6.8	6.0	7.7	7.5	
12b[cf]	4.57	4.80	5.17	4.25	3.90	1.32	5.18	5.26	3.43	3.49	4.4	6.9	6.0	9.2	9.4	
12c	4.51	4.52	3.77	3.87	3.74	1.28	5.15	5.21	3.39	3.49	4.7	7.0	5.7	8.7	9.3	
12f[dg]	4.53	4.68	4.93	4.08	3.83	1.25	5.18	5.24	3.34	3.48	*ca.* 5	7.1	*ca.* 6	*ca.* 9	*ca.* 9	
13[h]	4.45	4.56	3.46	3.09	4.41	1.41	5.16	5.21	3.40	3.47	4.6	7.0	0	4.2	1.0	1.3
14[ci]	4.61	4.39	3.74	4.06	3.83	1.39	5.16	5.22	3.42	3.46	5.4	7.0	6.1	3.7	1.6	

a) Benzyl CH_2 ; 5 arom.H : *ca* 7.35, $^2J(CH_2)$=12.4. b) lit.[14]. c) 333 K. d) 330 K. e) 335 K. f) Bz group : *ca.* 8.05 (m, 2H); *ca.* 7.55 (m, 1H); *ca.* 7.45 (m, 2H). g) Ac : 2.07. h) major isomer. i) OH-C(4) : 2.57 ; OH-C(5) : 2.88 ; J(4,OH-4)=9.1, J(5,OH-5)=3.0.

2) oxazane-diols.- ^{1}H-NMR data of diols and of their derivatives **8**, **9c**, **10**, **11a-c,f**, **12a-c,f** and **14** are collected in *Table 1*. Racemic allose diol (±)-**8** has already been studied and its configuration and conformation ascertained [14,25]. The same holds for its derivatives **9c**, **10** (*Figure 1*). These compounds are characterised by a large $^3J(4,5)$ coupling constant between the two axial H-C(5) and H-C(6) protons. The conformation is determined by the steric interaction between the Me-C(3) and the N-acyl groups [26a], Me-C(3) being axial and the dimethoxymethyl group at C(6) equatorial.



10a R = H
10d R , R = -SO_2-
10e R = Tf

11a R^2 = Bz R^3 = SO_3H
11b R^2 = H R^3 = Bz
11c R^2 = R^3 = H
11f R^2 = Ac R^3 = H

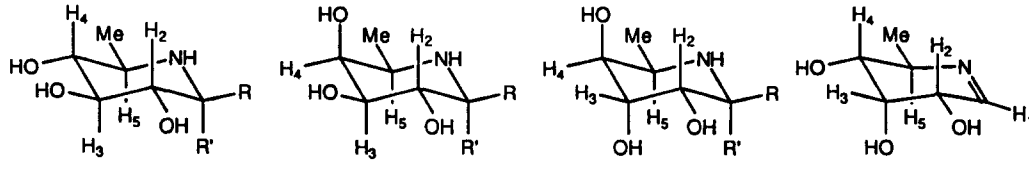
12a R^2 = SO_3H R^3 = Bz
12b R^2 = H R^3 = Bz
12c R^2 = R^3 = H
12f R^2 = H R^3 = Ac

14

Figure 1

The major diol and its derivatives **11a-c,f** which were obtained *via* a single inversion, are characterised by small coupling constants . A clearly resolved $^4J(3,5)$ W-coupling indicates that H-C(5) is equatorial which means that the hydroxyl inversion took place at C(5). To the contrary, the minor derivatives **12a-c,f** are characterised by two large $J(4,5)$ and $J(5,6)$ coupling constants. As a consequence H-C(4) is axial which demonstrates indeed that C(4) has been inverted. As to diol **14**, the comparison of the J values with those of the preceding diols **11a** or **12a** indicates an additional inversion of a hydroxyl group and demonstrates that **14** results from two inversions.

The ester derivatives **9c,10**, **11a,b,f**, **12a,b,f**, were characterised by a deshielding of H-C(4) or of H-C(5) in the α-position to the ester group at 4.5-5.5 ppm. ^{1}H-NMR data clearly show that in **11b** the benzoyl group migrated to C(4), while the acetyl group of the corresponding compound **11f** stayed put in position C(5).



2a (α) R = H R' = OH
2a (β) R = OH R' = H
2b R = R' = H
2c R = SO_3H R' = H

3a (α) R = H R' = OH
3a (β) R = OH R' = H
3b R = R' = H
3c R = SO_3H R' = H

6a (α) R = H R' = OH
6a (β) R = OH R' = H
6b R = R' = H
6c R = SO_3H R' = H

6a (i)

Figure 2

3) Amino-sugars and derivatives. - ^{1}H-NMR data of amino-sugars **2a**, **3a**, **6a** and of their derivatives are collected in *Table 2*. As for nojirimycin **1a** [27], the conformation is determined by the equatorial Me-group ; all compounds prove to be in the $^4C_1$(D) conformation (*Figure 2*). Glucose derivatives **2a-c** are characterised by large $^3J(2,3)$, $^3J(3,4)$ and $^3J(4,5)$ values. In the gulose series, these values are small with, in addition, a $^4J(1e,3)$ W-coupling between equatorial protons ; in the fucose series only $^3J(2,3)$ is large. The structure of the aminosugars were ascertained by comparison of the physical data of their 1-deoxy derivatives with those reported in the literature for **D-2b** [13,15], **L-3b** [13b,17], **D-6b** [15,18b] .

Table 2 [24]. ^{1}H-NMR spectra (D_2O, 300 K) of aminosugars **2a-c, 3a-c, 6a-c**, δ in ppm, *J* in Hz, internal standard D_4-TSP.

	He-C(1)	Ha-C(1)	H-C(2)	H-C(3)	H-C(4)	H-C(5)	Me(6)	*J*(1e,2)	*J*(1a,2)	*J*(2,3)	*J*(3,4)	*J*(4,5)	*J*(5,Me)	Others
2a(α)[a]	4.69		3.50	3.59	3.04	3.06	1.14	3.4		9.7	8.9	9.6	5.7	
2a(β)		4.15	3.18	3.33	3.06	2.63	1.17		8.1	9.3	9.5	9.6	6.3	
2a(i)[b]	7.54		4.09	3.64	3.33	3.46	1.35	1.0		8.5	10.0	8.8	6.8	2.8[c], 3.0[d]
2b	3.05	2.44	3.47	3.27	3.00	2.50	1.14	5.1	10.7	9.1	9.2	9.5	6.3	12.3[e]
2c		4.06	3.86	3.53	3.39	3.17	1.41		10.4	9.0	9.4	10.0	6.4	
3a(α)	4.72		3.78	3.79	3.76	2.88	1.13	3.0		f	3.3	1.5	6.7	
3a(β)		4.07	3.40	3.55	3.78	3.27	1.09		8.3	10.0	3.2	1.0	6.6	
3a(i)	7.64		4.17	3.82	3.95	3.70	1.32	1.0		9.4	*ca.* 2.6		7.3	3.4[c], 2.9[d]
3b	3.06	2.35	3.71	3.48	3.80	2.77	1.08	5.4	11.0	9.6	3.1	1.4	6.7	12.9[e]
3c		4.03	4.13	3.72	3.98	3.49	1.38		10.4	9.2	3.0	1.4	6.7	
6a(α)	4.64		3.84	3.97	3.74	3.46	1.11	3.8		3.1	3.8	2.0	6.8	1.6[g]
6a(β)		4.35	3.52	4.04	3.67	3.16	1.10		8.8	3.3	3.8	1.9	6.9	
6a(i)	7.69		4.08	4.22	f	3.70	1.28	2.0		4.1	2.6	f	7.4	2.8[c], 1.0[g]
6b	2.84	2.72	3.90	3.94	3.75	3.05	1.08	4.8	9.8	3.2	4.6	2.4	6.9	12.8[e], 1.0[g]
6c		4.22	4.31	4.12	3.94	3.74	1.39		10.6	1.7	4.3	1.6	6.8	

a) δ et *J* values calculated by simulation programm (Panic). b) 330 K. c) ^4J(1,5). d) ^5J(2,5). e) ^2J(1e,1a). f) not determinated. g) ^{4}J(1e,3).

As to the imine forms, their vicinal ^3J values between H-C(2), H-C(3), H-C(4), H-C(5) protons are similar to those of the corresponding α,β-anomers. As a consequence, their conformations appear in the corresponding half-chair $^4H_3$(D), as shown in *Figure 2* for **6a**(i). They are characterised by relatively large (3 Hz) allylic ^4J(1,5) and homoallylic ^5J(2,5) coupling constants corresponding to both *pseudo*-axial H-C(2) and H-C(5) protons [28].

The β-anomer of the aminosugars has an equatorial anomeric OH ; as a consequence the ^3J(1,2) value is large. For the same reason, the sulfite adducts **2c**, **3c**, **6c** are β-anomers, the sulfonic acid moiety being equatorial.

4) Amino-sugar behaviour. - In the conditions of their preparation (pH = *ca.* 8 in aqueous solution), amino-sugars **2a**, **3a**, **6a** are stable for a few days. Such compounds seem to be relatively stable in weakly acidic medium as proved by Legler for *manno*-nojirimycin [5], but rather unstable in strong acidic solutions [8]. Amino-sugars **2a**, **3a**, **6a** are equilibrium mixtures of three species, *i.e.* the expected α- and β-anomers and the imine forms (i). This equilibrium had been observed previously by us for amino-sugars **4a** and **5a** in the allose and talose series [14]. The proportions of the different species of **2a-6a** as a function of temperature have been determined by ^{1}H-NMR in D_2O and are reported in *Table 3*. Two conclusions can be drawn from these data :

- *Imine form.* This form is always present as a minor species and reaches (in D_2O) 30 % at 340 K for **3a** and **6a** in the gulose and fucose series. The proportion of the imine forms increases with temperature, which means that this form is thermodynamically the more stable one. Dehydratation of the α- and β-aminosugars to the corresponding imine is also an easy process.

Table 3 [24]. Proportions of α, β-anomers and of the imine form (i) for 6-deoxy-amino-sugars **2a-6a** (*ca.* 7.10^{-2} M in D_2O, ^{1}H-NMR determination) in comparison with the corresponding sugars (*ca.* 2 M) [30,31] as a function of temperature.

		(α)	(β)	(i)	furanoses	lit.
2a	300 K	56%	41%	3%		
	320 K	57%	37%	6%		
	340 K	55%	33%	12%		
6-deoxy-D-glucose	317 K	36%	64%			30
3a	300 K	44%	44%	12%		
	320 K	41%	40%	19%		
	340 K	36%	35%	29%		
L-fucose	304 K	28%	67%		α+β:5%	30
4a	300 K	37%	53%	10%		
	333 K	33%	48%	19%		
D-allose	317 K	17%	73%		α:3.7%, β:6%	31
5a	300 K	62%	35%	3%		
	320 K	60%	34%	6%		
	340 K	57%	32%	11%		
D-talose	317 K	37%	32%		α:17%, β:14%	31
6a	300 K	20%	65%	15%		
	320 K	20%	60%	20%		
	340 K	20%	50%	30%		
D-gulose	317 K	16%	78%		α+β:6%	31

It is interesting to notice that this latter imine form had not been observed so far but only suggested by *Paulsen* on ORD measurement grounds [26b]. These imine forms mimic rather well the cyclic oxocarbonium intermediate which is postulated during the glycosidase-catalysed hydrolysis of polysaccharides [1,29]. It is believed that they account for the glycosidase inibitory properties of the corresponding aminosugars [1,29].

-α,β-Anomeric proportions and anomeric effect. In *Table 3* are reported the anomeric proportions of some 6-deoxysugars [30] or carbohydrates [31] which correspond to the amino-sugars **2a-6a** (in D_2O). In all instances the α-anomer proportions are more important in the amino-sugars than in the corresponding 6-deoxysugars (or in the corresponding carbohydrates), the ratio being *ca.* 2.5 for **2a**, **3a**, and **4a** in the glucose, fucose and allose series, and of *ca.* 1.6 for **5a** and **6a** in the talose and gulose series.

The formation of a larger amount of the α-anomer can be interpreted by an increase of the anomeric effect in the amino-sugars of *ca.* 0.6 kcal/mole for the first group, of *ca.* 0.3 kcal/mole for the second one. The origin of this effect had been discussed previously [27,32]. For nojirimycin **1a**, the magnitude of the increase of the anomeric effect has been estimated at *ca.* 0.7 kcal/mole in D_2O [27].

Acknowledgement. - The support of the *Centre National de la Recherche Scientifique (URA-135)* is gratefully acknowledged. We also wish to thank the *Fondation pour l'École Nationale Supérieure de Chimie de Mulhouse* for a Ph.D-grant to H.S. and Th. Sifferlen for his collaboration.

EXPERIMENTAL PART

General. Flash chromatography (FC) : silica gel (*Merck 60*, 230-400 mesh). TLC : Al-roll silica gel (*Merck 60*, F_{254}). M.p. : *Kofler* hot bench or *Büchi-SMP-20* apparatus, corrected. IR spectra (ν in cm^{-1}) : *Perkin-Elmer 157 G* and *590 B* . ^1H- and ^{13}C-NMR spectra : *Bruker AC-F250*, usually at 300 K ; tetramethylsilane (TMS) or sodium trimethylsilylpropionate-D_4 (D_4-TSP) in D_2O (^1H-NMR) and $CDCl_3$, CD_3OD or (in D_2O) MeOH (^{13}C-NMR; δ($CDCl_3$)=77.0 ppm, δ(CD_3OD)=49.0, in D_2O δ(CH_3OH)=50.0, δ(dioxane)=67.4 with respect to TMS) as internal standards ; δ in ppm and *J* in Hz. ^{13}C-NMR assignments were ascertained by ^1H-^{13}C correlation measurements. $[\alpha]_D$ Values : *Schmidt Haensch Polartronic Universal* polarimeter. High resolution (HR)-MS were measured on a *MAT-311* spectrometer at the University of Rennes. Microanalyses were carried out by the "Service Central de Microanalyses" of the CNRS, at Vernaison, France.

Reagents and solvents. Ammonium benzoate, ammonium acetate, Na_2CO_3, $Ba(OH)_2.8H_2O$, conc. H_2SO_4 were obtained from Prolabo, $NaNO_2$ from Merck ; $RuCl_3.3H_2O$ from Aldrich ; SO_2 gaz, NBu_4BzO, $NaIO_4$, 5% Pd/C catalyst, Tf_2O from Fluka. $SOCl_2$, NEt_3, pyridine, DMF were distilled, dioxane was distilled from Na. Usual solvents were freshly distilled, CH_2Cl_2 was kept over Na_2CO_3, DMF and dioxane were kept over 4Å molecular sieves.

1. Diol derivatives.

Benzyl 6c-(dimethoxymethyl)-4t,5t-sulfinyldioxy-3r-methyl-1,2-oxazane-2-carboxylate ((±)-9a,b). Benzyl 6c-(dimethoxymethyl)-4t,5t-sulfonyldioxy-3r-methyl-1,2-oxazane-2-carboxylate ((±)-9c) and its (3R)-enantiomer D-9c. To a stirred soln of (±)-**8** [14,25] (1.0 g, 2.9 mmol) in CH_2Cl_2 (10 ml) at 0°C was added NEt_3 (1.6 ml, 11.4 mmol, 4 eq.) and in 10 mn a soln of $SOCl_2$ (0.32 ml, 4.4 mmol, 1.5 eq) in CH_2Cl_2 (1 ml). After 10 mn, the soln was diluted with Et_2O (30 ml), washed with H_2O (3 x 10 ml), dried ($MgSO_4$) and evaporated to give a crude 1:1 isomeric mixture of (±)-**9a,b** (1.2 g, quant.).

To a vigorously stirred soln of crude (±)-**9a,b** (1.2 g, 2.9 mmol) in $CHCl_3/CH_3CN/H_2O$ (2:2:3, 28 ml) at 0°C were added $RuCl_3.3H_2O$ (*ca.* 7 mg, 0.01 eq) and $NaIO_4$ (1.24 g, 5.8 mmol, 2 eq). After 1.5-3 h, the soln was diluted with Et_2O (20 ml), washed with H_2O, dried ($MgSO_4$) and evaporated. Crystallisation in Et_2O gave pure (±)-**9c** (0.97 g, 83 % from (±)-**8**).

D-9c (2.36 g, 80 %) was obtained from **D-8** [14] (2.5 g, 7.3 mmol) using the same procedure.

(±)-**9a,b** characterised by ^1H-NMR (C_6D_6, 342 K). (±)-**9a** : 5 arom.H (m, 7.0-7.3) ; 5.04 (or 5.10) (s, CH_2) ; 5.02 (dd, H-C(6)) ; 4.68 (dq, H-C(3)) ; 4.67 (dd, H-C(5)) ; 4.36 (d, H-C(1')) ; 3.61 (dd, H-C(4)) ; 3.12, 3.15 (2s, 2 OMe) ; 0.90 (d, Me-C(3)). *J*(1',6)=3.0, *J*(3,Me)=7.1, *J*(3,4)=1.4, *J*(4,5)=5.4, *J*(5,6)=9.3. (±)-**9b** : 5 arom.H (m, 7.0-7.3) ; 5.10 (or 5.04) (s, CH_2) ; 4.77 (dd, H-C(5)) ; 4.59 (dq, H-C(3)) ; 4.40 (dd,

H-C(4)) ; 4.28 (d, H-C(1')) ; 3.91 (dd, H-C(6)) ; 3.22, 3.21 (2s, 2 OMe) ; 0.88 (d, Me-C(6)) ; J(1',6)=3.0 ; J(3,Me)=7.1 ; J(3,4)=1.6 ; J(4,5)=5.1 ; J(5,6)=8.9.
(±)-9c : colourless crystals. Mp = 98-99°C. IR(KBr) : 2975, 2840, 1720, 1452, 1390, 1295, 1210, 1130, 1080, 992, 980, 880, 813, 755, 703. ^{1}H-NMR : *Table 1*. Anal. calc. for $C_{16}H_{21}NO_9S$ (403.40) : C 47.63, H 5.25, N 3.47, S 7.95 ; found : C 47.7, H 5.4, N 3.6, S 8.2.
D-9c : colourless resin. $[\alpha]_D^{20} = -68$ (c=2, $CHCl_3$). IR($CHCl_3$) : 2940, 2840, 1720, 1400, 1290, 1125, 1085, 1000. Anal. calc. for $C_{16}H_{21}NO_9S$ (403.40) : C 47.63, H 5.25, N 3.47, S 7.95 ; found : C 47.6, H 5.4, N 3.5, S 7.8.

Benzyl (3R)-6c-(dimethoxymethyl)-3r-methyl-4t,5t-bis(trifluoromethylsulfonyloxy)-1,2-oxazane-2-carboxylate, (D-10). To a soln of **D-8** [14] (0.1 g, 0.3 mmol) in CH_2Cl_2 (1.5 ml) were added at -10°C, pyridine (0.14 ml, 1.7 mmol, 5.4 eq.) and dropwise Tf_2O (0.13 ml, 0.8 mmol, 2.7 eq.). After 1 h, aq. 1 N Na_3PO_4 (3 ml) was added to the red soln and the resulting mixture was extracted with Et_2O (3x), the organic soln washed with H_2O, dried ($MgSO_4$) and evaporated to give pure **D-10** (0.17 g, 95 %).
10 : unstable colourless resin, characterised by ^{1}H-NMR : *Table 1*

2. Single inversion of cyclic sulfates.
a. Sharpless procedure [20b]. *Benzyl 5c-benzoyloxy-6c-(dimethoxymethyl)-4t-(hydroxysulfonyloxy)-3r-methyl-1,2-oxazane-2-carboxylate ((±)-11a) and benzyl 4c-benzoyloxy-6c-(dimethoxymethyl)-5t-(hydroxysulfonyloxy)-3r-methyl-1,2-oxazane-2-carboxylate ((±)-12a). Benzyl 4t-benzoyloxy-6c-(dimethoxymethyl)-5c-hydroxy-3r-methyl-1,2-oxazane-2-carboxylate ((±)-11b) and benzyl 4c-benzoyloxy-6c-(dimethoxymethyl)-5t-hydroxy-3r-methyl-1,2-oxazane-2-carboxylate ((±)-12b). Benzyl 6c-(dimethoxymethyl)-4t,5c-dihydroxy-3r-methyl-1,2-oxazane-2-carboxylate ((±)-11c) and its 4c,5t-dihydroxy isomer ((±)-12c).*

A soln of (±)-**9c** (1.5 g, 3.7 mmol) in DMF (15 ml) with $BzONH_4$ (1.02 g, 7.4 mmol, 2 eq) was stirred under Ar at 70°C for 24 h. Evaporation of the solvent gave crude (±)-**11a**, (±)-**12a** (75:25 isomeric mixture).

The crude mixture of (±)-**11a**, (±)**12a** (3.7 mmol) in dioxane (20 ml) was stirred at rt for 2 h with conc. H_2SO_4 (50 µl, 0.9 mmol, 0.25 eq.) and H_2O (20 µl, 0.12 mmol, 0.3 eq.). Excess Na_2CO_3 (0.2 g) was added under stirring. After 0.5 h, the solids were discarded by centrifugation and the solvent was evaporated to give crude (±)-**11b**, (±)-**12b** (75:25 isomeric mixture).

A soln of the crude mixture of (±)-**11b**, (±)-**12b** (3.7 mmol) in MeOH (20 ml) was stirred with Na_2CO_3 (0.9 g) for 7 days (or with conc NH_4OH (5 ml) for 4 h). The solids were discarded, the solvent was evaporated and the crude mixture (2.16 g) resolved by FC ($CHCl_3$/MeOH, 98:2) on SiO_2 (100 g) to give (±)-**11c** (0.91 g, 71 %) and (±)-**12c** (0.26 g, 20 %).
(±)-**11a**, (±)-**12a**, (±)-**11b**, (±)-**12b** were characterised by ^{1}H-NMR : *Table 1*.
(±)-**11c** : colourless resin. IR($CHCl_3$) : 3460, 3000, 2940, 2840, 1700, 1450, 1415, 1310, 1135, 1080, 1050. ^{1}H-NMR : *Table 1*. Anal. calc. for $C_{16}H_{23}NO_7$ (341.35) : C 56.29, H 6.79, N 4.10 ; found : C 56.2, H 6.9, N 4.4.
(±)-**12c** : colourless resin. IR($CHCl_3$) : 3510, 3000, 2940, 2840, 1705, 1452, 1410, 1330, 1298, 1130, 1068. ^{1}H-NMR : *Table 1*. Anal. calc. for $C_{16}H_{23}NO_7$ (341.35) : C 56.29, H 6.79, N 4.10 ; found : C 56.2, H 6.9, N 4.2.

b. Ring-opening with nitrite anion. *Benzyl (3R)-6c-(dimethoxymethyl)-5c-hydroxy-4t-(hydroxysulfonyloxy)-3r-methyl-1,2-oxazane-2-carboxylate (D-11d) and benzyl (3R)-6c-(dimethoxymethyl)-4c-hydroxy-5t-hydroxysulfonyloxy)-3r-methyl-1,2-oxazane-2-carboxylate (D-12d). Benzyl (3R)-6c-(dimethoxymethyl)-4t,5c-dihydroxy-3r-methyl-1,2-oxazane-2-carboxylate (D-11c) and its 4c,5t-dihydroxy isomer (D-12c)*

A soln of **D-9c** (2.1 g, 5.2 mmol) in DMF (21 ml) was stirred at 90°C for 4 h with $NaNO_2$ (3.57 g, 52 mmol, 10 eq.). After removal of the insoluble salts, evaporation of the solvent gave crude **D-11d**, **D-12d**, (70:30 isomeric mixture).

The soln of crude **D-11d**, **D-12d** (5.2 mmol) in dioxane (28 ml) was stirred at 40°C for 4 h with conc. H_2SO_4 (70 µl, 1.2 mmol, 0.5 eq) and H_2O (30 µl, 1.6 mmol, 0.3 eq.). Excess Na_2CO_3 (0.6 g) was added while stirring. After 0.5 h, the insoluble salts were discarded, the solvent was evaporated and the residue (2.2 g) resolved by FC ($CHCl_3$/MeOH, 98:2) to give **D-11c** (0.94 g, 53 %) and **D-12c** (0.41 g, 23 %).

D-11d(maj), **D-12d**(min) were characterised by ^{1}H-NMR ($CDCl_3$, 330 K) : 7.25 (m, 5 arom.H) ; 5.15 (s, CH_2) ; 4.73 (d, H-C(1')min) ; 4.70 (m, H-C(3) maj, H-C(5) min) ; 4.54 (s, H-C(1') maj, H-C(4) maj) ; 4.47 (quint., H-C(3) min) ; 4.09 (s, H-C(5) maj, H-C(6) maj) ; 3.94 (H-C(4) min) ; 3.82 (H-C(6) min) ; 3.38, 3.36 (2s, 2 OMe min) ; 3.32, 3.23 (2s, 2 OMe, maj) ; 1.45 (d, Me-C(3) maj) ; 1.24 (d, Me-C(3) min). For **D-11d** : only J(3,Me)=7.2 ; for **D-12d** : J(1',6)=2.0, J(3,4)=5.8, J(4,5)=9.0, J(5,6)=*ca.*10, J(3,Me)=7.0.
D-11c : colourless resin. $[\alpha]_D^{20} = -31$ (c=1, $CHCl_3$). Anal. calc. for $C_{16}H_{23}NO_7$ (341.35) : C 56.29, H 6,79, N 4.10 ; found C 56.1, H 6.9, N 4.2.
D-12c : Colourless resin. $[\alpha]_D^{20} = -7$ (c=2, $CHCl_3$). Anal. calc. for $C_{16}H_{23}NO_7$ (341.35): C 56.29, H 6.79, N 4.10 ; found : C 56.4, H 6.8, N 4.2.

3. Epoxide and its ring-opening

a. Benzyl 6c-(dimethoxymethyl)-4ξ,5ξ-epoxy-3r-methyl-1,2-oxazane-2-carboxylate ((±)-13) A soln. of (±)-**7** [25] (1.19 g, 3.8 mmol) and *m*-chloroperbenzoic acid (1.68 g, 8.6 mmol, 2 eq.) in CH_2Cl_2 was stirred at rt for 6 days. Na_2SO_3 (0.1 g) was added and the soln washed twice with aq. 1 M Na_2CO_3, with H_2O, dried ($MgSO_4$) and evaporated to give (±)-**13** as an isomeric mixture (70:30) (1.07 g, 85 %).
(±)-**13** : yellowish resin. IR($CHCl_3$) : 3005, 2940, 2840, 1710, 1450, 1410, 1360, 1297, 1125, 1082, 698. ^{1}H-NMR : *Table 1* for the major isomer ; some data for the minor isomer ($CDCl_3$) : 4.18 (d, 1H, J=*ca.* 6) ; 3.45, 3.47 (2s, 2 OMe) ; 1.36 (d, J=6.7, Me-C(3)). Anal. calc. for $C_{16}H_{21}NO_6$ (323.34) : C 59.43, H 6.55, N 4.33 ; found : C 59.5, H 6.8, N 4.3.

b. *Benzyl 4t,5c-dihydroxy-6c-(dimethoxymethyl)-3r-methyl-1,2-oxazane-2-carboxylate ((±)-11c).* To a soln of (±)-**13** (90 mg, 0.3 mmol) in DMF (0.9 ml) was added $NaNO_2$ (0.19 g, 3 mmol, 10 eq.) and the suspension stirred at 100° for 3d. The solid was discarded and the solvent evaporated. FC (AcOEt/cyclohexane 6:4) gave (±)-**11c** (49 mg, 52 %), identical with the major diol obtained above (*see 2a*).

4. Double inversion of D-9c and D-10.

*Benzyl (3*R*)-5c-acetoxy-6c-(dimethoxymethyl)-4t-hydroxy-3r-methyl-1,2-oxazane-2-carboxylate (D-11f) and its 4c-acetoxy-5t-hydroxy-isomer (D-12f). Benzyl (3*R*)-4c,5c-dihydroxy-6c-(dimethoxymethyl)-3r-methyl-1,2-oxazane-2-carboxylate (D-14)*
a. from D-9c. A soln of **D-9c** (1.2 g, 3 mmol) in DMF (12 ml) was stirred at 70°C for 16 h with ammonium acetate (0.91 g, 12 mmol, 4 eq.). Evaporation of DMF gave a crude mixture (75:25) of **D-11e**, **D-12e**, which were hydrolysed with conc. H_2SO_4 (50 µl, 0.9 mmol, 0.3 eq.) and H_2O(17 µl, 1 mmol) in dioxane (15 ml) at rt for 2 h. Excess Na_2CO_3 (0.63 g) was added while stirring ; after 0.5 h, the solids were removed by centrifugation and the solvent was evaporated. Soln of the residue in Et_2O (20 ml) was washed with H_2O (3x), dried ($MgSO_4$) and the solvent evaporated to give a crude isomeric mixture (75:25) of **D-11f**, **D-12f** which was dried by dissolution in toluene and evaporation.

To a stirred soln of the crude mixture of **D-11f**, **D-12f** (1.1 g, 3 mmol) in CH_2Cl_2 (6 ml) and pyridine (0.7 ml) at -10°C, was added Tf_2O (0.72 ml, 9 mmol, 3 eq.) dropwise. After 1 h, aq. 1 N Na_3PO_4 (12 ml) was added, the soln extracted with Et_2O, the organic soln washed with H_2O, dried ($MgSO_4$) and evaporated to give a crude mixture of **D-11g**, **D-12g**. Crude **D-11g**, **D-12g** in soln in DMF (10 ml) was stirred at 30°C overnight with $NaNO_2$ (0.61 g, 9 mmol, 3 eq.). Toluene (30 ml) was added, the solids were discarded and the solvents evaporated. The crude acetate mixture was treated with conc. aq. NH_3 (12 ml) in MeOH (35 ml) for 4 h at rt. Evaporation of the solvents and purification by FC (AcOEt/cyclohexane 1:1) gave pure **D-14** (0.74 g, 73 %).
b. from D-10. A soln of **D-10** (1.77 g, 2.9 mmol) in toluene (35 ml) and H_2O (3.5 ml) was stirred at 80°C overnight with NBu_4BzO (3.7 g, 10 mmol, 3 eq.). The mixture was evaporated and treated with excess Na_2CO_3 (2 g) in MeOH (30 ml) for 6 h at 50°C. After filtration, the solvent was evaporated, the residue dissolved in CH_2Cl_2 (30 ml) and the organic soln washed with aq. 1 N KOH and H_2O, dried ($MgSO_4$) and evaporated to give crude **D-14**. Purification by FC (AcOEt/cyclohexane 1:1) gave pure **D-14** (0.58 g, 58 %).
D-11f, **D-12f** : characterised by ^{1}H-NMR : *Table 1*.
D-14 : colourless resin. $[\alpha]_D^{20} = -19$ (c=1, $CHCl_3$). IR ($CHCl_3$) : 3500, 2940, 2840, 1725, 1450, 1405, 1345, 1290, 1245, 1135, 1175. ^{1}H-NMR : *Table 1*. Anal. calc. for $C_{16}H_{23}NO_7$ (341.55) : C 56.29, H 6.79, N 4.10 ; found : C 56.1, H 6.9, N 4.3.

5. 6-deoxy-amino-sugars.

a. general procedure for sulfite adducts [14] (cf lit.[8]). Oxazane-diol (0.85 g, 2.5 mmol) in EtOH (8 ml) was hydrogenolysed over 5 % Pd/C (50 mg and another 50 mg after 8 h) at 50°C for 24 h. The catalyst was discarded by centrifugation and the solvent evaporated. The ensuing acyclic acetal was dissolved in H_2O (4 ml) and hydrolysed in SO_2 atmosphere in a 1 l glas vessels at 40°C for 5-6 days until crystals appeared. EtOH (2 ml) was then added at 0°C and the crystallised sulfite adduct isolated. Reaction of SO_2 on the concentrated mother liquors at 0°C in H_2O (0.5 ml) and EtOH (0.5 ml) gave a second crop of the same sulfite adduct.

b. general procedure for amino-sugars [14]. A soln of the preceding sulfite adduct (0.1 g, 0.45 mmol) in H_2O (1 ml) was stirred with $Ba(OH)_2.8\ H_2O$ (0.16 g, 0.5 mmol, 1.1 eq.) for 2 h at rt. Precipitated $BaSO_3$ was discarded by centrifugation to give a aq. soln of amino-sugar as a mixture of α-anomer (α), β-anomer (β) and imine (i). ^{1}H-NMR : *Table 1*. Evaporation of H_2O at 40°C gave the aminosugars (*ca.* 80 mg, quant.) as a colourless resin. For the ^{1}H-RMN values of *Table 3*, sulfite adduct (8 mg, 0.035 mmol) and $Ba(OH)_2.8\ H_2O$ (12 mg, 0.038 mmol, 1.1 eq.) were used in D_2O (0.5 ml).

c. general procedure for 1-deoxyaminosugars [14].The previous soln of aminosugar (0.45 mmol) in H_2O (1 ml) was hydrogenolysed over 5 % Pd/C (10 mg) at rt for 1-2 h. Elimination of Pd/C by centrifugation and evaporation of H_2O gave pure 1-deoxy-aminosugar (*ca.* 65 mg, quant.) as a colourless resin.

d. glucose series.

*5-Amino-1,5,6-trideoxy-β-D-*gluco*-pyranose-1-sulfonic acid (D-2c).* General procedure a) with **D-11c** (0.85 g, 2.5 mmol), to give **D-2c** (0.373 g, 67 %).

D-2c : colourless crystals. Mp = 190-195°C (dec) (H_2O/EtOH). $[\alpha]_D^{20}$ = −8 (c=1, H_2O). IR (KBr) : 3485, 3370, 3105, 2960, 2780, 1640, 1590, 1430, 1350, 1245, 1192, 1092, 1050, 1017. ^{1}H-NMR (D_2O) : *Table 2*. ^{13}C-NMR (D_2O) : 71.2 C(1) ; 70.6 C(2) ; 76.6 C(3) ; 73.0 C(4) ; 56.8 C(5) ; 15.4 Me(6). Anal. calc. for $C_6H_{13}NO_6S$ (227.33) : C 31.71, H 5.76, N 6.16, S 14.11 ; found : C 31.5, H 5.6, N 5.9, S 14.2.

*5-Amino-1,5,6-trideoxy-β-DL-*gluco*-pyranose-1-sulfonic acid ((±)-2c).* General procedure a) with **(±)-11c** (0.7 g, 2.1 mmol) to give **(±)-2c** (0.34 g, 66 %).

(±)-2c : colourless crystals. Mp = 190-195°C (dec) (H_2O/EtOH). IR (KBr) : 3490, 3290, 3100, 2980, 2800, 2470, 1630, 1610, 1440, 1392, 1345, 1283, 1258, 1228, 1195, 1180, 1092, 1050, 1015. Anal. calc. for $C_6H_{13}NO_6S$, H_2O (245.24) : C 29.38, H 6.16, N 5.71, S 13.07 ; found : C 29.5, H 6.2, N 5.4, S 12.9.

*5-Amino-5,6-dideoxy-D-*gluco*-pyranose (6-deoxy-nojirimycin) (D-2a).* General procedure b) with **D-2c** (35 mg, 0.15 mmol) to give **D-2a**. ^{1}H-NMR : *Table 2*.

*5-Amino-5,6-dideoxy-DL-*gluco*-pyranose (6-deoxy-DL-nojirimycin) ((±)-2a).* General procedure b) with **(±)-2c** (0.1 g, 0.45 mml) to give **(±)-2a**.

1,5-imino-1,5,6-trideoxy-D-glucitol (1,6-dideoxy-nojirimycin)(D-2b). General procedure c) with **D-2a** (0.15 mmol) for 2 h at rt to give **D-2b** (23 mg, quant.).

D-2b : colourless resin. $[\alpha]_D^{20}$ = +13 (c=1, H_2O) (lit.[15] : $[\alpha]_D^{20}$ = +13 ; (c=1,H_2O) ; lit.[13a] : $[\alpha]_D^{23}$ = +12.0 (c=2.5, H_2O)). ^{1}H- and ^{13}C-NMR : identical data as in lit.[15]. ^{1}H-NMR : *Table 2*.

1,5-imino-1,5,6-trideoxy-DL-glucitol ((±)-2b). General procedure c) with **(±)-2a** (0.45 mmole) for 2 h at rt to give **(±)-2b** (67 mg, quant.) as a colourless resin.

(±)-2b was characterised as its tetraacetyl derivative : **(±)2b** (74 mg, from **(±)-2c**, 0.1 g, 0.45 mmol) was acetylated in Ac_2O (0.41 ml, 4.5 mmol, 10 eq.) and pyridine (0.8 ml) for 30 h at rt. After dilution with MeOH, evaporation gave an oil which was purified by FC (AcOEt) on SiO_2 (20 g) to give the tetraacetyl derivative (61 mg, 44 %) as colourless crystals. Mp = 104-5°C (*i*-Pr_2O/*i*-PrOH). IR (KBr) : 3410, 2970, 1750, 1735, 1640, 1440, 1380, 1235, 1210, 1070, 1042. ^{1}H-NMR ($CDCl_3$, 330 K) : 5.01 (t, *J*=4.0, 1H) ; 4.86 (q., *J*=2.9, H-C(2)) ; 4.80 (dt, *J*=0.6, 4.0, 1H), 4.51 (broad s, H-C(5)) ; 4.13 (broad s, Heq.-C(1)) ; 3.41 (broad d, *J*=15, Hax-C(1)) ; 2.08, 2.06, 2.05, 2.04 (4s, 4 Ac) ; 1.32 (d, *J*=7.2, Me-(6)). Anal. calc. for $C_{14}H_{21}NO_7$ (315.32) : C 53.32, H 6.71, N 4.44 ; found : C 53.4, H 6.7, N 4.5.

e. fucose series.

*5-Amino-1,5-dideoxy-β-D-*fuco*-pyranose-1-sulfonic acid (D-3c).* General procedure a) with **D-14** (0.32 g, 0.94 mmol) (hydrogenolysed for 30 h) to give **D-3c** (90 mg, 42 %)

D-3c : colourless crystals. Mp = 250-255°C (dec) (H_2O/EtOH). $[\alpha]_D^{20}$ = +9 (c=1, H_2O). IR (KBr) : 3360, 3080, 1560, 1430, 1260, 1205, 1150, 1140, 1120, 1105, 1047. ^{1}H-NMR : *Table 2*. ^{13}C-NMR (D_2O) : 71.8

C(1) ; 68.1 C(2) ; 74.1 C(3) ; 70.7 C(4) ; 56.8 C(5) ; 15.1 Me(6) (Some inexact data in lit.[19]). Anal. calc. for $C_6H_{13}NO_6S$ (227.23) : C 31.71, H 5.76, N 6.16, S 14.11 ; found : C 31.7, H 5.8, N 6.0, S 14.2.

5-Amino-5-deoxy-D-fuco-*pyranose (D*-fuco-*nojirimycin) (**D-3a**).* General procedure b) with **D-3c** (50 mg, 0.22 mmol) to give **D-3a**. ^{1}H-NMR : *Table 2*.

1,5-dideoxy-1,5-imino-D-fucitol (1-deoxy-D-fuco-*nojirimycin) (**D-3b**).* General procedure c) with **D-3a** (0.22 mmol) for 1 h to give **D-3b** (34 mg, quant.).

D-3b : colourless resin. $[\alpha]_D^{20}$ = +49 (c=1, H_2O) (lit.[17] : $[\alpha]_D^{20}$ = –46.9 (c=0.61, H_2O) ; lit.[11a] : $[\alpha]_D^{20}$ = –48.8 (c=0.64, H_2O), for the L-isomer). ^{1}H-NMR : *Table 1* (identical data as in lit.[17], similar data as in lit.[11a] for the L-enantiomer, as in lit.[13a] for the D-enantiomer). ^{13}C-NMR (D_2O) : 54.8 C(1) ; 69.7 C(2) ; 76.3 C(3) ; 73.9 C(4) ; 50.1 C(5) ; 17.5 Me(6) (similar data as in lit.[11a] for the L-isomer). MS (m/z(%)) : 147 (5), 129 (11), 112 (9), 73 (10), 58 (19), 57 (100), 56 (50), 44(97). HR-MS calc. for $C_6H_{13}NO_3$: 147.08954 ; found : 147.0887.

Remark : two lactams are sometimes formed (*ca.* 15 %) during longer hydrogenolysis, one being the D-fuconolactame (similar ^{13}C-NMR data as in lit.[36]).

f. gulose series.

5-amino-1,5,6-trideoxy-β-D-gulo-*pyranose-1-sulfonic acid (**D-6c**).* General procedure a) with **D-12c** (0.36 g, 1.05 mmol) to give **D-6c** (0.13 g, 55 %).

D-6c : colourless crystals. Mp = 210-215°C (dec) (H_2O/MeOH). $[\alpha]_D^{20}$ = –35 (c=1, H_2O). IR(KBr) : 3480, 3035, 2820, 1640, 1580, 1440, 1270, 1240, 1200, 1170, 1145, 1105, 1042, 1015, 998. ^{1}H-NMR : *Table 2*. ^{13}C-NMR (D_2O) : 68.6 C(1) ; 66.0 C(2) ; 71.0 C(3) ; 70.7 C(4) ; 53.1 C(5) ; 14.5 Me(6). Anal. calc. for $C_6H_{13}NO_6S$ (227.23) : C 31.71, H 5.76, N 6.16 ; S 14.11 ; found : C 31.8, H 6.1, N 6.2, S 14.1.

5-amino-1,5,6-trideoxy-β-DL-gulo-*pyranose-1-sulfonic acid ((±)-**6c**).* General procedure a) with (±)-**12c** (0.26 g, 0.75 mmol) to give (±)-**6c** (0.124 g, 70 %).

(±)-**6c** : colourless crystals. Mp = 210-215°C (dec) (H_2O/EtOH). IR(KBr) : 3500, 3360, 3290, 1640, 1580, 1417, 1230, 1210, 1142, 1125, 1105, 1053, 1040, 1012. Anal. calc. for $C_6H_{13}NO_6S$, 1/2 H_2O, (236.24) : C 30.50, H 5.97, N 5.92, S 13.97 ; found : C 30.4, H 6.0, N 5.6, S 13.6.

Remark : an intermediate, probably a acyclic SO_2-adduct, was formed in 30 % proportion and isomerised at 320 K to (±)-**6c**. ^{1}H-NMR (D_2O) : 4.67 (d, H-C(1)) ; 4.20 (dd, H-C(2)) ; 3.73 (dd, H-C(3)) ; 3.91 (dd, H-C(4)) ; 3.52 (quint, H-C(5)) ; 1.33 (d, Me(6)) ; *J*(1,2)=0.9, *J*(2,3)=9.4, *J*(3,4)= 1.3, *J*(4,5)=7.9, *J*(5.6)=6.7.

5-amino-1,5-dideoxy-D-gulo-*pyranose (6-deoxy-D*-gulo-*nojirimycin) (**D-6a**).* General procedure b) with **D-6c** (32 mg, 0.14 mmol) to give **D-6a**. ^{1}H-NMR : *Table 2*.

5-amino-1,5-dideoxy-DL-gulo-*pyranose (6-deoxy-DL*-gulo-*nojirimycin) ((±)-**6a**).* General procedure b) with (±)-**6c** (50 mg, 0.22 mmol) to give (±)-**6a**.

1,5-imino-1,5,6-trideoxy-D-gulitol (1,6-dideoxy-D-gulo-*nojirimycin) (**D-6b**).* General procedure c) with **D-6a** (0.14 mmol) for 2 h at rt to give **D-6b** (22 mg, quant.).

D-6b : colourless resin. ^{1}H-NMR : *Table 1*. ^{13}C-NMR (D_2O) : 45.2 C(1) ; 67.2 C(2) ; 71.7 C(3) ; 73.3 C(4) ; 49.3 C(5) ; 16.0 Me(6). Similar ^{1}H-NMR data and identical ^{13}C-NMR data as in lit.[15,18b].

1,5-imino-1,5,6-trideoxy-DL-gulitol (1,6-dideoxy-DL-gulo-*nojirimycin) ((±)-**6b**).* General procedure c) with (±)-**6a** (0.22 mmol) overnight at rt to give (±)-**6b** (32 mg, quant.) as a colourless resin.

(±)-**6b** was characterised as its tetraacetyl derivative : same procedure as for the tetraacetyl derivative of (±)-**2b**, with (±)-**6b** (from (±)-**6c**, 50 mg, 0.22 mmol), with Ac_2O (0.21 ml, 2.2 mmol, 10 eq.) in pyridine (0.41 ml) to give the crude product (50 mg). Crystallisation in *i*-Pr_2O/*i*-PrOH gave the tetraacetyl derivative (33 mg, 47 %) as colourless crystals. Mp = 145-7°C (*i*-Pr_2O/*i*-PrOH). Anal. calc. for $C_{14}H_{21}NO_7$ (315.32) : C 53.32, H 6.71, N 4.44 ; found : C 53.0, H 6.8, N 4.6.

REFERENCES and NOTES

1. Legler, G., *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 319.
2. Niwa, T.; Inouye, Sh.; Tsuruoka, T.; Koaze, Y.;Niida, T., *Agr. Biol, Chem.* **1970**, *34*, 966.
3. Reese, E. T.; Parrish, F. W.; Ettlinger, M., *Carbohydr. Res.* **1971**, *18*, 381.
4. Niwa, T.; Tsuruoka, T.; Goi, H.; Kodama, Y.; Itoh, J.; Inouye, Sh.; Yamada, Y.; Niida, T.; Nobe, M.; Ogawa, Y., *J. Antibiot.* **1984**, *37*, 1579.

5. Legler, G.; Jülich, E., *Carbohydr. Res.* **1984**, *128*, 61.
6. Legler, G.; Pohl, St., *Carbohydr. Res.* **1986**, *155*. 119.
7. Auberson, Y.; Vogel, P., *Angew. Chem., Int. Ed.* **1989**, *28*, 1498.
8. Paulsen, H.; Leupold, Fr.; Todt, Kl., *Liebigs Ann. Chem.* **1966**, *692*, 200 ; Paulsen, H.; Leupold, Fr., *Chem. Ber.* **1969**, *102*, 2822.
9. Inouye, Sh.; Tsuruoka, T.; Ito T.; Niida, T., *Tetrahedron* **1968**, *23*, 2125.
10. Winchester, Br.; Fleet, G. W. J., *Glycobiology* **1992**, *2*, 199.
11. a) Fleet, G. W. J.; Shaw, A. N.; Evans, St. V.; Fellows, L. E., *J. Chem. Soc., Chem. Comm.* **1985**, 841 ; b) Paulsen, H.; Matzke, M.; Orthen, Br.; Nuck, R.; Reutter, W., *Liebigs Ann. Chem.* **1990**, 953.
12. a) Brandstetter, T. W.; Davis, B.; Hyett, D.; Smith, C.; Hackett, L.; Winchester, Br. G.; Fleet, G. W. J., *Tetrahedron Lett.* **1995**, *36*, 7511 ; b) Zhou, P.; Salleh, H. M.; Chan, Ph. C. M.; Lajoie, G.; Honek, J., F.; Nambiar, P. T. Ch.; Ward, O. P., *Carbohydr. Res.* **1993**, *239*, 155.
13. a) Kajimoto, T.; Liu, K. K.-C.; Pederson, R. L.; Zhong, Z.; Ichikawa, Y.; Porco Jr, J. A.; Wong, Ch.-H., *J. Am. Chem. Soc.* **1991**, *113*, 6187 ; b) Liu, K. K.-C.; Kajimoto, T.; Chen, L.; Zhong, Z.; Ichikawa, Y.; Wong, Ch.-H., *J. Org. Chem.* **1991**, *56*, 6280.
14. Defoin, A.; Sarazin, H.; Streith, J., *Tetrahedron*, preceding publication ; *Tetrahedron Lett.* **1993**, *34*, 4327.
15. Defoin, A.; Sarazin, H.; Streith, J., *Helv. Chim. Acta* **1996**, *79*, 560 ; Defoin, A.; Sarazin, H.; Strehler, Ch.; Streith, J., *Tetrahedron Lett.* **1994**, *35*, 5653.
16. Hussain, A.; Wyatt, P. B., *Tetrahedron* **1993**, *49*, 2123.
17. Paulsen, H.; Matzke, M., *Liebigs Ann. Chem.* **1988**, 1121.
18. a) Fleet, G. W. J.; Petursson, S.; Campbell, A. L.; Mueller, R. A.; Behling, J. R.; Babiak, K. A.; Ng, J. S.; Scaros, M. G., *J. Chem. Soc., Perkin Trans. I* **1989**, 665 ; b) Shilvock, J. P.; Wheatley, J. R.; Davis, B.; Nash, R. J.; Griffiths, Rh. C.; Jones, M. G.; Müller, M.; Crook, S.; Watkin, D. J.; Smith, C.; Besra, G. S.; Brennan, P. J.; Fleet, G. W. J., *Tetrahedron Lett.* **1996**, *37*, 8569.
19. Defoin, A.; Sarazin, H.; Streith, J., *Synlett* **1995**, 1187 ; Defoin, A.; Sarazin, H.; Streith, J., Poster communications in *Cycloaddition and related Reactions : Theory and practice*, Vulcano Island, Italia, 21-24 june 1995 and in *First Euroconference on Carbohydrate mimics*, Strasbourg, France, 14-17 may 1995.
20. a) Gao, Y.; Sharpless, K. B., *J. Am. Chem. Soc.* **1988**, *110*, 7538 ; b) Kim, B. M.; Sharpless, K. B., *Tetrahedron Lett.* **1989**, *30*, 655.
21. Albert, R.; Dax, K.; Stütz, A.E., *Carbohydr. Res.* **1984**, *132*, 162.
22. Rao, A. S.; Paknikar, S. K.; Kirtane, J. G., *Tetrahedron* **1983**, *39*, 2323.
23. Binkley, R. W., *J. Carbohydr. Chem.* **1994**, *13*, 111.
24. For the discussion of ^{1}H-NMR data, prefixes (±)- or D- are omitted.
25. Defoin, A.; Fritz, H.; Geffroy, G.; Streith, J., *Helv. Chim. Acta* **1988**, *71*, 1642.
26. a) Paulsen, H.; Todt, Kl., *Chem. Ber.* **1967**, *100*, 3385 ; b) Paulsen, H.; Todt, Kl., *Adv. Carbohydr. Chem.* **1968**, *23*, 115.
27. Pinto, B. M.; Wolfe, S., *Tetrahedron Lett.* **1982**, *23*, 3687.
28. Barfield, M.; Chakrabarti, B., *Chem. Rev.* **1969**, *69*, 757 ; Barfield, M.; Spear, R. J.; Sternhell, S., *Chem. Rev.* **1976**, *76*, 593.
29. Sinnott, M. L., *Chem. Rev.* **1990**, *90*, 1171.
30. Angyal, S. J.; Pickles, V. A., *Austral. J. Chem.* **1972**, *25*, 1711, in *Beilstein's Handbuch der Organischen Chemie*, Springer Verlag: Berlin, 1977, Vol. *E 4/1*, pp. 4260, 4266.
31. Angyal, S. J.; Pickles, V. A., *Austral. J. Chem.* **1972**, *25*, 1695, in *Beilstein's Handbuch der Organischen Chemie*, Springer Verlag: Berlin, 1977, Vol.*E 4/1*, pp. 4299, 4333, 4345.
32. Defoin, A.; Fritz,H.; Schmidlin, Ch.; Streith, J., *Helv. Chim. Acta* **1987**, *70*, 554.
33. Fleet, G. W. J.; Ramsden, N. G.; Dwek, R. A.; Rademacher, T. W.; Fellows, L. E.; Nash, R. J.; Green, D. St. C.; Winchester, Br., *J. Chem. Soc., Chem. Comm.* **1988**, 483.

(*Received in Belgium* 4 *March* 1997; *accepted* 5 *August* 1997)