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Silica gel-catalysed addition of methyl nitroacetate to 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose and 2,3-*O*-isopropylidene-D-glyceraldehyde. Crystal structure of methyl 7-acetamido-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octopyranuronate

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Abstract

The addition of methyl nitroacetate to 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**5**) and to 2,3-*O*-isopropylidene-D-glyceraldehyde (**6**) in the presence of silica gel led stereoselectively to the formation of only (from **5**) or mainly (from **6**) two of the four possible nitroaldols in high yield. The catalytic action of silica gel was required in the reaction of **6**, but not in that of **5**. Isolation of a crystalline, reduced and *N*-acetylated derivative from the mixture of nitroaldols (**7** + **8**) obtained from **5** allowed for the determination of its crystal structure, showing that it has the 6*R*, 7*R* absolute configuration (one of the two possible 6,7-*threo* configurations) by X-ray diffraction methods. Therefore, the same 6*R* configuration was also assigned to the

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nitroaldols **7** and **8**, which on the basis of the easy α-epimerisation of the α-nitro esters should differ only in the configuration at C-7. A pair of amino alcohols obtained from the same mixture of nitroaldols were separately transformed into a 4,5-*cis*- and a 4,5-*trans*-oxazoline, the configurations of which were correlated with the C-6,7 relative configuration of the respective amino alcohols and also the respective nitroaldol. The Felkin model explained the high stereoselectivity observed. The configurations of the two predominant nitroaldols obtained from **6** were tentatively assigned by applying the Felkin model.

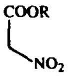
Keywords: Nitroaldol reaction; *aldehydo*-Sugars; Methyl nitroacetate; Stereoselectivity; Crystal structure of a 7-acetamido-octopyranuronic ester

1. Introduction

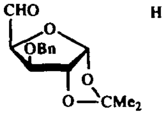
The nucleophilic addition of aliphatic nitro compounds to *aldehydo*-sugars has attracted attention because of its application to the synthesis of functionalised higher-carbon sugars, some of them being related to compounds of biological significance. The use of α-nitro esters in these reactions allows the simultaneous introduction of two functional groups in the lengthened carbon chain, a possibility explored by several authors. Thus, Paulsen et al. [1] studied the reaction of ethyl nitroacetate (**1a**) with 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose (**2**) in the absence of catalyst, and obtained a good yield of a 5 : 2 mixture of two of the four possible nitroaldol adducts (**3** and **4**), both of them having the *R* configuration at the new alcoholic carbon and differing in the (*R* or *S*) configuration of the carbon bearing the nitro function. This result was considered [1] to be consistent with the preferred attack of the nucleophile at the *re* face of the aldehydic carbonyl group in its preferred conformation. A study on the stereoselectivity of the addition of nitro compounds to sugar dialdehydes has been recently reported [2]. The reaction of nitroacetic esters with free aldoses in the presence of basic catalysts is more complex, the nitroaldol addition being followed by dehydration and an intramolecular Michael addition of an OH group to the α,β-unsaturated nitro ester, to afford finally 2-(*C*-glycosyl)-2-nitroacetic esters [3]. Similarly, the one-step reaction of *O*-protected *aldehydo*-sugars with two moles of methyl nitroacetate (**1b**) in the presence of diethylamine to yield isooxazoline *N*-oxides presumably involves the addition of nitroacetate to an intermediate α,β-unsaturated sugar nitro ester, followed by the intramolecular elimination of nitrous acid in the resulting dinitro compound [4]. Following our studies [5,6] on the synthesis of higher-carbon nitro and amino sugars, we have found that silica gel, even in the absence of solvent, is a good catalyst for the nitroaldol reaction of nitroacetic esters and certain *aldehydo*-sugars. We now report the results obtained in the reaction of **1b** with 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**5**) and with 2,3-*O*-isopropylidene-D-glyceraldehyde (**6**).

2. Results and discussion

The reaction of **1b** with 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**5**) in dry dichloromethane gave similar results both in the presence and in the



1a: R = Et
1b: R = Me



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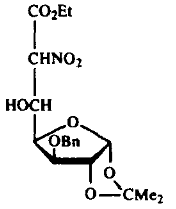

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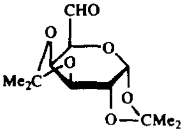
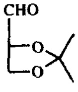


5



6

absence of Silica Gel 60. Thus, when the reaction was carried out by dissolving under stirring an equimolar mixture of the reactants in the minimal amount of dry dichloromethane and adding Silica Gel 60 (one half of the weight of **1b**), NMR and TLC indicated a 100% conversion, after 48 h at room temperature, into two of the four possible diastereomeric nitroaldols. In the absence of silica gel, completion of the reaction required ca. 8 h (NMR). After preparative TLC, a syrupy diastereomeric mixture was isolated in yields of 55% and 56%, respectively, but in the first case, the product was a 59 : 41 mixture of **7** and **8**, whereas in the latter case the ratio of the same isomers was 50 : 50 (^{1}H and ^{13}C NMR, Tables 1 and 2, respectively). The assignment of configurations was made as follows.

The mixture of the nitroaldols **7** and **8** obtained in the presence of silica gel was hydrogenated with Raney-nickel under different conditions. Hydrogenation in acetic anhydride at room temperature for 7 h led to a mixture, from which two main products were isolated after column chromatography. Eluted first was the *N*,*O*-diacetyl amino alcohol **9**. The second compound (**10**) eluted could be crystallised and studied by X-ray analysis, from which the total structure of **10** was shown to be methyl 7-acetamido-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octopyranuronate. Acetylation of **10** afforded an *N*,*O*-diacetyl derivative (**11**) different from **9**, the configuration of which, 6*R*, 7*R*, must be the same as that of **10**. A 6,7-*erythro* (6*R*, 7*S* or 6*S*, 7*R*) configuration is tentatively assigned to **9** by comparison of the $J_{7,\mathrm{NH}}$ values (9.5 Hz for **11**, 8.9 Hz for **9**) found in the ^{1}H NMR spectra (Table 1) with literature data [1] for similar compounds ($J_{threo} > J_{erythro}$).

When the hydrogenation of the mixture of **7** and **8** was performed in dry methanol at room temperature, followed by treatment with acetic anhydride in methanol at 0°C, a complex mixture was formed, from which two diastereomeric *N*-acetylamino alcohols could be separated by column chromatography. The $J_{7,\mathrm{NH}}$ values allowed to assign in principle a 6,7-*erythro* configuration (6*R*, 7*S* or 6*S*, 7*R*) to the first eluted compound (*J* 6.6 Hz), and a *threo* configuration (6*R*, 7*R* or 6*S*, 7*S*) to the second (*J* 9.0 Hz). The latter was identical with the amino alcohol **10** obtained by the first hydrogenation procedure, although it could not be crystallised.

The configurational assignment for **10** allowed to attribute the same 6*R*, 7*R* absolute configuration to the 6,7-*threo* products: one of the nitroaldols and the *N*,*O*-diacetyl amino alcohol **11** obtained by acetylation of **10**. For the 6,7-*erythro* products — the other nitroaldol, the other *N*,*O*-diacetyl amino alcohol **9** and the other *N*-acetyl amino alcohol obtained by the second hydrogenation method — the 6*R*, 7*S* configuration was

Table 1
^{1}H NMR data in $CDCl_3$ for compounds **7–16**

Compound		Chemical shifts (δ in ppm)													
		Me_2C	AcN	AcO	HO	MeO	H-1	H-2	H-3	H-4	H-5	H-6	H-7	NH	N=C–Me
(**7**+**8**) [a,b]	M	1.34s, 1.38s, 1.47s, 1.56s			[c]	3.89s	5.49d	4.35dd	4.67dd	4.47dd	4.02dd	4.70dd	5.56d		
	m	1.32s, 1.38s, 1.47s, 1.51s			[c]	3.87s	5.48d	4.33dd	4.67dd	4.46dd	3.84dd	4.56dd	5.60d		
(**7**+**8**) [d,e] (50 50)		1.31s, 1.32s, 1.33s, 1.37s,			3.28d	3.88s	5.48d	4.34dd	4.66dd	4.47dd	4.01dd	4.66ddd	5.55d		
		1.45s, 1.46s, 1.49s, 1.55s			3.29d	3.86s	5.47d	4.32dd	4.66dd	4.46dd	3.83da	4.55ddd	5.59d		
9 [d]		1.30s, 1.33s, 1.37s, 1.59s	2.05s	2.03s		3.70s	5.44d	4.33dd	4.61dd	4.20dd	3.85dd	5.52dd	5.17dd	6.34d [f]	
10 [g]		1.31s, 1.36s, 1.46s, 1.48s	2.05s		3.82d	3.75s	5.50d	4.31dd	4.62dd	4.42dd	3.75dd	4.33m	4.85dd	6.61d [f]	
11 [d]		1.31s, 1.32s, 1.44s, 1.51s	2.07s	2.04s		3.73s	5.52d	4.33dd	4.61dd	4.18dd	3.95dd	5.41dd	5.07dd	6.11d [f]	
12 [a]		1.33s, 1.36s, 1.41s, 1.55s	2.10s		[c]	3.74s	5.42d	4.32dd	4.62dd	4.43dd	3.68dd	4.49m “dd [h]	4.82dd “d [h]	6.85d [f]	
13 [a]		1.29s, 1.33s, 1.40s, 1.52s			[c]	3.70s	5.41d	4.28dd	4.60dd	4.43dd	←3.75m→		4.23d [fi]	2.15s [f] (2 H)	
14 [a]		1.28s, 1.30s, 1.43s, 1.51s			[c]	3.72s	5.47d	4.29dd	4.60dd	4.44dd	3.72dd	4.13dd	4.24dt [i] (2 H)	2.12s [f]	
15 [d]		1.28s, 1.40s, 1.48s, 1.58s				3.79s	5.53d	4.33dd	4.67dd	4.35dd	3.99dd	4.88dd	4.78dq		2.17d
16 [d]		1.26s, 1.27s (12 H)				3.71s	5.46d	4.27dd	4.56dd	4.22dd	3.76dd	4.94dd	4.65dq		1.96d

Table 1 (continued)

Compound	Coupling constants (J in Hz)								
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,HO}$	$J_{7,NH}$	$^5J_{7,Me}$
(**7**+**8**) [a,b] M	5.0	2.4	7.9	1.9	9.5	1.9	[c]		
m	4.8	2.4	7.9	1.9	9.5	3.1	[c]		
(**7**+**8**) [d,e]	4.9	2.5	7.9	1.6	9.5	1.7	7.1		
(50 50)	4.8	2.4	7.9	1.7	9.3	2.9	9.7		
9 [d]	5.1	2.6	7.8	1.8	9.8	1.8		8.9	
10 [g]	5.0	2.1	7.9	1.8	9.2	2.1	5.8	9.0	
11 [d]	4.9	2.5	7.8	1.8	9.3	2.3		9.5	
12 [a]	5.2	2.5	7.8	1.9	9.5	1.6 [h]	[c]	6.6	
13 [a]	5.1	2.2	7.5	≈ 0	[c]	≈ 5 [j]	[c]	[c]	
14 [a]	5.0	2.4	8.0	1.8	9.1	1.9	[c]	8.0	
15 [d]	4.9	2.4	8.0	1.9	9.5	10.0			1.1
16 [d]	5.0	2.4	7.9	1.9	6.0	6.7			1.4

[a] At 200 MHz.

[b] From procedure (a) (see under Experimental section): M, major component (59%); m, minor component (41%).

[c] Not observed.

[d] At 300 MHz.

[e] From procedure (b) (see under Experimental).

[f] Broad signal.

[g] At 500 MHz.

[h] 2.0 Hz after treatment with D_2O.

[i] Partially overlapped with the H-2 signal.

[j] Apparent J, since the signal is poorly resolved.

Table 2
^{13}C NMR data in CDCl$_3$ for compounds **7–12**, **15** and **16**

Compound	Chemical shifts (δ in ppm)												
	Me$_2$C	MeO	*Me*CO$_2$	*Me*CON	*Me*C=N	C-1	C-2–C-6	C-7	C-8	MeCO$_2$	MeCON	O–C–O	N=*C*–Me
(**7**+**8**)[a,b] M	24.3, 24.7, 25.5, 25.7	53.3				96.0	66.7, 69.4, 69.7, 70.3[c]	87.7	163.5			108.9 109.4	
m	24.3, 24.7, 25.5, 25.7	53.6				95.9	66.9, 69.0, 69.8, 70.5[c]	87.6	163.9			109.0 109.5	
9[d]	24.4, 24.7, 25.6, 25.7	52.0[e]	20.7	22.9		96.4	65.6, 69.9, 70.3, 70.6, 71.0	52.0[g]	169.4[f]	169.9[f]	170.0[f]	108.8 109.7	
10[g]	24.3, 24.7, 25.7, 25.8	52.4		23.0		96.1	66.8, 69.8, 70.5[c], 70.6	54.1	170.7[f]		171.5[f]	108.5 109.3	
11[g]	24.3, 24.6, 25.6, 25.7	51.5	20.4	22.9		96.0	65.4, 70.0, 70.3, 70.4, 70.6	52.4	168.6[f]	169.7[f]	171.0[f]	108.6 109.4	
12[a]	23.9, 24.3, 25.1, 25.2	51.5		22.2		95.8	66.8, 69.7, 69.8, 70.0[c]	55.6	170.0[f]		170.8[f]	108.0 108.6	
15[g]	24.2, 24.7, 25.5, 25.7	52.2			13.9	95.6	65.4, 69.0, 70.1[c], 70.7	77.8	170.2			108.9 109.2	167.2
16[g]	24.1, 24.7, 25.5, 25.9	52.3			13.8	96.0	70.2, 70.3, 70.4, 70.5, 71.4	79.7	171.4			109.3 109.5	166.3

[a] At 50.3 MHz.

[b] From procedure (a) (see under Experimental): M, major component; m, minor component. A sample obtained by procedure (b) showed identical data.

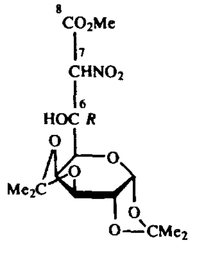
[c] Double intensity.

[d] At 125.8 MHz.

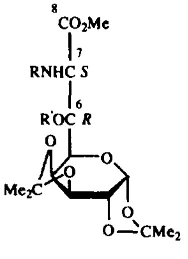
[e] Overlapped signals.

[f] These assignments may be interchanged.

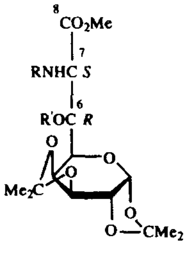
[g] At 75.5 MHz.



7 + 8



9 R = R' = Ac
12 R = Ac
13 R = R' = H

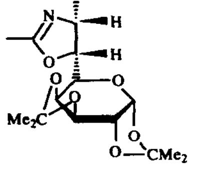


10 R = Ac, R' = H
11 R = R' = Ac
14 R = R' = H

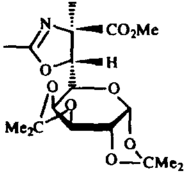
assigned considering the facile epimerisation at the α position of α-nitro esters. Thus, the structure of the last should be **12**.

Hydrogenation of the nitroaldol mixture (**7** + **8**) in glacial acetic acid for 12 h at room temperature led to a mixture of two amino alcohols (**13** and **14**), which after column chromatography were separately transformed by reaction with ethyl iminoacetate into the oxazoline derivatives **15** and **16**, respectively. The relative 6,7 configuration in the amino alcohols is correlated with the *cis* or *trans* relationship between H-4 and H-5 (heterocycle numbering) at the oxazoline ring, easily demonstrable [7] by the J value in the ^{1}H NMR spectrum (J_{cis} 10 Hz, J_{trans} 6.5 Hz). Thus, the 6,7-*erythro* configuration was assigned to **13** and the *threo* to **14** from the *cis* ($J_{6,7}$ 10.0 Hz, Table 1) and *trans* ($J_{6,7}$ 6.7 Hz) configurations of **15** and **16**, respectively. Since the 6R configuration is ascertained by chemical correlation with the parent nitroaldols, it follows that **13** and **15** have the 6R, 7S configuration while **14** and **16** are 6R, 7R configurated.

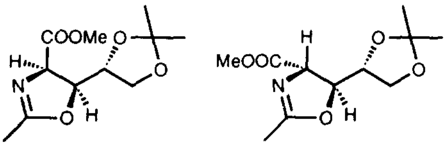
The high stereoselectivity observed in the nitroaldol reaction of **1b** with **5** may be explained in terms of Felkin's model [8]. By analogy with related studies [2], the preferred conformation of **5** in the transition state should be governed by polarity, as shown in Scheme 1, in which the attack of **1b** on the less hindered, *re* face of the carbonyl group is also shown to lead to the 6R product.



15



16

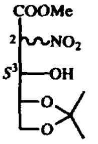


25 **26**

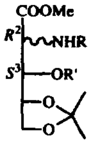
Scheme 1.

The reaction of **6** with **1b** was performed also in the presence and in the absence of Silica Gel 60. When **6** and **1b** were allowed to react at 0°C without any solvent, with stirring, by adding a weight of Silica Gel 60 similar to that of **1b**, the reaction was complete after 4 h (NMR). Preparative TLC afforded a mixture of mainly two (**17** and **18**) of the four possible diastereomeric nitroaldols (^{1}H and ^{13}C NMR, Tables 3 and 4, respectively), accompanied by minor amounts of the other two diastereomers (44 : 44 : 6 : 6 ratio). Here, the catalytic action of silica gel was evident, since the reaction did not progress, or only very slowly, in its absence.

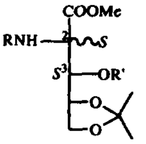
The three Raney-nickel catalysed hydrogenation methods described above for the nitroaldols obtained from **5** were applied to the crude mixture of nitroaldols **17** and **18** derived from **6**. As observed for similar compounds [1], the use of methanol as solvent in the hydrogenation led, after acetylation, to very poor yields of a mixture of mainly two *N*-acetylamino alcohols (**19** and **20**), which could not be separated by column chromatography (62 : 38 mixture and minor amounts of the other two diastereomers from the ^{1}H NMR spectrum, Table 3). Hydrogenation of the (**17** + **18**) mixture in acetic anhydride afforded a mixture of four products: two diastereomeric *N,O*-diacetylamino alcohols (**21** and **22**) and the same two *N*-acetylamino alcohols **19** and **20** mainly obtained by the first procedure. Column chromatography of this mixture separated the diacetylamino alcohols **21** and **22** (their configurational assignment was tentatively made), but the monoacetyl compounds **19** and **20** again were eluted together as a 59 : 41 mixture (^{1}H NMR, Table 3). By using glacial acetic acid as solvent in the hydrogenation, a mixture (^{1}H NMR) of two amino alcohols (**23** and **24**) was obtained, which was treated with ethyl iminoacetate similarly as for the amino alcohols **13** and **14**, to afford 54% of a 57 : 43 mixture (^{1}H NMR) of the oxazolines **25** and **26**, respectively. The *cis*



17 + 18



19 R = Ac, R' = H
21 R = R' = Ac
23 R = R' = H



20 R = Ac, R' = H
22 R = R' = Ac
24 R = R' = H

Table 3
^{1}H NMR data for compounds **17–22**, **25** and **26**

Compound	Chemical shifts (δ in ppm)											
	Me_2C	AcN	AcO	HO	MeO	H-2	H-3	H-4	H-5	H-5′	NH	N = C–Me
(**17** + **18**) [a,b]	1.33s, 1.35s (3H)			3.33d	3.89s	5.49d	←——4.0–1.27m——→					
(44 + 44%)	1.42s (3H)			3.44d	3.90s	5.50d						
(minor isomers)	1.45s			2.78d	3.86s	5.18d	←——4.0–4.5m——→					
(12%)	1.47s			3.06d	3.88s	5.26d						
(**17** + **18**) [a,c]	1.28s, 1.30s (3H)			3.42d	3.83s	5.41d [d]	4.11m	←——4.00–4.25m——→				
(in $CDCl_3$)	1.37s (3H)			3.5br	3.85s	5.46d [d]	4.21m					
(**19** + **20**) [a,b]	1.26s, 1.32s	2.01s		3.01 [e]	3.68s	4.73d [f]	3.66–3.70m	4.08–4.16m	←—3.89–4.04m—→		7.24d [f]	
[in$(CD_3)_2CO$] [a]	1.36s	2.02s			3.69s	4.81dd					7.54d [f]	
(in $CDCl_3$) [h]	1.29s, 1.32s	2.08s		5.1br	3.78s	4.80dd	3.7–3.9m	←——3.9–4.15m——→			6.36d [f]	
	1.33s, 1.42s	2.14s			3.79s	4.74dd					6.78d [f]	
21 (or **22**) [b]	1.22s, 1.27s	1.95s [i]	1.96s [i]		3.65s	5.14dd	5.10dd	4.20ddd	4.10dd	3.80dd	6.37d [f]	
(in $CDCl_3$)												
22 (or **21**) [b]	1.34s, 1.44s	2.10s [j]	2.10s [j]		3.73s	5.04dd	5.30dd	4.18ddd	4.00dd	3.80dd	6.30d [f]	
(in $CDCl_3$)												
(**25** + **26**) [c]	1.28s, 1.31s				3.67s	4.68dq	4.50dd	4.09m [j]	3.99dd	3.78dd		1.91d
(in $CDCl_3$)	1.17s, 1.23s				3.62s	4.49m	4.60dd	4.09m [j]	3.93dd	3.75dd		1.90d

Table 3 (continued)

Compound	Coupling constants (J in Hz)							
	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	$J_{2,NH}$	$J_{3,HO}$	$^{5}J_{2,Me}$
(**17** + **18**) [a,b]	3.5	[k]	[k]	[k]	[k]		8.7	
	1.9						6.0	
(minor isomers)	7.4						10.0	
	8.1						9.2	
(**17** + **18**) [a,c]	3.8	[k]	[k]	[k]	[k]		6.0	
	1.9							
(**19** + **20**) [a,b]	3.1	5.3	6.2	4.9	8.7	8.0		
[in $(CD_3)_2CO$] [g]						1.4		
(in $CDCl_3$) [h]	2.2	[k]	[k]	[k]	[k]	9.0		
	1.6					5.2		
21 (or **22**) [b]	2.4	8.7	6.3	5.0	8.8	8.0		
22 (or **21**) [b]	2.2	7.6	6.0	4.9	8.6	9.3		
(**25** + **26**) [c]	10.1	8.2	6.6	6.0	8.8			1.4
	6.6	6.2	4.7	5.0	8.8			1.3

[a] The other two diastereomers give rise to minor signals.

[b] At 200 MHz.

[c] At 300 MHz.

[d] The signal disappears slowly (5 days) after shaking the sample with D_2O.

[e] Included in the signal of H_2O present in the solvent.

[f] Broad signal.

[g] From the procedure (a) (see under Experimental section).

[h] From procedure (b) (see under Experimental section).

[i] These assignments may be interchanged.

[j] Overlapped signals.

[k] Complex coupling system.

Table 4
^{13}C NMR data for compounds **16–22**, **25** and **26**

Compound	Chemical shifts (δ in ppm)													
	Me$_2$C	MeO	*Me*CO$_2$	*Me*CON	*Me*C=N	C-1	C-2	C-3	C-4	C-5	Me*CO*$_2$	Me*C*ON	O–C–O	N=*C*–Me
(**17**+**18**)[a]	24.64, 24.70,	53.53				163.29	87.71	72.15[b]	74.37[b]	66.95			110.20	
(in CDCl$_3$)	26.61, 26.75	53.69				163.55	87.91	74.47[b]	75.57[b]	67.08			110.29	
(**19**+**20**)	24.61, 24.66,	51.66		20.64		170.21[c,d]	54.37	71.88[b]	73.41[b]	66.53		171.29[d]	109.26	
[in (CD$_3$)$_2$CO][a]	26.13, 26.41	51.93		21.83			55.32	75.11[b]	75.26[b]	66.86		171.70[d]	109.32	
(in CDCl$_3$)[e]	24.59, 24.75,	52.06[c]		22.34		169.51[d]	53.94	71.65[b]	73.82[b]	66.07		171.19[d]	109.06	
	26.11, 26.43			22.40		171.12[d]	56.00	74.82[b]	74.85[b]	66.63		171.70[d]	109.17	
21 (or **22**)[e]	24.68, 25.61	52.19[b]	20.60[d]	22.35[d]		169.07[d]	52.31[b]	72.83[d]	73.94[d]	66.79	169.93[d]	169.97[d]	109.43	
(in CDCl$_3$)														
22 (or **21**)[e]	24.96, 26.44	51.85[b]	20.31[d]	22.80[d]		169.19[d]	52.54[b]	72.63[d]	73.67[d]	65.68	170.11[d]	170.47[d]	109.66	
(in CDCl$_3$)														
(**25**+**26**)[e]	24.77, 26.08	52.27			13.52	171.12	81.23	69.50[b]	75.08[b]	65.58			109.77	166.37
(in CDCl$_3$)	24.56, 26.44	51.82			13.76	169.94	80.57	69.40[d]	72.99[d]	66.75			109.32	166.99

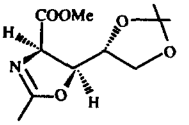
[a] At 50.3 MHz.

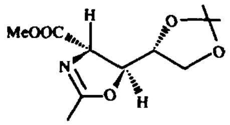
[b] These assignments may be interchanged.

[c] Double intensity.

[d] These assignments may be respectively interchanged.

[e] At 75.5 MHz.



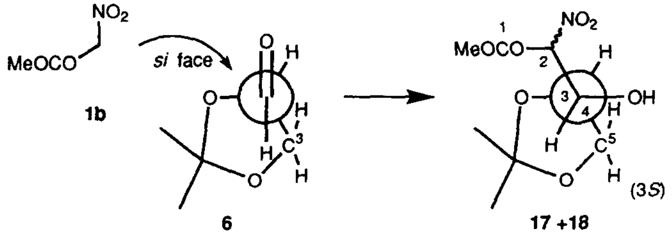


or *trans* relationship between H-4 and H-5 (heterocycle numbering) in each oxazoline was determined again by the $J_{2,3}$ value in the ^{1}H NMR spectrum [7] (Table 3, $J_{2,3}$ 10.1 Hz for the *cis* isomer **25**, and 6.6 Hz for the *trans* isomer **26**).

The configurational assignments for the new derivatives obtained from **6** were tentatively made by analogy with the parallel series of derivatives from **5** on the basis of mechanistic considerations. Thus, application of Felkin's model to the reaction of **1b** with **6** (Scheme 2) explains the preferential *S* configuration at position 3 of the two main nitroaldols formed, which should differ only in the configuration at the easily epimerisable position 2. The individual assignment of each pair of compounds was made bearing in mind the *cis* : *trans* ratio measured for the mixture **25**–**26**; the slight predominance seems to correspond to the *erythro* compounds **19, 21**, as is the case in the derivatives of **5**.

In conclusion, the nitroaldol reactions of **1b** with **5** and **6** catalysed by silica gel proceeded in almost quantitative yields with high stereoselectivity in the attack to the aldehydic carbonyl group. Only (from **5**) or mainly (from **6**) two of the four possible diastereomers were detected (NMR) and obtained as a mixture (yields after purification: 55% and 39% from **5** and **6**, respectively). The two diastereomers differ only in the configuration at the other new chiral center, the easily epimerisable nitro-substituted α-position.

X-ray structure analysis of **10**. — An ORTEP [9] view of the molecule along the *c* axis, together with the atomic numbering is shown in Fig. 1. Bond lengths and angles, shown in Table 5, agree with others analogues, and the typical asymmetry of endocyclic bonds for the pyranose ring O-15–C-1 and O-15–C-5 (1.384(8) and 1.434(8) Å, respectively) caused by the anomeric effect is observed [10]. The geometry observed for the pyranose ring is consistent with a twist–boat conformation. In terms of ring-pucker-



Scheme 2.

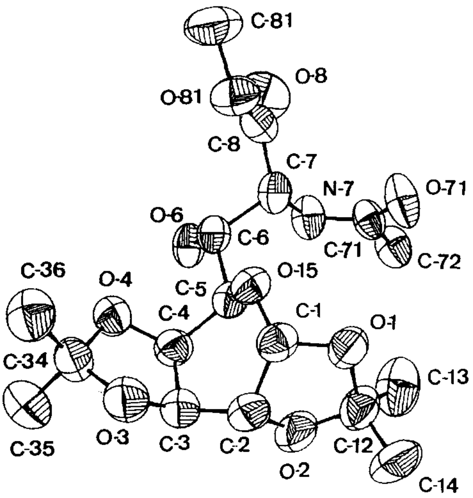


Fig. 1. An ORTEP view of **10** showing the atomic numbering. Thermal ellipsoids enclose 50% probability.

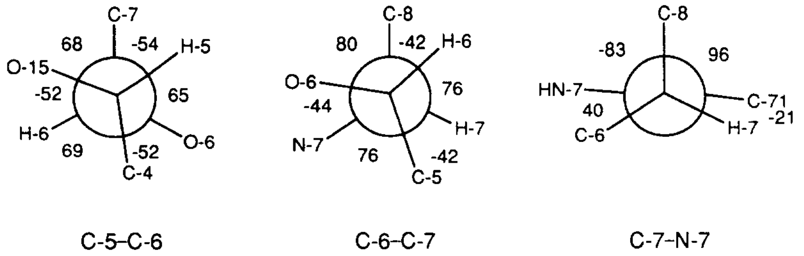
ing coordinates [11], amplitude and phase magnitudes are $Q = 0.615(8)$ Å, $\phi = -41(7)°$ and $\theta = 82(1)°$ for the sequence O-15–C-1–C-2–C-3–C-4–C-5. The asymmetric parameters [12] are ΔC_2(C-1) = 0.068(3) and ΔC_s(O-15–C-5) = 0.068(3). The geometry observed for the two dioxolane rings are twist and the ring-puckering coordinates are $Q = 0.317(8)$ Å and $\phi = 56(1)°$ for the sequence C-1–C-2–O-2–C-12–O-1 and $Q = 0.311(8)$ Å and $\phi = -54(1)°$ for the C-3–C-4–O-4–C-34–O-3 sequence. The asymmetric parameters are ΔC_2(O-1) = 0.011(3) and ΔC_2(C-4) = 0.003(3), respectively. The group –CO–OCH_3 is planar (max. dev. 0.005 Å) and the N–$COCH_3$ is nearly planar (max. dev. 0.016 Å). The chain C-8–C-7–C-6–C-5 is not planar and the substitution O-6, N-7 and O-8 are on the same side of the mean square plane. According to the Klyne and Prelog rules, the configurations around the chiral centre C-6 and C-7 are 6*R*, 7*R*. The dihedral angle between the C-7–H-7 and the N–H bonds has a value of 159.6°, in good agreement with the coupling constant ($J_{7,\mathrm{NH}}$ 9.0 Hz) found in $CHCl_3$ solution, as mentioned above. The Newman projections along the C-5–C-6, C-6–C-7, and C-7–N-7 bonds are shown in Fig. 2. The dihedral angles between the pyranose and dioxolane rings are 77.2 and 80.7°. The crystal cohesion is governed by van der Waals forces and one intermolecular H-bond, O-6 $\cdots$ O-71 $(x + 1/2, -y + 3/2, -z + 1)$ = 2.667(8) Å, O-6–H $\cdots$ O-71 = 145.6(4)°.

3. Experimental

General methods. — Solvents were evaporated in vacuo at < 40°C. Melting points were determined with a Gallenkamp MFB-595 apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 MC polarimeter at 589 (D) or 546 (V) nm. UV spectra were recorded with a Beckman DU-7 spectrophotometer and IR

Table 5
Bond distances (Å) and angles (°)

Bond lengths		Angles	
O-1–C-1	1.414(8)	C-1–O-1–C-12	110.4(5)
O-1–C-12	1.417(11)	C-2–O-2–C-12	106.3(7)
O-2–C-2	1.424(12)	C-3–O-3–C-34	106.4(6)
O-2–C-12	1.416(10)	C-4–O-4–C-34	107.9(5)
O-3–C-3	1.425(12)	C-1–O-15–C-5	115.0(5)
O-3–C-34	1.430(9)	C-8–O-81–C-81	118.4(7)
O-4–C-4	1.421(9)	C-7–N-7–C-71	122.4(6)
O-4–C-34	1.406(10)	O-1–C-1–O-15	110.6(5)
O-6–C-6	1.410(9)	O-15–C-1–C-2	116.1(6)
O-8–C-8	1.187(12)	O-1–C-1–C-2	103.2(6)
O-15–C-1	1.384(8)	O-2–C-2–C-1	102.9(6)
O-15–C-5	1.434(8)	C-1–C-2–C-3	114.3(6)
O-71–C-71	1.229(9)	O-2–C-2–C-3	108.8(8)
O-81–C-8	1.347(12)	O-3–C-3–C-2	107.5(8)
O-81–C-81	1.438(12)	C-2–C-3–C-4	114.2(6)
N-7–C-7	1.437(10)	O-3–C-3–C-4	103.3(6)
N-7–C-71	1.330(9)	O-4–C-4–C-3	105.4(6)
C-1–C-2	1.522(11)	C-3–C-4–C-5	113.0(6)
C-2–C-3	1.515(11)	O-4–C-4–C-5	109.6(5)
C-3–C-4	1.531(11)	O-15–C-5–C-4	110.5(5)
C-4–C-5	1.514(9)	C-4–C-5–C-6	112.8(5)
C-5–C-6	1.525(9)	O-15–C-5–C-6	105.4(5)
C-6–C-7	1.545(9)	O-6–C-6–C-5	109.3(5)
C-7–C-8	1.503(11)	C-5–C-6–C-7	109.9(5)
C-12–C-13	1.525(16)	O-6–C-6–C-7	108.4(5)
C-12–C-14	1.511(15)	O-8–C-8–O-81	123.2(8)
C-34–C-35	1.508(13)	O-81–C-8–C-7	108.5(7)
C-34–C-36	1.511(14)	O-8–C-8–C-7	128.2(9)
C-71–C-72	1.497(11)	C-6–C-7–C-8	110.9(5)
		N-7–C-7–C-8	111.7(6)
		N-7–C-7–C-6	109.5(6)
		O-1–C-12–O-2	105.3(6)
		O-2–C-12–C-14	110.6(7)
		O-2–C-12–C-13	110.1(7)
		O-1–C-12–C-14	109.6(9)
		O-1–C-12–C-13	107.7(8)
		C-13–C-12–C-14	113.0(8)
		O-3–C-34–O-4	105.0(5)
		O-4–C-34–C-36	108.5(7)
		O-4–C-34–C-35	110.3(7)
		O-3–C-34–C-36	109.1(7)
		O-3–C-34–C-35	111.2(6)
		C-35–C-34–C-36	112.1(7)
		O-71–C-71–N-7	119.8(7)
		N-7–C-71–C-72	116.7(6)
		O-71–C-71–C-72	123.3(6)



C-5–C-6 C-6–C-7 C-7–N-7

Fig. 2. The Newman projections along the C-5–C-6, C-6–C-7, and C-7–N-7 bonds of **10**.

spectra with a FTIR Bomem Michelson MB-120 spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded with a Varian XL-200 or a Bruker AMX-300 spectrometers. EI-mass spectra (70 eV) were obtained with a Kratos MS-80 RFA instrument with the ion-source at 200°C. The composition of ions was confirmed by accurate mass measurements at a resolving power of ≈ 10 000 (10% valley). TLC was performed on Silica Gel 60 F$_{254}$ (Merck) and detection with UV light or by charring with H$_2$SO$_4$. For preparative TLC, Silica Gel PSC-60 F$_{254}$ s (Merck) was used. Column chromatography was performed on Silica Gel 60 (Merck, 63–200 μm). Hydrogenations were achieved in a Gerhardt HY 1000 apparatus or in a Parr Pressure Reactor (600 mL).

*Methyl 7-deoxy-1,2 : 3,4-di-O-isopropylidene-7-nitro-*D-erythro- (**7**) *and* L-threo-(**8**)-α-D-galacto-*octopyranuronates.* — (a) To a cold (0°C), stirred solution of methyl nitroacetate (**1b**) [13] (0.24 g, 2.0 mmol) and 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**5**) [14] (0.52 g, 2.0 mmol) in the minimal amount of dry CH$_2$Cl$_2$ was added fresh activated Silica Gel 60 (Merck, 63–200 μm) (0.12 g). The temperature was left to reach 20°C. Monitoring of the reaction by ^{1}H NMR spectroscopy showed that, after 48 h at room temperature, the *aldehydo*-sugar had been totally consumed (100% conversion). The silica gel was then filtered off and washed with CH$_2$Cl$_2$ (3×10 mL). The filtrate and extracts were joined and the solvent was evaporated to give a syrupy product (0.75 g, 99%). Preparative TLC (3 : 1 EtOAc–hexane) (two irrigations) of a portion (0.14 g) of the crude product afforded a syrupy 59 : 41 mixture of the title isomers (80 mg, 55%); $[\alpha]_D^{25} - 43°$, $[\alpha]_V^{25} - 51°$ (*c* 1, CH$_2$Cl$_2$); λ_{max} (CH$_2$Cl$_2$) 221.3 and 309.2 nm; ν_{max} (film) 1757 (ester C=O), 1564 and 1387 cm^{-1} (NO$_2$). For the ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively. HRMS: *m/z* 362.1094 (calcd for C$_{15}$H$_{23}$NO$_{10}$–CH$_3$: 362.1087). Anal. Calcd for C$_{15}$H$_{23}$NO$_{10}$: C, 47.74; H, 6.14; N, 3.71. Found: C, 47.82; H, 6.21; N, 3.69.

(b) A mixture of **1b** (0.12 g, 1.0 mmol) and **5** (0.26 g, 1.0 mmol) in dry CH$_2$Cl$_2$ was stirred for a few minutes and then kept at room temperature. After 8 h, the aldehyde had totally disappeared (^{1}H NMR) (100% conversion). The solvent was then evaporated to give a syrupy product (0.35 g, 91%), a portion of which (0.19 g) was purified as indicated under (a) to afford a syrupy 1 : 1 mixture (NMR) or **7** and **8** (0.12 g, 56%). For the ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively.

Raney-nickel catalysed hydrogenation of the diastereomeric mixture of the nitroaldols **7** *and* **8** *obtained in the presence of silica gel.* — (a) Hydrogenation (2×10^5 Pa, room temperature) of the mixture of **7** and **8** (2.5 g, 6.7 mmol) in acetic anhydride (12 mL) in the presence of Raney-nickel (8.0 g) was monitored by TLC (4 : 1 EtOAc–hexane). After 7 h, the hydrogenation was stopped, the nickel was removed and the solution was coevaporated with toluene (5 × 20 mL) to give a greenish syrup, which was dissolved in Et_2O and decoloured by washing the ethereal solution several times with H_2O. Evaporation of the dried ($MgSO_4$) ethereal layer afforded 1.9 g of dry, colourless residue. Column chromatography (9 : 1 to 5 : 1 gradient of $CHCl_3$–acetone) of 1.5 g of this residue allowed to isolate, first, methyl 7-acetamido-6-O-acetyl-7-deoxy-1,2 : 3,4-di-O-isopropylidene-D-*erythro*-*α*-D-*galacto*-octopyranuronate (**9**) (0.54 g, 24%); $[\alpha]_D^{17}$ $-47°$ (*c* 1, $CHCl_3$); ν_{max} (film) 3420, 3057 (NH), 1750 (ester C=O), 1684 (amide I), and 1516 cm^{-1} (amide II). For the NMR data, see Tables 1 and 2. Anal. Calcd for $C_{19}H_{29}NO_{10}$: C, 52.89; H, 6.77; N, 3.25. Found: C, 52.64; H, 6.65; N, 2.70. HRMS: *m/z* 431.1802 (calcd: 431.1791).

Eluted second was methyl 7-acetamido-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-*α*-D-*galacto*-octopyranuronate (**10**) (0.54 g, 24%); mp 133–135°C; $[\alpha]_D^{20}$ $-53°$, $[\alpha]_v^{20}$ $-63°$ (*c* 1, CH_2Cl_2); ν_{max} (KBr) 3362, 3289 (OH and NH), 1759 (ester C=O), 1651 (amide I), and 1557 cm^{-1} (amide II). For the NMR data, see Tables 1 and 2. For the X-ray diffraction data, see below and Tables 5 and 6. Anal. Calcd for $C_{17}H_{27}NO_9$: C, 52.43; H, 6.98; N, 3.59. Found: C, 52.62; H, 7.26; N, 3.37.

Conventional treatment of **10** (100 mg, 0.26 mmol) in pyridine (1 mL) with acetic anhydride (1 mL) afforded amorphous methyl 7-acetamido-6-*O*-acetyl-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-*α*-D-*galacto*-octopyranuronate (**11**) (100 mg, 90%); $[\alpha]_D^{23}$ $-94°$, $[\alpha]_v^{23}$ $-109°$ (*c* 0.7, $CHCl_3$); ν_{max} (film) 3320 (NH), 1753 (ester C=O), 1663 (amide I), and 1532 cm^{-1} (amide II). For the NMR data, see Tables 1 and 2. HRMS: *m/z* 416.1553 (calc for $C_{19}H_{29}NO_{10}$–CH_3: 416.1557).

(b) A solution of the mixture of **7** and **8** (4.5 g, 11.9 mmol) in dry methanol (250 mL) was hydrogenated (10 atm) in the presence of Raney-nickel (3.8 g) at room temperature for 24 h. The nickel was filtered off and the filtrate was concentrated to give a residue (4.1 g), which was immediately redissolved in methanol (150 mL) and treated at 0°C with acetic anhydride (20 mL). After 24 h at 0°C and 12 h at room temperature, the mixture was several times coevaporated with toluene in vacuo to give a complex mixture (TLC) as a syrupy residue (3.75 g). An aliquot of this residue (3.5 g) was subjected to column chromatography (1 : 4 to 4 : 1 gradient of EtOAc–hexane), to afford, first, 1,2 : 3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (0.40 g), then methyl 7-acetamido-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-D-*erythro*-*α*-D-*galacto*-octopyranuronate (**12**) (0.19 g, 4.4%) as a syrup, $[\alpha]_D^{30}$ $-5°$ (*c* 1, $CHCl_3$); ν_{max} (film) 3354, 3311 (OH and NH), 1745 (ester C=O), 1660 (amide I), and 1554 cm^{-1} (amide II). For the NMR data, see Tables 1 and 2. HRMS: *m/z* 389.1724 (calcd for $C_{17}H_{27}NO_9$: 389.1678).

Eluted last was methyl 7-acetamido-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-*α*-D-*galacto*-octopyranuronate (**10**) (94 mg, 2.2%), $[\alpha]_D^{30}$ $-43°$ (*c* 1, $CHCl_3$); ν_{max} (film) 3349, 3312 (OH and NH), 1748 (ester C=O), 1651 (amide I), and 1539 cm^{-1} (amide II). For the NMR data, see Tables 1 and 2. HRMS: *m/z* 389.1696.

An intermediate fraction contained 80 mg (1.9%) of a mixture of **10** and **12**.

(c) To a solution of the mixture of **7** and **8** (1.0 g, 2.7 mmol) in glacial acetic acid (6 mL) was added a suspension of Raney-nickel (4.0 g) in the same solvent (8 mL). Hydrogenation of the mixture (2 × 10^5 Pa, room temperature) was monitored by TLC.

After 12 h, the starting material had been totally consumed. The nickel was then filtered off and the filtrate was concentrated to dryness to give a greenish residue, which was dissolved in ether and washed several times with H_2O. The dried ($MgSO_4$) ethereal layer was concentrated to yield a colourless residue (0.60 g), column chromatography of which (20 : 1 $CHCl_3$–MeOH) allowed to isolate, first, 1,2 : 3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.17 g), then methyl 7-amino-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-L-*threo*-α-D-*galacto*-octopyranuronate (**14**) (45 mg, 4.9%); ν_{max}(film) 3497, 3370 (OH and NH), and 1747 (ester C=O). For the ^1H NMR data, see Table 1. HRMS: m/z 332.1327 (calcd for $C_{15}H_{25}NO_8$–CH_3: 332.1345).

Eluted last was methyl 7-amino-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-D-*erythro*-α-D-*galacto*-octopyranuronate (**13**) (0.11 g, 12%); ν_{max}(film) 3548, 3290 (OH and NH), and 1745 (ester C=O). For the ^1H NMR data, see Table 1. HRMS: m/z 332.1340 (calcd for $C_{15}H_{25}NO_8$–CH_3: 332.1345).

An intermediate fraction contained 36 mg (3.9%) of a mixture of both isomers.

Oxazoline ring formation from **13** *and* **14**. — The amino alcohol **13** (75 mg, 0.22 mmol) was dissolved at 0°C in CH_2Cl_2 (1.5 mL) and to this solution was added ethyl iminoacetate hydrochloride (49.2 mg, 0.40 mmol) under N_2. After 6 h at 0°C, the mixture was poured into ice-water (3 mL) and extracted with CH_2Cl_2 (5 mL), then the dried ($MgSO_4$) organic layer was concentrated to give syrupy methyl 7-amino-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-6,7-*O*,*N*-ethylidyne-D-*erythro*-α-D-*galacto*-octopyranuronate (**15**) (60 mg, 72%); ν_{max} (film) 1752 (ester C=O) and 1680 cm^{-1} (C=N). For the NMR data, see Tables 1 and 2. Anal. Calcd for $C_{17}H_{25}NO_8 \cdot 0.75H_2O$: C, 53.04; H, 6.93; N, 3.64. Found: C, 52.94; H, 6.78; N, 3.24. HRMS: m/z 371.1573 (calcd for $C_{17}H_{25}NO_8$: 371.1580).

The same procedure, as applied to the aminoalcohol **14** (40 mg, 0.12 mmol) and ethyl iminoacetate hydrochloride (29.5 mg, 0.24 mmol) in CH_2Cl_2 (1 mL), afforded syrupy methyl 7-amino-7-deoxy-1,2 : 3,4-di-*O*-isopropylidene-6,7-*O*,*N*-ethylidyne-L-*threo*-α-D-*galacto*-octopyranuronate (**16**) (41 mg, 92%); ν_{max} (film) 1745 (ester C=O) and 1670 cm^{-1} (C=N). For the NMR data, see Tables 1 and 2. HRMS: m/z 371.1603 (calcd for $C_{17}H_{25}NO_8$: 371.1580).

*Methyl 2-deoxy-4,5-*O*-isopropylidene-2-nitro-*D*-ribonate* (**17**) *and -*D*-arabinonate* (**18**).— (a) To a mixture of **6** [15] (0.78 g, 6 mmol) and **1b** (0.71 g, 6 mmol), stirred at 0°C for 2–3 min, was added fresh activated Silica Gel 60 (Merck, 63–200 μm) (0.72 g), the temperature was left to reach 20°C and the stirring was continued until NMR showed the complete disappearance of **6** (4 h). The mixture was then extracted with CH_2Cl_2 (3 × 5 mL) and the combined extracts were concentrated to give a colourless, chromatographically homogeneous (TLC, 1 : 1 ether–hexane) syrup (1.25 g, 80%). An aliquot (0.100 g) of this product was purified by preparative TLC (4 : 1 $CHCl_3$–acetone) to afford a 44 : 44 : 6 : 6 mixture of mainly **17** and **18**, with the other two diastereomers, as a viscous, colourless liquid (49 mg, 39%), bp 125°C (0.15 torr); $[\alpha]_D^{25}$ +18°, $[\alpha]_v^{25}$ −8° (*c* 1, $CHCl_3$); ν_{max} (film) 3530–3380 (OH), 1751 (ester C=O), 1566 and 1375 cm^{-1} (NO_2). For the NMR data, see Tables 3 and 4. Anal. Calcd for $C_9H_{15}NO_7$: C, 43.37; H, 6.07; N, 5.62. Found: C, 43.34; H, 6.10; N, 5.26. HRMS: m/z 234.0579 (calcd for $C_9H_{15}NO_7$–CH_3: 234.0610).

(b) An attempt to perform the reaction without any catalyst was unsuccessful: A mixture of **6** (0.39 g, 3 mmol) and **1b** (0.36 g, 3 mmol) was stirred at 0°C for 2–3 min, and then the temperature was left to reach 20°C. Monitoring the reaction by ^{1}H NMR showed that the progress of the reaction was very slow. Thus, the signal of the aldehydic proton of **6** could be clearly observed even after 7 days, when signals of side products started to emerge.

Raney-nickel catalysed hydrogenation of the diastereomeric mixture of nitroaldols **17** *and* **18** *obtained in the presence of silica gel.* — (a) A solution of the crude mixture of **17** and **18** (0.6 g, 2.4 mmol) in dry MeOH (20 mL) was hydrogenated (10^6 Pa) in the presence of Raney-nickel (0.93 g) at room temperature for 24 h (TLC monitoring, 6 : 1 $CHCl_3$–acetone). The nickel was filtered off and the filtrate was concentrated to give a residue (0.19 g), which was immediately redissolved in methanol (12 mL) and treated dropwise at 0°C with acetic anhydride (1.0 mL). After 24 h at 0°C, the solvents were evaporated to afford a syrup (0.19 g), column chromatography of which (9 : 1 to 6 : 1 gradient of $CHCl_3$–acetone) allowed to obtain 22.5 mg (3.5%) of a mixture of methyl 2-acetamido-2-deoxy-4,5-*O*-isopropylidene-D-ribonate (**19**) and -D-arabinonate (**20**) with minor amounts of the other two diastereomers; ν_{max} (film) 3615, 3242 (OH and NH), 1748 (ester C=O), 1651 (amide I), and 1557 cm^{-1} (amide II). For the NMR data, see Tables 3 and 4. HRMS: m/z 261.1224 (calcd for $C_{11}H_{19}NO_6$: 261.1207).

(b) A solution of the mixture of **17** and **18** (2.75 g, 11 mmol) in acetic anhydride (20 mL) was hydrogenated (2×10^5 Pa, room temperature) in the presence of Raney-nickel (8 g) for 24 h. The nickel was then removed and the solution was concentrated to give an oil, an aqueous solution of which was successively treated with ether (5 × 30 mL) and CH_2Cl_2 (3 × 30 mL). The combined, dried ($MgSO_4$) organic layers were concentrated to give an oily residue (1.9 g), an aliquot of which (1.5 g) was subjected to column chromatography (9 : 1 to 5 : 1 gradient of $CHCl_3$–acetone). Eluted first was methyl 2-acetamido-3-*O*-acetyl-2-deoxy-4,5-*O*-isopropylidene-D-ribonate (**21**) or -D-arabinonate (**22**) (0.22 g, 8.7%); ν_{max} (film) 3312 (NH), 1749 (ester C=O), 1682 (amide I), and 1508 cm^{-1} (amide II). For the NMR data, see Tables 3 and 4. HRMS: m/z 288.1085 (calcd for $C_{13}H_{21}NO_7$–CH_3: 288.1078).

Eluted second was a mixture of the two diastereomers **21** and **22** (0.15 g, 6.0%).

Eluted third was **22** or **21** (93 mg, 3.7%); ν_{max} (film) 3292 (NH), 1749 (ester C=O), 1668, 1653 (amide I), and 1506 cm^{-1} (amide II). For the NMR data, see Tables 3 and 4. HRMS: m/z 288.1096 (calcd for $C_{13}H_{21}NO_7$–CH_3: 288.1078).

Eluted last was a mixture of **19** and **20** with $< 5\%$ of the other two diastereomers (0.31 g, 14%); ν_{max} 3340br (NH and OH), 1748 (ester C=O), 1655 (amide I), and 1521 cm^{-1} (amide II). For the NMR data, see Tables 3 and 4. HRMS: m/z 246.0977 (calcd for $C_{11}H_{19}NO_6$–CH_3: 246.0976).

An intermediate fraction contained 0.11 g (4.4%) of a mixture of the products of the third and the last fractions.

(c) To a solution of the mixture of **17** and **18** (2.0 g, 8.0 mmol) in glacial acetic acid (6 mL) was added a suspension of Raney-nickel (6.0 g) in the same solvent (12 mL). The mixture was hydrogenated at 3×10^5 Pa and room temperature for 24 h, the nickel was then filtered off, and the filtrate was concentrated to give a greenish residue. An aqueous solution of this residue was filtered through a bed of Silica Gel 60 (Merck, 63–200 μm), which adsorbed much more strongly the nickel(II) salts than the reduction products; these were desorbed percolating thoroughly with absolute ethanol. Evaporation of the solvent yielded a syrupy residue, TLC of which (15 : 1 $CHCl_3$–MeOH) showed the presence of two diastereomers: methyl 2-amino-2-deoxy-4,5-*O*-isopropylidene-D-ribonate (**23**) and -D-arabinonate (**24**) (0.95 g, 54%); ν_{max} (film) 3337br (OH and NH) and 1738 cm^{-1} (ester C=O).

Oxazoline ring formation from the mixture of **23** *and* **24**. — The crude mixture of aminoalcohols **23** and **24** (0.75 g, 3.4 mmol) was dissolved at 0°C in dry CH_2Cl_2 (30 mL) and ethyl iminoacetate hydrochloride (0.84 g, 6.8 mmol) was added under argon. The reaction mixture was stirred at 0°C for 6 h, then poured into ice-water (30 mL) and extracted with CH_2Cl_2 (3×30 mL). The combined, dried ($MgSO_4$) extracts were concentrated to give a residue (0.40 g), which was purified by column chromatography (30 : 1 to 10 : 1 gradient of $CHCl_3$–MeOH) to afford a mixture of *cis* and *trans* oxazolines: methyl 2-amino-2-deoxy-4,5-*O*-isopropylidene-2,3-*N*,*O*-ethylidyne-D-ribonate (**25**) and -D-arabinonate (**26**) (154 mg, 18%); ν_{max} (film) 1752 (ester C=O) and 1680 cm^{-1} (C=N). For the NMR data, see Tables 3 and 4. HRMS: m/z 242.1029 and 228.0878 (calcd for $C_{11}H_{17}NO_5$–H: 242.1028, and for M–CH_3: 228.0872).

Crystal analysis for **10**.[1] — The compound crystallised as colourless prisms. A crystal of dimensions $0.32 \times 0.28 \times 0.60$ mm was used for X-ray investigations, that belonged to the orthorombic system with systematic absences consistent with the space group $P2_12_12_1$. Accurate cell dimensions and crystal orientation matrix, determined on a ENRAF CAD-4 diffractometer by least-squares treatment of the setting angles of 25 reflections in the range $6 < \theta < 15°$, were $a = 14.164(3)$, $b = 24.697(5)$ and $c = 5.703(1)$ Å. The unit cell volume V was 1995.0(6) $Å^3$, $Z = 4$, $D_c = 1.30$ g cm^{-3}, $F(000) = 832$, and the absorption coefficient μ was 0.098 mm^{-1}.

Intensity data were collected in the $\omega - 2\theta$ scan mode, using Mo-K_α radiation up to $\theta = 30°$ for a total of 3304 reflections ($h - 0$ to 19, $k - 0$ to 34, $l - 0$ to 8). Three standard reflections $(\bar{1}\ 0\ 3)$, $(3\ 9\ 1)$ and $(\bar{1}\ 6\ 1)$, monitored every 100 reflections, showed statistical fluctuations; 1433 observed reflections $[I > 3\sigma(I_0)]$ were used for structure determination. Data were corrected for Lorentz and polarisation factors, extinction factors were ignored, and an empirical absorption correction following the DIFABS procedure [16] was applied to the isotropically refined data.

The structure was solved by the direct methods program MULTAN80 [17]. The E-map, computed for the phase set with the lowest combined figure of merit, showed all the non-hydrogen atoms, and the initial residual calculated for these atom positions was 0.163. The structure was refined isotropically ($R = 0.091$, unit weights) and then anisotropically, minimising the function $\Sigma\omega(|F_0| - |F_c|)^2$, where $\omega = 1/\sigma^2(F_0)$, together with anisotropic refinement of the overall scale factor. Subsequent difference Fourier syntheses revealed most of the hydrogen atoms, and those remaining were included in the later refinement in the positions calculated geometrically. The tempera-

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[1] Lists of the hydrogen coordinates and thermal parameters have been deposited with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK, citing the reference Carbohydrate Research, 271 (1995) 79–99.

Table 6
Atomic coordinates and thermal parameters for non-hydrogen atoms

Atom	x/a	y/b	z/c	U_{eq} [a]
O	0.0706(3)	0.6556(2)	0.1098(9)	57(1)
O-1	−0.0672(3)	0.6062(2)	0.0974(12)	75(2)
O-2	0.0044(4)	0.5468(2)	0.3386(14)	90(2)
O-3	0.2309(4)	0.5623(2)	0.0540(12)	82(2)
O-4	0.2687(3)	0.6369(2)	0.2610(12)	73(2)
O-6	0.1817(3)	0.7164(2)	0.6133(11)	67(2)
O-8	0.0737(7)	0.8448(3)	0.5064(16)	115(3)
O-71	−0.1428(4)	0.7484(3)	0.4605(11)	87(2)
O-81	0.1034(5)	0.8155(2)	0.1439(12)	85(2)
N-7	−0.0009(4)	0.7428(3)	0.6220(12)	69(2)
C-1	0.0297(5)	0.6075(3)	0.0377(15)	64(2)
C-2	0.0682(6)	0.5561(3)	0.1498(19)	75(3)
C-3	0.1673(5)	0.5616(3)	0.2476(20)	74(3)
C-4	0.1865(5)	0.6156(3)	0.3702(16)	64(2)
C-5	0.1059(5)	0.6555(3)	0.3454(13)	56(2)
C-6	0.1357(4)	0.7138(3)	0.3942(13)	56(2)
C-8	0.0747(6)	0.8091(3)	0.3675(18)	72(3)
C-7	0.0477(5)	0.7508(3)	0.4033(14)	62(2)
C-12	−0.0855(6)	0.5640(4)	0.2592(18)	80(3)
C-13	−0.1419(8)	0.5879(6)	0.4622(22)	114(5)
C-14	−0.1363(8)	0.5182(4)	0.1364(32)	119(5)
C-34	0.3087(5)	0.5956(3)	0.1227(18)	72(3)
C-35	0.3801(7)	0.5639(4)	0.2630(20)	90(3)
C-36	0.3519(7)	0.6211(5)	−0.0931(18)	89(3)
C-71	−0.0946(5)	0.7424(3)	0.6377(14)	62(2)
C-72	−0.1356(6)	0.7314(4)	0.8750(16)	78(3)
C-81	0.1362(10)	0.8680(4)	0.0712(27)	113(5)

[a] $U_{eq} = (1/3)\Sigma[U_{ij} a_i^* a_j^* a_i a_j \cos(a_i a_j)] \times 10^4$.

ture factors of the hydrogen atoms were fixed with the equivalent U_{iso} values of the carrier atoms. The final R and R_w values were 0.051 and 0.070, respectively. In the final cycle of the refinement, the average shift/e.s.d. was 0.079. The final difference Fourier synthesis showed maximum and minimum electron densities of 0.20 and −0.30 e Å^{-3}, respectively. The atomic scattering factors used were taken from the International Tables for the X-Ray Crystallography [18], and all calculations performed with the X-ray system of crystallographic programs [19]. The final coordinates are listed in Table 6.

The bond lengths (Å) and angles (°) in Table 5 were calculated by the program PARST, written by Nardelli [20].

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