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SYNTHESIS OF AMINO SUGARS VIA ISOXAZOLINES

NITRILE OXIDE–FURAN ADDUCTS AS KEY INTERMEDIATES IN THE ISOXAZOLINE ROUTE TOWARDS NOVEL AMINO SUGAR DERIVATIVES[1–3]

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Abstract—New variations for 1,3-dipolar nitrile oxide cycloadditions to reluctant dipolarophiles furan and 2-methylfuran are presented. The furoisoxazoline adducts **6** and **7** are shown to represent highly advanced, yet versatile precursors for derivatives of novel C_6 and C_7 amino sugar derivatives, accessible by subsequent highly stereoselective modification (addition of HO/OCH_3 or HO/OH) and/or $LiAlH_4$ reduction.

INTRODUCTION

Isoxazolines with additional oxy functions play a key role in a general scheme to synthesize amino polyols, amino sugars or amino acids from respective alkene and nitrile oxide building blocks.[6] In each step of the *isoxazoline route*[7] (cycloaddition, chemo-regioselective modification, and reductive cleavage) significant stereoselection is achieved.[6] With fully substituted aminodeoxyaldoses as the target class (cf. **A**), the specific problem to be solved at the isoxazoline precursor stage is to get access to the two series of 4-oxygenated isoxazolines, i.e. **B** and **C** of Scheme 1.

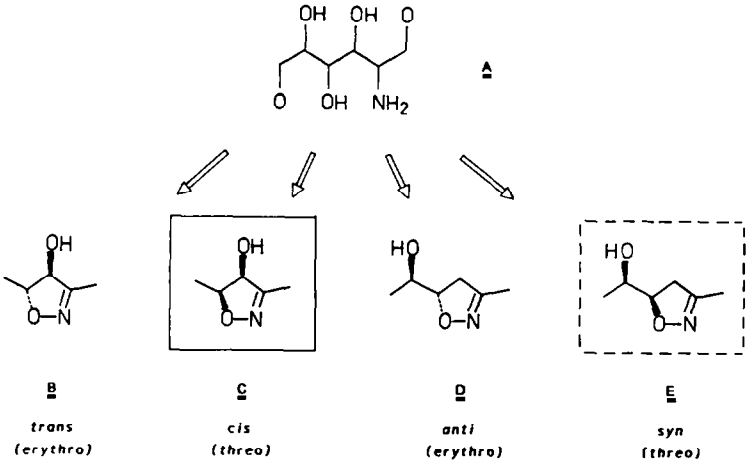
The 4,5-*trans*(*erythro*) configuration, as depicted in **B**, could be obtained by regio- and stereoselective *endo*-deprotonation/hydroxylation.[9] Subsequent reduction by lithium aluminum hydride[10,11] gave access to the *ribo* series (synthesis of D,L-phytosphingosine).[9,11] It seemed equally desirable to build up the 4,5-*cis* arrangement, as shown by **C**, as this would create *xylo* and/or *arabino*/*lyxo* units on reduction.[3,4,6]

Another problem concerns generating either relative configuration at the fourth stereocentre, located in the side-chain of respective isoxazolines, cf. **D** and **E**. Cycloadditions to derivatives of α-chiral allylic alcohols were shown to lead to *erythro* products **D** preferentially,[12] which are precursors to *ribo* compounds such as D-lividosamine.[13] However, the strategy leading to intermediates of type **C**, detailed below, implies an obvious solution to generate the (additional) *threo*(*syn*) relationship as shown in **E**.

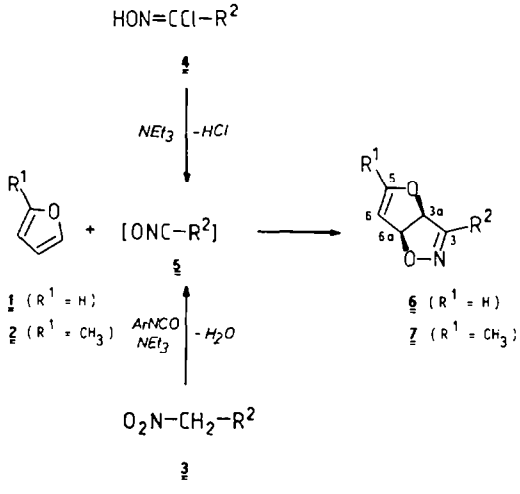
NITRILE OXIDE–FURAN CYCLOADDITIONS

Cycloaddition constitutes the most straightforward approach to *cis*-4-oxygenated isoxazolines **C** (and *trans* isomers **B**). Yet, nitrile oxides are known to cycloadd to vinyl ethers or esters to furnish the undesired 5-oxygenated derivatives with high regioselection.[14] This is well rationalized for the parent compounds using MO arguments,[14–17] and apparently applies likewise to variously substituted enol derivatives that we have prepared and submitted to nitrile oxide cycloadditions.[4]

Our efforts, based on results of *aryl* nitrile oxide reactions with furans as reported by Caramella, Grünanger, Houk and co-workers[18,19] at first gave low yields of monocycloadducts when *aliphatic* nitrile oxides were used. This is not surprising, as nitrile oxide dimerization to give furoxans is the usual, dominating reaction when sluggishly reacting dipolarophiles are



Scheme 1.[8]



Scheme 2.†

† Racemic compounds, here and in the following.

used under the "standard" conditions of the Mukaiyama procedure.[15,20] A further difficulty in these reactions is the work-up, as the by-products N,N'-diphenyl urea and others[21] often hamper the isolation of the pure adducts. A systematic study then established optimum conditions to obtain furan adducts **6** from aceto- and benzonitrile oxides **5d** and **e**, respectively, as well as from glycolonitrile and glyoxylonitrile oxide derivatives **5a–c** (Scheme 2 and Table 1).

The addition of boron trifluoride–ether complex in catalytic amounts (procedures D and G, see Table 1) led to a major improvement in the benzo- and acetonitrile oxide cases. The corresponding 3-phenyl- and 3-methyl-3a,6a-dihydrofuro[2,3-d]isoxazoles ("furo-isoxazolines") **6e** and **d**, respectively, could be isolated easily, as the usual furoxan formation was not observed.[22] This could not be extended to the reactions of the other nitrile oxides **5a–c**, however, probably due to the lability of the protecting groups towards the Lewis acid catalyst. For these nitrile oxides the use of dilution conditions with rather long addition/reaction periods and 1,4-diisocyanatobenzene as the dehydrating agent proved successful (see Table 1, procedures B and C). Satisfactory results were obtained, regardless of the purity of the diisocyanate used: (a) reactions with a very impure sample (assay *ca* 30%; amorphous, almost insoluble) could be run in an autoclave for 2–4 weeks, producing up to 20 g of adduct in one run (Table 1, procedure B); (b) with pure diisocyanate (crystalline) the reactions proceeded faster; the nitro compounds **3a–c** were added to a suspension of the diisocyanate in a dilution set-up with refluxing furan **1** or 2-methylfuran **2**, and the adducts were obtained pure after flash chromatography (procedure C, Table 1 and Experimental).

The successful outcome of these reactions, optimized in the course of several years, constitutes the basis for many synthetically useful, highly regio- and stereoselective transformations of the furoisoxazolines,[3,4,6] some of which are described below.

ADDITIONS TO THE FURAN PART OF FUROISOXAZOLINES

Furoisoxazolines **6** and **7** correspond to isoxazolines of type **C** (Scheme 1); they represent highly advanced precursors of racemic amino sugars, as seen by

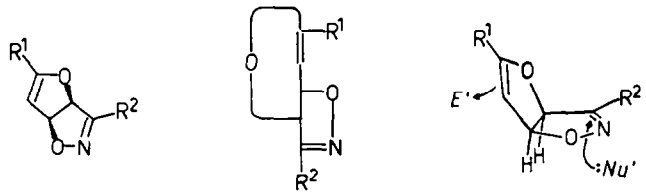
Table 1. Yield of furoisoxazolines **6, 7**

Compound	R^1	R^2	Equiv. of **1** or **2**	Yield (%)	Procedure[a]
6a	H	CH_2O^tBu	10	25.5	A
			56	40	B
			240	*66–78*	C
6b	H	$CH(OEt)_2$	140	45	B
			240	*68–76*	C
6c	H		80	23	B
			240	*71*	C
6d	H	CH_3	28	7	A[b]
			28	*28*	D
6e	H	Ph	1400	(91 GLC)	E[c]
			69	12.2	E[c]
			11	18.5	F
			70	*48*	G
7a	H_3C	CH_2O^tBu	40	44	B
			200	*68*	C
7b	H_3C	$CH(OEt)_2$	57	52	B
			200	*68*	C
7c	H_3C		61	48	B
			200	*61*	C

[a] For details see Experimental. Procedure A: phenyl isocyanate, dilution set-up. Procedure B: 1,4-diisocyanatobenzene (assay 30%); reaction with **1** run in autoclave at 70–80°, with **2** in flask at reflux. Procedure C: diisocyanate (pure); dilution set-up. Procedure D: carried out as in A, but $F_3B \cdot OEt_2$ added. Procedure E: Huisgen's *in situ* method, HCl elimination with Et_3N, addition time 2 hr (cf. Ref. 14*a*); work-up by chromatography (preparative run). Procedure F: similar to E, but dilution set-up. Procedure G: as in F, but $F_3B \cdot OEt_2$ as catalyst.

[b] Ref. 4*a*.

[c] Ref. 18*b*.



6, 7 F G

Scheme 3.

comparison with the classic Fischer projection formula F (Scheme 3).[23–26]

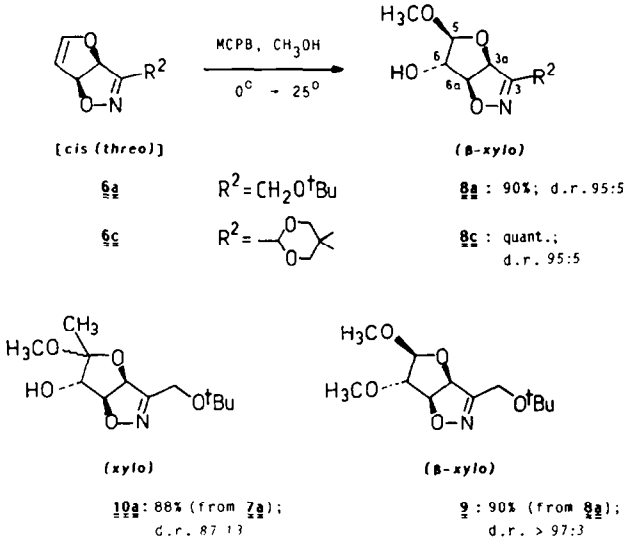
Due to the nature of the two double bonds, electrophiles E′ should add to the electron-rich C=C bond of the dihydrofuran moiety, whereas nucleophiles like "hydride" from $LiAlH_4$ will attack the C=N bond of the isoxazoline part. For both, approach to the bicyclic structure from the *exo* face will be highly preferred.

Addition of HO/OCH_3 *by oxidation with MCPB in methanol*

The furoisoxazolines **6** and **7**, respectively, are labile towards acid: attempted methanol addition in the presence of a catalytic amount of *p*-toluenesulfonic acid caused **6a** to open to the corresponding α-furyl oxime. *m*-Chloroperbenzoic acid in methanol though, gave the desired methyl *trans*-hydroxyfuranoside **8a** in 90% yield, in a 95:5 diastereomer ratio (d.r.).† This parallels literature reports on the analogous reaction with dihydropyran (*trans/cis* 90:10),[27] and is rationalized by prior *exo*-epoxidation and, again, highly stereoselective epoxide opening by methanol[27] (Scheme 4).

Treatment of the furanoside **8a**, an analytically pure oil, with methyl iodide/potassium hydroxide in DMSO[28] gave a crystalline methyl ether, **9**, in 90% yield, as a single diastereomer. The MCPB oxidation of the furoisoxazoline acetal **6c** likewise furnished the protected dialdehyde **8c** in high yield, as a 95:5 anomer mixture with *xylo* configuration. Oxidation of the methylfuran adduct **7a** proved less selective, as the corresponding methyl furanoside **10a** (88%) consisted of an 87:13 mixture.

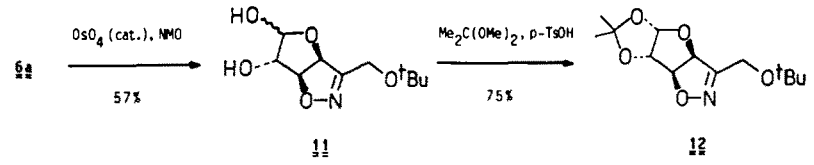
The configuration of these furanosides becomes evident from ^1H- and ^{13}C-NMR data, and from the comparison of these with literature data of related compounds.[26] Notably, the ^1H-NMR spectra of **8a**, **c**



Scheme 4.

† To indicate the (dia)stereoselectivity of a reaction, we prefer the use of *(dia)stereomer percent ratios*. In our view, this is more useful than (i) numbers like 3.7:1, 19:1, 240:1, etc.; (ii) diastereoselectivity expressed by "d.s.", i.e. the main diastereomer's percent figure [cf. S. Thaisrivongs and D. Seebach, *J. Am. Chem. Soc.* **105**, 7407 (1983), footnote 13] or (iii) the use of "diastereomer excess" figures "d.e." (likewise: "e.e."). The use of diastereomer percent ratios, by contrast, directly relates to the yield attainable; it also favours the evaluation of these figures in terms of free enthalpy differences of diastereomeric transition states.

and **9** show singlets for the absorptions of H-5 and H-6 (for the numbering see Scheme 4), indicative of a *trans*, *trans* arrangement of the H atoms at C-5, C-6 and C-6a. Further, the ^{13}C-NMR absorptions of the anomeric carbon atoms at *ca* 110 (major isomers) and 103 ppm (minor isomers) for **8a** and **c** show that the 5-OMe and 6-OH substituents of the furanoside part must be arranged in a *trans* fashion in the major, and *cis* in the minor components. The reference values, taken from β/α-methyl *xylo*- and *lyxo*-furanosides, are *ca* 109.5 and



Scheme 5.

103 ppm for the anomeric carbon atoms (*β*-D-*xylo*: 109.7, *α*-D-*lyxo*: 109.2, both with MeO/OH *trans*; *β*-D-*lyxo*: 103.3, *α*-D-*xylo*: 103.0 ppm, for *cis* arrangements).[29] Considering the *cis*-fusion of the two 5-membered rings[30] (J_{3a6a} = 7.5–8 Hz for **8a**, **c**, **9** and **10a**), the main products of these oxidations, **8a** and **c** (and **9**), can safely be assigned the *β*-*xylo* configuration. Accordingly, the major isomer **10a** obtained by oxidation of the methylfuran adduct **7a**, is assigned the *xylo* configuration also. The minor isomer (J_{6a} = 3–5 Hz) may belong to the *lyxo* series. The relative configuration at the anomeric centre of **10a** could not be established.

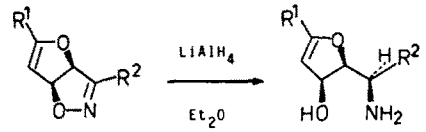
Addition of HO/OH *by oxidation with osmium tetroxide/NMO*

The bis-hydroxylation of the C=C enol ether bond of **6a** was effected with the osmium tetroxide/N-methyl morpholine-N-oxide system,[29] which had been applied successfully in the furan/nitrone cycloadduct series.[23] A 57% yield of a 1:1 mixture of anomers **11** resulted; this, on ketalization with dimethoxypropane/*p*-toluenesulfonic acid, afforded a single acetonide **12**, as judged from ^{13}C-NMR. The ^{1}H-NMR couplings of **12** indicated the *anti*-fusion of the tricycle corresponding to the *α*-*xylo* configuration (Scheme 5), in accord with literature data.[23,26] Thus, both the *β*- and *α*-anomer of the *xylo* series were accessible from furoisoxazoline **6a**.

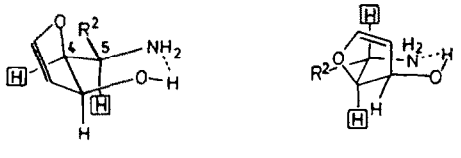
ADDITION TO THE ISOXAZOLINE PART OF FUROISOXAZOLINES

Synthesis of xylo *and* ido-*aminodeoxysugar derivatives by LAH reduction*

The furoisoxazolines **6** and **7** were reduced with lithium aluminum hydride (LAH) in ether, according to the previously reported procedure.[10,32] As expected from earlier results with related substrates (cyclopentane analogues),[10,32] the corresponding amino alcohols **13** and **14**—i.e. aminodeoxy furanoid glycals



6, **7** (*threo*) **13**, **14** (*xylo*)



H (*xylo*) **I** (*lyxo*)

Table 2. Stereoselective reduction of furoisoxazolines **6**, **7** to produce furanoid aminodeoxy glycals **13**, **14**

Compound	R^1	R^2	Yield (%)	d.r.[a]
13a	H	CH_2O^tBu	86	>95:5
13b	H	$CH(OEt)_2$	88[b]	94:6
13c	H		72[c]	94:6
13d	H	CH_3	35	>95:5
13e	H	Ph	—[d]	—
14a	H_3C	CH_2O^tBu	63	>97:3
14b	H_3C	$CH(OEt)_2$	67	94:6
14c	H_3C		72	93:7

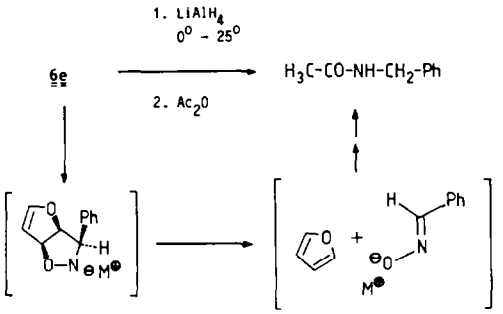
[a] From peak ratios/integrals of ^{13}C-NMR recordings at 100.6 MHz (**13a** at 22.6 MHz); cf. Ref. 32.
[b] Slightly deviating elemental analysis.
[c] 84% of spectroscopically pure crude product.
[d] See text.

—generally were obtained in good yield and diastereoselection (Table 2).

The ^{13}C-NMR data of these dihydrofuran derivatives **13** and **14**, on comparison with those of the cyclopentane series[32] (*xylo*/*lyxo* ≥ 96:4), did not permit unambiguous assignment of their configurations. However, the small but very consistent shift differences of the signal pairs of diastereomers confirm that the main isomer in each case had the *same relative* configuration. The ^{1}H-NMR data are more informative. The coupling constants $J_{4,5}$ (for **13b–d**; $J_{2,3}$ for **14b**, **c**) of the major diastereomers show values of 2.5–3.0 Hz throughout. This is in accord only with the *xylo* arrangement, since by analogy with other *γ*-amino alcohol diastereomers,[13,32] these amino alcohols are likely to exist as H-bridged species with preferred conformations **H** and **I** as depicted left. A more conclusive argument for the predominant formation of the *xylo* isomers is, that hydride delivery from the *exo* face corresponds to the major pathway observed in all LAH reductions of bicyclic or *cis*-4,5-disubstituted isoxazolines met so far.[4,32–34]

As seen from Table 2, the d.r. figures of the methyl and t-butoxymethyl products **13d**, **a** and **14a** are somewhat higher than those found for the acetals **13b**, **c**, **14b**, and **c**. In terms of energy ($\Delta\Delta G^{\ddagger}$) this represents an effect of *ca* 0.5 kcal mol^{-1} (**13d** vs **14c**). This decrease in stereoselectivity on adding ether functions in the isoxazoline 3- or 5-side-chains has been encountered before.[11,13]

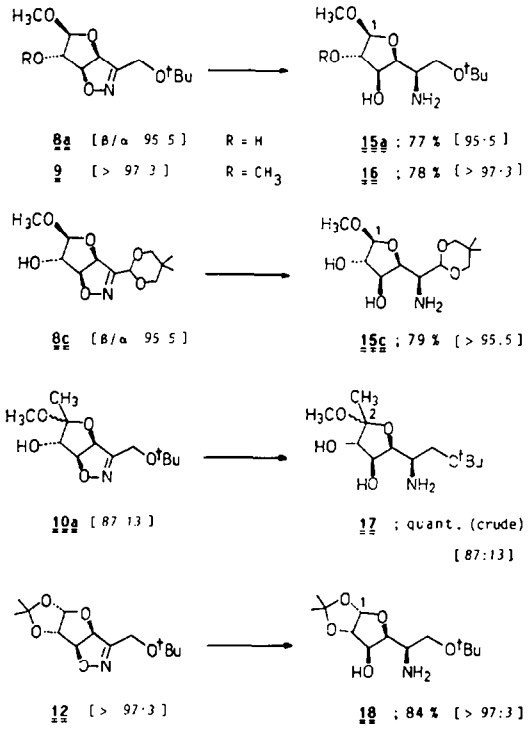
The LAH reduction of the phenyl compound **6e** failed to produce any of the expected amino alcohol. Work-up with acetic anhydride gave a mixture containing up to 50% of N-benzylacetamide, isolated by flash chromatography and identified by NMR, IR and m.p. comparison with an authentic sample. We



Scheme 6.

interpret this to be the result of a novel anionic [2 + 3$^{\ominus}$] cycloreversion,[35] taking place after hydride addition to the C=N bond. The intermediate, with a severely crowded *endo*-phenyl group, collapses to give the "aromatic" furan and a phenyl-stabilized oximate, which is reduced further by excess LAH (Scheme 6).

The methyl furanosides **8a**, **c**, **9**, **10a**, and the acetonide **12** were reduced successfully by the usual procedure, see Scheme 7. The diastereomer composition of the products in each case corresponded to that of the starting compounds. This again demonstrates uniform hydride delivery to the *exo* face (*vide infra*) of the *cis*-fused bi- or tricyclic isoxazolines. The values of the coupling constants $J_{4,5}$ of 4.0, 3.3, and 2.0 Hz in the spectra of **15a**, **16**, and **18**, respectively, agree well with that expected for a *threo* (*anti*) configuration at these centres. For a related compound of the *gluco* series (nojirimycin), epimeric at C-5 (CH—NH_2), a value of 8.7 Hz was reported.[23] The couplings in the



Scheme 7. Stereoselective synthesis of aminodeoxy furanosides.

furanose part show the relative configuration there unchanged. The furanosides **15a**, **16**, and the acetonide **18** are thus assigned the *β-ido* and *α-ido* configuration, respectively, with conformations corresponding to that shown by **H**.

The configuration of the 6-amino-1,6-dideoxy-ketoheptose derivative **17** cannot be deduced on this basis, as the respective coupling amounts to 6.0 Hz. However, by analogy with the steric course of LAH reductions of the other cases, the *ido* configuration of the major diastereomer seems likely. The same argument applies to the dialdose derivative **15c**. In this case only a poorly resolved ^{1}H-NMR spectrum was obtained. However, the ^{13}C-NMR chemical shift values, in particular that for C-4, strongly suggest the same configuration, i.e. *ido*, when compared with those obtained from **15a** (Table 3).

To summarize some of the merits of the approach outlined, *xylo* furanoid glycals of aminodeoxy aldoses, dialdoses or ketoaldoses are accessible in two steps, with high stereoselectivity, and overall yields of 41 (**14b**)–67% (**13a, b**). With MCPB oxidation included, 3-step routes to 5-amino-5-deoxy-*ido*-furanosides of both the α- and β-type are at hand, with 28–51% overall yields (for **18** and **15a**, respectively); the *ido*-dialdose furanoside **15c** is prepared in 69% from the nitroacetaldehyde acetal **3c**. Besides the potential use of these compounds as versatile intermediates, it is worth noting that these compounds are (racemic) 5-epimers/analogues of nojirimycin (D-*gluco* series), a potent inhibitor of intestinal mammalian di- and oligosaccharases.[37] If desired, removal of the t-butyl or neopentylidene protecting groups should be feasible (for the former, this has been successful with the case of 4-deoxyristosamine,[38] for the latter in the course of a synthesis of D-lividosamine[13]). The synthesis of *enantiomerically pure* amino sugars (derivatives) by this approach, on the other hand, seems difficult, as preliminary experiments with *R*-glyceronitrile oxide acetonide/2-methylfuran gave a 1:1 mixture of adducts.[39]

CONCLUSION

Furoisoxazolines **6** and **7**, obtained in one step by cycloaddition of aliphatic nitrile oxides with furan **1** or 2-methylfuran **2**, are precursors in the synthesis of racemic amino sugars of both familiar and novel structures. Additional reactions to the enol ether C=C bond of these cycloadducts, as described, include the highly stereoselective attachment of HO/OCH_3 and HO/OH groups.[40] Due to the shape of the [3.3.0]-bicyclic skeleton of furo- and dihydrofuro-isoxazolines, LAH reductions likewise show high diastereoselection, to lead to a variety of amino sugar derivatives of the *xylo* and *ido* series, respectively.

This approach lends itself to many variations, in which many of the following features may be combined at will.

(1) Synthesis of amino sugars of different chain length as determined by choice of building blocks.

(2) Choice of oxidation states at both the nitrile oxide and the furan termini.

(3) Production of furanoid glycals, or of β- or α-furanose structures.

(4) As indicated,[6] oxidative C=C fission at the

Table 3. ^{13}C-NMR chemical shifts of furanoid glycals **13**, **14**, and furanose derivatives **15–18**[a]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	Other
13a	148.5	106.3	83.0	74.2	51.0	65.2	t-Bu: 27.5, 73.4
13b	148.3 (148.6)	106.4 (104.9)	80.7 (82.1)	74.3 (73.5)	52.8 (54.0)	104.0 (102.5)	$(OEt)_2$: 15.2, 62.7, 63.7
13c	148.4 (148.7)	106.1 (104.4)	80.6 (81.8)	74.1 (73.1)	53.3 (54.1)	101.7 (100.2)	CMe_2: 21.5, 23.0, 30.1; CH_2: 76.9
13d	148.8	106.3	86.3	73.6	46.2	22.6	
15a	109.9 (102.6)	80.6 (78.5)[b]	78.1	81.6 (78.9)[b]	52.0 (51.7)	64.8 (63.5)	t-Bu: 27.5, 73.2; OMe: 55.6 (55.8)
16	108.0	91.2	75.8	81.5	52.2	65.5	t-Bu: 27.6, 73.2; 2 OMe: 55.6, 57.6
15c	111.2	81.5	78.7	82.0	55.2	102.9	CMe_2: 21.9, 23.4, 31.1; OMe: 56.0; 2 CH_2: 78.1, 78.2
18	105.1	85.8	77.4[b]	78.5[b]	52.0	65.8	t-Bu: 27.5, 73.1; CMe_2: 26.3, 26.9, 111.3
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	
17	16.7 (19.7)	109.8 (103.4)	81.8 (79.7)	78.9	82.2 (85.1)	52.2 (51.6)	63.9 (64.9)	t-Bu: 27.5, 73.1; OCH_3 48.8 (48.6)
14a	13.8	158.4	101.5	84.3	75.2	51.0	65.0	t-Bu: 27.5, 73.3
	C-7	C-6	C-5	C-4	C-3	C-2	C-1	
14b	13.7	158.3 (158.7)	101.8 (100.5)	81.6 (83.0)	75.6 (74.8)	53.1 (54.2)	104.2 (104.0)	$(OEt)_2$: 15.1, 15.7, 62.9, 63.7
14c	13.8	158.4 (159.0)	101.9[b] (100.4)[b]	81.7 (82.4)	75.4 (74.5)	53.7 (54.2)	101.7[b] (100.2)[b]	CMe_2: 21.7, 23.0, 30.3; CH_2: 77.0

[a] Mostly recorded as $CDCl_3$ solutions at 100.6 MHz (see Experimental); δ in ppm; ( ): minor isomer.
[b] Tentative assignment.

furoisoxazoline stage results in chain-shortening at the furan terminus, to give rise to C_5 derivatives from furan/or 2-methylfuran/C_2-nitroalkane building blocks. These extensions of the above approach, including means to achieve stereo*control* in the isoxazoline reduction, will be the subject of a future report.[40]

EXPERIMENTAL

For general remarks see Ref. 13 and earlier papers cited therein.

Starting materials

Preparation of nitrile oxide precursors **3a**, **b**,[41] **c**, and **4d**, see procedures and quotes given in Ref. 13.

Furoisoxazolines **6** *and* **7**

3 - t - *Butoxymethyl* - 3*a*,6*a* - *dihydrofuro*[2,3 - d]*isoxazole* (**6a**); *Procedure A*: 30 ml (330 mmol) of phenylisocyanate and 20 g (135 mmol) of **3a** in a dilution set-up were added to a soln of 1 ml (3.6 mmol) of Et_3N in 100 ml of furan (**1**) at reflux (50–60°; addition rate *ca* 1.2 mmol h^{-1} for **3a**, *ca* 7 mmol h^{-1} for isocyanate; total *ca* 100 hr). The ppt formed was filtered off, and excess furan removed by distillation to leave 17.82 g of a brown oil. Kugelrohr distillation (95°/0.05 Torr) gave 13.47 g of a yellow oil, consisting of **6a** and furoxan (2.2:1 by ^{1}H-NMR). Fractional distillation (Spaltrohr column) afforded 6.78 g (25.5%; b.p. 80°/0.05 Torr) of **6a** as a slightly yellow, analytically pure oil. IR (film): 3100 (w), 2980, 1610, 1395, 1370, 1190, 1050, 920, 890, 810, 720 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.26 [$C(CH_3)_3$], 4.14 and 4.34 (AB, CH_2), 5.26 (6-H), 5.78 (6a-H), 5.88 (3a-H), 6.56 (5-H); coupling constants: $J_{3a}J_{6a}$ = 8.5, J_{56} = 3, J_{56a} = 1, J_{66a} = 2, J_{AB} = 8.5 Hz. ^{13}C-NMR ($CDCl_3$): δ 27.3 [$C(\underline{C}H_3)_3$], 55.4 (CH_2), 74.2 [$\underline{C}(CH_3)_3$], 86.7 and 88.8 (C-3a, C-6a), 101.0 (C-6), 148.9 (C-5), 154.4 (C-3). (Found: C, 60.76; H, 7.57; N, 7.46. Calc for $C_{10}H_{15}NO_3$ (197.2): C, 60.90; H, 7.67; N, 7.10%.)

Procedure B: 36.75 g (250 mmol) of **3a**, 112 g of 1,4-diisocyanatobenzene (Bayer, assay *ca* 30%), 2 ml (14.4 mmol) of Et_3N, and 11 (14 mol) of furan (**1**), were stirred at 70–80° for 24 hr in a 2 l autoclave. On distillation of the mixture excess furan (780 ml) was recovered, the residue treated with 1 l of CH_2Cl_2, filtered and concentrated *in vacuo*. This left 35.78 g of a slightly yellow oil (**6a**:furoxan 4:1, from ^{1}H-NMR); fractional distillation as above gave 19.67 g (40%) of analytically pure **6a**.

Procedure C: A soln of 294 mg (2.0 mmol) of **3a** in 25 ml of **1** at 50° bath temp by means of a dilution set-up was added to a suspension of diisocyanate (641 mg, 4.0 mmol; pure, with m.p. 91–92°) and Et_3N (0.1 ml, 0.72 mmol) in furan (10 ml; total *ca* 480 mmol) within 2 d and stirred at 25° for another 3 d. The mixture was filtered through silica and concentrated to give 412 mg of a yellow oil, of which 250 mg were submitted to flash chromatography on silica (pet ether/EtOAc 95:5) to afford 186 mg (78%) of colorless, pure **6a** and 20 mg (12%) of 4,5-bis-(t-butoxymethyl)furoxan [^{1}H-NMR ($CDCl_3$): δ 1.26 and 1.29 (CH_3), 4.42 and 4.56 (CH_2)]. A 10 mmol run gave 1.29 g (66%) of pure **6a**.

3 - *Diethoxymethyl* - 3a,6a - *dihydrofuro*[2,3 - d]*isoxazole* (**6b**): According to *Procedure C*, a 2 mmol run gave 498 mg of crude material as a brown oil, of which 300 mg were purified as above; yield of **6b** 194 mg (76%), pale yellow oil; b.p. 90–93°/0.05 Torr. A 10 mmol run gave 68%, a 150 mmol run (*Procedure B*) gave 14.35 g (45%; 55% based on **3b** consumed) of analytically pure **6b**. IR (film): 3100 (w), 2980, 1600, 1050 (sb), 900 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.23 (2 CH_3), 3.36–3.40 (2 CH_2), 5.33 [$C\underline{H}(OEt)_2$], 5.26 (dm, 6-H), 5.80 (dm, 6a-H), 5.93 (d, 3a-H), 6.63 (dm, 5-H); coupling constants: J_{3a6a} = 8.5, J_{56} = 2.5 Hz. ^{13}C-NMR ($CDCl_3$): δ 15.0 and 15.1 (CH_3), 63.2 and 63.3 (CH_2), 88.0 and 88.2 (C-3a, C-6a), 96.9 [$\underline{C}H(OEt)_2$], 100.8 (C-6), 149.5 (C-5), 153.6 (C-3). (Found: C, 56.25; H, 7.38; N, 6.53. Calc for $C_{10}H_{15}NO_4$ (213.2): C, 56.33; H, 7.09; N, 6.57%.)

3 - (5,5 - *Dimethyl* - 1,3 - *dioxan* - 2 - *yl*) - 3a,6a - *dihydrofuro*[2,3 - d]*isoxazole* (**6c**). From 1.752 g (10 mmol) of **3c** in 125 ml of furan, with 3.203 g (20 mmol) of diisocyanate and 0.5 ml (3.6 mmol) of Et_3N in 50 ml of **1** (total 2.45 mol); addition time 4 d at 50°, then another 4 d at 50° and 3 d at 25° according to *Procedure C*. For work-up the crude product was

filtered through basic alumina to afford 2.173 g of a light-yellow oil. 1.087 g of this material was purified by flash chromatography (column 50 × 2.5 cm; pet ether–EtOAc 8:1). Yield of **6c** 800 mg (71%) as a colourless oil, that crystallized on standing (m.p. 54–56°). IR (KBr): 3100 (w), 2960, 1620 (w), 1470, 1140, 1110, 1050, 1020, 900 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.78 and 1.27 (5'-CH_{3ax} and 5'-CH_{3eq}), 3.57 and 3.59 (d, 4'- and 6'-H_{ax}), 3.74 and 3.76 (dd, 4'- and 6-H_{eq}), 5.32 (dd, 6-H), 5.43 (s, 2'-H), 5.85 (ddd, 6a-H), 5.96 (d, 3a-H), 6.62 (5-H); coupling constants: J_{3a6a} = 8.5, J_{56} = 2.5, J_{56a} = 1.0, J_{66a} = 2.5; J_{gem} = 11, ^4J = 2.5 Hz (dioxane part). ^{13}C-NMR ($CDCl_3$): δ 21.8, 22.8 (2 5'-CH_3), 30.3 (C-5'), 77.2 (C-4', C-6'), 87.7 and 88.4 (C-3a, C-6a), 96.0 (C-2'), 100.6 (C-6), 149.7 (C-5), 152.8 (C-3). (Found: C, 58.43; H, 6.79; N, 6.59. Calc for $C_{11}H_{15}NO_4$ (225.2): C, 58.66; H, 6.71; N, 6.22%.)

3 - *Methyl* - 3a,6a - *dihydrofuro*[3,3 - d]*isoxazole* **6d**; *Procedure D*: A soln of 3.75 g (50 mmol) of nitroethane (**3d**) in 50 ml of **1** in a dilution set-up during 8 d was added at RT to a mixture of 20 ml (182 mmol) of phenyl isocyanate/10 drops (*ca* 2 mmol) of $F_3B \cdot OEt_2$/0.5 ml of Et_3N in 50 ml of **1** (total: 1.4 mol of furan). After removal of solids and excess furan the crude product was dissolved in ether and passed through basic alumina (10 g), then concentrated *in vacuo* to leave 3.47 g of a light-yellow oil. Pure furoisoxazoline **6d** was obtained therefrom by column chromatography (30 g of silica; cyclohexane–EtOAc 7.5:1); yield 1.76 g (28%) of a colourless oil, b.p. 53–55°/0.05 Torr. IR (film): 3100 (w), 1680, 1610, 1440, 1145, 1060 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 90 MHz): δ 1.3 (CH_3), 5.2 (dd, 6-H), 5.6 (m, 3a-H), 5.8 (m, 6a-H), 6.5 (dm, 5-H); coupling constants: J_{3a6a} = 8, J_{56} = 3, J_{56a} = 1, J_{66a} = 2 Hz. ^{13}C-NMR ($CDCl_3$): δ 11.4 (CH_3), 85.9 and 90.8 (C-3a, C-6a), 101.2 (C-6), 148.3 (C-5), 152.2 (C-3). (Found: C, 57.58; H, 5.43; N, 11.21. Calc for $C_6H_7NO_2$: C, 57.59; H, 5.64; N, 11.19%.)

3 - *Phenyl* - 3a,6a - *dihydrofuro*[2,3 - d]*isoxazole* **6e**; *Procedure G*: 15.54 g (100 mmol) of hydroximolyl chloride **4e** in 100 ml of furan at 25° were added within 10 d to a soln of 28 ml (200 mmol) of Et_3N and 10 drops (*ca* 2 mmol) of $F_3B \cdot OEt_2$ in 400 ml of **1** (total of furan: 7 mol). Furan (430 ml) was recovered from the mixture by distillation. The remainders were dissolved in 100 ml of CH_2Cl_2, washed with water (2 × 100 ml), dried (Na_2SO_4), and concentrated *in vacuo* to leave 16.34 g of a brown solid, containing **6e**, diphenylfuroxan, and Et_3NHCl (^{1}H-NMR). After column chromatography (80 g of silica; cyclohexane–EtOAc 4:1) 8.89 g (48%) of **6e** was obtained; colourless oil, solidifying after several days, m.p. 44–46° (lit.[18b] 45–46°). IR (CCl_4): 3060 (w), 1610, 1360, 1140, 1060, 900 cm^{-1}. ^{1}H-NMR in agreement with data of Ref. 18*b*. ^{13}C-NMR ($CDCl_3$): δ 87.6 and 88.4 (C-3a, C-6a), 100.9 (C-6); 127.1, 128.0, 128.5 and 129.8 (C_6H_5), 148.6 (C-5), 153.8 (C-3). (Found: C, 70.78; H, 4.75; N, 7.53. Calc for $C_{11}H_9NO_2$ (187.2): C, 70.58; H, 4.85; N, 7.48%.)

3 - t - *Butoxymethyl* - 5 - *methyl* - 3a,6a - *dihydrofuro*[2,3 - d]*isoxazole* (**7a**): According to *Procedure C*, from 1.472 g (10.0 mmol) of **3a**, addition at 80° (bath temp) within 3 d, stirring continued at 80° for 3 d; filtration through celite, distillation of excess 2-methylfuran (**2**) (100 ml of **2** recovered), filtration through basic alumina. Crude product: 2.352 g of a brown oil; flash chromatography of 1.176 g of this material yielded 716 mg (68%) of analytically pure **7a** as a yellow oil. Application of *Procedure B* (in a flask; 26 d at reflux; see preparation of **6a**) gave 44% of pure **7a** after fractional distillation with a Spaltrohr column (200 mmol of **3a**; 18.73 g of **7a**, b.p. 80–90°/*ca* 0.005 Torr). IR (CCl_4): 2990, 1660, 1380, 1190, 1075, 1040, 940, 905 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 90 MHz): δ 1.27 [s, $C(CH_3)_3$], 1.86 (m, 3-CH_3), 4.20 and 4.40 (AB, CH_2), 4.93 (m, 6-H), 5.71 (dm, 6a-H), 5.90 (3a-H); J_{3a6a} = 8, J_{AB} = 12 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 13.0 (5-CH_3), 27.2 [$C(\underline{C}H_3)_3$], 55.6 (CH_2), 74.0 [$\underline{C}(CH_3)_3$], 87.9 and 88.2 (C-3a, C-6a), 97.0 (C-6), 154.4 (C-3), 159.2 (C-5). (Found: C, 62.62; H, 8.09; N, 6.50. Calc for $C_{11}H_{17}NO_3$ (211.1): C, 62.54; H, 8.11; N, 6.63%.)

3 - *Diethoxymethyl* - 5 - *methyl* - 3a,6a - *dihydrofuro*[2,3 - d]*isoxazole* **7b**: According to *Procedure C* as applied to **7a**. From 1.632 g (10 mmol) of **3b**, addition in 2 d, stirring at 80° continued for 10 d. Filtration of the crude product through silica gave 1.728 g of dark-yellow oil; after flash chromatography (pet ether–ethyl acetate 9:1) 1.374 g (61%) of **7b**; orange oil, analytically pure. From a 100 mmol run (*Procedure B*, cp. **7a**) 12.52 g (52%) of **7b** were collected after Kugelrohr distillation (b.p. 90°/0.05 Torr; yellow oil). IR (film): 3100 (w), 2970, 1685, 1660, 1550, 1380, 1210, 1110, 1050, 940, 920 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 90 MHz): δ 1.2 (m, 2 CH_3), 1.9 (m, 5-CH_3), 3.4–4.0 (m, 2 CH_2), 5.0 (m, 6-H), 5.3 [s, $C\underline{H}(OEt)_2$], 5.7 (dm, 6a-H), 5.9 (d, 3a-H); J_{3a6a} = 8.5 Hz. ^{13}C-NMR ($CDCl_3$): δ 13.3, 15.0 and 15.1 (3 CH_3), 62.2 and 63.2 (2 CH_2), 88.3 and 89.3 (C-3a, C-6a), 96.6 [$CH(OEt)_2$], 97.2 (C-6), 153.7 (C-3), 159.9 (C-5). (Found: C, 58.25; H, 7.50; N, 6.16. Calc for $C_{11}H_{17}NO_4$ (227.3): C, 58.14; H, 7.54; N, 6.16%.)

3 - (5,5 - *Dimethyl* - 1,3 - *dioxan* - 2 - *yl*) - 5 - *methyl* - 3a,6a - *dihydrofuro*[2,3 - d]*isoxazole* **7c**: *Procedure C* was used, starting with 1.752 g (10 mmol) of **3c**; addition time 3 d at 80°; after further reaction for 15 d at 80° TLC showed unreacted **3c**, so 0.5 ml of Et_3N and 10 mmol of diisocyanate were added and the reaction continued for a total of 28 d; the usual work-up including flash chromatography (cp. **7a**) gave 1.341 g (56%) of a yellow solid, m.p. 80–82°. IR (KBr): 3120 (w), 2960, 1660, 1210, 1100, 1030, 980, 930, 900 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.78 and 1.26 (2 5'-CH_3), 1.89 (m, 5-CH_3), 3.58 and 3.59 (d, 4'- and 6'-H_{ax}), 3.73 and 3.75 (dd, 4'- and 6'-H_{eq}), 4.97 (m, 6-H), 5.40 (s, 2'-H), 5.78 (dm, 6a-H), 5.92 (d, 3a-H); J_{3a6a} = 8.5; J_{gem} = 11.0, ^4J = 3.0 Hz (dioxane part). ^{13}C-NMR ($CDCl_3$): δ 13.2 (5-CH_3), 21.8 and 22.8 (2 5'-CH_3), 30.3 (C-5'), 77.2 and 77.3 (C-4', C-6'), 88.0 and 89.6 (C-3a, C-6a), 96.0 and 96.4 (C-2', C-6), 153.1 (C-3), 160.1 (C-5). (Found: C, 60.54; H, 7.44; N, 6.10. Calc for $C_{12}H_{17}NO_4$ (239.3): C, 60.24; H, 7.16; N, 5.85%.)

MCPB oxidation of furoisoxazolines **6a**, **c** *and* **7a**

β - Xylo - 3 - t - *butoxymethyl* - 6 - *hydroxy* - 5 - *methoxytetrahydrofuro*[2,3 - d]*isoxazole* **8a**: A soln of 1.73 g (10 mmol) of MCPB (85%) in 10 ml of MeOH at 0° within 15 min was added to 986 mg (5 mmol) of **6a**, dissolved in 30 ml of MeOH, and the mixture stirred for 16 hr at RT. 10 g of dried, strongly basic ion exchange resin (Lewatit® M600 G3, Bayer; the Cl^- form was treated with 2 N NaOH, until complete exchange was seen by $AgNO_3$-monitoring. Washing with MeOH, then acetone, and drying over P_2O_5 gave a resin, which was used preferentially in a shaking apparatus to avoid excessive abrasion) were added and the mixture shaken for 16 hr. Filtration through basic alumina, removal of the solvent on a rotary evaporator and drying over P_2O_5/KOH left 1.10 g (90%) of analytically pure **8a** as a yellow syrup, d.r. 95:5 (^{13}C-NMR), b.p. 180°/0.05 Torr (Kugelrohr). IR (CCl_4): 3620 (w), 3445 (mb), 2980, 2825 (w), 1370, 1190, 1110, 1080, 1050 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 1.3 [$C(CH_3)_3$], 3.2 (b, OH), 3.3 (s, OCH_3), 4.2 and 4.3 (AB, 3-CH_2), 4.4 (s, 6-H), 4.8 (d, 6a-H), 5.0 (s, 5-H), 5.7 (d, 3a-H); J_{3a6a} = 8 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz; 90:10 isomer mixture, obtained by running the reaction at 50°), *β-xylo* isomer (major): δ 27.5 [$C(\underline{C}H_3)_3$], 55.1 (5-OCH_3), 55.6 (3-CH_2), 74.5 [$\underline{C}(CH_3)_3$], 79.6, 87.7 and 88.0 (C-6a, C-3a), 110.5 (C-5), 157.6 (C-3). α-*Xylo* isomer (minor): δ 78.8 (C-6), 84.9 (C-6a), 88.8 (C-3a), 103.6 (C-5), 156.9 (C-3). (Found: C, 54.08; H, 7.67; N, 5.45. Calc for $C_{11}H_{19}NO_5$ (245.3): C, 53.86; H, 7.80; N, 5.71%.)

Methyl ether **9** *from* **8a**: 900 mg (16 mmol) of powdered KOH were added to 6 ml of dry DMSO and the mixture stirred for 5 min at 25°, then mixed with 990 mg (4 mmol) of **8a** in 2 ml of DMSO. After stirring for 2 min, 0.5 ml (8 mmol) of MeI were injected, causing the mixture to warm up. After 30 min the mixture was versed into 20 ml of water, extracted with CH_2Cl_2 (2 × 20 ml), and the organic solutes, after drying, concentrated to leave a greasy brown solid. This was taken up in CH_2Cl_2 and the soln filtered through basic alumina to give, after crystallization from pet ether, 220 mg of colourless crystals. The mother liquor, treated as above, gave a second crop of identical material (total: 930 mg, 90%; m.p. 77–78°) as a single isomer (d.r. > 97:3 from ^{13}C-NMR). IR ($CDCl_3$): 2990, 1460 (w), 1110, 1050, 1020, 950, 880 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 1.2 [$C(CH_3)_3$], 3.2 and 3.4 (5- and 6-OCH_3), 3.8 (s, 6-H), 4.1 and 4.3 (AB, 3-CH_2), 4.7 (d, 6a-H), 4.9 (s, 5-H), 5.6 (d, 3a-

H); $J_{3a6a} = 8$, $J_{AB} = 12$ Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 27.5 [C($\underline{C}H_3)_3$], 55.4 (3-CH_2), 55.1 and 57.7 (5- and 6-OCH_3), 74.3 [$\underline{C}(CH_3)_3$], 85.1 (C-6), 87.3 (C-6a), 89.3 (C-3a), 108.0 (C-5), 157.4 (C-3). (Found: C, 55.62; H, 8.15; N, 5.46. Calc for $C_{12}H_{21}NO_5$ (256.0): C, 55.59; H, 8.16; N, 5.40%.)

β-Xylo-3-(5,5-*dimethyl*-1,3-*dioxan*-2-*yl*)-6-*hydroxy*-5-*methoxytetrahydrofuro*[2,3-d]*isoxazole* (**8c**): As described with **8a**, 676 mg (3 mmol) of **6c** were converted to **8c** (845 mg, "103"%), obtained as an analytically pure, pale-yellow oil with a d.r. of 95:5 (^{13}C-NMR). IR (film): 3450 (mb), 2970, 1470 (m), 1100, 1040, 890 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.77 and 1.25 (2 5'-CH_3), 3.3 (s, 5-OCH_3), 3.57 and 3.74 (A and B of two AB, 4'- and 6'-CH_2), 4.35 (sb, OH), 4.39 (s, 6-H), 4.84 (d, 6a-H), 4.99 (s, 5-H), 5.40 (s, 2'-H), 5.75 (d, 3a-H); $J_{3a6a} = 7.5$, $J_{AB} = 11.5$ Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz), *β-xylo* isomer (major): δ 21.8 and 22.9 (2 5'-CH_3), 30.3 (C-5'), 55.1 (5-OCH_3), 77.2 (C-4', C-6'), 78.9 (C-6), 86.5 (C-6a), 88.7 (C-3a), 95.8 (C-2'), 110.1 (C-5), 155.8 (C-3). *α-Xylo* isomer: δ 59.9 (5-OCH_3), 78.6 (C-6), 84.1 (C-6a), 86.9 (C-3a), 95.6 (C-2'), 103.2 (C-5). (Found: C, 53.09; H, 7.06, N, 5.10. Calc for $C_{12}H_{19}NO_6$ (273.3): C, 52.94; H, 7.03; N, 5.14%.)

Xylo-3-t-*butoxymethyl*-6-*hydroxy*-5-*methoxy*-5-*methyltetrahydrofuro*[2,3-d]*isoxazole* **10a** *and isomer*: From 1.056 g (5 mmol) of **7a**, as described above for **8a**, **10a** was obtained as a yellow, analytically pure oil (1.137 g, 80%; d.r. 87:13 from ^{13}C-NMR peak ratios). IR (film): 3420 (mb), 2980, 1470 (w), 1370, 1200, 1105, 1055, 890 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz), major isomer (*xylo*): δ 1.25 [s, C($CH_3)_3$], 1.45 (s, 5-CH_3), 2.8 (sb, OH), 3.19 (s, 5-OCH_3), 4.22 and 4.36 (s each, 3-CH_AH_B), 4.25 (s, 6-H), 4.81 (d, 6a-H), 5.68 (d, 3a-H); $J_{3a6a} = 8$, $J_{AB} = 11.5$ Hz. Minor isomer: δ 1.24 [s, C($CH_3)_3$], 1.42 (s, 5-CH_3), 3.35 (s, 5-OCH_3), 3.92 (d, 6-H), 4.20 and 4.32 (d each, 3-CH_AH_B), 4.89 (dd, 6a-H), 5.35 (d, 3a-H); $J_{3a6a} = 8$, $J_{66a} = 3.5$, $J_{AB} = 12$ Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz), major isomer (*xylo*): δ 16.0 (5-CH_3), 27.4 [C($\underline{C}H_3)_3$], 48.7 (5-OCH_3), 55.7 (3-CH_2), 74.4 [$\underline{C}(CH_3)_3$], 80.5 (C-6), 86.6 (C-6a), 89.0 (C-3a), 111.4 (C-5), 157.0 (C-3). Minor isomer: δ 17.8 (5-CH_3), 48.9 (5-OCH_3), 84.1 and 84.8 (C-6, C-6a), 90.4 (C-3a), 106.0 (C-5). (Found: C, 55.37; H, 8.17; N, 5.40. Calc for $C_{12}H_{21}NO_5$ (259.3): C, 55.58; H, 8.16; N, 5.40%.)

Osmium tetroxide oxidation of furoisoxazoline **6a**

β/α-Xylo-3-t-*butoxymethyl*-5,6-*dihydroxytetrahydrofuro*[2,3-d]*isoxazole* **11**: A soln of *ca* 10 mg (0.04 mmol) of OsO_4 in 4 ml of 80% aqueous acetone was warmed to 60°, then supplied with 0.70 g (5.2 mmol) of N-morpholine N-oxide hydrate (NMO). To this mixture within 3 hr a soln of 1.97 g (10 mmol) of furoisoxazoline **6a** in 10 ml of 80% acetone was dropped and some more NMO (1.40 g, 10.4 mmol) added portionwise. The mixture was kept at 60° and stirred for 2 hr; acetone then was removed by distillation, affording a dark-brown oily residue, which was extracted with EtOAc (3 × 10 ml). The organic solvents were combined, washed (twice with 1 N HCl/brine, once with sat $NaHCO_3$/brine), dried over Na_2SO_4, and concentrated *in vacuo*, to leave 1.61 g of a brown oil, solidifying after several days. 1.0 g of this material was recrystallized from ether to furnish 0.87 g (57%) of colourless crystals of **11**, m.p. 102–107°, d.r. 1:1 (^{13}C-NMR). IR ($CHCl_3$): 3620, 2980, 1390 (m), 1360, 1060, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 1.2 [s, C($CH_3)_3$], 3.5 (bs, OH), 4.2 (AB, J = 12 Hz; 3-CH_2), 4.6–5.7 (m, 4 C$\underline{H}$O). ^{13}C-NMR ($CDCl_3$/H_3CCN 1:1, 100.6 MHz) of 1:1 anomer mixture: δ 27.0 [C($\underline{C}H_3)_3$], 54.9 and 55.1 (3-CH_2), 74.1 [$\underline{C}(CH_3)_3$], 75.1 and 79.9 (C-6), 83.6, 87.0, 87.2, and 87.7 (C-3a, C-6a), 97.0 (C-5 of *β*-**11**), 103.6 (C-5 of *α*-**11**). (Found: C, 52.01, H, 7.67; N, 5.99. Calc for $C_{10}H_{17}NO_5$ (231.2): C, 51.94, H, 7.41; N, 6.06%.)

α-Acetonide of β/α-**11**, α-xylo-3-t-*butoxymethyl*-5,6-O-*isopropylidenetetrahydrofuro*[2,3-d]*isoxazole* (**12**): 1.11 g (4.8 mmol) of the hemiacetal **11**, 680 mg (6.5 mmol) of 2,2-dimethoxypropane, and a catalytic amount of *p*-TsOH were dissolved in 15 ml of benzene, and the mixture refluxed for 3 hr, *ca* 10 ml of solvents were distilled off slowly (azeotropic mixture of benzene–MeOH), and the remainders diluted with 10 ml of CH_2Cl_2. To this 3 g of basic ion exchange resin (see **8a**) were added. The mixture was shaken overnight and gave, after removal of solvents, 1.28 g of a slightly impure (^{1}H-NMR) brown oil. Pure **12** was obtained on addition of 10 ml of CH_2Cl_2, subsequent filtration through basic alumina and removal of solvents; 1.05 g of a yellow oil, that crystallized on addition of a small quantity of pet ether, to afford 980 mg (75%) of colourless, crystalline **12**, m.p. 52–53°. IR (CCl_4): 3000, 1460 (m), 1390, 1230, 1200, 1170, 1080, 1030, 890 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.24 [s, C($CH_3)_3$], 1.35 and 1.50 [$C(CH_3)_2$], 4.18 and 4.27 (d each, 3-CH_AH_B), 4.75 (d, 6-H), 4.92 (d, 6a-H), 5.65 (d, 3a-H), 5.79 (d, 5-H); $J_{3a6a} = 6.6$, $J_{56} = 3.5$, $J_{AB} = 12$ Hz. (Found: C, 57.98; H, 7.82; N, 5.05. Calc for $C_{13}H_{21}NO_5$ (271.3): C, 57.55; H, 7.80; N, 5.02%.)

Stereoselective LAH reduction of furoisoxazolines **6**, **7**; *synthesis of* xylo-*aminodeoxy furanoid glycals* **13**, **14**

6-t-*Butyl ether of* xylo-*hexose furanoid glycal* **13a**: *General procedure.* Cf. Ref. 32. LAH reductions were conducted in an inert atmosphere (N_2); LAH was kept in dry ether at 0° and the isoxazoline added as an ether soln or, if less soluble, as a pure substance. The reactions were monitored by TLC analyses. After hydrolysis of the mixture (per gramme of $LiAlH_4$: 1.0 ml of H_2O, 0.75 ml of 20% NaOH, 1–3.5 ml H_2O until the ppt became colourless and granular[42]). CH_2Cl_2 was added, stirred for *ca* 1 d, solids filtered off and washed thoroughly with CH_2Cl_2, and concentrated and dried *in vacuo*. Reduction of **6a** (1.25 g, 6.34 mmol) with LAH (502 mg, 13.2 mmol) in ether (15 and 20 ml); reaction time 2 hr at RT; yield 1.10 g (86%) of **13a**, colourless crystals, m.p. 74–75°, d.r. of crude product > 95:5 (^{13}C-NMR, 22.6 MHz). IR (CCl_4): 3400 (m), 3300 (mb), 3100 (w), 2980, 1615, 1365, 1195, 1150, 1090, 1035 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 90 MHz): δ 1.2 [s, C($\underline{C}H_3)_3$], 2.8 (b, OH, NH_2), 3.3–3.5 (AB of CH_2 and m of H-5), 4.1 and 4.3 (dm, 4-H), 4.9 (ddd, 3-H), 5.3 (dd, 2-H), 6.6 ("d", 1-H); $J_{12} = 3$, $J_{13} = 1$, $J_{23} = 3$, $J_{34} = 8$ Hz. ^{13}C-NMR see Table 3. (Found: C, 59.47; H, 9.58; N, 6.83. Calc for $C_{10}H_{19}NO_3$ (201.3): C, 59.68; H, 9.52; H, 6.69%.)

6-*Diethyl acetal of* xylo-*hexodialdose furanoid glycal*, **13b**: From **6b** (640 mg, 3 mmol) with LAH (270 mg, 7.1 mmol) in ether (5 and 5 ml), hydrolysis after 2 d and further stirring for 1 d, then another 2 d after addition of 20 ml of CH_2Cl_2/Na_2SO_4; crude product as a slightly impure yellow oil (573 mg, 88%, d.r. 94:6), that decomposed partly on attempted chromatographic separation. IR (CCl_4): 3390 (w), 3300 (mb), 2980, 1665 (m), 1110, 1060, 1020, 930, 870 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.23 (m, 2 CH_3), 3.31 (dd, 5-H), 3.55 (sb, OH, NH_2), 3.5–3.8 (m, 2 CH_2), 4.48 (d, H-6), 4.49 (dd, 4-H), 4.85 (dd, 3-H), 5.16 (dd, 2-H), 6.58 (d, 1-H); $J_{12} = 4.5$, $J_{23} = 2.5$, $J_{34} = 8.0$, $J_{45} = 2.5$, $J_{56} = 7.5$ Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): see Table 3. (Found: C, 55.71; H, 9.41; N, 6.84. Calc for $C_{10}H_{19}NO_4$ (217.3): C, 55.28; H, 8.81; N, 6.45%.)

6-*Neopentylglycol acetal of* xylo-*hexodialdose furanoid glycal* **13c**: From **6c** (676 mg, 3 mmol) and LAH (190 mg, 5 mmol) in ether (20 ml); hydrolysis after 90 min at 0° and 14 d at RT, then stirring with CH_2Cl_2 (10 ml) for 14 d at RT; crude product as a yellow solid (577 mg, 84%, m.p. 87–90°, d.r. 94:6); pure product as colourless crystals (from ether, 476 mg, 72%, m.p. 92–93°). IR (CCl_4): 3400 (w), 3320 (wb), 2980, 1610, 1150, 1100, 1040, 1030, 990, 930 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz, from crude product): δ 0.75 and 1.18 (2 × s, $CH_{3\,eq}$ and $CH_{3\,ax}$), 3.05 (sb, OH, NH_2), 3.32 (dd, 5-H), 3.45 and 3.48 (2 d of $C\underline{H}_{ax}H_{eq}$), 3.64 and 3.68 (2 dd of $CH_{ax}\underline{H}_{eq}$), 4.45 (d, 6-H), 4.45 (dd, 4-H), 4.91 (ddd, 3-H), 5.24 (dd, 2-H), 6.56 (db, 1-H); $J_{12} = 2.7$, $J_{13} = 1.0$, $J_{23} = 2.7$, $J_{34} = 7.7$, $J_{45} = 2.7$, $J_{56} = 6.0$; $J_{gem} = 11.5$, $^4J = 2.7$ Hz (dioxane part). ^{13}C-NMR ($CDCl_3$, 100.6 MHz, crude product): see Table 3. (Found: C, 57.54; H, 8.29; N, 6.07. Calc for $C_{11}H_{19}NO_4$ (229.3): C, 57.63; H, 8.35; N, 6.11%.)

1,4-*Anhydro*-5-*amino*-2,5-*dideoxy*-xylo-*hex*-1-*enitol* **13d**: From **6d** (375.4 mg, 3 mmol) with LAH (233 mg, 6.1 mmol) in ether (5 and 10 ml), hydrolysis after 2.5 hr at RT; colourless crystals (134 mg, 35%, m.p. 105–106°, d.r. > 95:5). IR (CCl_4): 3400 (w), 3280 (wb), 3060 (w), 2980, 1615, 1260, 1150, 1100, 1040, 920 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 60

MHz): δ 1.3 (d, CH_3), 3.0 (sb, OH, NH_2), 3.4 (dq, 5-H), 4.1 (dd, 4-H), 4.9 (ddd, 3-H), 5.2 (dd, 2-H), 6.6 (db, 1-H); J_{12} = 2, J_{13} = 1, J_{23} = 3, J_{34} = 8, J_{45} = 3, J_{56} = 6 Hz. ^{13}C-NMR ($CDCl_3$, 22.6 MHz): see Table 3. (Found: C, 55.78; H, 8.59; N, 10.71. Calc for $C_6H_{11}NO_2$ (129.2): C, 55.80; H, 8.58; N, 10.84%.)

7-O-t-*Butyl* xylo-*heptulose furanoid glycal* **14a**: From **7a** (634 mg, 3 mmol) with LAH (114 mg, 3 mmol) in ether (5 and 5 ml), hydrolysis after 2 hr at 0° and 14 hr at RT; analytically pure, "crude" product (yellow oil, 410 mg, 63%, d.r. > 97 : 3). IR (CCl_4): 3380 (w), 3300 (wb), 2960, 1665 (m), 1380, 1360, 1180, 1080 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.20 [s, $C(CH_3)_3$], 1.84 [sb, 1-H (CH_3)], 3.3–3.5 [m, 6-H, 7-H (CH_2), OH, NH_2], 4.22 (dd, 5-H), 4.83 (dm, 4-H), 4.90 (m, 3-H); J_{45} = 7, J_{56} = 4 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): see Table 3. (Found: C, 61.37; H, 10.12; N, 6.51. Calc for $C_{11}H_{21}NO_3$ (215.3): C, 61.37; H, 9.83; N, 6.19%.)

Diethyl acetal of xylo-*heptos-6-ulose furanoid glycal* **14b**: From **7b** (730 mg, 3.2 mmol) with LAH (114 mg, 3 mmol) in ether (5 and 5 ml), hydrolysis after 16 hr at RT with additional stirring for 1 d after addition of CH_2Cl_2 (20 ml). The crude product (yellow–brown oil, 529 mg, 76%, d.r. 94 : 6) was purified by addition of ether, filtration from a yellow, fluffy ppt to give **7b** as an analytically pure, brown oil (497 mg, 67%). IR (CCl_4): 3380 (w), 3300 (w), 2960, 1665 (m), 1110, 1060, 1020, 930 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.2 (mc, 2 CH_3), 1.88 [sb, 7-H (CH_3)], 3.29 (dd, 2-H), 3.5–3.8 (m, 2 CH_2, OH, NH_2), 4.46 (d, 1-H), 4.49 (dd, 3-H), 4.87 (db, 4-H), 4.90 (sb, 5-H); J_{12} = 7.5, J_{23} = 3.0, J_{34} = 7.5 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz, from crude product): see Table 3 for data of 96 : 4 isomers. Impurities (< 10%) in crude product: δ 61.9, 93.1, 99.4, 125.5, 147.8. (Found: C, 57.37; H, 8.92; N, 6.21. Calc for $C_{11}H_{21}NO_4$ (231.3): C, 57.12; H, 9.15; N, 6.06%.)

Neopentyl glycol acetal of xylo-*heptos-6-ulose furanoid glycal* **14c**: From **7c** (718 mg, 3 mmol) with LAH (190 mg, 5 mmol) in ether (20 ml); hydrolysis after 2 d at RT; stirring for another d after addition of CH_2Cl_2 (10 ml). Crude product (685 mg, 94%) as a yellow oil; colourless crystals from ether/pet ether (crops of 431 and 95 mg, total 72%; m.p. 86–87 and 82–83°). A slightly impure third fraction was obtained in the form of light-yellow crystals (101 mg, 14%; m.p. 74–78°). IR (CCl_4): 3400 (m), 3320 (mb), 2960, 1670, 1380, 1170, 1100, 1030, 1000, 930, 920 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 0.74 and 1.18 (2 s, $CH_{3\,eq}$ and $CH_{3\,ax}$), 1.86 [m, 7-H (CH_3)], 3.0 (sb, OH, NH_2), 3.29 (dd, 2-H), 3.46 and 3.49 (2 d of $CH_{ax}H_{eq}$), 3.63 and 3.67 (2 dd of $CH_{ax}H_{eq}$), 4.45 (d, 1-H), 4.49 (dd, 3-H), 4.85 (dm, 4-H), 4.90 (m, 5-H); J_{12} = 6.0, J_{23} = 3.0, J_{34} = 7.5; J_{gem} = 11, ^4J = 2.7 Hz (dioxane part). ^{13}C-NMR ($CDCl_3$, 400 MHz, from crude product): see Table 3 for data of 93 : 7 isomers. Impurities (< 10%) in crude product: δ 45.4, 70.8. (Found: C, 59.46; H, 8.66; N, 5.69. Calc for $C_{12}H_{21}NO_4$ (243.3): C, 59.24; H, 8.70; N, 5.76%.)

Stereoselective LAH reduction of dihydrofuroisoxazolines **8a, c, 9, 10, 12**; *synthesis of aminodeoxy* ido-*furanoses* **15a, c, 16–18**

Methyl 5-*amino*-6-O-t-*butyl*-5-*deoxy*-β-*idofuranoside* **15a**: According to the general procedure outlined for **13a**; from **8a** (β/α 95 : 5; 736 mg, 3 mmol) with LAH (228 mg, 6 mmol) in ether (30 and 5 ml). Hydrolysis after 14 hr at RT, stirring continued for 5 d with addition of Na_2SO_4, and for 12 hr after adding ether/CH_2Cl_2 (30 ml of each); light-yellow syrup (580 mg, 77%). IR (film): 3380 (sb), 2980, 1190, 1070, 1020, 810 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.20 [s, $C(CH_3)_3$], 3.17 (ddd, 5-H), 3.30 (dd, 6-H_A), 3.40 (s, OCH_3), 3.40 (m, 6-H_B, 2 OH, NH_2), 4.10 (sb, 2-H), 4.11 (d, 3-H), 4.21 (dd, 4-H), 4.81 (s, 1-H); J_{34} = 5.0, J_{45} = 4.0, J_{5A} = 7.0, J_{5B} = 5.5, J_{AB} = 8.5 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): see Table 3. (Found: C, 53.10; H, 9.02; N, 5.65. Calc for $C_{11}H_{23}NO_5$ (249.3): C, 52.99; H, 9.30; N, 5.62%.)

Methyl 5-*amino*-6-O-t-*butyl*-5-*deoxy*-2-O-*methyl*-β-*idofuranoside* **16**: From **9** (β/α > 97 : 3; 778 mg, 3 mmol) in ether (5 ml) with LAH (227 mg, 6 mmol). After 14 hr at RT more ether (10 ml) was added, and hydrolyzed as usual 4 hr later. Yield of **16**: 620 mg (78%) as a yellow oil; d.r. > 97 : 3. IR (film): 3400 (sb), 2990, 1190, 1110, 935 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.20 [s, $C(CH_3)_3$], 3.18 (ddd, 5-H), 3.30 (6-H_A), 3.40 and 3.41 (2 s, 2 OCH_3), 3.40 (m, 6-H_B, OH, NH_2), 3.68 (bs, 2-H), 4.12 (dd, 4-H), 4.25 (dd, 3-H), 4.82 (s, 1-H); J_{23} = 1.0, J_{34} = 4.8, J_{45} = 3.3, J_{5A} = 7.5, J_{5B} = 5.7, J_{AB} = 8.5 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): see Table 3. (Found: C, 54.64; H, 9.40; N, 4.97. Calc for $C_{12}H_{25}NO_5$ (263.3): C, 54.73; H, 9.57; N, 5.32%.)

Methyl 5-*amino*-5-*deoxy*-6,6-O-*neopentylidene*-β-ido-*hexodialdo*-1,4-*furanoside* **15c**: From **8c** (470 mg, 1.7 mmol) in ether (20 ml), and LAH (332 mg, 8.5 mmol), added in portions; hydrolysis after 12 hr at RT, treatment with CH_2Cl_2 (10 ml)/Na_2SO_4 for another hour. The crude product (colourless solid, 434 mg, 92%, m.p. (dec.) 136–138°; d.r. > 95 : 5), crystallized from MeOH, gave colourless crystals (371 mg, 79%, m.p. 141–142°), IR (KBr): 3360, 2960, 1120, 1100, 1050, 1020 cm^{-1}. ^{1}H-NMR ($CDCl_3$/CD_3OD 5 : 1, 400 MHz): δ 0.74 and 1.17 (2 s, $CH_{3\,eq}$ and $CH_{3\,ax}$), 3.44 and 3.46 (s and d(?), OCH_3 and 5-H), 3.65 (m, 2 CH_2), 4.10 (s, 2-H), 4.15 (m, 3-H), 4.40 (d, 6-H), 4.50 (bs, 4-H), 4.83 (s, 1-H); J_{56} = 6.5 Hz. ^{13}C-NMR (CD_3OD, 100.6 MHz): see Table 3. (Found: C, 51.58; H, 8.52; N, 4.65. Calc for $C_{12}H_{23}NO_6$ (277.3): C, 51.97; H, 8.36; N, 5.05%.)

Methyl 6-*amino*-7-O-t-*butyl*-1,6-*dideoxy*-ido-*hept*-2-*ulofuranoside* **17**: From **10a** (517 mg, 2 mmol) with LAH (304 mg, 8 mmol) in ether (5 and 5 ml); hydrolysis after 2 hr at 0° and 14 hr at RT; work-up by addition of CH_2Cl_2 (10 ml), stirring for 1 d, filtering, removal of solvent, and drying over P_2O_5/KOH *in vacuo*. Colourless, slowly solidifying oil (554 mg "105"%, d.r. 87 : 13; m.p. 69–70° (main part) and 74–75°). IR (CCl_4): 3380 (mb), 2960, 1360, 1190, 1080, 1020 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.20 [s, $C(CH_3)_3$], 1.42 [s, 1-H (CH_3)], 3.13 (ddd, 6-H), 3.30 (s and sb, OCH_3 and OH, NH_2), 3.31 and 3.48 (2 dd, 7-H_A and 7-H_B), 4.02 (d, 3-H), 4.10 (dd, 4-H), 4.17 (dd, 5-H); J_{34} = 1.0, J_{45} = 4.5, J_{56} = 6.0, J_{6A} = 7.0, J_{6B} = 4.5, J_{AB} = 8.5 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): see Table 3. (Found: C, 54.64; H, 9.40; N, 4.97. Calc for $C_{12}H_{25}NO_5$ (263.3): C, 54.73; H, 9.57; N, 5.32%.)

5-*Amino*-6-O-t-*butyl*-5-*deoxy*-1,2-O-*isopropylidene*-α-*idofuranose* **18**: From **12** (271 mg, 1 mmol, d.r. > 97 : 3) in ether (5 ml) with LAH (90 mg, 2.37 mmol) added portionwise; hydrolysis after 4 d at RT, with stirring continued for 2 hr at RT, then with CH_2Cl_2 (20 ml)/Na_2SO_4 added, for another 2 hr. Colourless oil, slowly solidifying (231 mg, 84%, m.p. 53–55°; d.r. > 97 : 3). IR (CCl_4): 3400 (w), 3000, 1220, 1200, 1170, 1075, 1020 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.20 [s, $C(CH_3)_3$], 1.30 and 1.48 [2 s, $C(CH_3)_2$], 3.21 (ddd, 5-H), 3.32 and 3.41 (2 dd, 6-H_A, 6-H_B), 4.11 (dd, 4-H), 4.25 (d, 3-H), 4.47 (d, 2-H), 5.93 (d, 1-H); J_{12} = 3.5, J_{34} = 3.0, J_{45} = 2.0, J_{5A} = 7–7.3, J_{5B} = 8.5 Hz. ^{13}C-NMR ($CDCl_3$, 100.6 MHz): see Table 3. (Found: C, 56.88; H, 8.89; N, 5.10. Calc for $C_{13}H_{25}NO_5$ (273.3): C, 56.71; H, 9.15; N, 5.09%.)

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REFERENCES

[1] Syntheses *via* isoxazolines, Part 16. For Part 15 see Ref. 12*b*.
[2] The concept of this approach was presented first at Hannover, November 1980, and at the Chemiedozententagung, Tübingen, March 1981, see Abstract A 18.
[3] Preliminary communication: I. Müller and V. Jäger, *Tetrahedron Lett.* 4777 (1982).
[4a] I. Müller, Diploma Thesis, Universität Würzburg (1980); [b] Part of the Ph.D. Thesis of I.M., Universität Würzburg (1984).

[5] Present address: Organisch-Chemisches Institut der Universität, CH-8057 Zürich, Switzerland.

[6] For a review see V. Jäger, H. Grund, V. Buß, W. Schwab, I. Müller, R. Schohe, R. Franz and R. Ehrler, *Bull. Soc. Chim. Belg.* **92**, 1039 (1983).

[7] V. Jäger and H. Grund, *Angew. Chem.* **88**, 27 (1976); *Ibid. Int. Ed. Engl.* **15**, 50 (1976).

[8] For a discussion on the use of *syn/anti* stereodescriptors see S. Masumune, S. A. Ali, D. L. Snitman and D. S. Garvey, *Angew. Chem.* **92**, 573 (1980); *Ibid. Int. Ed. Engl.* **19**, 557 (1980); see also V. Prelog and G. Helmchen, *Angew. Chem.* **94**, 614 (1982); *Ibid. Int. Ed. Engl.* **21**, 567 (1982); D. Seebach and V. Prelog, *Angew. Chem.* **94**, 696 (1982); *Ibid. Int. Ed. Engl.* **21**, 654 (1982).

[9] W. Schwab and V. Jäger, *Angew. Chem.* **93**, 578 (1981); *Ibid. Int. Ed. Engl.* **20**, 603 (1981).

[10] V. Jäger, V. Buß and W. Schwab, *Tetrahedron Lett.* 3133 (1978).

[11] V. Jäger, W. Schwab and V. Buß, *Angew. Chem.* **93**, 576 (1981); *Ibid. Int. Ed. Engl.* **20**, 601 (1981).

[12a] V. Jäger, R. Schohe and E. F. Paulus, *Tetrahedron Lett.* 5501 (1983); [b] K. N. Houk, S. R. Moses, Y.-D. Wu, N. G. Rondan, V. Jäger, R. Schohe and F. R. Fronczek, *J. Am. Chem. Soc.* **106**, 3880 (1984).

[13] V. Jäger and R. Schohe, *Tetrahedron* **40**, 2199 (1984).

[14a] K. Bast, M. Christl, R. Huisgen, W. Mack and R. Sustmann, *Chem. Ber.* **106**, 3258 (1973); [b] P. Caramella, T. Bandiera, P. Grünanger and E. Marinone Albini, *Tetrahedron* **40**, 441 (1984), and literature cited therein.

[15a] Reviews: C. Grundmann and P. Grünanger, *The Nitrile Oxides*. Springer, Berlin (1971); [b] A. Padwa (Editor), 1,3-*Dipolar Cycloaddition Chemistry*. Wiley-Interscience, New York (1984); [c] P. Caramella and P. Grünanger in Ref. 15*b*, Vol. 1, Chap. 3, p. 291.

[16] Reviews: R. Huisgen, *J. Org. Chem.* **41**, 403 (1976); R. Huisgen in Ref. 15*b*, Vol. 1, Chap. 1, p. 1.

[17] K. N. Houk and K. Yamaguchi in Ref. 15*b*, Vol. 2, Chap. 13, p. 407.

[18a] P. Grünanger and I. Grasso, *Gazz. Chim. Ital.* **85**, 1271 (1955); A. Corsico Coda, P. Grünanger and G. Veronesi, *Tetrahedron Lett.* 2911 (1966); [b] P. Caramella, G. Cellerino, A. Corsico Coda, A. Gamba Invernizzi, P. Grünanger, K. N. Houk and F. Marinone Albini, *J. Org. Chem.* **41**, 3349 (1976).

[19] Cf. a recent *intra*molecular case: O. Tsuge, K. Ueno and S. Kanemasa, *Chem. Lett.* 285 (1984).

[20] T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.* **82**, 5339 (1960); cp. R. Huisgen, W. Mack and E. Anneser, *Angew. Chem.* **73**, 656 (1961), and Ref. 12 (Christl).

[21] On longer reaction times, the isocyanate dehydrating agent is consumed slowly, probably due to oligomerization by the tertiary amine. Further, isocyanate slowly adds N,N'-diphenylurea: H. J. Günther, Dissertation, Universität Gießen (1978).

[22] BF_3 is known to alter the nitrile oxide dimerization course: S. Morocchi, A. Ricca, A. Selva and A. Zanarotti, *Chim. Ind. (Milan)* **50**, 558 (1968); *Gazz. Chim. Ital.* **99**, 1965 (1969). For use of BF_3 in nitrile oxide cycloadditions with nitriles and ketones, see S. Morrocchi, A. Ricca and L. Velo, *Tetrahedron Lett.* 331 (1967).

[23] A related approach to amino sugars, using optically active N-glycosyl nitrone/furan cycloadducts, was developed by Prof. Vasella. In a stereochemically complementary way, this led to the synthesis of D-nojirimycin: A. Vasella and R. Voeffray, *Helv. Chim. Acta* **65**, 1134 (1982); R. Voeffray, Dissertation, Universität Zürich (1983).

[24] For other nitrone-based routes to amino sugars, via 4-oxygenated isoxazolidines, see P. M. Wovkulich and M. R. Uskoković, *J. Am. Chem. Soc.* **103**, 3956 (1981); C. M. Dicken and P. DeShong, *J. Org. Chem.* **47**, 2047 (1982); P. DeShong, C. M. Dicken, J. M. Leginus and R. R. White, *J. Am. Chem. Soc.* **106**, 5598 (1984); cp. P. DeShong and J. M. Leginus, *Ibid.* **105**, 1686 (1983).

[25] Cf. Nitrone–furan cycloadditions: L. Fišera, J. Kováč and J. Poliačikova, *Heterocycles* **12**, 1005 (1979); L. Fišera, J. Kováč, J. Poliačikova and J. Leško, *Monatsh. Chem.* **111**, 909 (1980); L. Fišera, A. Gaplovský, H.-J. Timpe and J. Kováč, *Coll. Czech. Chem. Commun.* **46**, 1504 (1981); L. Fišera, S. Laudar and H.-J. Timpe, *Z. Chem.* **23**, 148 (1983).

[26] Cf. use of furan–aldehyde photocycloadditions in carbohydrate synthesis: T. Kozluk and A. Zamojski, *Tetrahedron* **39**, 805 (1983); A. Zamojski and G. Grynkiewicz, *The Total Synthesis of Natural Products* (Edited by J. Apsimon), Vol. 6, p. 141 ff. Wiley-Interscience, New York (1984). See also: S. L. Schreiber and K. Satake, *J. Am. Chem. Soc.* **105**, 6723 (1983); S. L. Schreiber and A. H. Hoveyda, *Ibid.* **106**, 7200 (1984).

[27] A. A. Frimer, *Synthesis* 579 (1977); see also Ref. 26; H. Meerwein, *Methoden der Organischen Chemie* (Edited by Houben, Weyl and Müller), 4th edn., Vol. 6/3, p. 118 ff. G. Thieme Verlag, Stuttgart (1965); C. L. Stevens and J. Tazuma, *J. Am. Chem. Soc.* **76**, 715 (1954); B. F. Coles, J. R. L. Smith and R. C. Garner, *J. Chem. Soc. Perkin Trans. I* 2664 (1979); J. J. Havel and K. H. Chan, *J. Org. Chem.* **41**, 513 (1976); P. Jarglis and F. W. Lichtenthaler, *Tetrahedron Lett.* 3781 (1982).

[28] R. A. W. Johnstone and M. E. Rose, *Tetrahedron* **35**, 2169 (1979).

[29] R. G. S. Ritchie, N. Cyr, B. Korsch, H. J. Koch and A. S. Perkin, *Can. J. Chem.* **53**, 1424 (1975); see also J. Urban, M. Marek, J. Jarý and P. Sedmera, *Coll. Czech. Chem. Commun.* **45**, 2779 (1980).

[30] Cf. all-carbon analogues: L. A. Paquette, *Top Curr. Chem.* **79**, 41 (1979).

[31] V. Van Rheenen, D. Y. Cha and R. C. Kelly, *Tetrahedron Lett.* 1973 (1976); V. Van Rheenen, D. Y. Cha and W. M. Hartley, *Org. Synth.* **58**, 43 (1978). Review: M. Schröder, *Chem. Rev.* **80**, 187 (1980); see also J. K. Cha, W. J. Christ and Y. Kishi, *Tetrahedron* **40**, 2247 (1984), and literature cited.

[32] V. Jäger and V. Buß, *Liebigs Ann. Chem.* 101 (1980); V. Jäger, V. Buß and W. Schwab, *Ibid.* 122 (1980).

[33] V. Jäger, I. Müller and E. F. Paulus, *Tetrahedron Lett.* 2997 (1985).

[34] R. Ehrler, Dissertation, Universität Würzburg, to be completed (1985).

[35] For an excellent review on 1,3-dipolar cycloreversions see G. Bianchi and R. Gandolfi, 1,3-*Dipolar Cycloaddition Chemistry* (Edited by A. Padwa), Vol. 2, p. 451. Wiley, New York (1984).

[36] These rules apparently apply also to the case of 1,3-diols: R. W. Hoffmann and U. Weidmann, *Chem. Ber.* (1985), in press. We thank Prof. Hoffmann, Marburg, for a preprint of this work.

[37] E. Truscheit, W. Frommer, B. Junge, L. Müller, D. D. Schmidt and W. Wingender, *Angew. Chem.* **93**, 738 (1981); *Ibid. Int. Ed. Engl.* **20**, 744 (1981).

[38] W. Schwab and V. Jäger, unpublished results (1980/1); W. Schwab, Dissertation, Universität Gießen (1981).

[39] B. Häfele and V. Jäger, unpublished results (1984).

[40] Additions of other group combinations (H/OCH_3; Br/Br; Br/OR; I/OR) occur with similar high stereoselectivity: Ref. 4; presented at the 3*rd Convegno Sulle Reazioni Pericicliche*, Naples, October (1984).

[41] L. René and R. Royer, *Synthesis* 878 (1981).

[42] Cf. L. F. Fieser and M. L. Fieser, *Reagents for Organic Synthesis*, p. 584. Wiley, New York (1967).