α-Amino Polyhydroxy Tetronic and Pentonic Acids from Bromodeoxyaldonolactones*

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Treatment of either 2-bromo-2-deoxy-L-threono- (**3**) or L-erythrono-1,4-lactone (**6**) with NaN_3 gave identical mixtures of 2-azido-2-deoxy-L-threono- (**7**) and -L-erythronolactone (**8**). Similar treatment of 2-bromo-2-deoxy-D-xylono-1,4-lactone (**13**) gave a 1:1 mixture of 2-azido-2-deoxy-D-xylono- (**15**) and -D-lyxono-1,4-lactone (**16**), while the 2-bromo-2-deoxy-D-arabinono-1,4-lactone (**24**) gave a 1:1 mixture of 2-azido-2-deoxy-D-arabinono- (**26**) and D-ribono-1,4-lactone (**27**). All isomers could be separated by either flash chromatography or crystallization. Catalytic hydrogenation of the azido lactones gave the corresponding amino lactones, as hydrochlorides, or the α-amino acids. The azido lactone **15** was converted into 2-acetamido-2-deoxy-D-xylose (**21**), while **26** gave 2-amino-2-deoxy-D-arabinose · HCl (**35**). The epimeric mixtures of azido lactones (**15**, **16**) or (**26**, **27**) were converted in a one-pot synthesis into 2-acetamido-5-*O*-acetyl-2,3-dideoxy-D-*threo*-pentono-1,4-lactone (**37**). The intermediate was shown to be 2-acetamido-5-*O*-acetyl-2,3-dideoxy-D-*glycero*-pent-2-eno-1,4-lactone (**36**), which was prepared from the fully acetylated amino lactones (**32**, **33**). The 2-bromo lactones, as well as the 2-azido lactones, were shown to equilibrate under basic conditions.

The α-amino-β-hydroxy acids are an important class of amino acids which are fundamental components in peptidases,[1] may act as enzyme inhibitors[2] or can be used as pharmaceuticals.[3] The necessity of having only one enantiomer has resulted in the appearance of several methods for the enantioselective synthesis of such compounds.[4,5,6] Optically active α-amino polyhydroxy acids may also be obtained from aldonic acids having the appropriate stereochemistry. Thus, using bromodeoxyaldonolactones, readily available from aldonic acids, we have recently described the preparation of amino acids and amino sugars by nucleophilic substitution with the azide ion.[7,8] Continuing this work, we now describe the reactions of 2-bromo-2-deoxy-tetrono- and -pentonolactones with azide ion.

Results and discussion

2-Bromo-2-deoxy-D-xylono- (**13**) and D-arabinono-1,4-lactone (**24**) were obtained by treatment of D-lyxono- and D-ribono-1,4-lactone, respectively, with hydrogen bromide in acetic acid (HBA).[9] Treatment of either potassium L-erythronate (**1**) or calcium L-threonate (**4**) with HBA yielded the 2,4-dibromo-2,4-dideoxy-L-threonic (**2**) and -L-erythronic acid (**5**), respectively, previously isolated as their methyl esters.[8] When the acids **2** and **5** were kept in aqueous solution at a pH of ca. 3, an intramolecular nucleophilic attack by the carboxylate on C-4 took place, leading to the 1,4-lactones **3** and **6**, respectively.

When either of the 2-bromo-2-deoxylactones (**3**) or (**6**) was treated with sodium azide in acetonitrile, the same mixture of the 2-azido-2-deoxy-L-threono- (**7**) and -L-erythronolactone (**8**) in a 2:3 ratio was obtained. The azido lactones could be separated by chromatography. Treatment of

*Part IX. For Part VIII, see Ref. 7.

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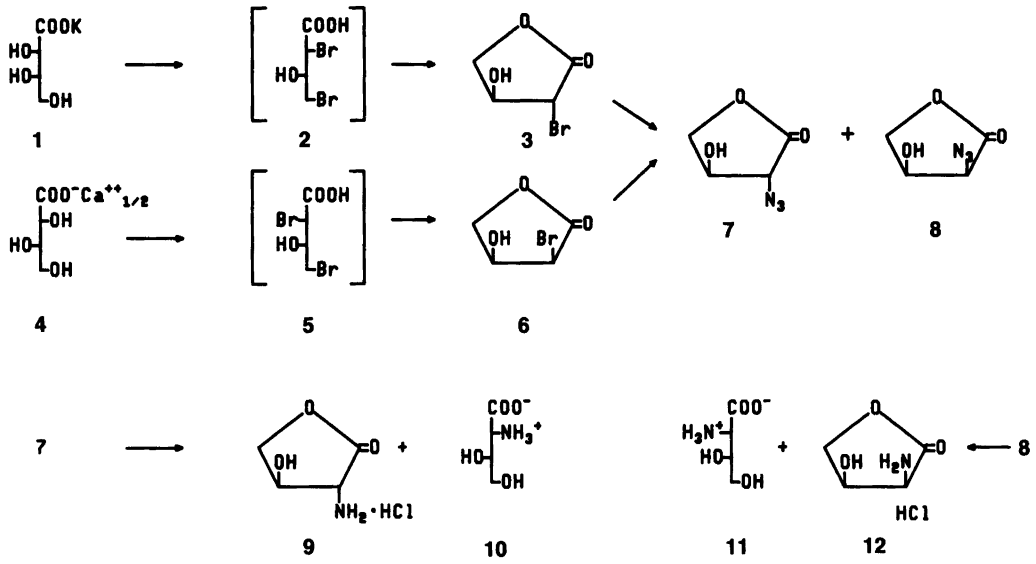
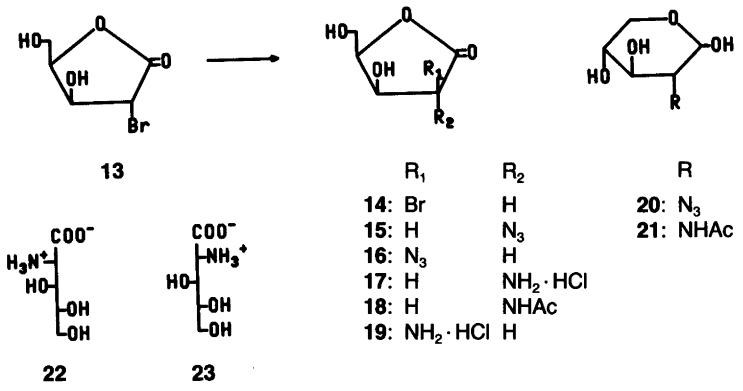


either 2-bromo-2-deoxy-D-xylono- (**13**) or -D-arabinono-1,4-lactone (**24**) under similar conditions gave 1:1 mixtures of 2-azido-2-deoxylactones **15** and **16**, and **26** and **27**, respectively. Chromatographic separation yielded the pure isomers, the *xylo* (**15**) and *arabino* (**26**) isomers being crystalline. Direct crystallization from the crude mixture of **26** and **27** gave **26** in 30–35 % yield. Catalytic hydrogenation of the azido lactones afforded the corresponding amino lactones in admixture with the α-amino acids. Thus, from the *threo* azido lactone **7** the 2-amino lactone **9** as well as the amino acid **10** could be prepared and isolated in a crystalline state. Similarly, the *erythro* isomer **8** gave the crystalline 2-amino lactone **12** and the amino acid **11**. These four isomers of α-amino-β-γ-dihydroxy butyric acid, as well as of their γ-lactone hydrochloride, have been described,[10,11] thus proving the L-*threo* configuration of **9** and **10** as well as the L-*erythro* configuration of **11** and **12** (the data for the compounds with D- and L-*threo*-configurations have been interchanged in Ref. 10).

In order to prove the configurations of the 2-azido lactones **15** and **16**, one of them (**15**) was treated with sodium borohydride to give a 2-azido-2-deoxy pentose (**20**). A ^{1}H NMR spectrum showed the presence of two anomers having J_{12} 4.0 and 8.0 Hz, respectively, confirming the *xylo* configuration. Furthermore, hydrogenation and acetylation gave the known 2-acetamido-2-deoxy-D-xylose (**21**).[12] The azido lactone **15** was hydrogenated in aqueous hydrochloric acid yielding the syrupy 2-amino-γ-lactone hydrochloride (**17**), together with a small amount of the δ-lactone, as seen from the ^{13}C NMR spectrum. The 2-amino-2-deoxy-D-xylono-γ- and δ-lactones, as a mixture, have been synthesised, together with the D-*arabino* isomer, from D-glyceraldehyde.[13] The free amino acid (**23**) was obtained as an amorphous substance by basifying the hydrochloride (**17**). Treatment of **23** in methanol with acetic anhydride gave the crystalline 2-acetamido-γ-lactone (**18**). The L-enantioner of **18** has been described,[3] together with other derivatives of the naturally occurring 2-amino-2-deoxy-L-xylonic acid and of the corresponding D-isomer (**23**). The L-enantiomer of **23**, the so-called polyoxamic acid, is a constituent of polyoxines, a family of antifungal antibiotics.[3]

The 2-azido-2-deoxy-D-lyxono lactone (**16**) was similarly converted into the amino lactone **19** and 2-amino-2-deoxy-D-lyxonic acid (**22**). From the mixture of azido lactones, having *arabino* (**26**) and *ribo* (**27**) configuration, one isomer (**26**) could be crystallized directly. Conversion to the 2-azido sugar (**34**), and subsequent reduction to 2-amino-2-deoxy-D-arabinose hydrochloride (**35**)[12] proved the *arabino* configuration of **26**. Hence, **27** was shown to be the *ribo* isomer. Cata-



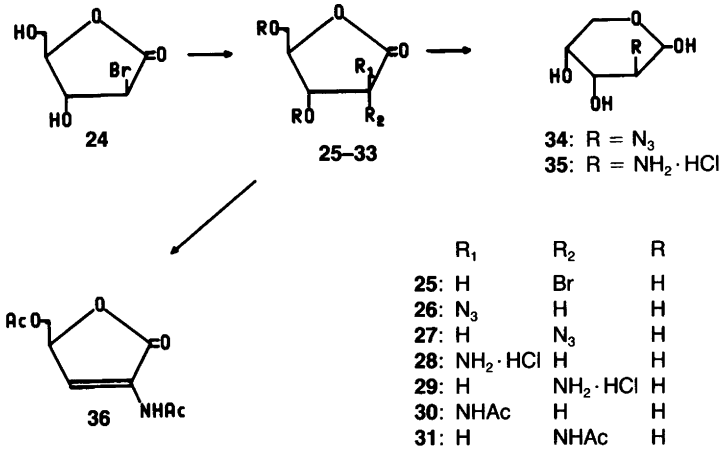
13

	R_1	R_2	R
14:	Br	H	
15:	H	N_3	
16:	N_3	H	
17:	H	$NH_2 \cdot HCl$	
18:	H	NHAc	
19:	$NH_2 \cdot HCl$	H	
20:			N_3
21:			NHAc

22 23

lytic hydrogenation of **26** and **27** produced the crystalline hydrochlorides of the 2-amino lactones **28**[13] and **29**, respectively.

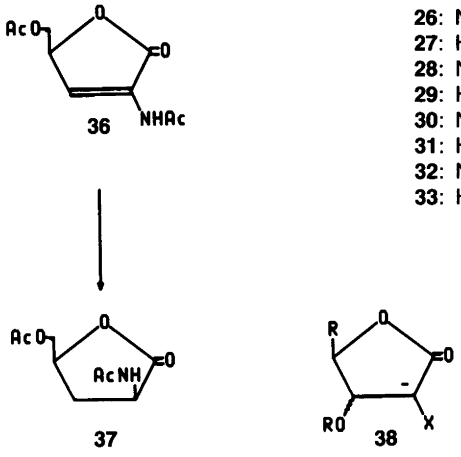
The convenient synthesis of 3-deoxyaldonolactones from acetylated aldonolactones[14] might be extended to the preparation of 2-amino-2,3-dideoxyaldonolactones from 2-azido lactones. All four isomers, **26** and **27**, and **15** and **16**, would be expected to give the same compound (**37**). Thus, the crude mixture of **26** and **27** was hydrogenated in the presence of acetic anhydride to give the acetamido compounds **30** and **31**, which were subsequently *O*-acetylated to **32** and **33**, respectively. Elimination of acetic acid by treatment with potassium fluoride in ethyl acetate gave the crystalline 2,3-unsaturated 2-acetamido lactone



24 25–33

34: R = N_3
35: R = $NH_2 \cdot HCl$

	R_1	R_2	R
25:	H	Br	H
26:	N_3	H	H
27:	H	N_3	H
28:	$NH_2 \cdot HCl$	H	H
29:	H	$NH_2 \cdot HCl$	H
30:	NHAc	H	H
31:	H	NHAc	H
32:	NHAc	H	Ac
33:	H	NHAc	Ac



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(**36**). Hydrogenation of the double bond yielded 2-acetamido-5-*O*-acetyl-2,3-dideoxy-D-*threo*-pentono-1,4-lactone (**37**). More conveniently, the synthesis of **37** could be performed as a one-pot procedure by catalytic hydrogenation of the crude mixture of azido lactones (**26** and **27**, or **15** and **16**) in the presence of acetic anhydride and triethylamine. A derivative of 2-amino-2,3-dideoxy-D-*threo*-pentono-1,4-lactone has previously been synthesised from D-xylose[15] with the aim of preparing clavalin, a β-lactam antibiotic.

The nucleophilic substitution of 2-bromo-2-deoxytetrono and -pentono lactones with azide ion gave ca. 1:1 mixtures of 2-azido lactones; this contrasts with the corresponding reactions of bromodeoxyhexonolactones,[7] for which the epimeric ratio was found to be ca. 95:5. We did observe[7] that an epimerisation at C-2 of the 2-bromo-2-deoxyhexonolactones took place in DMF in the presence of bromide ions. Similarly, a mixture of **3** and **6** was obtained when the 2-bromo-2-deoxy-L-threono lactone (**3**) was boiled in acetonitrile in the presence of 0.1 molar equiv. of sodium bromide; the reaction is probably an S_N2 displacement. However, we have also observed that a base may cause a similar isomerisation. Thus, the 2-bromoxylono lactone (**13**) in the presence of sodium azide in water showed, after 1.5 h at room temperature, the presence of the *lyxo* isomer (**14**) (**13**:**14** ~ 3:2), while the *arabino* isomer (**24**) in acetonitrile in the presence of triethylamine instantaneously gave a 1:1 mixture of **24** and the *ribo* isomer (**25**). These reactions probably proceed via abstraction of the α-hydrogen atom to give the carbanion **38** (X = Br) as an intermediate. The same intermediate (**38**, X = N_3) is probably responsible for the isomerisation of pure 2-azido lactones in the presence of azide ions. Thus, **8** was stable in boiling acetonitrile, but addition of sodium azide gave, after 3 h, **8** and **7** in the ratio 2:1.

Preparation of α-azido lactones by nucleophilic displacement has been reported to be an S_N2 process with no isomerisation.[16] The leaving group used was the reactive triflate, allowing the reaction to take place at −20 °C. However, a similar substitution was reported[17] to proceed with retention. The use of lithium azide to substitute a (4-chlorophenyl)sulfonyl group was reported to give pure inversion.[15] When the 2-bromoxylono lactone (**13**) was treated in DMF with lithium azide at −10 °C → +25 °C, the 2-azido lactones with *lyxo* (**16**) and *xylo* (**15**) configuration were formed in the ratio 4:1, while the ratio was 1:1 when sodium azide was used. Other experiments have indicated that lithium azide is more reactive, allowing substitutions to proceed at lower temperatures and thus with less isomerisation.

In conclusion, a nucleophilic substitution α to a carboxyl function may, in principle, always give two isomeric products, the ratio varying between 9:0.5 and 1:1. But, as described in this paper and in the preceding paper in this series,[7] optically pure azido lactones, and hence α-amino hydroxy acids and aminodeoxy sugars, can easily be obtained from bromodeoxy lactones.

Experimental

Melting points are uncorrected. Optical rotations were measured using a Perkin Elmer 241 polarimeter. NMR Spectra were recorded on Bruker WH-90 and AM-500 NMR instruments. Dioxane (67.40 ppm) was used as internal reference for ^{13}C NMR spectra, and acetone (δ 2.22) for ^1H NMR spectra in D_2O. TMS was used as the reference for spectra in $CDCl_3$. Column chromatography was performed on silica gel 60 (40–63 μm, Merck 9385) using the flash technique. Evaporations were carried out in vacuum at 50 °C, unless otherwise indicated. Microanalyses were performed by NOVO Microanalytical Laboratory, Bagsværd, Denmark.

2-Bromo-2-deoxy-L-threono-1,4-lactone (**3**). Potassium L-erythronate (**1**)[8,18] (16.6 g) was stirred with 170 ml of a 32 % solution of hydrogen bromide in acetic acid (HBA) for 1.5 h at room temperature. Water (400 ml) was then added and the mixture was allowed to stand for 2 h. Concentration left a residue containing the dibromo acid (**2**). ^{13}C NMR (D_2O): 171.5 ppm (C-1), 71.4 (C-3), 52.6 (C-2), 35.3 (C-4). An aqueous solution of Na_2CO_3 was added until pH = 3. Concentration left a residue which was dissolved in water (60 ml); the aqueous solution was extracted with EtOAc (6×50 ml). The combined extracts were dried (Na_2SO_4), treated with activated carbon, and concentrated to give the syrupy 2-bromo lactone (**3**) (13.7 g, 79 %), which was pure as judged from ^{13}C NMR spectra (D_2O): 174.9 ppm (C-1), 75.0 (t, *J* 155 Hz, C-4), 74.5 (d, *J* 158 Hz, C-3), 42.6 (d, *J* 163 Hz, C-2). A sample

was purified further by distillation, b.p. 150–160 °C/2 mmHg; $[\alpha]_D^{20}$ +14° (*c* 5.0, $CHCl_3$). Anal. $C_4H_5BrO_3$: C, H, Br.

2-Bromo-2-deoxy-L-erythrono-1,4-lactone (**6**). Calcium L-threonate[8,19] (**4**) (10.0 g) was treated with HBA (100 ml) for 1.5 h at room temperature as described above. The residue containing the dibromo acid (**5**) [^{13}C NMR (D_2O: 171.7 ppm (C-1), 71.2 (C-3), 46.7 (C-2), 36.8 (C-4)] was adjusted to pH 3 and worked up as described above to give the 2-bromo lactone (**6**) (8.5 g, 73 %) as a syrup, which was pure as judged from ^{13}C NMR spectra (D_2O): 170.7 ppm (s, C-1); 71.1 (t, *J* 155 Hz, C-4), 66.1 (d, *J* 159 Hz, C-3), 44.5 (d, *J* 154 Hz, C-2). A sample was distilled, b.p. 135–145 °C/1–2 mmHg; $[\alpha]_D^{20}$ +5.0° (*c* 4, $CHCl_3$). Anal. $C_4H_5BrO_3$: C, H, Br.

2-Azido-2-deoxy-L-threono- (**7**) *and -L-erythrono-1,4-lactone* (**8**). *a: From* **3**. The 2-bromo lactone **3** (8.6 g) was boiled under reflux in acetonitrile (125 ml) together with NaN_3 (15 g) for 2.5 h with protection from light. After filtration and concentration, the residue was dissolved in EtOAc (50 ml) and the solution was washed twice with water (10 ml). The organic layer was dried (Na_2SO_4), treated with activated carbon and concentrated to give a product (5.9 g, 87 %) containing the two azido lactones **7** and **8** in the ratio 2:3, as seen from a ^{13}C NMR spectrum. The compounds were separated by flash chromatography (EtOAc/Hexane, 1:1) to give 2-azido-2-deoxy-L-threono-1,4-lactone (**7**) (1.3 g, 19 %) as a syrup. ^{13}C NMR (D_2O): 174.3 ppm (C-1), 71.1 (d and t, C-3 and C-4), 63.8 (d, C-2). A mixed fraction (1.0 g, 14 %) was then isolated, followed by syrupy 2-azido-2-deoxy-L-erythrono-1,4-lactone (**8**) (2.0 g, 30 %). ^{13}C NMR (D_2O): 174.5 ppm (C-1), 74.2 (t, C-4), 69.6 (d, C-3), 61.3 (d, C-2).

b: From **6**. The bromo lactone **6** (14.3 g) was boiled under reflux in acetonitrile (150 ml) together with sodium azide (28 g) for 5 h with protection from light. Filtration and concentration gave a residue which was worked up as described above to give 7.5 g (66 %) of a mixture of the 2-azido lactones **7** and **8** in the ratio 2:3, as seen from the ^{13}C NMR spectrum.

2-Amino-2-deoxy-L-threono-1,4-lactonehydrochloride (**9**). The azido lactone **7** (900 mg) in water (25 ml) and 12 M HCl (1 ml) was hydrogenated (70 atm. H_2) in the presence of 5 % palladium-on-carbon (100 mg) over night. Filtration and concentration gave a residue which contained the lactone **9** together with the acid hydrochloride. Crystallization from EtOH gave **9** (300 mg, 31 %); m.p. 173–175 °C. Recrystallization from EtOH/EtOAc/$CHCl_3$ gave a product with m.p. 174–176 °C; $[\alpha]_D^{20}$ +27.3° (*c* 0.6, H_2O); [lit.[10] m.p. 175–175.5 °C; $[\alpha]_D$ +26° (D and L are interconverted); cf.[20] m.p. 163 °C, $[\alpha]_D$ −29.5° for the D enantiomer]. ^{13}C NMR (D_2O): 172.4 ppm (C-1), 71.8 (C-4), 69.9 (C-3), 56.1 (C-2). The mother-liquor from crystallization of **9** was boiled in water (20 ml) for 1.5 h and the solution was poured on a column of ion-exchange resin (Amberlite IR-120, H^+, 20 ml). Elution with water until neutral, followed by elution with aqueous ammonia (12.5 %, 250 ml) gave, after concentration of the ammoniacal eluate, 2-amino-2-deoxy-L-threonic acid (**10**) (0.26 g, 31 %); m.p. 208–212 °C. Recrystallization from H_2O/MeOH gave **10** with m.p. 210–212 °C; $[\alpha]_D^{20}$ +12.8° (*c* 0.6, H_2O); (lit.[11]) m.p. 214–215 °C, $[\alpha]_D^{20}$ +13.1° (*c* 4.8, H_2O).

2-Amino-2-deoxy-L-erythrono-1,4-lactone hydrochloride (**12**). The 2-azido lactone **8** (1.0 g) in water (25 ml) and 12 M HCl (1 ml) was hydrogenated, and the reaction mixture worked up as described above to give a crystalline residue (~1 g). Crystallization from EtOH gave **12** (750 mg, 70 %); m.p. 170–174 °C. Recrystallization from EtOH/EtOAc gave a product with m.p. 175–177 °C; $[\alpha]_D$ +54.3° (*c* 0.5, H_2O); [lit.[10] m.p. 176°; $[\alpha]_D$ +55.6° (*c* 1.5, H_2O)]. ^{13}C NMR (D_2O): 173.6 ppm (C-1), 75.9 (C-4), 67.1 (C-3), 52.9 (C-2). The mother-liquor was treated as described above to give 2-amino-2-deoxy-L-erythronic acid (**11**), which was crystallized from H_2O/MeOH (70 mg, 7 %); m.p. 190–193 °C. Recrystallization from the same solvent gave **11** with m.p. 192–194 °C; $[\alpha]_D$ −7.8 (*c* 0.7, H_2O); [lit.[10] m.p. 194–195 °C; $[\alpha]_D^{23}$ −11.3; (*c* 7.2, H_2O)].

2-Azido-2-deoxy-D-xylono- (**15**) *and -D-lyxono-1,4-lactone* (**16**). The 2-Bromo-2-deoxy-D-xylono-1,4-lactone (**13**) (5.0 g) and NaN_3 (5 g) in CH_3CN (50 ml) were boiled for 6 h with protection from light. Filtration and concentration gave a residue to which EtOAc (50 ml) was added,

followed by filtration and concentration. The resulting syrup was dissolved in water (10 ml) and the solution was extracted with EtOAc (10×20 ml). The combined extracts were dried (Na_2SO_4) and concentrated to give 3.9 g (95 %) of a mixture of the azido lactones **15** and **16** in ca. 1:1 ratio. Flash chromatography (EtOAc/hexane, 3:1) gave 1.2 g (29 %) of the *xylo* isomer **14**. ^{13}C NMR (D_2O): 174.9 ppm (C-1), 82.1 (C-4), 72.5 (C-3), 64.0 (C-5), 59.8 (C-2). Crystallization from ether gave 0.57 g (14 %); m.p. 80–82 °C; $[\alpha]_D^{20}$ +222° (*c* 1.5, EtOAc). Anal. $C_5H_7N_3O_4$: C, H, N. A mixture (0.74 g, 18 %) of **15** and **16** was then isolated, followed by the *lyxo* isomer (**16**) (1.27 g, 31 %) which was pure as judged from a ^{13}C NMR spectrum (D_2O): 175.5 ppm (C-1), 83.9 (C-4), 71.0 (C-3), 63.2 (C-5), 60.6 (C-2).

2-Amino-2-deoxy-D-xylonic acid (**23**). A mixture of the azido lactone **15** (500 mg), water (10 ml) and 4 M HCl (1.1 ml) was stirred in an H_2 atmosphere in the presence of 5 % palladium-on-carbon (100 mg) overnight. Filtration and concentration gave a syrupy residue (~700 mg) containing 2-amino-2-deoxy-D-xylono-1,4-lactone hydrochloride (**17**), as seen from a ^{13}C NMR spectrum (D_2O): 171.8 ppm (C-1), 81.9 (C-4), 70.2 (C-3), 59.3 (C-5), 55.2 (C-2). A minor component was present, probably the corresponding 1,5-lactone[13]: 170.8 ppm (C-1), 73.3 (C-4), 68.0 (C-3), 63.0 (C-5), 57.2 (C-2). The product was basified on a column of ion-exchange resin (Amberlite IR 120 H^+, 15 ml) by elution with aqueous ammonia as described above to give **23** (200 mg, 42 %) as a syrup. ^{13}C NMR (D_2O): 173.5 ppm (C-1), 73.9 (C-4), 69.0 (C-3), 63.3 (C-5), 58.8 (C-2). The amino acid could not be induced to crystallize.

2-Acetamido-2-deoxy-D-xylono-1,4-lactone (**18**). 2-Amino-2-deoxy-D-xylonic acid (**23**) (250 mg) was suspended in MeOH (10 ml) containing acetic anhydride (1 ml). The mixture was stirred overnight and then concentrated. The residue was purified by flash chromatography ($CHCl_3$/MeOH, 10:1) to give **18** (115 mg, 40 %); m.p. 136–140 °C; (lit.[3] m.p. 146–150 °C, 150–152 °C[21]). ^1H NMR (500 MHz, $CDCl_3$, DMSO as reference): δ 8.05 (d, NH), 5.30 (d, OH-3, *J* 6.0 Hz), 4.50 (m, H-2, H-3 and H-4), 3.90 (ddd, H-5, $J_{55'}$ 12.0, J_{50H} and J_{45} 6.0 and 3.0), 3.75 (ddd, H-5′, $J_{45'}$ and $J_{5'OH}$ 3.0 and 6.0), 1.95 (s, NAc).

2-Azido-2-deoxy-D-xylose (**20**). A solution of the 2-azido lactone **15** (600 mg) in water (20 ml) was cooled to 0 °C. Ion-exchange resin (Amberlite IR 120, H^+, 15 ml) was added, and $NaBH_4$ (400 mg) was added with stirring in the course of 30 min, keeping the pH at 5–6. After another 30 min the mixture was filtered and concentrated, and the residue was co-concentrated twice with methanol to give the azido sugar (**20**) (0.47 g, 95 %) as a syrup; α:β ratio 2:3. ^{13}C NMR (D_2O): α-anomer: 92.4 ppm (C-1), 72.7, 67.8, 65.8, 64.5 (C-2, C-3, C-4, C-5); β-anomer: 96.8 ppm (C-1), 75.5, 70.2, 66.2, 62.5 (C-2, C-3, C-4, C-5). ^1H NMR (500 MHz, D_2O): α-anomer: δ 5.35 (d, H-1, J_{12} 4.0 Hz), 3.2–4.3 (H-2, H-3, H-4, H-5); β-anomer: 4.67 (d, H-1, J_{12} 8.0 Hz), 3.2–4.3 (H-2, H-3, H-4, H-5).

2-Acetamido-2-deoxy-D-xylose (**21**). A mixture of the 2-azido sugar **20** (470 mg), CH_3OH (20 ml) and Ac_2O (1.0 ml) was stirred in an H_2 atmosphere overnight in the presence of 5 % palladium-on-carbon (100 mg). Filtration and concentration gave a residue (530 mg, ~100 %) which crystallized on addition of EtOH to give α-**21**; m.p. 176–184 °C. Recrystallization from ethanol/hexane gave a product with m.p. 182–184 °C; $[\alpha]_D$ +26.8° → +6.0° (*c* 1.2, H_2O); [lit.[12] m.p. 186–190 °C; $[\alpha]_D$ +55° → 7.8° (*c* 0.64, H_2O)]. ^{13}C NMR (D_2O): α-anomer: 92.0 ppm (C-1), 71.8, 70.8 (C-3, C-4), 62.0 (C-5), 54.9 (C-2), 175.3 and 22.9 (NAc); β-anomer: 96.6 (C-1), 70.4, 66.1 (C-3, C-4, C-5), 57.5 (C-2), 177.8 and 23.1 (NAc).

2-Amino-2-deoxy-D-lyxonic acid (**22**). A mixture of 2-azido lactone **16** (2.58 g), water (40 ml) and 4M HCl (5.6 ml) was stirred in an H_2 atmosphere for 8 h in the presence of 5 % palladium-on-carbon (200 mg). Filtration and concentration gave the syrupy 2-amino lactone hydrochloride (**19**) (2.12 g, 77 %), as seen from the ^{13}C NMR spectrum (D_2O): 173.1 ppm (s, C-1), 84.4 (d, C-4), 67.9 (d, C-3), 60.2 (t, C-5), 53.7 (d, C-2). The product could not be crystallized. The product (650 mg) was basified on a column of Amberlite IR 120 (H^+, 20 ml) as described above. This gave 2-amino-2-deoxy-D-lyxonic acid (**22**) as a syrup (500 mg, 65 %). ^{13}C NMR (D_2O): 172.6 ppm (C-1), 72.8 (C-4), 68.5 (C-3), 63.5 (C-5), 59.7 (C-2).

2-Azido-2-deoxy-D-arabinono- (**26**) *and -D-ribono-1,4-lactone* (**28**). The 2-bromo-2-deoxy-D-arabino lactone (**24**)[9] (5.0 g) was treated with NaN_3 (5.0 g) in boiling CH_3CN (7 h) as described above to give a syrup (3.5 g, 85 %) consisting of the 2-azido lactones **26** and **27** in a ratio of ca. 1:1. Addition of ether gave 1.3 g (32 %) of the *arabino* isomer (**26**); m.p. 105–111 °C. Recrystallization from ethyl acetate/hexane gave **26** with m.p. 118–120 °C; $[\alpha]_D^{20}$ −76° (*c* 1.6, EtOAc). Anal. $C_5H_7N_3O_4$: C, H, N. ^{13}C NMR (D_2O): 173.8 ppm (C-1), 83.5 (C-4), 72.0 (C-3), 65.3 (C-2), 60.0 (C-5). The mother-liquor from crystallization of **26** contained **26** and the *ribo* isomer (**27**) in a ca. 1:4 ratio. ^{13}C NMR (D_2O) of **27**: 175.7 ppm (C-1), 88.5 (C-4), 71.7 (C-3), 61.9, 61.5 (C-2, C-5). Pure **27** is reported to be crystalline.[17]

2-Amino-2-deoxy-D-arabinono-1,4-lactone hydrochloride (**28**). The 2-azido lactone **26** (1.0 g) was hydrogenated for 2 h as described above. The residue, which crystallized on addition of EtOH, gave the amino lactone hydrochloride **28** (800 mg, 75 %); m.p. 166–170 °C. Recrystallization from water/acetone gave a product with m.p. 172–173 °C; $[\alpha]_D^{20}$ +45.0° (*c* 1.8, H_2O); (lit.[13] for the amino lactone: m.p. 175 °C; $[\alpha]_D$ +44°). Anal. $C_5H_{10}ClNO_4$: C, H, Cl, N. ^{13}C NMR (D_2O): 171.0 ppm (C-1), 84.1 (C-4), 70.0 (C-3), 59.7 (C-5), 56.7 (C-2).

2-Amino-2-deoxy-D-ribono-1,4-lactone hydrochloride (**29**). Crude 2-azido-2-deoxy-D-ribono lactone (**27**) (2.4 g) (obtained as described above from crystallization of **26**, and containing ~20 % of the latter) was hydrogenated for 5 h as usual. Work-up gave a crystalline residue (1.7 g, 67 %); m.p. 183–185 °C. Recrystallization from H_2O (a few drops)/acetone gave **29** with m.p. 190–191 °C; $[\alpha]_D^{20}$ +6.0° (*c* 1.9, H_2O). Anal. $C_5H_{10}ClNO_4$: C, H, N, Cl. ^{13}C NMR (D_2O): 173.1 ppm (C-1), 88.9 (C-4), 67.9 (C-3), 60.4 (C-5), 51.9 (C-2).

2-Azido-2-deoxy-D-arabinose (**34**). To a solution of borane dimethylsulfide adduct (3.5 ml, 10 M) in THF (10 ml) was slowly added 2-methyl-2-butene (7.5 ml) under N_2, and the mixture was then kept at room temperature for 5 h. The azido lactone **26** (1.0 g) in THF (10 ml) was added slowly at 0 °C, and the mixture was allowed to reach room temperature overnight. Water (10 ml) was then added and the mixture was boiled for 1 h. Concentration gave a residue which was dissolved in water and extracted three times with dichloromethane. The aqueous phase was concentrated to give syrupy 2-azido-2-deoxy-D-arabinose (**34**) (800 mg, 79 %). ^{13}C NMR (D_2O): α-anomer: 96.7 ppm (C-1), 72.1 (C-3), 68.6, 67.4, 65.6 (C-2, C-4, C-5); β-anomer: 92.5 (C-1), 69.2, 68.1 (C-3, C-4), 63.4, 61.4 (C-2, C-5). ^1H NMR (500 MHz, D_2O): α-anomer: δ 4.61 (d, H-1, J_{12} 8.0 Hz), 3.54 (dd, H-2, J_{23} 10.5 Hz), 3.6–4.2 (m, H-3, H-4, H-5); β-anomer: δ 5.42 (d, H-1, J_{12} 3.5 Hz), 3.6–4.2 (m, H-2, H-3, H-4, H-5).

2-Amino-2-deoxy-D-arabinose hydrochloride (**35**). A solution of the azido sugar **34** (800 mg) in water (20 ml) containing 1.2 ml 4 M HCl was stirred in a hydrogen atmosphere overnight in the presence of palladium-on-carbon (5 %, 200 mg). Filtration and concentration gave a product which crystallized on addition of EtOH. This gave **35** (500 mg, 59 %); m.p. 151–153 °C; $[\alpha]_D^{20}$ −153° (3 min) → −120° (20 h) (*c* 1.4, H_2O); (lit.[12] m.p. 154–157 °C; $[\alpha]_D$ −158° → −120°). ^{13}C NMR (D_2O): 94.1 ppm (C-1, β), 90.2 (C-1, α), 69.7, 68.7, 68.2, 67.5, 66.3, 63.2 (C-3, C-4, C-5), 55.4, 52.1 (C-2).

*5-O-Acetyl-2-acetamido-2,3-dideoxy-D-*glycero*-pent-2-eno-1,4-lacton* (**36**). The 2-bromo lactone **24** (or the isomeric bromo lactone **13**) (5.0 g) was treated with sodium azide as described above to give a mixture of the 2-azido lactones **26** and **27** (3.85 g, 94 %). The mixture was dissolved in CH_3OH (50 ml) together with acetic anhydride (8 ml) and stirred in a hydrogen atmosphere for 3 h in the presence of palladium-on-carbon (5 %, 500 mg). Filtration and concentration gave a ca. 1:1 mixture of the acetamido compounds **30** and **31** (~5 g). ^{13}C NMR (D_2O): 177.5, 174.1, 175.2, 175.0 ppm (C-1 and carbonyl), 88.6, 83.8 (C-4), 71.4, 69.7 (C-3), 61.6, 60.7 (C-5), 58.2, 53.6 (C-2), 22.6 (NAc), 21.4 (OAc). Acetic anhydride (15 ml) and 60 % aqueous $HClO_4$ (a few drops) were added, and after 1 h water was added; after a further 15 min NaOAc was added until neutral. The residue obtained on concentration was dissolved in EtOAc and the solution was filtered through silica gel. The filtrate was concentrated to give the acetates **32** and **33** (~6.4 g) (ca. 1:1). ^{13}C NMR ($CDCl_3$): 172.6, 170.8, 170.1, 169.8, 169.4 ppm (C-1 and carbonyl), 80.3, 77.8 (C-4), 73.1, 70.1 (C-3), 62.7, 62.4 (C-5), 54.8, 49.4

(C-2), 21.7 (NAc), 20.0 (OAc). The product was stirred in dry EtOAc (100 ml) with KF (10 g) for 5 h, after which the solution was filtered and concentrated to give a crystalline residue (3.6 g) of **36**; addition of ether gave 3.0 g (59 %) of **36**, m.p. 150–154 °C. Recrystallization from ethyl acetate/hexane gave **36** with m.p. 153–154.5 °C; $[\alpha]_D^{20}$ +35.8° (*c* 0.7, EtOAc) (Reported[21] for the L-isomer: m.p. 160–161 °C; $[\alpha]_D$ was not reported). Anal. $C_9H_{11}NO_5$: C, H, N. ^{13}C NMR ($CDCl_3$): 170.0, 169.2, 168.8 ppm (C-1 and carbonyl), 126.7 (C-2), 124.7 (C-3), 78.8 (C-4), 63.2 (C-5), 23.0 (NAc) and 20.1 (OAc).

*5-O-Acetyl-2-acetamido-2,3-dideoxy-D-*threo*-pentono-1,4-lactone* (**37**). *a: From azido lactones.* A crude mixture of the azido lactones **26** and **27** (4.2 g) was hydrogenated in EtOAc (100 ml) containing Et_3N (16.8 ml), acetic anhydride (8.0 ml) and palladium-on-carbon (5 %, 600 mg) at ca. 50 atm. overnight. Filtration and concentration gave a residue which was dissolved in water (200 ml). The solution was extracted with CH_2Cl_2 (10 ml) which was discarded. The CH_2Cl_2 probably contained a small portion of 2,3-oxazolidines. The aqueous phase was then subjected to continuous extraction with EtOAc for 3 h. The organic phase was dried (Na_2SO_4), filtered and concentrated to give syrupy **37** (3.0 g, 58 %), which was pure as seen from a ^{13}C NMR spectrum ($CDCl_3$): 174.1, 170.6, 170.2 ppm (C-1 and carbonyl), 74.5 (C-4), 64.2 (C-5), 49.1 (C-2), 30.1 (C-3), 22.0 (NAc), 20.1 (OAc). A sample was purified by kugelrohr distillation: bp ~240–250°/0.5 mmHg; $[\alpha]_D^{20}$ +46.9° (*c* 0.7, EtOAc). Anal. $C_9H_{13}NO_5$: C, H, N. Starting from the *xylo,lyxo* azide lactones (**15** and **16**) (4.0 g) and using the same procedure, 2.4 g (48 %) of **37** was obtained. A ^{13}C NMR spectrum was identical with that of the product described above.

b: From **36**. The unsaturated lactone **36** (1.0 g) was hydrogenated in EtOH (50 ml) in the presence of palladium-on-carbon (5 %, 100 mg) at 100 atm. Filtration and concentration gave **37** (1.0 g, 99 %), which was pure as seen from a ^{13}C NMR spectrum, identical with that described above. $[\alpha]_D^{20}$ +46.3° (*c* 0.24, EtOAc).

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