

Base-Catalyzed Rearrangement of 6-Bromo-3,6-dideoxy-aldohexono-1,4-lactones*

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Upon treatment of 3-deoxy-D-*arabino* and 3-deoxy-D-*xylo*-hexono-1,4-lactone with hydrogen bromide in acetic acid (HBA), 6-bromo-3,6-dideoxy-D-*arabino*- and 6-bromo-3,6-dideoxy-D-*xylo*-hexono-1,4-lactone are produced. When reacted with anhydrous potassium carbonate in acetone the two bromodeoxylactones are converted into epoxides. Exposed to excess aqueous potassium hydroxide, the bromodeoxylactones, or the epoxides, rearrange to give 3-deoxy-L-*ribo*- and 3-deoxy-L-*lyxo*-hexono-1,4-lactone. Consequently, inversion at both C-4 and C-5 has taken place. In both cases, considerable amounts of anhydrides are formed along with the lactones. The mechanism of the base-induced rearrangements is discussed. The various 6-bromodeoxylactones undergo hydrogenolysis to give the corresponding 3,6-dideoxyhexono-1,4-lactones. On reduction, the 3,6-dideoxy-D-*arabino*-hexono-1,4-lactone affords 3,6-dideoxy-D-*arabino*-hexose (tyvelose).

Continuing our work on bromodeoxylactones,^{1,4} we recently became interested in their behaviour towards nucleophiles.^{5,6} In a previous paper,⁶ the base catalyzed rearrangement of 6-bromo-2,6-dideoxy-D-*arabino*-hexono-1,4-lactone into 2-deoxy-L-*ribo*-hexono-1,4-lactone was described. We now report on the behaviour of 6-bromo-3,6-dideoxy-D-*arabino*-(*3a*) and 6-bromo-3,6-dideoxy-D-*xylo*-hexono-1,4-lactone (*16a*) towards base.

Certain 3-deoxy-aldono-1,4-lactones can be prepared from fully acetylated aldono-1,4-lactones by a reductive elimination reaction.⁷ Thus, the two 3-deoxy-D-hexono-1,4-lactones, *1a* and *15a*, utilized in the present study, were obtained from the D-glucono- and D-galactono-lactones, respectively. The corresponding 6-bromo-3,6-dideoxy-hexono-lactones *3a* and *16a* were obtained in high yields by treatment of *1a* (or the corresponding salt (*6*)) and *15a*, respectively, with hydrogen bromide in acetic acid. When treated with

excess aqueous potassium hydroxide, the 6-bromo-lactone (*3a*) gave a mixture of two products; according to ¹³C NMR spectroscopy the major component consisted of a 3-deoxy-aldohexonate. After acetylation, the virtually homogeneous acetylated 3-deoxy-hexono-1,4-lactone (*8b*) was obtained in 55% yield. Deacetylation afforded the free lactone (*8a*) which was identified as the enantiomer of the known 3-deoxy-D-*ribo*-hexono-1,4-lactone.^{8,9} Obviously, the reaction of the 6-bromolactone (*3a*) with aqueous potassium hydroxide is accompanied by inversion at both C-4 and C-5. After esterification and acetylation, the minor product exhibited NMR-data in accordance with the 2,5-anhydride structure (*12b*, R₁ = OCH₃).

The base-catalyzed rearrangements of 6-bromo-6-deoxy-lactones are probably initiated by the formation of a 5,6-epoxide.⁶ Upon reaction of the 6-bromo-3,6-dideoxy-lactone (*3a*) with anhydrous potassium carbonate in acetone, a crystalline 5,6-epoxide (*5*) can indeed be isolated. On treatment with aqueous potassium hydroxide the latter gave the same products as were obtained

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Table 1. ^{13}C NMR spectra of 3-deoxy-aldono-1,4-lactones and of potassium salts of 3-deoxy-aldonic acids in $\text{H}_2\text{O} + \text{D}_2\text{O}$ solutions

Compound	Chemical shifts, ppm					
	C-1	C-2	C-3	C-4	C-5	C-6
1a	180.0	68.7*	32.1	78.0	72.1*	62.5
2a, 8a	180.4	67.8*	31.5	79.9	72.7*	62.7
15a	180.0	68.6*	33.1	78.4	72.8*	62.7
25a	—	67.6*	33.5	79.6	73.6*	62.8
6	182.9	70.3	38.4	75.9	70.3	63.2
14	182.6	71.9	38.3	75.6	71.9	63.9
11, 20	182.6	69.2*	38.8	75.6	70.3*	63.8
22	182.6	69.9*	38.3	74.2	71.1*	63.7
5	179.7	68.4	31.5	76.6	52.5	45.1
7	182.1	69.7	38.7	67.7	55.9	46.1
13	181.5	70.8	37.4	55.7	62.6*	61.4*
18	179.9	68.4	33.7	78.4	53.9	45.7
21	182.2	69.8*	38.9	69.9*	57.1	46.7
19	—	—	33.5	59.2	56.1	60.4

*May be interconverted.

from the 6-bromolactone (3a) under similar conditions. To study the rearrangements more closely, the reactions were monitored by ^{13}C -NMR spectroscopy. When the epoxide 5 was treated with an equivalent of potassium hydroxide in water, the lactone opened, and the anion 7 was observed (Table 1). When more base (1.5 equivalent) was added, the rearranged epoxide (13) rapidly appeared, together with the 3-deoxy-L-ribo-hexonate (14) and the 2,5-anhydride (12a, $\text{R}_1 = \text{O}^-$). After 30 min at room temperature the reaction was complete and the rearranged aldinate 14 and the anhydride (12a, $\text{R}_1 = \text{O}^-$) were present in a 5:1 ratio. In the strong basic solution the equilibrium between the 5,6-epoxide (7) and the 3,4-epoxide (13) was rapidly shifted^{6,10} towards the latter, which, in turn, opened up with inversion at C-4 through neighbouring group participation from the carboxylate ion in a five-membered transition state. The competing reaction (attack of OH-2 on C-5 in 7 to give a 2,5-anhydride) was not observed in the corresponding rearrangement of the 6-bromo-2,6-dideoxy-D-arabino-hexono-1,4-lactone with strong base to 2-deoxy-L-ribo-hexonic acid.⁶ The epoxide 5 was also treated with aqueous potassium carbonate and the reaction was followed by ^{13}C NMR spectroscopy. When 1.1 mol of carbonate was used, 7 was initially formed but in the course of three

days underwent ring-opening to give equal amounts of two isomeric 3-deoxy-aldohexonates with *arabino*- (6) and *xylo*- (11) configurations. When 3 moles of carbonate were used, the spectrum, after one day revealed the presence of 6 and 11 in the ratio 7:1.

The 3-deoxy-L-ribo-hexono-1,4-lactone (8a), upon reaction with HBA, was converted into the 6-bromo-3,6-dideoxy-L-ribo-hexono-1,4-lactone (9a). When the latter was treated with an excess of aqueous potassium hydroxide a ^{13}C NMR spectrum showed that a 3-deoxy-aldohexonate with D-*arabino*-configuration (6) had been formed together with a minor quantity of a 2,5-anhydride. The mixture was not further investigated.

When the 6-bromo-3,6-dideoxy-D-*xylo*-hexono-1,4-lactone (16a) was treated with potassium carbonate under anhydrous conditions, the crystalline 5,6 epoxide (18) could be isolated in good yield. Treatment of the latter, or the bromide (16a), with strong aqueous potassium hydroxide gave, according to ^{13}C NMR data, a mixture of three compounds. After acetylation the 3-deoxy-lactone (25b) could be crystallized in 15% yield. Hence, inversions at C-4 and C-5 had taken place also in this case, yet without representing the main reaction. When the reaction mixture was treated with methanol and sulfuric acid, followed by acetylation, 25b could be iso-

lated after chromatography, along with the 2,6-anhydride (23b, $R_1 = \text{OCH}_3$), and the 2,5-anhydride (24b, $R_1 = \text{OCH}_3$). The structures of the latter two followed from their ^1H and ^{13}C NMR spectra. The compounds 25b, 24b ($R_1 = \text{OCH}_3$) and 23b ($R_1 = \text{OCH}_3$) were isolated in a ratio of about 1:3.5:5.

Treatment of the epoxide (18) in water with one equivalent of potassium hydroxide, gave the anion 21, as seen from a ^{13}C NMR spectrum. Immediately after the addition of another 1.3 equivalent of potassium hydroxide, a spectrum revealed the presence of the anhydrides 23a ($R_1 = \text{O}^-$) and 24a ($R_1 = \text{O}^-$), accompanied by a trace of the rearranged epoxide 19 and the 3-deoxy-L-xylo-aldohexonate (22). In this case the rearrangement of the epoxide 21 to the 3,4-epoxide (19) was not the favoured reaction. The weaker base, potassium carbonate in water, reacted with 18 to give solely the ring-opened product, 3-deoxy-D-xylo-hexonate (20).

In summary, the base catalyzed reactions of 6-bromo-3,6-dideoxy-lactones, via 5,6-epoxides, are dependent on the structures of the bromolactones. Within the *arabino* (3a)- or *ribo* (9a)-series, inversions at C-4 and C-5 constitute the predominant features, as is the case for the corresponding 6-bromo-2,6-dideoxy-lactones.⁶ In the case of the *xylo*-configuration (16a), the formation of 2,6- (23) and 2,5 (24)-anhydrides becomes the major reaction; similar anhydride formation is observed on exposing 6-bromo-2,6-dideoxy-D-xylo-hexonolactone to base.¹¹

The 6-bromo-3,6-dideoxy-lactones (3a), (9a) and (16a) were converted into the corresponding 3,6-dideoxylactones 4a, 10a and 17a, respectively, upon hydrogenolysis. Reduction of the latter (with di-(3-methyl-2-butyl)-borane) afforded the corresponding hexoses, as previously reported for the D-xylo-isomer¹² and here for the 3,6-dideoxy-D-*arabino*-hexose (tyvelose).

^{13}C NMR chemical shifts of the 3-deoxy- and the 3,6-dideoxy-hexono-1,4-lactones, as well as their acetates, are presented in the experimental part. Assignments were confirmed through selective proton-decoupling experiments. The reported ^{13}C NMR chemical shifts of a series of racemic acetylated 3-deoxy- and 3,6-dideoxy-hexono-1,4-lactones,¹⁵ are in agreement with our results only insofar as the signals of all C-2 epimeric lactones be interchanged. Thus, the data reported for the *arabino* isomers¹³ belong to com-

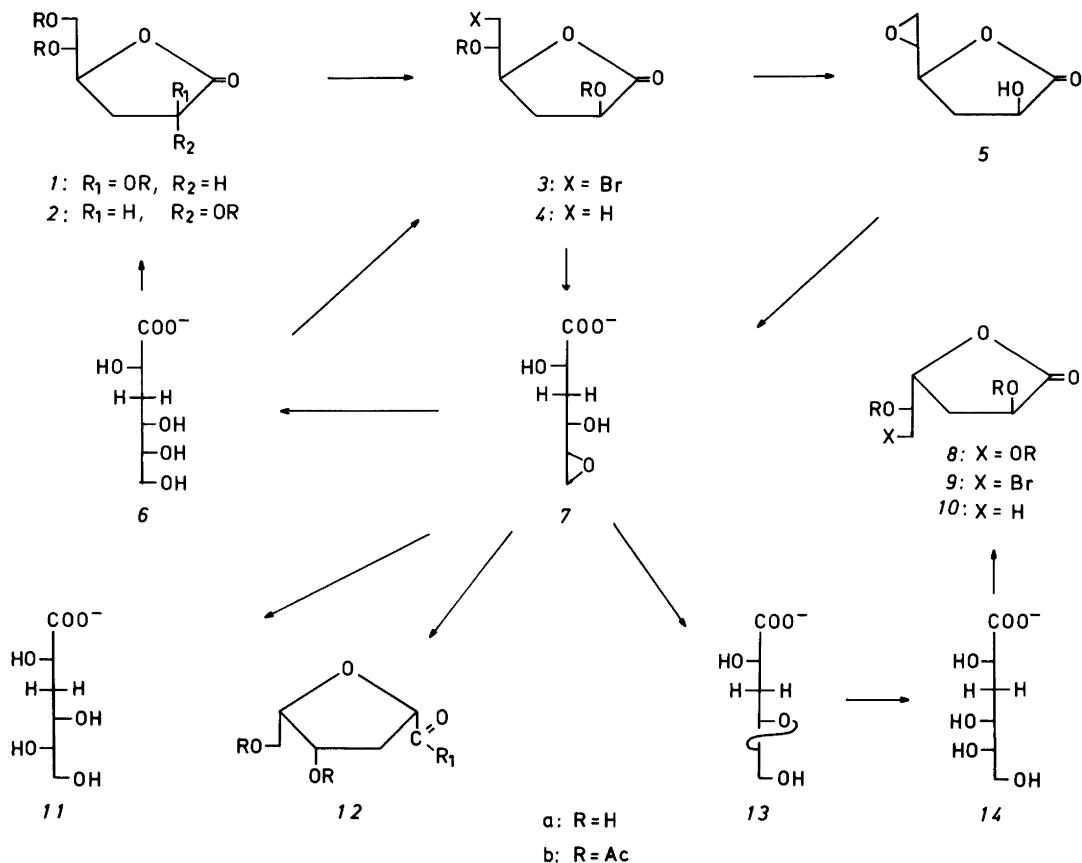
pounds having *ribo*-configurations. This also followed from the observed base-induced isomerisation of the 3-deoxy-D-*arabino*-hexonolactone (1a) to the *ribo*-isomer (2a).

Experimental

Melting points are uncorrected. Optical rotations were measured on a Perkin Elmer 141 polarimeter. NMR spectra were obtained on Bruker WH-90, HX-270 and AM-500 instruments. Dioxane (67.40 ppm) was used as internal reference for ^{13}C NMR spectra and acetone (δ 2.12) for ^1H NMR spectra in D_2O . TMS was used as the reference for spectra in CDCl_3 . Column chromatography was performed on silicagel 60 (40–63 μm , Merck 9385) using the "flash technique".¹⁴ Evaporations were performed in vacuum at 50°C, when not otherwise indicated. Microanalyses were performed by NOVO microanalytical laboratory.

The course of the base-catalysed reaction of the crystalline 5,6-epoxides 5 and 18 were followed on samples prepared by dissolving the compound (500 mg) in D_2O (0.5 ml) in a 10 mm NMR sample tube; the appropriate amounts (see discussion) of potassium hydroxide or carbonate, dissolved in H_2O , were added at 0°C, bringing the total volume of the solution to ~1.5 ml; a few drops of dioxane served as the internal reference. The solutions were kept at room temperature and ^{13}C NMR spectra were measured at intervals at 22.63 MHz.

6-Bromo-3,6-dideoxy-D-arabino-hexono-1,4-lactone (3a). Calcium 3-deoxy-D-*arabino*-hexonate dihydrate (15 g) (6),^{7,9} was stirred with 30% hydrogen bromide in acetic acid (HBA) (150 ml) for 3 h. Then methanol (300 ml) was added and the mixture was left standing overnight. After repeated evaporations (at 60°C) with water the residue was dissolved in water (30 ml) and extracted with ethyl acetate (10×30 ml); the extract was dried (Na_2SO_4), treated with activated carbon, filtered and evaporated to give a pale syrup (14.9 g, 95.6%) of pure 3a as apparent from a ^{13}C NMR spectrum. ^{13}C NMR (D_2O): 179.6 ppm (C-1); 78.1 (C-4); 71.5, 68.6 (C-2, C-5); 34.5, 32.6 (C-3, C-6). On standing in water the lactone opens partially to the corresponding acid: 179.0 ppm (C-1); 74.3 (C-4); 69.5, 68.0 (C-2, C-5); 37.4, 36.9 (C-3, C-6). An analytical sample of the



lactone **3a** was obtained by flash chromatography (ethyl acetate-pentane, 2:1). $[\alpha]_D^{20} - 4.9^\circ$ (c 2.3, EtOAc). Anal. $C_6H_5BrO_4$: C, H, Br.

3,6-Dideoxy-D-arabino-hexono-1,4-lactone (4a). The bromolactone (**3**) (3.18 g) was dissolved in ethyl acetate (30 ml) together with triethylamine (6 ml) and 5% palladium on carbon (300 mg) and stirred in a hydrogen atmosphere (1 atm.) overnight. Filtration and evaporation gave **4a** contaminated with some triethylamine hydrobromide, as seen from a ^{13}C NMR spectrum. The product was purified by flash chromatography giving 1.4 g (70%) of pure **4a**. $[\alpha]_D^{20} - 13.3^\circ$ (c 3.0, EtOAc). Anal. $C_6H_{10}O_4$: C, H. ^{13}C NMR (D_2O): 180.2 ppm (C-1); 81.3 (C-4); 68.8, 67.2 (C-2, C-5); 31.0 (C-3); 17.2 (C-6).

2,5-Di-O-acetyl-3,6-dideoxy-D-arabino-hexono-1,4-lactone (4b). In another experiment crude **4a**,

prepared from 2.0 g of **3a**, was acetylated with acetic anhydride (4 ml) and a few drops of aqueous perchloric acid (60%) for 1 h. Work-up in the usual way gave **4b** (1.5 g, 73.5%) as a syrup which was homogeneous as estimated from its ^{13}C NMR spectrum ($CDCl_3$): 171.6 ppm (C-1); 77.1 (C-4); 68.9, 67.9 (C-5, C-2); 29.1 (C-3); 14.5 (C-6); 169.6, 169.3, 20.5, 20.0 (OAc).

A crystalline sample was obtained by flash chromatography (ethyl acetate-pentane, 2:1). Recrystallisation from ether-pentane gave an analytical specimen of **4b**, with m.p. 76–78°C. $[\alpha]_D^{20} + 54.3^\circ$ (c 2.5, $CHCl_3$). Anal. $C_{10}H_{14}O_6$: C, H.

3,6-Dideoxy-D-arabino-hexose. A solution of di-(3 methyl-2-butyl)-borane was prepared under argon from the borane-dimethyl sulfide complex (3.4 ml) in THF (10 ml) and 2-methyl-2-butene (7.15 ml) in THF (10 ml).¹⁵ The solution was

cooled in ice, and dried; **4a** (830 mg) in THF (10 ml) was added in the course of 15 min at 0°C, and then left overnight at room temperature. Water (10 ml) was added and the mixture refluxed for 3 h and concentrated. Water was added again, and the mixture was extracted 3 times with dichloromethane, the aqueous phase was concentrated, and coevaporated twice with methanol, to give the sugar (800 mg ~ 100%). Purification by flash chromatography and recrystallization from acetonitrile gave a product with m.p. 82–85°C. $[\alpha]_D^{20} + 31.9^\circ$ (lit.¹⁶ m.p. 97–99°C, $[\alpha] = +23^\circ$). A ¹³C NMR (125 MHz) spectrum (D₂O) revealed that the α-pyranose was the main product: 93.5 ppm. (C-1); 70.5, 68.9, 67.9 (C-2, C-4, C-5); 33.7 (C-3); 17.6 (C-6), accompanied by the β-pyranose, 95.4 (C-1), and the α-furanose form, 102.9 (C-1); 82.7 (C-4).

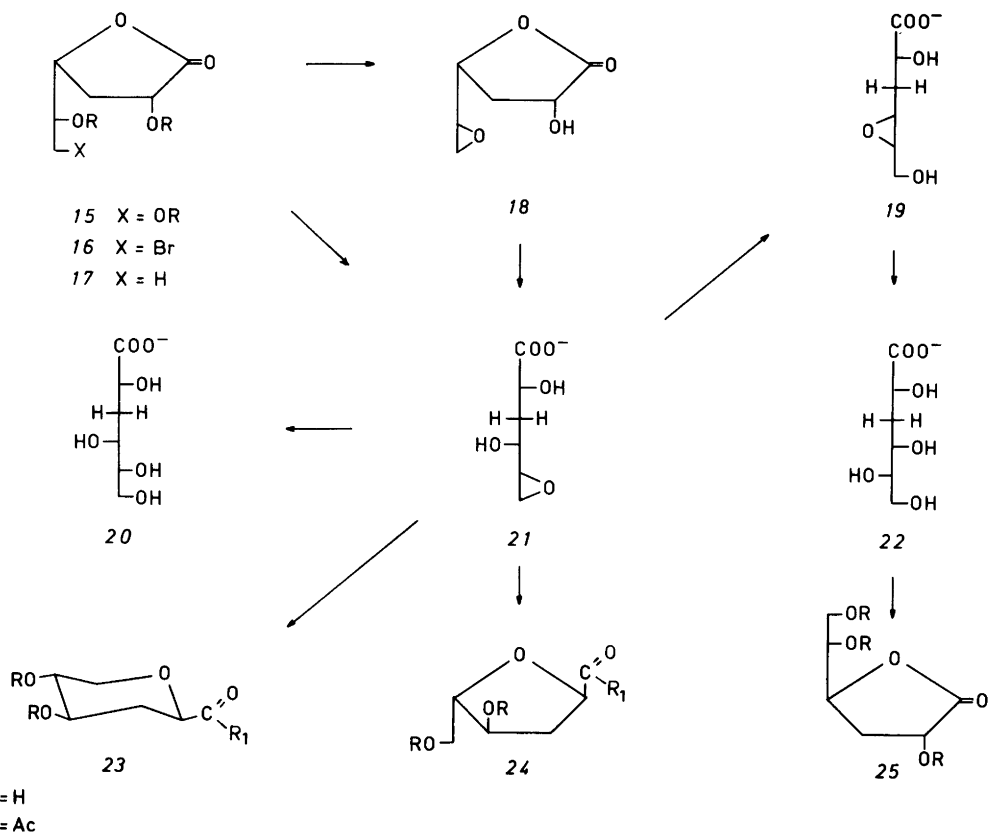
5,6-Anhydro-3-deoxy-D-arabino-hexono-1,4-lactone (5). The 6-bromolactone (**3a**) (10.0 g) was dissolved in anhydrous acetone (30 ml) and stirred with potassium carbonate (40 g) for 1.5 h. Filtration and treatment of the filtrate with charcoal and MgSO₄ for 15 min followed by filtration and concentration, gave a crude product (6 g, 94%), which crystallized. Addition of ether gave **5** (4.2 g); m.p. 76–80°C sufficiently pure for further use. An analytical specimen was obtained by recrystallizations from ethyl acetate to give a product with m.p. 82–82.5°C. $[\alpha]_D^{20} - 20.1^\circ$ (c 0.9, EtOAc). Anal. C₆H₈O₄: C, H. ¹³C NMR (CDCl₃): 176.8 ppm (C-1); 75.7 (C-4); 67.7 (C-2); 51.0 (C-5); 44.0 (C-6); 31.3 (C-3).

Tri-O-acetyl-3-deoxy-L-ribo-hexono-1,4-lactone (8b). The crude 6-bromolactone (**3a**), prepared from Ca-metasaccharinate (**6**) (3.0 g, 13.8 mmol), was dissolved in water (15 ml), and potassium hydroxide (6 g) was added with vigorous stirring. After 30 min the mixture was neutralized with conc. hydrochloric acid and concentrated. Acetic acid (10 ml) was added to the salt cake together with conc. hydrochloric acid (3 ml). After filtration the filter cake was washed with acetic acid, and the combined filtrates were concentrated. Acetic acid (5 ml) was added and evaporated; this was repeated. The residue was acetylated with acetic anhydride (10 ml) and aqueous perchloric acid (60%, 1 ml) for 1 h. Work-up in the usual way gave a product (2.2 g, 56%) which was almost pure **8b** as seen from a ¹³C NMR spec-

trum. A sample was purified by flash chromatography (ethyl acetate-pentane, 1:1) giving pure **8b**. $[\alpha]_D^{20} - 28.3^\circ$ (c 6.4, CHCl₃); reported¹⁷ for the D-enantiomer: $[\alpha]_D + 14.0^\circ$. Anal. C₁₂H₁₆O₈: C, H. ¹³C NMR (CDCl₃): 171.6 ppm (C-1); 75.2 (C-4); 70.7, 67.0 (C-2, C-5); 61.1 (C-6) and 29.1 (C-3); 169.8, 169.2, 169.15, 20.1, 20.0 (OAc). ¹H NMR (500 MHz) (CDCl₃): δ 5.43 (H-2, *J*₂₃ 9.0, *J*_{23'} 7.5 Hz); 2.71 (H-3, *J*₃₄ 4.0, *J*_{33'} 14.0); 2.36 (H-3', *J*_{3,4} 8.5); 4.82 (H-4, *J*₄₅ 4.0); 5.25 (H-5, *J*₅₆ 4.5, *J*_{56'} 5.0); 4.31 (H-6, *J*_{66'} 12.0); 4.16 (H-6'); 2.15, 2.10, 2.08 (OAc).

3-Deoxy-L-ribo-hexono-1,4-lactone (8a). Crude **8b** (7.3 g), prepared from **6** (10 g) as described above, was treated with sodium methoxide in methanol, followed by treatment with acid ion exchange resin (IR 120, H⁺). Filtration, treatment with charcoal, filtration, and evaporation at 50°C for 30 min gave a semicrystalline product⁸ of **8a** (3.85 g, 49.7%, based on **6**). A sample was crystallized from ethanol to give a product with m.p. 104–105°C; $[\alpha]_D^{20} - 27.0^\circ$ (c 1.4, H₂O) (reported⁹ for the D-enantiomer: m.p. 108–109°C, $[\alpha]_D + 27.0^\circ$). Anal. C₆H₁₀O₅: C, H. ¹³C NMR (D₂O): 180.4 ppm (C-1); 79.7 (C-4), 72.6, 67.7 (C-2, C-5); 62.7 (C-6); 31.4 (C-3).

Treatment of 6-bromo-3,6-dideoxy-D-arabino-hexono-1,4-lactone (3a) with potassium hydroxide. The 6-bromolactone (**3a**) prepared from Ca-metasaccharinate (**6**) (3.0 g) as described above, was dissolved in water (15 ml) and potassium hydroxide (6 g) was added in one portion. After stirring for 1 h the mixture was neutralized with conc. hydrochloric acid and concentrated. The ¹³C NMR spectrum showed **14** to be the major product, contaminated with a minor product (83.3 ppm, 78.6, 72.4, 61.2 and 39.9). Methanol (60 ml) was added together with conc. H₂SO₄ (2 ml) and the mixture was refluxed overnight, after which time the salts were filtered off, and the filtrate was neutralized with pyridine and concentrated. Acetylation overnight in pyridine (15 ml) with acetic anhydride (15 ml) and work-up in the usual way gave a syrup (3.1 g), which contained the acetylated lactone **8b** as the main product, contaminated with a minor product in the ratio of about 4.7:1. Flash chromatography (ethyl acetate-pentane, 2:1) gave pure **8b** (1.1 g), mixed fractions, and almost pure **12b** (R₁ = OCH₃). Judged from the ¹³C NMR spectra of the



fractions, **8b** was formed in 60% yield and **12b** ($R_1 = \text{OCH}_3$) in 14% yield. For **12b** ($R_1 = \text{OCH}_3$) the following signals were observed: ^{13}C NMR (CDCl_3): 171.9 ppm (C-1); 79.8 (C-5); 75.9, 72.6 (C-2, C-4); 62.5 (C-6); 36.9 (C-3); 52.1 (OCH_3); 170.5, 20.6 (OAc). ^1H NMR (500 MHz) (CDCl_3): δ 4.58 (H-2, J_{23} 9.0 Hz, $J_{23'}$ 4.0), 2.60 (H-3, J_{34} 5.6, $J_{33'}$ 14.5), 2.31 (H-3', $J_{3'4}$ 2.1), 5.39 (H-4, J_{45} 3.6), 4.38 (H-6, J_{56} 7.2, $J_{66'}$ 14.5), 4.3–4.2 (H-5, H-6').

6-Bromo-3,6-dideoxy-L-ribo-hexono-1,4-lactone (9a). The lactone (**8a**) (1.0 g) was dissolved in HBA (10 ml). After 3 h at room temperature, methanol (30 ml) was added, and the mixture was refluxed for 2 h. Evaporation and repeated coevaporation with water gave the 6-bromolactone (**9a**) (1.4 g, 100%) in almost pure form as

evidenced by a ^{13}C NMR spectrum. Purification by flash chromatography (ethyl acetate-pentane, 2:1) gave pure **9a** (790 mg, 59%) as a syrup. $[\alpha]_D^{20} = -38.4^\circ$ (c 4.5, EtOAc). Anal. $\text{C}_6\text{H}_9\text{BrO}_4$: C, H, Br. ^{13}C NMR (D_2O): 179.3 ppm (C-1); 79.1 (C-4); 71.0, 66.9 (C-5, C-2); 34.3, 30.8 (C-6, C-3).

Di-O-acetyl-3,6-dideoxy-L-ribo-hexono-1,4-lactone (10b). Calcium metasaccharinate (**6**) (5.0 g) was converted, as described above, into crude **3a**, which in turn was dissolved in water (20 ml) and treated with potassium hydroxide (15 g) for 30 min. After neutralisation with conc. hydrochloric acid and concentration, a salt cake was obtained containing **14** as the major product. Treatment with HBA (50 ml) for 2 h, followed by reaction with methanol (100 ml) over night and evaporation gave crude **9a**. Water was added and evaporated again; this was repeated twice, followed

by co-evaporation twice with ethyl acetate. The syrup was dissolved in ethyl acetate (50 ml) and ethanol (50 ml), dried (MgSO_4), and triethylamine (20 ml) was added. After filtration more triethylamine (20 ml) was added together with 5% palladium on carbon (500 mg), and the mixture was stirred in a hydrogen atmosphere overnight (1 atm.). Filtration and concentration gave almost pure *10a* (1.6 g, 47.6%) as seen from the ^{13}C NMR spectrum (D_2O): 180.7 ppm (C-1); 83.2 (C-4); 68.7, 68.0 (C-2, C-5); 30.6 (C-3); 18.0 (C-6). Acetylation with acetic anhydride (4 ml) and aqueous perchloric acid (60%) gave, after work-up in the usual way, 1.7 g (65.9%) of *10b*. Purification by flash chromatography (ethyl acetate-pentane, 1:2) gave pure *10b* as a syrup. $[\alpha]_D^{20} - 39.2^\circ$ (*c* 2.7, CHCl_3). Anal. $\text{C}_{10}\text{H}_{14}\text{O}_6$: C, H. ^1H NMR (500 MHz) (CDCl_3): 5.47 (H-2, J_{23} 9.0 Hz, $J_{23'}$ 7.8); 2.69 (H-3, J_{34} 3.3, $J_{33'}$ 14.0); 2.31 (H-3', J_{34} 9.0); 4.61 (H-4, J_{45} 3.5); 5.13 (H-5, J_{56} 6.5); 1.21 (H-6).

3,6-Dideoxy-L-ribo-hexono-1,4-lactone (10a). The 6-bromolactone (*9a*) (690 mg) in ethyl acetate (10 ml) and ethanol (2 ml) was subjected to hydrogenolysis overnight in the presence of triethylamine (1 ml) and 5% palladium on carbon (100 mg). Filtration, concentration and coevaporation twice with ethyl acetate left syrupy *10a* (450 mg, 100%), which was pure according to its ^{13}C NMR spectrum, identical to the one described above.

6-Bromo-3,6-dideoxy-D-xylo-hexono-1,4-lactone (16a). 3-Deoxy-D-xylo-hexono-1,4-lactone (*15'*) (10.0 g) was treated with HBA (100 ml) for 3 h at room temperature. Methanol (200 ml) was then added and the mixture was boiled for 2 h (or left overnight at room temperature). The mixture was evaporated (at 60°C), and evaporation was continued for ~15 min. Water (20 ml) was added and again evaporated (~15 min); the procedure was repeated. Then water (20 ml) was added and the solution was extracted with ethyl acetate (6×25 ml); the extract was dried (Na_2SO_4) and concentrated. This left a crude product (14 g, ~100%) which could be crystallized from ether to give 11.5 g (82%) of *16a*, m.p. $111\text{--}114^\circ\text{C}$. A sample was recrystallized twice from ethyl acetate, raising the m.p. to $114\text{--}116^\circ\text{C}$. $[\alpha]_D^{25} - 27.7^\circ$ (*c* 1.4, EtOAc). Anal. $\text{C}_8\text{H}_9\text{BrO}_4$: C, H, Br. ^{13}C NMR (D_2O): 179.8 ppm (C-1); 79.2 (C-4); 71.9

(C-5); 68.6 (C-2); 34.1 (C-6, $J_{\text{CH}} = 153$ Hz); 33.2 (C-3, $J_{\text{CH}} = 141$ and 131 Hz). The signals were assigned through selective ^1H -decoupling.

5,6-Anhydro-3-deoxy-D-xylo-hexono-1,4-lactone (18). The 6-bromolactone (*16a*) (1.28 g) was dissolved in dry acetone (25 ml); anhydrous potassium carbonate (5 g) was added and the mixture was stirred for 1 h. Filtration and concentration gave a product which crystallized from chloroform to give *18* (637 mg, 79.6%); m.p. $74\text{--}78^\circ\text{C}$. A sample was recrystallized twice from chloroform to give *18*, with m.p. $80\text{--}81^\circ\text{C}$. $[\alpha]_D^{20} - 5.8^\circ$ (*c* 0.5, EtOAc). Anal. $\text{C}_6\text{H}_8\text{O}_4$: C, H. ^1H NMR (CDCl_3): δ 4.50 (H-2, J_{23} 8.5 Hz, $J_{23'}$ 9.0); 2.73 (H-3, J_{34} 6.2, $J_{33'}$ 9.0); 2.21 (H-3', J_{34} 9.0); 4.40 (H-4, J_{45} 4.8); 3.20 (H-5, J_{56} 4.5, $J_{56'}$ 2.5); 2.94 (H-6, $J_{66'}$ 4.5); 2.88 (H-6'); 3.18 (OH). ^{13}C NMR (CDCl_3): 177.2 ppm (C-1); 75.6 (C-4); 67.6 (C-2); 52.4 (C-5); 44.3 (C-6); 33.4 (C-3).

Tri-O-acetyl-3-deoxy-L-xylo-hexono-1,4-lactone (25b). The 6-bromolactone (*16a*) (3.0 g, 13.3 mmol) was dissolved in water (15 ml) and potassium hydroxide (2.3 g, 41.1 mmol) was added in one portion with stirring. After 30 min the mixture was neutralized with conc. hydrochloric acid and concentrated. Acetic acid (5 ml) was added together with conc. hydrochloric acid (1 ml) and the mixture was concentrated (for ~20 min at 60°C). This was repeated with additional acetic acid (5 ml). A ^{13}C NMR spectrum of the residue showed the presence of three compounds. Acetylation with acetic anhydride (15 ml) and perchloric acid gave a crystalline product, *25b* (550 mg, 16%), which could be recrystallized from ether-pentane to give a product (352 mg, 9.5%) with m.p. $96\text{--}98^\circ\text{C}$. Recrystallisation from the same solvent gave pure *25b*, m.p. $97.5\text{--}98.5^\circ\text{C}$, $[\alpha]_D^{20} + 10.9^\circ$ (*c* 0.3, CHCl_3). Anal. $\text{C}_{12}\text{H}_{16}\text{O}_8$: C, H. ^1H NMR (500 MHz, CDCl_3): δ 5.42 (H-2, $J_{23} = J_{23'}$ 8.7 Hz); 2.5 (H-3, J_{34} 3.0, $J_{33'}$ 13.8); 2.40 (H-3', J_{34} 9.0); 4.88 (H-4, J_{45} 2.4); 5.22 (H-5, J_{56} 5.3, $J_{56'}$ 7.1); 4.36 (H-6, $J_{66'}$ 11.7); 4.18 (H-6'); 2.24, 2.33, 2.08 (OAc). ^{13}C NMR (125 MHz, CDCl_3): 171.9 ppm (C-1); 75.5 (C-4); 71.3 (C-5); 66.8 (C-2); 61.6 (C-6); 30.4 (C-3); 170.2, 169.6, 20.5, 20.2 (OAc).

Treatment of 6-bromo-3,6-dideoxy-D-xylo-hexono-1,4-lactone (16a) with potassium hydroxide. The 6-bromolactone (*16a*) (3.0 g) was

treated with potassium hydroxide and worked up as described above to give a crude product containing three components. The mixture was boiled with methanol (30 ml) and conc. H_2SO_4 (1 ml) overnight. Neutralization with pyridine followed by removal of the solvents left a residue to which pyridine was added and again evaporated. Acetylation with acetic anhydride (15 ml) and pyridine (15 ml) for 3 h at room temperature gave a crude product (2.4 g), which was separated by flash chromatography (ethyl acetate-pentane, 1:1). The first fraction (553 mg, 16 % consisted of pure **23b** ($R_1 = \text{OCH}_3$). ^{13}C NMR (CDCl_3): 169.9 ppm (C-1); 73.3, 69.7, 68.5 (C-2, C-4, C-5); 65.9 (C-6); 31.9 (C-3); 52.2 (OCH_3); 169.8, 169.7, 20.7, 20.6 (OAc). ^1H NMR (500 MHz, CDCl_3): δ 4.14 (H-2, J_{23e} 3.25, J_{23a} 10.25); 2.50 (H-3e, J_{3e4} 5.0, J_{3a3e} 13.25); 1.88 (H-3a, J_{3a4} 10.0); 5.02 (H-4, J_{45} 8.75); 4.92 (H-5, J_{56e} 5.0, J_{56a} 8.75); 4.25 (H-6e, J_{6e6a} 11.5); 3.38 (H-6a); 3.78 (OCH_3); 2.07, 2.08 (OAc). The next fractions contained mixtures of **23b** and **24b**, both ($R_1 = \text{OCH}_3$), followed by pure **24b** ($R_1 = \text{OCH}_3$) (45 mg, 1.3 %). ^{13}C NMR (CDCl_3): 173.2 ppm (C-1); 82.6 (C-5); 76.5, 74.6 (C-2, C-4); 63.6 (C-6); 36.0 (C-3); 52.0 (OCH_3); 171.1, 170.7, 20.6 (OAc). ^1H NMR (CDCl_3): δ 4.68 (H-2, J_{23} 9.0 Hz, J_{23} 3.0); 2.53 (H-3, J_{34} 6.4, $J_{33'}$ 14.0); 2.31 (H-3', $J_{3'4}$ 2.4); 5.08 (H-4, J_{45} 2.4); 4.38 (H-5, J_{56} 4.3, $J_{56'}$ 5.0); 4.22 (H-6, $J_{66'}$ 12.0); 4.14 (H-6'); 3.75 (OCH_3); 2.07, 2.00 (OAc). – The last fraction (220 mg, 6 %) contained almost pure **25b**, which crystallized; m.p. 95–97°C. Based on the ^{13}C NMR spectra of the fractions isolated, the compounds **23b** and **24b**, (both $R_1 = \text{OCH}_3$), together with **25b** were formed in about 30, 22 and 8 %, respectively.

Di-O-acetyl-3,6-dideoxy-D-xylo-hexono-1,4-lactone (17b). The bromolactone **16a** (1.5 g) in methanol (5 ml) and ethyl acetate (25 ml) was subjected to hydrogenolysis overnight in the presence of triethylamine (2 ml) and 5 % palladium on carbon (200 mg). Filtration and concentration left a product (**17a**) contaminated with triethylamine hydrobromide. Acetylation with acetic anhydride and aqueous perchloric acid (60 %) in the usual way gave **17b** (1.4 g, 91.5 %); m.p. 78–82°C; (reported⁷ m.p. 86–87°C). ^{13}C NMR (CDCl_3): 171.4 ppm (C-1); 77.2 (C-4); 69.8 (C-5); 67.8 (C-2); 30.4 (C-3); 15.3 (C-6); 20.6 and 20.2 (OAc). The ^{13}C NMR signals were assigned through selective ^1H -decoupling. The chemical

shifts reported previously⁷ for C-2 and C-5 have here been interconverted.

Isomerisation of 3-deoxy-D-arabino-hexono-1,4-lactone (1a) with sodium hydroxide. The Ca metasaccharinate (**6**)⁷ was deionised with Amberlite IR 120 (H^+), and concentrated at 60°C for 20 min to give the lactone **1a** (see Table 1 for ^{13}C NMR data). A sample was acetylated to give **1b**. ^{13}C NMR (CDCl_3): 171.5 ppm (C-1); 74.4 (C-4); 68.0, 70.7 (C-2, C-5); 61.6 (C-6); 30.4 (C-3). The data previously reported for **1b**⁷ should be corrected to those presented here. **1a** (553 mg, 3.4 mmol) was dissolved in water (6 ml) together with sodium hydroxide (486 mg, 12.2 mmol) and the solution was heated to 150°C for 24 h. The mixture was concentrated, acidified with conc. hydrochloric acid and concentrated to give a mixture of two lactones in equal amounts, having the *arabino-* (**1a**) and *ribo-*configurations (**2a**), respectively (see Table 1 for ^{13}C NMR data). The mixture was acetylated to give a mixture of **1b**, the ^{13}C chemical shifts of which were identical with those given above, and of tri-*O*-acetyl-3-deoxy-D-*ribo*-hexono-1,4-lactone **2b** with the following ^{13}C NMR data (CDCl_3): 171.7 ppm (C-1); 74.4 (C-4); 70.7, 68.0 (C-5, C-2); 61.6 (C-6); 30.4 (C-3); 170.0, 169.5, 20.4, 20.3 (OAc).

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