

Preparation of 3-Deoxy-aldonolactones by Hydrogenolysis of Acetylated Aldonolactones

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Acetylated aldo-1,4-lactones, when treated with hydrogen in the presence of triethylamine and palladium on carbon, form acetylated 3-deoxy-aldono-1,4-lactones in high yield through elimination of the 3-acetoxy group and subsequent stereospecific hydrogenation of the unsaturated intermediate. Thus, acetylated *D*-galactono-1,4-lactone (1) yields tri-*O*-acetyl-3-deoxy-*D*-xylohexono-1,4-lactone (3*a*). Acetylated *D*-mannono- or *D*-glucono-1,4-lactone both give 3-deoxy-*D*-arabino-hexono-1,4-lactone (10*a*), whereas the four acetylated *D*-pentono-1,4-lactones (14–17) all afford di-*O*-acetyl-*D*-threo-pentono-1,4-lactone (18*a*). *D*-Gluconolactone can be converted into (*R*)- γ -caprolactone (27) on treatment with hydrogen bromide followed by a series of reductions. Similarly, *D*-lyxonolactone produces 2,3-dideoxy-*D*-glycero-pentono-1,4-lactone (29).

Acylated aldonolactones readily undergo β -elimination to give 2,3-unsaturated lactones. Thus Lederkremer *et al.* found that benzylation of aldonolactones in pyridine under mild conditions yielded fully benzyolated lactones which under more forced conditions eliminated benzoic acid to give 2,3-unsaturated lactones. The latter could be hydrogenated to 3-deoxy-lactones.^{1,2} Acetylation of *D*-glucono-1,5-lactone in pyridine gave similar results.^{3,4} However, the elimination of acylated lactones in pyridine is sometimes difficult to control since the initially formed 2,3-unsaturated lactones readily undergo further eliminations.^{4,5}

We have found that when aldonolactones are acetylated under acidic conditions, using sulfuric or perchloric acid as catalyst, elimination does not take place and fully acetylated lactones are easily obtained. Furthermore, treatment of the latter with hydrogen in the presence of palladium and tri-

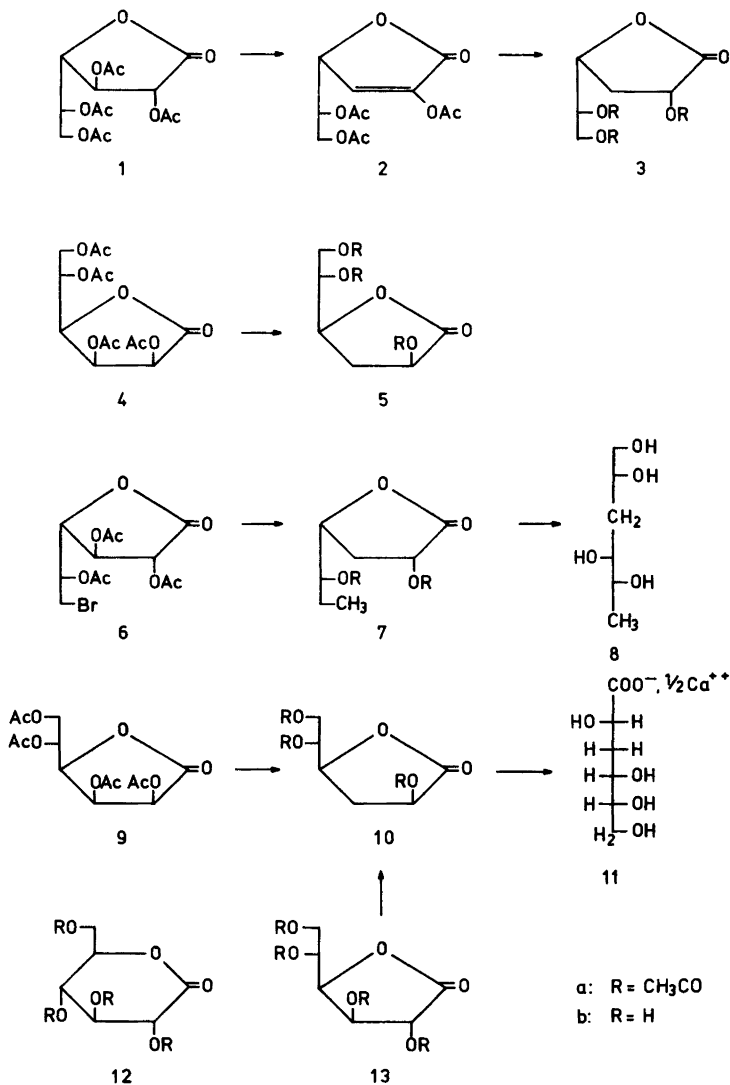
ethylamine results in simultaneous elimination and hydrogenation and produces acetylated 3-deoxy-aldonolactones in high yields. Using this procedure isolation of the 2,3-unsaturated lactones is avoided.

When tetra-*O*-acetyl-*D*-galactono-1,4-lactone (1) was hydrogenolyzed in ethyl acetate and triethylamine using 5% palladium on carbon as catalyst the 3-deoxy-lactone (3*a*) was obtained as the sole product and after deacetylation the known⁶ crystalline 3-deoxy-*D*-xylohexono-1,4-lactone (3*b*) was isolated in 80% yield. The 3-deoxy-lactone (3*a*) is undoubtedly formed by elimination, catalyzed by triethylamine, to give the unsaturated lactone (2), which is subsequently reduced to 3*a*.

Using catalytic hydrogenolysis as described above, a number of acetylated aldonolactones have been converted into 3-deoxylactones. In most cases only one of the C-2 epimeric 3-deoxylactones was detected. It is important to use a good quality catalyst since slow hydrogenation leads to coloured by-products, probably because the unsaturated lactone undergoes further elimination if allowed to accumulate.

Hydrogenolysis of tetra-*O*-acetyl-*L*-gulono-1,4-lactone (4) gave the acetylated 3-deoxy-lactone (5*a*). After deacetylation 3-deoxy-*L*-xylohexono-1,4-lactone (5*b*), the enantiomer of 3*b*, was isolated in 72% yield. Similarly, the acetylated 6-bromo-6-deoxy-*D*-galactono-1,4-lactone (6)⁸ gave the 3,6-dideoxy-lactone (7*a*) in 93% yield, the 3-*O*-acetyl group and the bromine atom being removed in one step. Deacetylation of 7*a* gave 3,6-dideoxy-*D*-xylohexono-1,4-lactone (7*b*), which was in turn reduced to the known⁹ 3,6-dideoxy-*D*-xylohexitol (8).

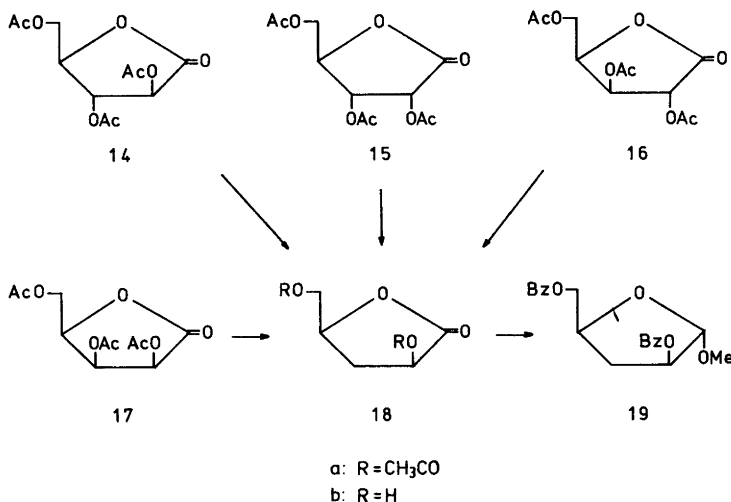
Analogous hydrogenolysis of tetra-*O*-acetyl-*D*-mannono-1,4-lactone (9) gave tri-*O*-acetyl-3-deoxy-*D*-arabino-hexono 1,4-lactone (10*a*) as the



only detectable product; deacetylation furnished the known lactone (*10b*).¹⁰ Similar hydrogenolysis of tetra-*O*-acetyl-*D*-glucono-1,4-lactone (*13a*) would be expected also to give *10a*; however, *13a* is not available readily in a pure state. Heating of *D*-glucono-1,5-lactone (*12b*) in acetic acid in the presence of sulfuric acid produces a solution which contains predominantly the 1,4-lactone (*13b*).¹¹ Acetylation of this solution gave *13a*, contaminated with ca. 15% of the corresponding 1,5-lactone (*12a*). Hydrogenolysis of this mixture yielded *10a* which was deacetylated and converted into the calcium

salt (*11*), isolated in a 50% overall yield from *D*-glucono-1,5-lactone (*12b*). Hydrogenolysis of the acetylated 1,5-lactone (*12a*) was in our hands not stereospecific,³ but gave a mixture of tri-*O*-acetyl-3-deoxy-*D*-arabino- and *D*-ribo-hexono-1,5-lactones.

The hydrogenolysis of the four isomeric tri-*O*-acetyl-*D*-pentono-1,4-lactones (*14*, *15*, *16* and *17*) was also studied. They all yielded di-*O*-acetyl-3-deoxy-*D*-threo-pentono-1,4-lactone (*18a*); the C-2 epimeric *D*-erythro-lactone was not observed. The structure of *18a* was ascertained through its conversion into the known¹² methyl di-*O*-benzoyl-3-



deoxy- α -D-threo-pentofuranoside (19).

It was also found that an acetoxy group can be removed from C-3 of an acetylated 2-deoxy-lactone using the procedure described above. Thus hydrogenolysis of di-*O*-acetyl-2,6-dideoxy-*D*-arabino-hexono-1,4-lactone (20), or of the 6-bromolactone (23), gave the acetylated trideoxy-lactone (21); its enantiomer (25) was prepared analogously from (22). Racemic mixtures of 21 and 25 have been synthesized previously,¹³ whereas 25 has been obtained also from natural sources.¹⁴

Finally, (R)- γ -caprolactone (27) was prepared through a series of simple reactions starting with *D*-gluconolactone, which can be readily converted into the 6-bromo-2,6-dideoxy-lactone (23).^{8,15} Treatment of the latter with zinc in acetic acid furnished a high yield of the unsaturated lactone (24), which on hydrogenation yielded (26). Hydrogenolysis of 26 at room temperature as described above was slow, but at ca. 70 °C it was smoothly converted into 27. The latter has been found to be a pheromone and it has been synthesized in several different ways.^{16–18} The optical rotation of the 27 described in the present paper was very close to that of the product prepared from (S)-glutamic acid.¹⁶ Hydrogenolysis of the 2-deoxylactone (28*b*) yielded the *D*-2,3-dideoxylactone (29*b*), isolated as the crystalline tosylate (29*c*), which has previously been synthesized from (S)-glutamic acid.¹⁶ The crude, acetylated 2-deoxy-lactone (28*b*) was prepared from potassium *D*-lyxonate as previously described¹⁵ without isolation of any intermediates.

EXPERIMENTAL

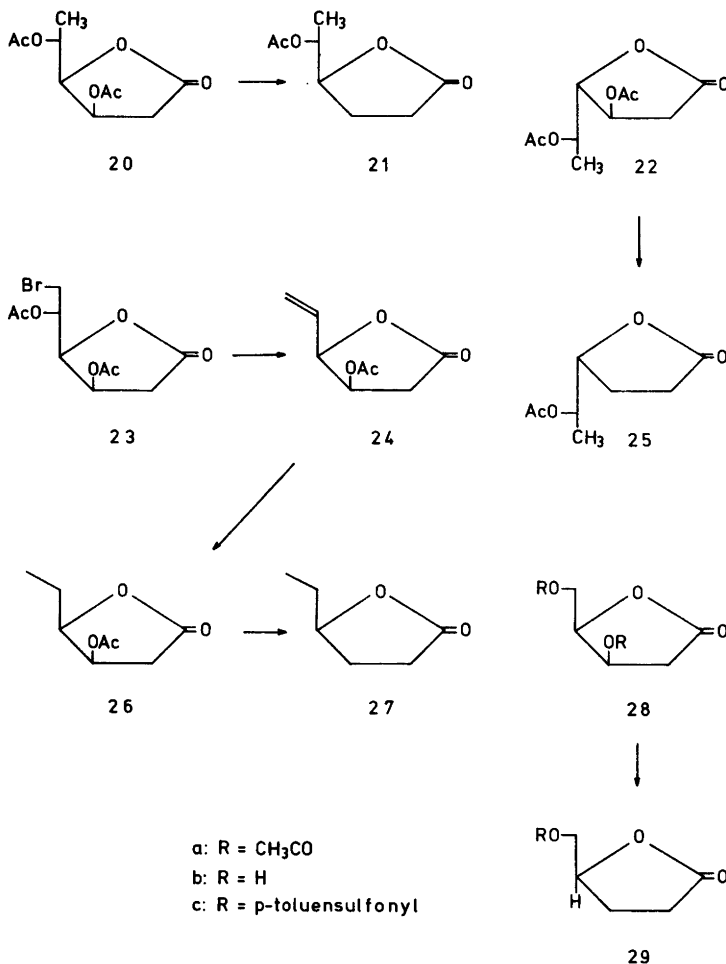
Melting points are uncorrected. Optical rotations were measured on a Perkin Elmer 141 polarimeter. NMR spectra were obtained on Bruker WH-90 and HX-270 instruments. Acetylated products were measured in CDCl₃ and nonacetylated compounds in D₂O. Acetone (δ 2.12) was used as internal reference for ¹H NMR spectra and dioxane (67.40 p.p.m.) for ¹³C NMR spectra in D₂O. Microanalyses were performed by NOVO microanalytical laboratory.

Unless otherwise stated all hydrogenolysis reactions were carried out at room temperature and at either 3 atm pressure in a Parr type of apparatus or at ca. 100 atm in a steel autoclave.

*Preparation of acetylated hexono- and pentono-1,4-lactones.*¹⁹ A suspension of the 1,4-lactone (5.0 g) in acetic anhydride (50 ml) containing 5 drops of 60% aqueous perchloric acid was kept at room temperature for 30 min. Ice and water were then added and after 1/2 h the solution was extracted with dichloromethane. The extract was washed 3 times with water, dried and evaporated. The residue thus obtained consisted of the crude, acetylated 1,4-lactone.

Alternatively, a salt of the aldonic acid (10 g) was suspended in a mixture of acetic acid (50 ml) and conc. sulfuric acid (5 ml) and the suspension was heated to 80–90 °C for 30 min. It was then cooled to room temperature and acetic anhydride (30 ml) was added. After stirring for 30 min the mixture was worked up as described above.

Using these procedures the following acetylated lactones were prepared. Their structures were in all



cases confirmed through their ¹H and ¹³C NMR spectra. Only data from the latter are given and signals from the acetyl groups are omitted.

Tetra-O-acetyl-D-galactono-1,4-lactone (1) was prepared from *D-galactono-1,4-lactone* and crystallized from ethanol, yield 90%, m.p. 66.5–68 °C, $[\alpha]_D^{20} -19.7^\circ$ (c 1.5, CHCl₃), reported¹⁹ m.p. 67–68 °C, $[\alpha]_D -20^\circ$. ¹³C-NMR: 170.0 ppm (C-1); 77.1 (C-4); 71.9 and 71.8 (C-2,3); 68.0 (C-5); 61.3 (C-6).

Tetra-O-acetyl-L-gulono-1,4-lactone (4) was obtained in 90% yield as a syrup from *L-gulono-1,4-lactone* (reported¹⁹ m.p. 103–104 °C). ¹³C NMR: 170.1 ppm (C-1); 76.2 (C-4); 69.0, 68.4, and 67.9 (C-2,3,5); 61.3 (C-6).

Tetra-O-acetyl-D-mannono-1,4-lactone (9) from *D-mannono-1,4-lactone*²⁰ in 99% yield after crystallization from ethanol–water, m.p. 114–115 °C. Recrystallization gave a product with m.p. 119–

120 °C (reported¹⁹ m.p. 121 °C) ¹³C NMR: 170.0 ppm (C-1); 74.5 (C-4); 68.2, 67.7, and 66.5 (C-2,3,5); 61.7 (C-6).

Tri-O-acetyl-D-arabono-1,4-lactone (14) from *D-arabono-1,4-lactone*.²¹ Crystallization from ethyl acetate gave 69%, m.p. 55–56 °C, $[\alpha]_D^{25} +51.6^\circ$ (c 4.5, CHCl₃), (reported²¹ m.p. 81, 68–69, and 52–54 °C, $[\alpha]_D +53.2^\circ$). ¹³C NMR: 167.5 ppm (C-1); 76.6 (C-4); 71.7 and 71.4 (C-2,3); 61.3 (C-5).

Potassium *D-arabonate* gave 60% of 14, m.p. 55–56 °C.

Tri-O-acetyl-D-ribo-1,4-lactone (15) was obtained in 75% yield from *D-ribo-1,4-lactone* as a syrup (reported²² m.p. 54–56 °C). ¹³C NMR: 168.7 ppm (C-1); 79.8 (C-4); 69.3 and 65.9 (C-2,3); 62.3 (C-5).

Tri-O-acetyl-D-xylono-1,4-lactone (16) was prepared from *D-xylono-1,4-lactone*²³ in 42% yield

after crystallization from ethyl acetate, m.p. 94–95°C, $[\alpha]_D^{20}$ 71.8° (c 3.0, CHCl₃), (reported²⁴ m.p. 99°C, $[\alpha]_D$ +62.4° (EtOH)). ¹³C NMR: 167.9 ppm (C-1); 74.4 (C-4); 71.6 and 69.8 (C-2, 3); 60.1 (C-5).

Ammonium D-xylonate²³ yielded 37% of 16, m.p. 91–94°C.

Tri-*O*-acetyl-D-lyxono-1,4-lactone (17) was obtained from D-lyxono-1,4-lactone in 96% yield as a syrup. ¹³C NMR: 168.7 (C-1); 75.5 (C-4); 69.0 and 67.6 (C-2, 3); 60.7 (C-5).

3-Deoxy-D-xylo-hexono-1,4-lactone (3b). Tetra-*O*-acetyl-D-galactono-1,4-lactone (1) (10.0 g) in ethyl acetate (100 ml) and triethylamine (10 ml) was hydrogenolyzed for 3 h at 3 atm. pressure in the presence of 5% palladium on carbon (1.0 g). The mixture was then filtered and the filtrate was washed twice with 4 M hydrochloric acid, dried and evaporated. This gave 8.0 g (99%) of tri-*O*-acetyl-3-deoxy-D-xylo-hexono-1,4-lactone (3a) as a syrup. ¹H NMR: δ 5.31 (H-2); 5.01 (H-5); 4.51 (H-4); 4.18 (H-6); 4.00 (H-6'); 2.57 (H-3); 2.00 (H-3'). J_{23} 9.0 Hz; $J_{23'}$ 10.5; $J_{33'}$ 12.9; J_{34} 6.0; $J_{3'4}$ 9.0; J_{45} ; J_{56} 4.5; $J_{56'}$ 6.0; $J_{66'}$ 12.0. ¹³C NMR: 171.4 ppm (C-1); 74.3 (C-4); 70.4 (C-2); 67.6 (C-5); 61.7 (C-6); 30.0 (C-3).

The acetylated lactone (3a) (7.3 g) was kept overnight in water (40 ml) and ethanol (40 ml) containing potassium hydroxide (4.0 g). The solution was then passed through an ion exchange resin (Amberlite IR-120, H⁺) and evaporated. The residue was crystallized from methanol to give 4.0 g (80%) of 3b, m.p. 140°C. Recrystallization furnished a product with m.p. 142–143°C, $[\alpha]_D = -45.6°$ (c 1.3, H₂O) (reported⁶ m.p. 142–143°C, $[\alpha]_D -47.8°$). ¹³C NMR: 178.7 ppm (C-1); 78.4 (C-4); 72.9 (C-5); 68.6 (C-2); 62.7 (C-6); 33.1 (C-3).

3-Deoxy-L-xylo-hexono-1,4-lactone (5b). Tetra-*O*-acetyl-L-gulonolactone (4) (4.0 g) was hydrogenolyzed for 3 h at 3 atm. pressure as described above to give 3.0 g (95%) of tri-*O*-acetyl-3-deoxy-L-xylo-hexono-1,4-lactone (5a) as a syrup. Its ¹H and ¹³C NMR spectra were identical with those of 3a.

Deacetylation of 5a as described above yielded 1.5 g (72%) of 5b, m.p. 140°C. Recrystallization from methanol–ether gave a product with m.p. 142°C, $[\alpha]_D^{20} +44.8°$ (c 1.5, H₂O). Anal. C₆H₁₀O₅; C, H. ¹H and ¹³C NMR data were identical with those of 3b.

Di-*O*-acetyl-3,6-dideoxy-D-xylo-hexono-1,4-lactone (7a). Tri-*O*-acetyl-6-bromo-6-deoxy-D-galactono-1,4-lactone⁸ (6) (5.0 g) was hydrogenolyzed in ethyl acetate (75 ml) and triethylamine (10 ml) for 3 h at 3 atm. pressure in the presence of 5% palladium on carbon (500 mg). Work-up as described above and crystallization from ether–pentane gave 2.9 g (93%) of 7a, m.p. 75–77°C. Two additional recrystallizations gave a product with m.p. 86–87°C, $[\alpha]_D^{20} -22.8°$ (c 1.1, CHCl₃). Anal. C₁₀H₁₄O₆; C, H. ¹H NMR: δ 5.51 (H-2); 5.02 (H-5); 4.47 (H-4); 2.72 (H-3); 1.99 (H-3'); 1.32 (H-6). J_{23} 8.8 Hz; $J_{23'}$ 10.5;

$J_{33'}$ 12.5; J_{34} 5.5; $J_{3'4}$ 10.4; J_{45} 5.3; J_{56} 6.5. ¹³C NMR: 171.4 ppm (C-1); 77.2 (C-4); 69.8 (C-2); 67.8 (C-5); 30.4 (C-3); 15.4 (C-6).

3,6-Dideoxy-D-xylo-hexono-1,4-lactone (7b). Deacetylation of 7a (3.0 g) as described above and crystallization from ether gave 1.3 g (75%) of 7b, m.p. 80–81°C. Recrystallization from ethyl acetate yielded a product with m.p. 85–86°C, $[\alpha]_D^{20} -50.8°$ (c 1.2, H₂O). Anal. C₆H₁₀O₅; C, H. ¹³C NMR: 180.1 ppm (C-1); 82.1 (C-4); 69.6 (C-5); 68.6 (C-2); 33.6 (C-3); 18.0 (C-6).

3,6-Dideoxy-D-xylo-hexitol (8). A solution of the lactone 7b (0.4 g) in ether (15 ml) was stirred overnight with lithium aluminiumhydride (200 mg). After addition of excess 1 M hydrochloric acid the mixture was deionized with a mixed bed ion exchange resin (Amberlite MB-3). Evaporation of the resulting solution gave 250 mg (61%), m.p. 90°C from ethanol $[\alpha]_D^{20} +52°$ (c 2.0, H₂O), (reported⁹ m.p. 92–94°C $[\alpha]_D +54°$).

3-Deoxy-D-arabino-hexono-1,4-lactone (10b). Tetra-*O*-acetyl-D-mannono-1,4-lactone (9) (10.0 g) was hydrogenolyzed in ethyl acetate (100 ml) and triethylamine (10 ml) for 20 h at room temperature in the presence of 5% palladium on carbon (1.0 g). Work-up as described above gave 8.2 g (~100%) of syrupy tri-*O*-acetyl-3-deoxy-D-arabino-hexono-1,4-lactone (10a). ¹³C NMR: 179.7 ppm (C-1); 75.3 (C-4); 68.5 and 67.7 (C-2, 5); 63.1 (C-6); 36.8 (C-3). Its ¹H NMR spectrum was identical with that described previously.³

Deacetylation of 10a (8.2 g) as described above gave 4.7 g (~100%) of 10b as a syrup. ¹³C NMR: 178.6 ppm (C-1); 77.7 (C-4); 71.8 and 68.5 (C-2, 5); 62.2 (C-6); 31.8 (C-3). The spectrum was identical with that of an authentic sample of 10b.¹⁰

Calcium 3-deoxy-D-arabino-hexonate (11). To D-glucono-1,5-lactone (12b) (10.0 g) was added acetic acid (20 ml), water (0.5 ml), and two drops of conc. sulfuric acid and the mixture was boiled for ca. 5 min. until a clear solution was obtained. The solution was then cooled and acetic anhydride (50 ml) and sulfuric acid (10 drops) was added. After 10 min. ice and water was added and the mixture was extracted with dichloromethane (3 × 50 ml). The extract was washed with water, dried and evaporated leaving 17.9 g (92%) of a syrup which consisted mainly of tetra-*O*-acetyl-D-glucono-1,4-lactone (13a) as seen from ¹H and ¹³C NMR spectra.

This product was hydrogenolyzed at 100 atm. pressure overnight to give 14.0 g (97%) of crude 10a which was subsequently deacetylated as described above to yield 7.2 g (81%) of syrupy 3-deoxy-D-arabino-hexono-1,4-lactone (10b), identical with the product described above. The lactone (10b) was converted into the calcium salt (11) by treatment with calcium hydroxide.¹⁰ Crystallization from water gave 5.5 g (50% based on D-glucono-1,5-

lactone) of **11**, m.p. 161–162 °C, $[\alpha]_D^{20} - 22^\circ$ (c 2.0, H₂O), (reported¹⁰ $[\alpha]_D - 24^\circ$). ¹³C NMR: 182.6 ppm (C-1); 75.6, 70.3 and 69.5 (C-2, 4, 5); 63.3 (C-6); 37.9 (C-3). The spectrum was identical with that of an authentic sample.¹⁰

Hydrogenolysis of tetra-O-acetyl-D-glucono-1,5-lactono (12a). Hydrogenolysis of 1.5 g of **12a**¹⁹ at 100 atm. pressure followed by deacetylation as described above gave 0.46 g (72 %) of a mixture of **10b** and 3-deoxy-D-ribo-hexono-1,4-lactone in a ratio of 3:1 as seen from a ¹³C NMR spectrum. An authentic sample of the ribono-lactone was prepared according to Ref. 10.

Di-O-acetyl-3-deoxy-D-threo-pentono-1,4-lactone (18a). Each of the acetylated D-pentono-1,4-lactones, **14**, **15**, **16**, and **17**, was hydrogenolyzed as described above, either at 100 atm pressure for 5–24 h or at 3 atm for 24–28 h. Work-up and crystallization from ether followed by recrystallization from ethyl acetate gave **18a** with m.p. 69–71 °C, $[\alpha]_D^{25} + 51.2^\circ$ (c 1.3, CHCl₃). Anal. C₉H₁₂O₆: C, H. ¹H NMR (270 MHz): δ 5.50 (H-2); 4.66 (H-4); 4.37 (H-5); 4.19 (H-5'); 2.76 (H-3); 1.99 (H-3'). J_{23} 8.7 Hz; $J_{23'}$ 10.2; $J_{33'}$ 13.0; J_{34} 6.2; $J_{3'4'}$ 9.8; J_{45} 3.0; $J_{45'}$ 5.6; $J_{55'}$ 12.3 ¹³C NMR: 171.5 ppm (C-1); 73.8 (C-4); 67.7 (C-2); 63.7 (C-5); 29.8 (C-3).

The four acetylated pentono-lactones all gave the 3-deoxy-lactone (**18a**) by this procedure, no isomeric deoxy-lactones were observed. The rate of hydrogenolysis differed. Thus the arabino-lactone (**14**) was completely hydrogenolyzed by treatment with hydrogen for 5 h at 100 atm and gave **18a** in 83 % yield. The ribo-lactone (**15**) required 48 h reaction and gave 55 % of **18a**.

Methyl 3,5-di-O-benzoyl-3-deoxy-α-D-threo-pentofuranoside (19). The acetylated lactone (**18a**) (1.5 g) was deacetylated with potassium hydroxide as described above to give 0.89 g (97 %) of syrupy 3-deoxy-D-threo-pentono-1,4-lactone (**18b**).²⁵ ¹³C NMR: 181.1 ppm (C-1); 79.9 (C-4); 69.7 (C-2); 63.9 (C-5); 33.7 (C-3).

The latter product was dried in vacuum and suspended in THF (80 ml) under an argon atmosphere. To the ice-cooled and stirred suspension was added a solution of diisoamylborane, prepared from the borane-dimethylsulfide complex (4.2 ml) and 2-methyl-2-butene (8.7 ml) in THF (12 ml).²⁶ The solution was kept overnight at room temperature. Water (10 ml) was then added and the mixture was boiled for 2 h. After cooling it was extracted with dichloromethane (3 × 30 ml); the aqueous phase was evaporated leaving 700 mg (75 %) of syrupy 3-deoxy-D-threo-pentose,²⁵ characterized through its ¹H and ¹³C NMR spectra.

The product was dissolved in methanol (50 ml) containing acetyl chloride (1 ml) and the solution was kept for 20 h. It was then neutralized with silver carbonate, filtered, and evaporated leaving 674 mg

of crude product. A ¹³C NMR spectrum showed that it contained mainly methyl 3-deoxy-α-D-threo-pentofuranoside showing the following signals: 111.3 ppm (C-1); 81.0 (C-4); 76.3 (C-2); 65.7 (C-5); 56.6 (OMe); 35.4 (C-3); $J_{C-1, H-1}$ 170 Hz.

Benzoylation with benzoyl chloride in pyridine gave 1.5 g of a syrup which was purified by chromatography on a column of silica gel using ethyl acetate-pentane (1:4) as eluant. The main fraction gave 536 mg of methyl 2,5-di-O-benzoyl-3-deoxy-α-D-threo-pentofuranoside (**19**) which was crystallized from ether–pentane, m.p. 86–87 °C $[\alpha]_D^{25}$ 38.2 (c 1.0, CHCl₃), (reported¹² 89–89.5 °, $[\alpha]_D$ 36.7°). ¹H NMR (90 MHz); δ 5.33 (H-2); 5.13 (H-1); 4.3–4.7 (H-4, 5); 3.40 (OMe); 2.69 (H-3); 1.96 (H-3'). $J_{12} \approx 0$ Hz; J_{23} 6.5; $J_{23'}$ 1.6; $J_{33'}$ 13.5; J_{34} 8.0; $J_{3'4}$ 5.0.

5-O-Acetyl-2,3,6-trideoxy-D-erythro-hexono-1,4-lactone (21). A solution of di-O-acetyl-2,6-dideoxy-D-arabino-hexono-1,4-lactone (**20**) (8.1 g) and triethylamine (8.0 ml) in ethyl acetate (30 ml) was treated with hydrogen for 18 h at room temperature and a pressure of 100 atm. in the presence of 5 % palladium on carbon (500 mg). Work-up as described above gave 4.5 g (74 %) of **21** as a colourless liquid which was pure as seen from a ¹H NMR spectrum. Distillation in vacuum gave 4.1 g (73 %), b.p. 110 °C (1 mm), $[\alpha]_D^{20} + 30.4^\circ$ (c 9.5, CHCl₃). Anal. C₈H₁₂O₄: C, H. ¹H NMR (270 MHz): δ 5.11 (H-5); 4.50 (H-4); 2.55 (H-2') 2.52 (H-2); 2.31 (H-3'); 2.13 (H-3); 2.04 (OAc); 1.27 (H-5); $J_{22'}$ 18.0 Hz; J_{23} 8.0 and 8.7; $J_{2'3}$ 6.9 and 9.6; $J_{33'}$ 14.3; J_{34} 6.4 and 7.6; J_{45} 3.8; J_{56} 6.5. ¹³C NMR: 176.0 ppm (C-1); 79.3 (C-4); 69.7 (C-5); 27.1 (C-2); 21.6 (C-3); 14.2 (C-6). The D,L-form has been synthesized.²⁷

Alternatively, the 6-bromo-lactone (**23**)¹⁵ (10.0 g) in ethyl acetate (75 ml) and triethylamine (15 ml) was hydrogenolyzed as described above to give 4.7 g (84 %) of **21**. Distillation yielded 3.5 g (63 %), b.p. 110 °C (1 mm), $[\alpha]_D^{20} + 30.0^\circ$ (c 6.7, CHCl₃).

5-O-Acetyl-2,3,6-trideoxy-L-erythro-hexono-1,4-lactone (25). Hydrogenolysis of di-O-acetyl-2,6-dideoxy-L-arabino-hexono-1,4-lactone¹⁵ (**25**) (8.9 g) as described above gave 5.0 g (75 %) of crude **25**. Distillation yielded 4.8 g (72 %) of a product with b.p. 110 °C (1 mm), $[\alpha]_D^{20} - 30.4^\circ$ (c 8.2, CHCl₃). Anal. C₈H₁₂O₄: C, H. ¹H and ¹³C NMR spectra were identical with those of the enantiomer (**21**).

3-O-Acetyl-5,6-didehydro-2,5,6-trideoxy-D-threo-hexono-1,4-lactone (24). A solution of the 6-bromo-lactone (**23**) (14.7 g) in a mixture of acetic acid (140 ml) and water (60 ml) was stirred and cooled in ice. Zinc dust (80 g) was added in portions in the course of 2 h and the mixture was stirred for an additional h. The zinc was filtered off and washed with water and dichloromethane. The filtrate was extracted four times with dichloromethane and the extract was washed with water and dried. Evaporation left 6.5 g (80 %) of **24** as a colourless liquid which was pure as

seen from a ^1H NMR spectrum. In a series of preparations the yield varied between 80 and 90%. Distillation in vacuum gave 4.9 g (60%) of 24, b.p. 110°C (1 mm), $[\alpha]_D^{20} + 70.8^\circ$ (c 5.4, CHCl_3). Anal. $\text{C}_8\text{H}_{10}\text{O}_4$: C, H. ^1H NMR (270 MHz): δ 5.84 (H-5); 5.54 (H-3); 5.48 (H-6); 5.39 (H-6'); 5.04 (H-4); 2.92 (H-2) 2.62 (H-2). J_{22} 18.3 Hz; J_{23} 1.9; $J_{2,3}$ 6.3; $J_{3,4}$ 4.5; $J_{4,5}$ 6.3; $J_{4,6} = J_{4,6'}$ ~1; $J_{5,6}$ 17.5; $J_{5,6'}$ 10.5; $J_{6,6'}$ 1.2. ^{13}C NMR: 173.4 ppm (C-1); 129.3 (C-5); 119.5 (C-6); 82.1 (C-4); 70.4 (C-3); 35.3 (C-2).

3-O-Acetyl-2,5,6-trideoxy-D-threo-hexono-1,4-lactone (26). The 6-bromo-lactone (23) (11.5 g) was treated with zinc in acetic acid as described above to give 5.2 g of crude 24. This was hydrogenated at 1 atm. pressure in ethyl acetate (20 ml) in the presence of 5% palladium on carbon (200 mg). Filtration and evaporation gave 5.2 g (82%) of 26 which was pure as seen from a ^1H NMR spectrum. Distillation in vacuum gave 4.5 g (70%) of 26, b.p. 110°C (1 mm), $[\alpha]_D^{20} + 31.4^\circ$ (c. 8.0, CHCl_3). Anal. $\text{C}_8\text{H}_{12}\text{O}_4$: C, H. ^1H NMR (270 MHz): δ 5.47 (H-3); 4.52 (H-4); 2.91 (H-2); 2.55 (H-2); 1.81 (H-5'); 1.70 (H-5); 1.02 (H-6). J_{23} 1; $J_{2,3}$ 5.6; $J_{3,4}$ 4.2; $J_{4,5}$ 5.6; $J_{4,5'}$ 9.6; $J_{5,6}$ 7.2. ^{13}C NMR: 173.3 ppm (C-1); 82.9 (C-4); 69.4 (C-3); 35.5 (C-2); 20.6 (C-5); 8.6 (C-6).

(R)-(+)- γ -Caprolactone (27). A solution of the crude, unsaturated lactone (24) (9.0 g), prepared as described above, in ethyl acetate (40 ml) was hydrogenated at 1 atm. pressure in the presence of 5% palladium on carbon (500 mg) until hydrogen was no longer consumed (ca. 5 h). The suspension was then transferred to an autoclave, triethylamine (8 ml) was added, and it was hydrogenolyzed overnight at 100 atm. and 70°C. The catalyst was then filtered off and the solution was washed twice with 2 M hydrochloric acid and once with water, dried and evaporated. The residue (5.5 g) (91%) consisted of the lactone (27) as a colourless liquid which was pure as seen from a ^1H NMR spectrum. Distillation in vacuum gave 3.9 g (65%) of 27, b.p. 57–60°C (1 mm), $[\alpha]_D^{20} + 51.9^\circ$ (c 7.5, MeOH); (reported¹⁶ $[\alpha]_D^{20} + 53.2^\circ$ (MeOH)). NMR: δ 4.44 (H-4); 2.52 (H-2); 2.34 and 1.87 (H-3); 1.70 (H-5); 0.99 (H-6). ^{13}C NMR: 177.0 ppm (C-1); 81.8 (C-4); 28.4, 28.0, and 27.0 (C-2,3,5); 9.0 (C-6).

2,3-Dideoxy-D-glycero-pentono-1,4-lactone (29b). Potassium D-lyxonate (10 g) was stirred with a 32% solution of hydrogen bromide in acetic acid (100 ml) for 1 h at room temperature. Methanol (200 ml) was then added and the mixture was kept overnight. Evaporation gave a residue which was dissolved in water (20 ml) and extracted with ethyl acetate (6 \times 25 ml). The extract was dried and evaporated leaving 12 g of crude 2-bromo-2-deoxy-D-xylono-1,4-lactone.¹⁵ This product was hydrogenolyzed for 2 h at 100 atm. pressure in ethyl acetate (100 ml) and triethylamine (10 ml) using 500 mg of 5% palladium on carbon as catalyst. Filtration and evaporation

gave crude 2-deoxy-D-threo-pentono-1,4-lactone (28b).¹⁵ Acetic anhydride (20 ml) and 60% aqueous perchloric acid (5 ml) was added. After 1 h, water was added and the mixture was extracted with dichloromethane. The extract was dried and evaporated leaving 7.0 g (66%) of di-O-acetyl-2-deoxy-D-threo-pentono-1,4-lactone (28a) which was pure as seen from a ^{13}C NMR spectrum.¹⁵

Hydrogenolysis of the latter product for 20 h at 100 atm. in ethyl acetate (100 ml) and triethylamine (10 ml) with 1.0 g of 5% Pd/C and work-up as described above gave 7 g of crude 5-O-acetyl-2,3-dideoxy-D-glycero-pentono-1,4-lactone (29a). ^{13}C NMR: 176.6 (C-1); 77.2 (C-4); 64.9 (C-5); 27.7 (C-2); 23.3 (C-3).

Deacetylation with potassium hydroxide followed by deionization and evaporation gave a product which was completely lactonized by evaporation with a few ml of 2 M hydrochloric acid at 50°C. This left 3.5 g (62% based on potassium lyxonate) of syrupy 28b. ^{13}C NMR data: 183.8 (C-1); 84.3 (C-4); 64.8 (C-5); 30.3 (C-2); 24.5 (C-3).

5-O-p-Toluenesulfonyl-2,3-dideoxy-D-glycero-pentono-1,4-lactone (29c). The crude lactone (29b) (1.4 g) in pyridine (8 ml) was stirred overnight at 0°C with *p*-toluenesulfonyl chloride (3.0 g). Water was then added and the mixture was extracted with dichloromethane. The extract was washed with 2 M hydrochloric acid and with water, dried and evaporated. This gave 2.72 g (83%) of 29c with m.p. 79–80°C. Recrystallization from ethyl acetate–ether gave a product with m.p. 84–85°C, $[\alpha]_D^{20} + 45.9^\circ$ (c 1.5, CHCl_3); (reported¹⁶ m.p. 85–87°C $[\alpha]_D + 47.0^\circ$). A ^1H NMR spectrum further confirmed the structure.

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