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β-Elimination of protected aldono-1,4-lactones as a general approach to the synthesis of 2-keto-3-deoxyaldonic acids containing four to six carbon atoms

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Abstract

The well-known β-elimination of protected aldonolactones is used for the synthesis of the short-chain 2-keto-3-deoxyaldonic acids **1–4** containing four to six carbon atoms. The key step is the facile β-elimination step which generates the desired 2-keto-3-deoxy acids as protected enol 1,4-lactones in excellent yields. Smooth deprotection then leads to the 2-keto-3-deoxyaldonic acids. In the case of the protected D-galactono-1,4-lactone **6** an epimerisation is observed during the elimination process. This enables the synthesis of both 2-keto-3-deoxy-D-hexonic acids with either D-*erythro* (**1**) or D-*threo* (**2**) configuration in good to excellent yields in only three steps starting with commercially available D-galactono-1,4-lactone (**5**).

Keywords: Aldono-1,4-lactones; β-Elimination; Ketodeoxyaldonic acids; Synthesis

1. Introduction

The 2-keto-3-deoxyaldonic acids **1–3** are well-known metabolites in the oxidative degradation pathway of aldoses leading to pyruvate and small hydroxy aldehydes [1]. There are also some reports about their occurrence in polysaccharides. 3-Deoxy-D-*threo*-hex-2-ulosonic acid (**2**) was identified as part of an extracellular polysaccharide in *Azotobacter vinelandii* [2]. A corresponding 3-deoxy-L-*glycero*-pent-2-ulosonic acid

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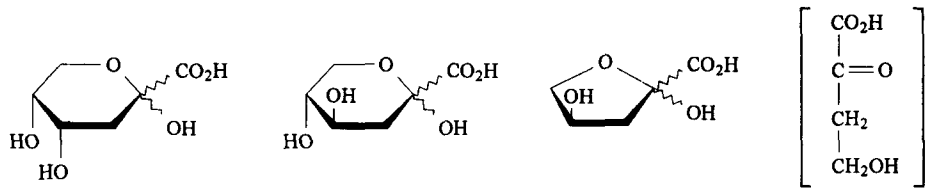


Scheme 1.

occurs as a component of the repeating unit of the capsular polysaccharide of *Klebsiella* K38 [3].

For the chemical synthesis of this family of compounds four major approaches have previously been used: (*i*) condensation of oxalacetic acid with aldoses leading to diastereomeric mixtures of the desired compounds [4]; (*ii*) selective oxidation of 3-deoxyaldonic acids by the action of sodium perchlorate in the presence of vanadium(V) oxide in mediocre yields [5]; (*iii*) cyanohydrin synthesis and base-catalysed cyclisation to imidolactones, elimination, and stepwise hydrolysis in an overall yield of ca. 6% [6]; (iv) chain extension of aldoses by a one- or two-carbon synthon including a comparatively complex synthesis of the starting materials [7].

To our knowledge only one approach dealing with the synthesis of **2** employing β-elimination was reported by Anker and co-workers [8]. This synthetic sequence started with D-glucono-1,5-lactone and allowed the synthesis of **2** in a six-step reaction in an overall yield of 45%.

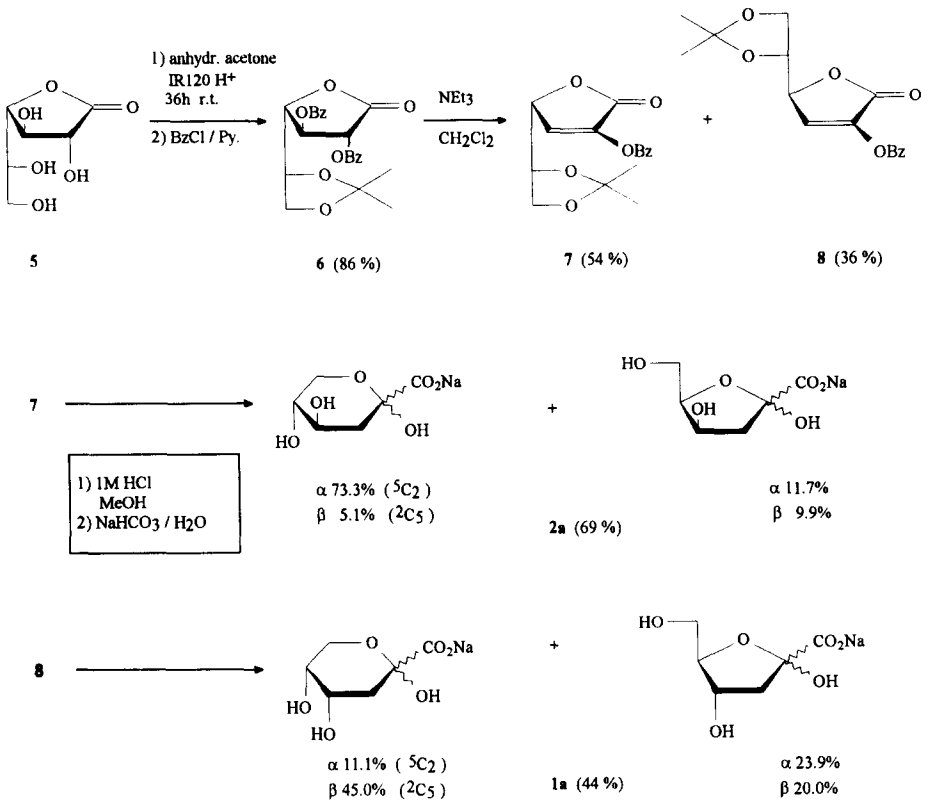
2. Results and discussion

The investigation presented in this paper focuses on a more general approach which can be used for the 2-keto-3-deoxyaldonic acids **1–4**. Starting with the aldono-1,4-lactones (**5, 9, 13**) the selective protection of the hydroxy groups in the side chain was followed by benzoylation of the remaining hydroxy groups at C-2 and C-3.

β-Elimination in protected aldonolactones was first observed as a side reaction during base-catalysed acetylations and benzoylations of unprotected lactones [9]. De Lederkremer et al. [10] isolated several elimination products by treatment of perbenzoylated lactones with bases such as pyridine or triethylamine and discussed an E_{1cb} mechanism for the elimination step [11]. Pedersen and his co-workers [12] used the synthetic potential of this reaction for the synthesis of 3-deoxyaldonic acids and 3-deoxyaldoses by combining the triethylamine-catalysed elimination of peracetylated aldonolactones with the in situ reduction of the initially formed enol intermediate to give 3-deoxyaldonolactones.

Our initial task was to develop a suitable protecting group pattern which would prohibit further elimination and enable smooth deprotection to give the labile free acids.

In the case of D-galactono-1,4-lactone (**5**) a quantitative selective isopropylidenation (TLC) of the side-chain hydroxy groups was achieved by treatment of **5** with Amberlite



Scheme 2.

IR-120 (H^+) ion-exchange resin in anhydrous acetone. The crude material could be subjected, without further purification, to benzoylation of the remaining hydroxy groups to yield the fully protected product **6** in 86% overall yield. β-Elimination was carried out in dichloromethane with a catalytic to a molar amount of triethylamine and led to the simultaneous formation (TLC) of the two products **7** and **8** in 56 and 33% yield, respectively. Until now all attempts to change the product ratio by variation of temperature, the reaction time, and the amount of catalyst have been unsuccessful.

After separation by column chromatography the two products were identified as C-4 epimers by comparison of NMR data values and optical rotation. The coupling constant $J_{4,5}$ 4 Hz for **7** proved the D-*threo* configuration which is similar to that of the starting material (**6**: $J_{4,5}$ 4 Hz). On the other hand the coupling constant $J_{4,5}$ 8 Hz for **8** indicated the D-*erythro* configuration. All other ^1H and ^{13}C signals of both these compounds were similar and clearly proved the 2-enolactone structure. The difference in optical rotation of −55.4° for **8** and +19.8° for **7** further supported the idea that epimerisation at C-4 occurred during the elimination and caused the formation of the two diastereomeric compounds **7** and **8**.

Deprotection was carried out for both products in a two-step reaction which could be performed in situ. The cleavage of the isopropylidene group was achieved first by

treatment with hydrochloric acid in anhydrous methanol; an addition of aqueous sodium hydrogen carbonate to pH 8 then led to deprotection of the enol and simultaneous lactone opening. Following evaporation the raw material was separated from inorganic salts and sodium benzoate by chromatography on a Sephadex G10 column.

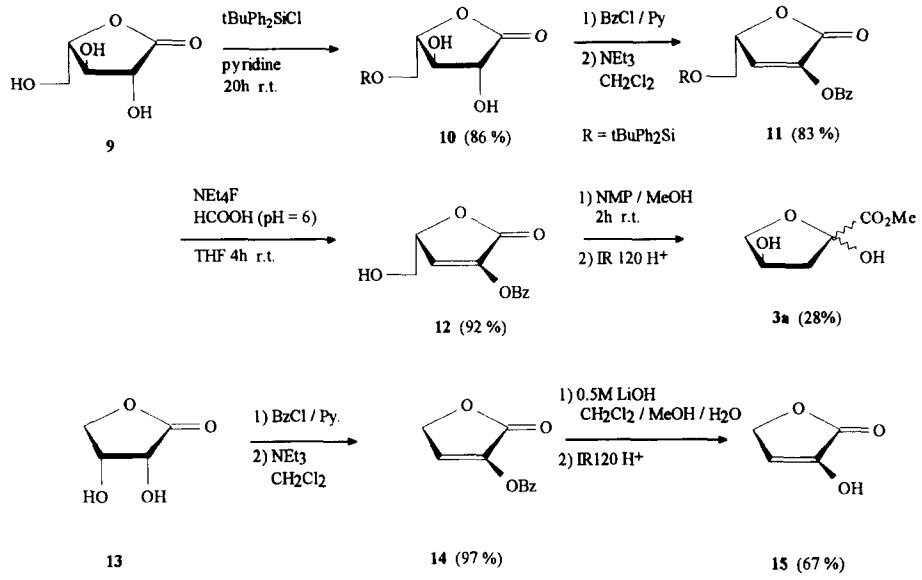
The sodium salts **1a** and **2a** of the 2-keto-3-deoxyhexonic acids **1** and **2** could be obtained in 44 and 69% yield, respectively. The NMR spectra in D_2O indicated for both compounds a mixture of anomeric pyranose and furanose structures; **2a** could be identified as the product previously described by Anker and his co-workers [8] and **1a** as its D-*erythro* isomer based on evaluation of coupling constants.

In the case of the L-arabinono-1,4-lactone **9** the selective protection of the side-chain hydroxy group at C-5 could be achieved by silylation with 1.2 equivalents of *tert*-butylchlorodiphenylsilane in anhydrous pyridine in 80% yield after column chromatography. In contrast to the previous results of Fleet and his co-workers [13], who used the same reagent but added imidazole for protection of the primary hydroxy group in D-*glycero*-D-*gluco*-heptono-1,4-lactone, no significant silylation at the corresponding 2 position could be observed in this case. The crude material formed by benzoylation of the remaining hydroxy groups at C-2 and C-3 could be subjected to β-elimination without further purification and gave 83% of the 3-deoxy-2-enolactone **11**.

This product was desilylated with tetrabutylammonium fluoride at pH 6 to give compound **12** in 92% yield. Its enantiomeric purity was proved by esterification with Mosher's reagent [14]. The NMR spectra of the ester showed only one set of signals which indicated the formation of only one enantiomer during the course of β-elimination as determined by ^{1}H NMR. The configuration was supposed to be L-*glycero* by comparison of the optical rotation value of **11** with that of the diastereomeric compounds **7** and **8**.

Again the deprotection procedure as described for **7** and **8** seemed to be successful as seen by TLC; however, the workup procedure caused decomposition probably because of the instability of the sodium salt of **3**. In order to avoid this problem the very mild debenzoylation method with *N*-methylpyrrolidine in methanol and tetrahydrofuran was used [15]. After two hours the reaction mixture was acidified by addition of Amberlite IR-120 (H^+) resin, and stirring was continued for 30 min in order to form the methyl ester **3a** of the acid **3**. The crude material was purified by column chromatography which enabled the isolation of compound **3a** in 28% yield, in addition to 18% starting material. The NMR spectra showed two anomeric 3-deoxy-L-*glycero*-pent-2-ulofuranosonic acid methyl esters. An unequivocal assignment of the α and β configuration was not possible because of similar coupling constants.

D-Erythrono-1,4-lactone (**13**) could be directly subjected to the same benzoylation and β-elimination sequence as described for **10** to obtain **14** in 97% yield. The deprotected acid has already been described as unstable and impossible to isolate [10]. For that reason the deprotection was carried out in a two-phase system containing water, methanol, and chloroform by slow addition of 0.5 M aqueous lithium hydroxide to pH 9. After removal of the organic layer the aqueous layer was acidified by the addition of Amberlite IR-120 (H^+) resin in order to form the more stable lactone derivative **15** which could be extracted with diethyl ether and crystallised in 67% yield by partial evaporation of the solvent. In contrast to an earlier report by Lane and Dekker [16], who



9 10 (86 %) 11 (83 %) 12 (92 %) 3a (28%) 13 14 (97 %) 15 (67 %)

Scheme 3.

proposed a ketone structure for **15**, the NMR spectra in D_2O showed only evidence for the presence of the enol form.

In summary it should be pointed out that the approach developed via β-elimination was successful for the synthesis of all the desired 2-keto-3-deoxyaldonic acids, incorporating some modifications of the deprotecting procedures. Compounds **1a** and **2a** could both be prepared from D-galactono-1,4-lactone (**5**) in 12.5 and 33% overall yield by a three-step synthesis. For **3a** the overall yield following the four-step reaction sequence was only 17% mainly due to the instability of the keto acid **3**. In the case of **15** the synthesis was shortened to only two steps with an overall yield of 65%.

The application of this synthetic strategy to aldono-1,4-lactones with elongated side chains such as the well-known 3-deoxy-D-*arabino*-hept-2-ulosonic acid or 3-deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) by a combination of the protective group techniques is under investigation.

3. Experimental

2,3-Di-O-benzoyl-5,6-O-isopropylidene-D-galactono-1,4-lactone (**6**).—D-Galactono-1,4-lactone (**5**) (20 g; 55.8 mmol) was dissolved in anhyd DMF (50 mL). 2,2-Dimethoxypropane (50 mL) and Amberlite IR-120(H^+) (1 g) were added and the mixture was stirred for 38 h. After complete reaction (TLC 1:1 toluene–EtOAc) the ion-exchange resin was removed by filtration and the solution was evaporated to 50 mL. Benzoyl chloride (27.8 mL, 223.2 mmol) dissolved in anhyd pyridine (37.4 mL) was added dropwise at 0°C. After 3 h at room temperature, the mixture was poured into ice–water

and the product was extracted with CH_2Cl_2. The organic layer was washed several times with saturated aq $NaHCO_3$, dried over $MgSO_4$, evaporated, and finally purified by column chromatography (20:1 → 5:1 toluene–EtOAc) to yield **6** (20.5 g, 86%) as a syrup; $[\alpha]_D^{20}$ +59.0° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^1H (400 MHz), δ 8.20–8.00, 7.60–7.10 (m, m, 10 H, Bz), 6.10 (d, 1 H, $J_{2,3}$ 5.5 Hz, H-2), 5.95 (dd ~ t, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 4.65 (m, 2 H, H-4, H-5), 4.20 (dd, 1 H, $J_{5,6a}$ 6.5,$J_{6a,6b}$ 8.0 Hz, H-6a), 4.10 (dd, 1 H, $J_{5,6b}$ 6.0 Hz, H-6b), 1.55, 1.45 (2 s, each 3 H, CMe_2); ^{13}C (100 MHz) δ 168.5 (C-1), 165.0, 164.6 (C-Bz), 133.9, 133.3 (C-Bz), 129.6–128.3 (C-Bz), 110.0 (CMe_2), 74.3, 73.9, 73.8, 71.9 (C-2, C-3, C-4, C-5), 64.5 (C-6), 25.3, 24.8 (CMe_2).

*2-O-Benzoyl-3-deoxy-5,6-O-isopropylidene-*D-threo-*hex-2-enono-1,4-lactone* (**7**) *and 2-O-benzoyl-3-deoxy-5,6-O-isopropylidene-*D-erythro-*hex-2-enono-1,4-lactone* (**8**).—A solution of **6** (14 g, 32.9 mmol) in CH_2Cl_2 (200 mL) was treated with triethylamine (3.83 mL, 32.8 mmol). After 3 h the solvents were evaporated and the crude residue was subjected to several azeotropic distillations with toluene. The isomer separation was achieved by column chromatography (10:1 → 5:1 toluene–EtOAc) to yield **7** (5.58 g, 56%) as a white solid; mp 79–82°C; $[\alpha]_D^{20}$ +19.8° (*c* 1.0, $CHCl_3$); and **8** (3.36 g, 33%) as a white solid; mp 67–70°C; $[\alpha]_D^{20}$ −55.4° (*c* 1.0, $CHCl_3$). NMR data for **7** ($CDCl_3$): ^1H (400 MHz), δ 8.15, 7.60, 7.45 (m, m, m, 2 H, 1 H, 2 H, Bz), 7.35 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 5.10 (dd, 1 H, $J_{4,5}$ 4.0 Hz, H-4), 4.40 (ddd, 1 H, $J_{5,6a}$ 6.5, $J_{5,6b}$ 5.5 Hz, H-5), 4.10 (dd, 1 H, $J_{6a,6b}$ 8.6 Hz, H-6a), 3.85 (dd, 1 H, H-6b), 1.40, 1.30 (2 s, each 3 H, CMe_2); ^{13}C (100 MHz), δ 165.8 (C-1), 162.2 (C-Bz), 138.4 (C-2), 133.8 (C-Bz), 129.9, 128.4 (C-Bz), 129.5 (C-3), 110.0 (CMe_2), 77.6 (C-4), 74.0 (C-5), 64.0 (C-6), 25.4, 24.4 (CMe_2). Anal. Calcd for **7** $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.60; H, 5.29. NMR data for **8** ($CDCl_3$): ^1H (400 MHz), δ 8.15, 7.60, 7.48 (m, m, m, 2 H, 1 H, 2 H, Bz), 7.53 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 4.90 (dd, 1 H, $J_{4,5}$ 8.0 Hz, H-4), 4.15 (dd, 1 H, $J_{5,6a}$ 6.0 Hz, H-6a), 4.08 (dd, 1 H, $J_{5,6b}$ 4.0, $J_{6a,6b}$ 9.0 Hz, H-6b), 4.00 (ddd, 1 H, H-5), 1.50, 1.40 (2 s, each 3 H, CMe_2); ^{13}C (100 MHz), δ 165.0 (C-1), 161.4 (C-Bz), 137.4 (C-2), 133.9 (C-Bz), 131.5 (C-3), 129.9, 128.2 (C-Bz), 109.3 (CMe_2), 78.5 (C-4), 75.9 (C-5), 65.4 (C-6), 25.4, 23.6 (CMe_2). Anal. Calcd for **8** $C_{16}H_{16}O_6$: C, 63.15; H, 5.30. Found: C, 63.35; H, 5.33.

*Sodium 3-deoxy-α,β-*D-threo-*hex-2-ulo-pyranosonate and -furanosonate* (**2a**).—To a solution of **7** (1.46 g, 5 mmol) in MeOH (50 mL) was added 1 M methanolic HCl (5 mL) and the solution was stirred until the starting material had disappeared (TLC, 1:1 toluene–EtOAc. Following addition of saturated aq $NaHCO_3$ to pH 8.5 the inorganic salts were removed by filtration and the solution was concentrated by freeze-drying. The crude product was finally purified by chromatography on a Sephadex G 10 column to yield compound **2a** (810 mg, 69%). NMR data (D_2O/CD_3CN): *α-Pyranose (73.3%)* ^1H (400 MHz), δ 3.90 (m, 1 H, H-4), 3.85 (m, 1 H, H-5), 3.63 (m, 2 H, H-6a, H-6b), 2.20 (dd, 1 H, $J_{3a,3b}$ 13.0, $J_{3a,4}$ 5.0 Hz, H-3a), 1.83 (dd, 1 H, $J_{3b,4}$ 11.5 Hz, H-3b); *β-Pyranose (5.1%)* ^1H (400 MHz), δ 4.57 (ddd ~ dt, 1 H, $J_{3a,4}$ 5.0, $J_{3b,4}$ 4.0, $J_{4,5}$ 4.0 Hz, H-4), 4.20 (m, 1 H, H-5), 3.90 (m, 1 H, H-6a), 3.85 (m, 1 H, H-6b), 2.60 (dd, 1 H, $J_{3a,3b}$ 13.0 Hz, H-3a), 2.20 (m, 1 H, H-3b); *α-Furanose (11.7%)* ^1H (400 MHz), δ 4.10 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12 Hz, H-6a), 3.85 (m, 1 H, H-4), 3.63 (m, 1 H, H-5), 3.52 (dd, 1 H, $J_{5,6b}$ 7.0 Hz, H-6b), 2.59 (dd, 1 H, $J_{3a,3b}$ 13.0, $J_{3a,4}$ 6.0 Hz, H-3a), 1.72 (dd, 1 H, $J_{3b,4}$ 8.0 Hz, H-3b); *β-Furanose (9.9%)* ^1H (400 MHz), δ 4.50 (ddd ~ q, 1 H, $J_{3a,4}$ 4.0, $J_{3b,4}$

4.0, $J_{4,5}$ 4.0 Hz, H-4), 4.32 (ddd, 1 H, $J_{5,6a}$ 4.0, $J_{5,6b}$ 7.0 Hz, H-5), 3.90 (m, 1 H, H-6a), 3.85 (m, 1 H, H-6b), 2.40 (m, 2 H, H-3a, H-3b). Anal. Calcd for $C_6H_9O_6Na \cdot H_2O$: C, 33.04; H, 5.08. Found C, 33.16; H, 5.06.

*Sodium 3-deoxy-α,β-*D-erythro-*hex-2-ulo-pyranosonate and -furanosonate* (**1a**).—**8** (1.07 g, 3.6 mmol) was subjected to the same procedure as described for **7** to yield **1a** (364 mg, 44%). NMR data (D_2O/CD_3CN): *α-Pyranose (11.1%)* ^{1}H (400 MHz), δ 3.95 (m, 1 H, H-4), 3.80 (dd, 1 H, $J_{5,6a}$ 7.0, $J_{6a,6b}$ 11.5 Hz, H-6a), 3.73 (m, 1 H, H-5), 3.55 (m, 1 H, H-6b), 2.08 (dd, 1 H, $J_{3a,4}$ 3.5, $J_{3a,3b}$ 13.5 Hz, H-3a), 1.84 (dd, 1 H, $J_{3,4}$ 7.5 Hz, H-3b); *β-Pyranose (45%)* ^{1}H (400 MHz), δ 3.97 (ddd, 1 H, $J_{3a,4}$ 13.0, $J_{3b,4}$ 5.0, $J_{4,5}$ 3.0 Hz, H-4), 3.90 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.5 Hz, H-6a), 3.75 (m, 1 H, H-5), 3.69 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 1.92 (dd ~ t, 1 H, $J_{3a,3b}$ 13.0 Hz, H-3a), 1.77 (dd, 1 H, H-3b); *α-Furanose (23.9%)* ^{1}H (400 MHz), δ 4.25 (m, 1 H, H-4), 4.10 (m, 1 H, H-5), 3.63 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 11.5 Hz, H-6a), 3.55 (m, 1 H, H-6b), 2.45 (dd, 1 H, $J_{3,4}$ 7.0, $J_{3a,3b}$ 14.0 Hz, H-3a), 1.95 (dd, 1 H, $J_{3b,4}$ 3.0 Hz, H-3b); *β-Furanose (20.0%)* ^{1}H (400 MHz), δ 4.25 (m, 1 H, H-4), 3.92 (m, 1 H, H-5), 3.69 (m, 1 H, H-6a), 3.55 (m, 1 H, H-6b), 2.24 (dd, 1 H, $J_{3a,4}$ 7.0, $J_{3a,3b}$ 13.5 Hz, H-3a), 2.19 (dd, 1 H, $J_{3b,4}$ 6.5 Hz, H-3b). Anal. Calcd for $C_6H_9O_6Na \cdot H_2O$: C, 33.04; H, 5.08. Found C, 33.08; H, 5.05.

5-O-tert-*Butyldiphenylsilyl-*L-*arabinono-1,4-lactone* (**10**).—A solution of L-arabinono-1,4-lactone (**9**) (1.0 g, 6.75 mmol) in anhyd pyridine (15 mL) was treated with *tert*-butylchlorodiphenylsilane (2.2 mL, 8.5 mmol) and stirred for 16 h at room temperature. After addition of MeOH (2 mL) the solution was stirred for an additional 30 min and concentrated in vacuo. Column chromatography (1:1 toluene–EtOAc) afforded **10** (2.08 g, 80%); mp 110°C; $[\alpha]_D^{20}$ −35.1° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H (400 MHz), δ 7.60–7.50, 7.40–7.28 (m, m, 6 H, 4 H, Ph), 4.39 (m, 2 H, H-2, H-3), 4.12 (ddd, 1 H, $J_{3,4}$ 7.0, $J_{4,5a}$ 3.0, $J_{4,5b}$ 3.0 Hz, H-4), 3.87 (dd, 1 H, $J_{5a,5b}$ 11.5 Hz, H-5a), 3.77 (dd, 1 H, H-5b), 2.22 (s, 2 H, 2 OH), 0.95 (s, 9 H, *t*-Bu); ^{13}C (100 MHz), δ 174.0 (C-1), 137.4 (C-Ph), 135.2, 129.6, 127.5 (C-Ph), 80.4 (C-4), 74.4, 73.2 (C-2, C-3), 61.2 (C-5), 26.3 (C-*t*-Bu), 18.8 (C-*t*-Bu). Anal. Calcd for $C_{21}H_{26}O_5Si$: C, 65.26; H, 6.78. Found: C, 65.19; H, 6.88.

2-O-*Benzoyl-*5-O-tert-*butyldiphenylsilyl-*L-*glycero-pent-2-enono-1,4-lactone* (**11**).—To a solution of **10** (4.17 g, 10.8 mmol) in anhyd pyridine (20 mL) was added benzoyl chloride (4.6 mL, 40 mmol) at 0°C and the solution was stirred for an additional hour at room temperature. The mixture was diluted with CH_2Cl_2 and poured into ice–water. The organic layer was washed several times with saturated aq $NaHCO_3$, dried over $MgSO_4$, and concentrated to 30 mL. This solution was treated with triethylamine for β-elimination. After 2 h at room temperature the solvents were evaporated and column chromatography (8:1 toluene–EtOAc) afforded **11** (4.25 g, 83%) as a syrup; $[\alpha]_D^{20}$ +11.6° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H (400 MHz), δ 8.10–7.90, 7.50–7.20 (m, m, 15 H, 5 H Bz, 10 H Ph), 7.18 (d, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 4.95 (ddd ~ dt, 1 H, $J_{4,5a}$ 4.5, $J_{4,5b}$ 4.5 Hz, H-4), 3.80 (dd, 1 H, $J_{5a,5b}$ 11.0 Hz, H-5a), 3.73 (dd, 1 H, H-5b), 0.95 (s, 9 H, *t*-Bu); ^{13}C (100 MHz), δ 171.0 (C-1), 162.4 (C-Bz), 139.0 (C-Bz), 138.1 (C-2), 135–127 (C-Bz, C-Ph), 130.7 (C-Ph), 79.0 (C-4), 63.3 (C-5), 26.4 (C-*t*-Bu), 18.8 (C-*t*-Bu). Anal. Calcd for $C_{28}H_{28}O_5Si$: C, 71.16; H, 5.98. Found: C, 70.78; H, 6.07.

2-O-*Benzoyl-*L-glycero-*pent-2-enono-1,4-lactone* (**12**).—A solution of **11** (1.69 g, 3.58 mmol) in anhyd THF (50 mL) was treated with conc. formic acid until pH 5–6, and

a 1.1 M solution of tetrabutylammonium fluoride in THF (3.4 mL, 3.7 mmol) was added at 0°C. After stirring for 4 h at room temperature the solution was diluted with CH_2Cl_2 (20 mL) and water (20 mL). The organic layer was separated, washed twice with water, dried over $MgSO_4$, and concentrated in vacuo. Column chromatography (1:1 toluene–EtOAc) afforded **12** (790 mg, 92%) as a white solid; mp 109°C; $[\alpha]_D^{20}$ +11.2° (c 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H (400 MHz), δ 8.10, 7.78, 7.43 (m, m, m, 5 H, Bz), 7.33 (d, 1 H, $J_{3,4}$ 2.0 Hz H-3), 5.11 (ddd, 1 H, $J_{4,5}$ 4.0, $J_{4,5a}$ 5.0 Hz, H-4), 3.98 (dd, 1 H, $J_{5a,5b}$ 12.0 Hz, H-5a), 3.88 (dd, 1 H, H-5b), 2.05 (s, 1 H, OH); ^{13}C (100 MHz), δ 165.7 (C-1), 160.9 (C-Bz), 136.6 (C-2), 132.2 (C-3), 130.8–126.7 (C-Bz), 126.0 (C-Bz), 78.7 (C-4), 59.4 (C-5). Anal. Calcd for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.44; H, 4.35.

Methyl α,β-L-glycero-*pent-2-ulopyranosonate* (**3a**).—A solution of **12** (200 mg, 0.83 mmol) in anhyd THF (5 mL) and anhyd MeOH (5 mL) was treated with two drops of *N*-methylpyrrolidine (NMP). After 2 h at room temperature Amberlite IR-120 (H^+) (~ 100 mg) was added and stirring was continued for an additional 30 min. The ion-exchange resin was removed by filtration and the solvents were evaporated. Column chromatography (5:1 → 1:1 toluene–acetone) afforded **3a** (38 mg, 28%) as a syrup and reisolated starting material **12** (34 mg, 18%). NMR data (D_2O/CD_3CN) *anomer 1*: ^{1}H (400 MHz), δ 4.44 (dddd ~ ddt, 1 H, $J_{3a,4}$ 6.0, $J_{3b,4}$ 3.0, $J_{4,5a}$ 5.5, $J_{4,5b}$ 2.0 Hz, H-4), 3.95 (dd, 1 H, $J_{5a,5b}$ 9.5 Hz, H-5a), 3.85 (m, 1 H, H-5b), 3.73 (s, 3 H, OMe), 2.32 (dd, 1 H, $J_{3a,3b}$ 14.0 Hz, H-3a), 2.12 (ddd, 1 H, $J_{3b,5b}$ 1.0 Hz, H-3b); *anomer 2*: ^{1}H (400 MHz), δ 4.39 (m, 1 H, H-4), 4.12 (dd, 1 H, $J_{4,5a}$ 5.5, $J_{5a.5b}$ 9.5 Hz, H-5a), 3.81 (dd, 1 H, $J_{4,5b}$ 2.5 Hz, H-5b), 3.69 (s, 3 H, OMe), 2.29 (dd, 1 H, $J_{3a,3b}$ 14.5, $J_{3a,4}$ 7.0 Hz, H-3a), 2.06 (dd, 1 H, $J_{3b,4}$ 2.0 Hz, H-3b). Anal. Calcd for $C_6H_{10}O_5$: C, 44.45; H, 6.22. Found: C, 44.28; H, 6.23.

2-Benzoyloxy-2-buten-4-olide (**14**).—A solution of D-erythrono-1,4-lactone (**13**) (2 g, 17.0 mmol) in anhyd DMF (20 mL) and anhyd pyridine (5.5 mL) was treated at 0°C with benzoyl chloride (7.9 mL, 68.0 mmol). After complete benzoylation (TLC: 3:1 toluene–EtOAc), the mixture was diluted with CH_2Cl_2 (30 mL) and poured into ice water. The organic layer was washed several times with saturated aq $NaHCO_3$, dried over $MgSO_4$, and concentrated in vacuo. The crude syrup was dissolved in CH_2Cl_2 (50 mL) and treated with triethylamine (5 mL, 36 mmol) for 2 h. The solvents were removed in vacuo and, after several azeotropic distillations with toluene, **14** (3.43 g, 98%) could be obtained by crystallisation from MeCN; mp 108°C. NMR data ($CDCl_3$): ^{1}H (400 MHz), δ 7.97, 7.45 (m, m, 2 H, 1 H, 3 H Bz), 7.30 (m, 3 H, H-3, 2 H Bz), 4.77 (d, 2 H, $J_{3,4}$ 2.0 Hz, H-4a, H-4b); ^{13}C (100 MHz), δ 166.7 (C-1), 162.3 (C-Bz), 137.2 (C-2), 133.8 (C-Bz), 129.9, 128.2 (C-Bz), 129.7 (C-3), 67.4 (C-4). Anal. Calcd for $C_{11}H_8O_4$: C, 64.71; H, 3.95. Found: C, 64.52; H, 3.81.

2-Hydroxy-2-buten-4-olide (**15**).—To a solution of **14** (1.5 g, 4.9 mmol) in MeOH (20 mL) and $CHCl_3$ (10 mL) was added a solution of LiOH (3.91 g, 9.31 mmol) in water (20 mL) dropwise at 0°C, keeping the pH below 9. Water (50 mL) was added and the layers were separated. The aqueous layer was acidified by the addition of Amberlite IR-120 (H^+) and concentrated by freeze-drying to a volume of ca. 10 mL. The product was extracted several times with diethyl ether and crystallised by concentration of the organic layer at 0°C to yield **15** (330 mg, 67%); mp 106°C (Lit. [16]: mp 106–107°C).

NMR data ($CDCl_3$): ^1H (400 MHz), δ 6.23 (t, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 4.62 (d, 2 H, H-4a, H-4b); ^{13}C (100 MHz), δ 171.1 (C-1), 141.4 (C-2), 114.0 (C-3), 67.2 (C-4).

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References

[1] R. Weinberg and M. Doudoroff, *J. Biol. Chem.*, 217 (1955) 607–624; A.S. Dahms, *Biochem. Biophys. Res. Commun.*, 60 (1974) 1433–1458; A.S. Dahms and R.L. Andersen, *ibid.*, 36 (1969) 809–812; A.H. Stouthamer, *Biochim. Biophys. Acta*, 48 (1961) 484–500; C.W. Schuster, *Methods Enzymol.*, 9 (1966) 524–528; J.R. Andreesen and G. Gottschalk, *Arch. Microbiol.*, 114 (1969) 158–172; G. Ashwell, A.J. Wahba, and J. Hichmann, *Biochim. Biophys. Acta*, 30 (1958) 186–187; J.M. Merrick and S. Roseman, *Methods Enzymol.*, 9 (1966) 657–660; M.A. Cynkin and G. Ashwell, *J. Biol. Chem.*, 235 (1960) 1576–1578; H.P. Meloch and W.A. Wood, *ibid.*, 239 (1964) 3505–3514.

[2] D. Claus, *Biochem. Biophys. Res. Commun.*, 20 (1965) 745–751.

[3] B. Lindberg, K. Samuelson, and W. Nimmich, *Carbohydr. Res.*, 30 (1973) 63–70.

[4] J.W. Cornforth and M.E. Firth, *J. Biol. Chem.*, 68 (1958) 57–61; M.A. Ghalambor, E.M. Levine, and E.C. Heath, *ibid.*, 241 (1966) 3207–3211; D. Portsmouth, *Carbohydr. Res.*, 8 (1968) 193–204.

[5] D. Charon and L. Szabó, *J. Chem. Soc., Perkin Trans. 1*, (1973) 1175–1179; F. Trigalo, W. Jackymeczyk, J.C. Young, and L. Szabó, *ibid.*, (1975) 593–598; F. Trigalo, M. Level, and L. Szabó, *ibid.*, (1975) 600–602.

[6] R. Kuhn, D. Weiser, and H. Fischer, *Justus Liebigs Ann. Chem.*, 628 (1959) 207–239; G.B. Paerels, *Recl. Trav. Chim. Pays-Bas*, 80 (1961) 985–988; G.B. Paerels and H.W. Geluk, *ibid.*, 89 (1970) 813–824.

[7] R. Ramage, A.M. MacLeod, and G.W. Rose, *Tetrahedron*, 47 (1991) 5625–5636.

[8] R. Plantier-Royon, F. Carderra, and D. Anker, *J. Carbohydr. Chem.*, 10 (1991) 787–811.

[9] I. Dijong and U. Wittkötter, *Chem. Ber.*, 104 (1971) 2090–2102.

[10] R.M. de Lederkremer and M.I. Litter, *Carbohydr. Res.*, 20 (1971) 442–444; M.I. Litter, and R.M. de Lederkremer, *ibid.*, 26 (1973) 431–434; R.M. de Lederkremer, M.I. Litter, and L.F. Sala, *ibid.*, 36 (1974) 185–187.

[11] L.O. Jeroncic, O.J. Varela, A.F. Cirelli, and R.M. de Lederkremer, *Tetrahedron*, 40 (1984) 1425–1430.

[12] K. Bock, I. Lundt, and C. Pedersen, *Acta Chem. Scand., Ser. B*, 35 (1981) 155–162.

[13] W.F. Collin, G.W.J. Fleet, M. Haraldsson, I. Cenci di Bello, and B. Winchester, *Carbohydr. Res.*, 202 (1990) 105–116.

[14] J.A. Dale, D.L. Dull, and H.S. Mosher, *J. Org. Chem.*, 34 (1969) 2543–2549.

[15] O. Moradei, S. Leit, C. du Mortier, A.F. Cirelli, and J. Thiem, *J. Carbohydr. Chem.*, 12 (1993) 13–22.

[16] R.S. Lane and E.E. Dekker, *Biochemistry*, 8 (1969) 2958–2965.