ELSEVIER

Carbohydrate Research 303 (1997) 185–191

CARBOHYDRATE RESEARCH

A two step synthesis of 3-deoxy-D- or L-glycono-1,4-lactones and 2-*O*-alkyl-3-deoxy-D-glycono-1,4-lactones from D- or L-glyconolactones

Caroline Choquet-Farnier, Imane Stasik, Daniel Beaupère *

Laboratoire de Chimie Organique, Université de Picardie Jules Verne, 33 rue Saint-Leu, F-80039 Amiens, France

Received 24 March 1997; accepted in revised form 4 June 1997

Abstract

Treatment of unprotected D- or L-glyconolactones with sodium hydride and alkyl halides, in dimethylsulfoxide, led to the corresponding 2-*O*-alkyl-3-deoxy-2-enono-1,4-lactones. Hydrogenolysis of 2-*O*-benzyl derivatives by catalytic hydrogen transfer with palladium on charcoal and cyclohexene as hydrogen donor gave 3-deoxy-hex- or pent-2-enono-1,4-lactones in the enolic forms. Reduction of 2-*O*-benzyl-enonolactones with ammonium formate as hydrogen donor afforded 3-deoxy-D- or L-glycono-1,4-lactones when 2-*O*-alkyl ethers gave the corresponding ethers. © 1997 Elsevier Science Ltd.

Keywords: Glyconolactones; 3-Deoxy-glycono-1,4-lactones; Catalytic hydrogen transfer; (Ammonium formate: cyclohexene: palladium: hydrogenation reagent)

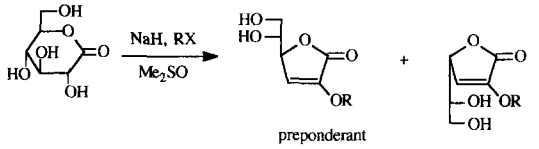
1. Introduction

3-Deoxy-glyconolactones, useful intermediates for the synthesis of natural 3-deoxy sugars such as abequose [1], ascarylose [2] or nonactin antibiotic derivatives [3], were previously obtained from peracylated glyconolactones [4–7]. Treatment of peracetylated hexono- and pentono-1,4-lactones with triethylamine and hydrogen in the presence of palladium on charcoal induced simultaneous elimination and reduction to give the corresponding peracetylated 3-deoxylactones stereospecifically [8]. Similarly, 2,3,5,6-tetra-*O*-benzoyl-L-gulono-1,4-lactone and 2,3,5-tri-*O*-benzoyl-D-ribono-1,4-lactone gave the corresponding 3-deoxylactones in 73% and 68% yield, respectively [9]. Perbenzoylated 3-deoxyglyconolactones were also obtained after isolation of the corresponding hex-2-enono-lactones, followed by a hydrogenation step with hydrogen and palladium on charcoal [4–7].

We recently reported [10] that treatment of D-glucono-1,5-lactone with sodium hydride and various alkyl halides (RX), at room temperature, afforded the corresponding butenolide derivatives in a one-pot procedure (Scheme 1). This alkylation-elimination reaction was applied to L-gulono- and L-mannono-

* Corresponding author.

PII S0008-6215(97)00164-X



Scheme 1.

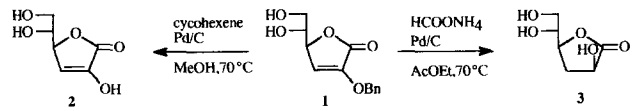
1,4-lactones [10] and is now extended to D-galactono- and D-ribono-1,4-lactones.

2. Results and discussion

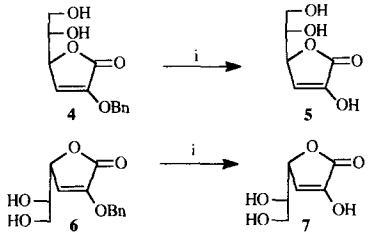
Two hypotheses may explain the regioselective etherification and elimination steps in the former results. On one hand, in basic media, glyconolactone would result in the corresponding 3-deoxy-2-enono-1,4-lactone which could be etherified at the more acidic enolic hydroxyl group. This possibility cannot be ruled out although no 2-enono-1,4-lactone was detected when D-glucono-1,5-lactone was treated with sodium hydride in dimethylsulfoxide. On the other hand, the etherification step may occur before the elimination step. When the benzylation of D-glucono-1,5-lactone was performed at 0 °C, small amounts of 2-*O*-benzyl and 2,3-di-*O*-benzyl-D-glucono-1,4-lactones were isolated. Each benzylated derivatives reacted with sodium hydride and benzyl bromide in dimethylsulfoxide to give 2-*O*-benzyl-3-deoxy-D-*erythro*-hex-2-enono-1,4-lactone, which brings supports this hypothesis. The epimerisation at C-4 was always observed in basic media but was limited, due to the use of a low amount of base [10].

The reduction of the 2-enono-lactones was then investigated for access to 3-deoxy-D-glycono-1,4-lactones. We previously reported that catalytic hydrogen transfer was a very selective method to remove benzyl groups by hydrogenolysis [11] or reduction of double bonds [12]. This selectivity was shown to be dependent on the hydrogen donor. We first tested cyclohexene and ammonium formate, respectively, as hydrogen donors in the presence of palladium on charcoal using the 2-*O*-benzyl-3-deoxy-D-*erythro*-hex-2-enono-1,4-lactone, as a substrate (**1**).

When the butenolide **1** was treated with cyclohexene in methanol at 70 °C, **2** was obtained quantitatively by hydrogenolysis of the benzyl group. Reduction of the ethylenic system was not observed. NMR Spectroscopy showed it to exist in the enol form (Scheme 2). When applied to butenolides **4** and **6**, this hydrogenolysis procedure led to unprotected enonolactones **5** and **7**, which were isolated in 94% and 97% yield, respectively (Scheme 3).



Scheme 2.



Scheme 3. (i) Cyclohexene, Pd/C, MeOH, 70 °C.

A different result was obtained when the butenolide **1** was treated with ammonium formate as hydrogen donor (2 equiv) and palladium on charcoal as catalyst. Ethyl acetate was used as solvent at 70 °C for 2 h, since methanol resulted in the opening of the lactone affording the corresponding methyl ester. 3-Deoxy-D-*arabino*-hexono-1,4-lactone (**3**) was isolated as the sole product in 90% yield (Scheme 2). Hydrogenolysis and reduction occurred at the same time. As expected, hydrogenation of the ethylenic system took place stereoselectively [5,8,13]. This specificity was attributed to the steric hindrance of the side chain at C-4, which induces the reduction from the opposite face of the molecule. Acetylated derivative of **3** showed the same coupling as 2,5,6-tri-*O*-acetyl-3-deoxy-D-*arabino*-hexono-1,4-lactone ($J_{2,3}$ 8.4 Hz and $J_{2,3'}$ 10.7 Hz) [14]. Moreover, a 2D-NOESY experiment showed that distances between H-3–4 and H-2–3 were shorter than thoses between H-3′–4 and H-2–3′ respectively and confirmed the *arabino* configuration.

Using the ammonium formate-palladium on charcoal system, a number of 3-deoxy-glycono-1,4-lactones were prepared (Table 1).

The stereoselective reduction of L-gulono and L-mannono-1,4-lactone derivatives (**4**, **6**) gave only the 3-deoxylactones **8** and **9** in 98% and 96% yield

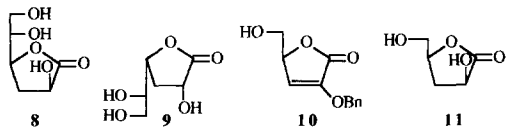
Table 1
Reduction of 2-*O*-benzyl-enonolactones with ammmonium formate

Substrate	Time (h)	Product	Yield %
4	1.5	**8**	98
6	2.0	**9**	96
10	1.5	**11**	100

Table 2
Reduction of 2-*O*-alkyl-enonolactones with ammmonium formate

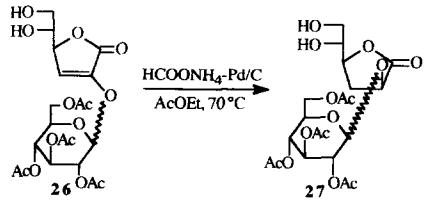
Substrate	Time (h)	Product	Yield %
12	3.0	**13**	90
14	1.0	**15**	100
16	1.0	**17**	100
18	1.3	**19**	90
20	2.0	**21**	100
22	1.5	**23**	91
24	1.0	**25**	100

respectively. For **8**, 2D-NOESY experiment allowed the same conclusion as for **3** and coupling constants $J_{2,3}$ 8.5 Hz and $J_{2,3'}$ 10.8 Hz were similar to those reported for 2,3,6-tri-*O*-acetyl-3-deoxy-L-*lyxo*-hexono-1,4-lactone [8]. Lactones **9** and **3** are enantiomeric and then display the same spectroscopic characteristics. 3-Deoxy-D-*threo*-pentono-1,4-lactone **11**, which was expected from the stereoselective reduction of D-*glycero*-pent-2-enono-1,4-lactone derivative **10**, showed coupling constants $J_{2,3}$ 8.6 Hz and $J_{2,3'}$ 10.6 Hz, similar to those reported for 3-deoxylactones **3** and **8**.

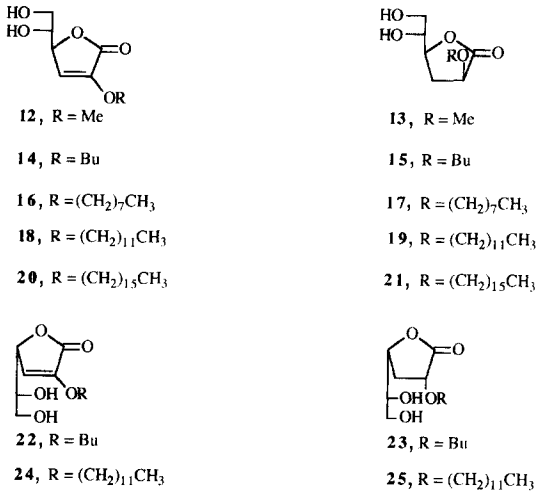


The ammonium formate–palladium on charcoal hydrogenation system was applied to other 2-*O*-alkyl-enono-1,4-lactones, which are not hydrogenolysable, to get 2-*O*-alkyl-3-deoxy-D-glycono-1,4-lactones (Table 2).

The C-2 configuration of 3-deoxylactones depends on the C-4 configuration of the starting butenolide: 2-*O*-alkyl-3-deoxy-D-*erythro*-hex-2-enono-1,4-lactones (**12**, **14**, **18**, **20**, **24**) gave the 2-*O*-alkyl-3-deoxy-D-*arabino*-hexono-1,4-lactones (**13**, **15**, **19**, **21**, **25**) in 90%–100% yield, whereas 2-*O*-butyl and 2-*O*-dodecyl-3-deoxy-D-*threo*-hexono-1,4-lactones (**16**, **22**) gave the 2-*O*-alkyl-3-deoxy-D-*xylo*-hexono-1,4-lactones (**17**, **23**) in 91% and 100% yield, respectively.



Scheme 4.



When applied to the disaccharide enonolactone **26**, this method needed a longer reaction time but led to 2-*O*-(2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl)-3-deoxy-D-*arabino*-hexono-1,4-lactone (**27**) (α/β = 16/9) quantitatively (Scheme 4).

In conclusion, 3-deoxy-D- or L-*arabino* and D- or L-*xylo*-hexono-1,4-lactones and 3-deoxy-D-*threo*-pentono-1,4-lactone can be efficiently prepared from D-glucono-1,5-lactone, L-mannono-, D-galactono-, L-gulono- and D-ribono-1,4-lactones, respectively, in two steps. In a first step, a one-pot procedure involving a regioselective alkylation and elimination results in the 2-*O*-alkyl-3-deoxy-hex- or pent-2-enono-1,4-lactones. This is followed by the stereoselective hydrogenation by catalytic hydrogen transfer. For 2-*O*-benzyl-2-enono-1,4-lactones, the use of cyclohexene and palladium on charcoal led to 3-deoxy-hex- or pent-2-enono-1,4-lactones. By using ammonium formate as hydrogen donor, 3-deoxy-hexono- or pentono-1,4-lactones were obtained. For all the 2-*O*-alkyl substituted unsaturated lactones, the ammonium formate reduction gave the 2-*O*-alkyl-3-deoxy-D-*arabino*- or *xylo*-hexono-1,4-lactones.

3. Experimental

General methods.—^{1}H and ^{13}C NMR spectra and 2D-NOESY experiments were recorded in Me_2SO-d_6, $CDCl_3$ or CD_3OD with Me_4Si as internal standard on a Bruker 300 MHz spectrometer. Optical rotation values were measured with a JASCO DIP-370 digital polarimeter, using a sodium lamp, at 20 °C. Column chromatography was performed on silica gel (E.

Merck 230–400 mesh) using EtOAc–petroleum ether. Analytical TLC was performed on E. Merck glass backed silica gel sheets (Silica Gel F_{254}) and EtOAc–petroleum ether as eluent.

General procedure for synthesis of enonolactones. —A soln of the lactone (1 g, 5.6 mM) and sodium hydride in anhyd Me_2SO (30 mL) was stirred for 1 h under an inert atmosphere. The alkyl halide was added at 0 °C. The mixture was stirred at room temperature for 24 h, then MeOH was added and the soln was concd, at 40 °C, under reduced pressure. The crude product was purified by column chromatography using EtOAc–petroleum ether.

2-O-Benzyl-3-deoxy-D-erythro-*hex-2-enono-1,4-lactone* (**1**).—From D-glucono-1,5-lactone, NaH (0.26 g, 11 mM, 2 equiv) and BnBr (1.34 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether and EtOAc), **1** was isolated as a solid (1.2 g, 85%); mp 115–116 °C, lit. 125–126 °C [13]; $[\alpha]_D$ −16.6° (*c* 1, MeOH), lit. −19.1° (*c* 1, MeOH) [13]; ^{1}H NMR (Me_2SO-d_6): δ 6.62 (d, 1 H, $J_{3,4}$ 1.7 Hz, H-3), 5.08 (dd, 1 H, $J_{4,5}$ 4.3 Hz, H-4), 3.77 (m, 1 H, H-5), 3.55 (d, 2 H, $J_{5,6}$ 5.3, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.2 (C-1), 145.3 (C-2), 116.9 (C-3), 79.1 (C-4), 71.5 (C-5), 62.5 (C-6). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.40%; H, 5.60%. Found: C, 62.20%; H, 5.70%.

2-O-Benzyl-3-deoxy-L-threo-*hex-2-enono-1,4-lactone* (**4**).—From L-gulono-1,4-lactone, NaH (0.26 g, 11 mM, 2 equiv) and BnBr (1.34 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether and EtOAc), **4** was isolated as a solid (0.71 g, 51%); mp 162–163 °C; $[\alpha]_D$ +36.0° (*c* 1.02, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.56 (d, 1 H, $J_{3,4}$ 1.1 Hz, H-3), 5.07 (dd, 1 H, $J_{4,5}$ 3.8 Hz, H-4), 3.60 (m, 1 H, H-5), 3.45 (d, 2 H, $J_{5,6}$ 5.9, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.4 (C-1), 144.9 (C-2), 117.6 (C-3), 78.9 (C-4), 71.3 (C-5), 62.3 (C-6). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.40%; H, 5.60%. Found: C, 62.27%; H, 5.71%.

2-O-Benzyl-3-deoxy-L-erythro-*hex-2-enono-1,4-lactone* (**6**).—From L-mannono-1,4-lactone, NaH (0.26 g, 11 mM, 2 equiv) and BnBr (1.34 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether and EtOAc), **6** was isolated as a solid (0.85 g, 61%); mp 119–120 °C; $[\alpha]_D$ +18.4° (*c* 1.02, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.50 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 4.9 Hz, H-4), 3.78 (m, 1 H, H-5), 3.65 (d, 2 H, $J_{5,6}$ 5, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.2 (C-1), 145.2 (C-2), 116.7 (C-3), 79.1 (C-4), 71.3 (C-5), 62.4 (C-6). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.40%; H, 5.60%. Found: C, 62.46%; H, 5.76%.

2-O-Benzyl-3-deoxy-D-glycero-*pent-2-enono-1,4-lactone* (**10**).—From D-ribono-1,4-lactone (1 g, 6.75 mM), NaH (0.49 g, 20.3 mM, 3 equiv) and BnBr (1.34 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (EtOAc), **10** was isolated as a solid (0.59 g, 40%); mp 98–100 °C, lit. 100–101 °C [15]; $[\alpha]_D$ +9.2° (*c* 0.9, MeOH), lit. +11,4° (*c* 1, MeOH) [15]; ^{1}H NMR ($CDCl_3$): δ 6.07 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 4.86 (m, 1 H, $J_{4,5}$ 3.4 Hz, H-4), 3.73 (dd, 1 H, $J_{4,5'}$ 5.3 Hz, H-5), 3.50 (dd, 1 H, $J_{5,5'}$ 12.4, H-5′); ^{13}C NMR ($CDCl_3$): δ 167.6 (C-1), 145.2 (C-2), 115.0 (C-3), 80.4 (C-4), 61.8 (C-5). Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45%; H, 5.45%. Found: C, 65.50%; H, 5.76%.

3-Deoxy-2-O-methyl-D-erythro-*hex-2-enono-1,4-lactone* (**12**).—From D-glucono-1,5-lactone, NaH (0.26 g, 11 mM, 2 equiv) and MeI (0.7 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (EtOAc), **12** was isolated as a solid (0.61 g, 63%); mp 66–69 °C; $[\alpha]_D$ −36.1° (*c* 1.05, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.47 (d, 1 H, $J_{3,4}$ 1.9 Hz, H-3), 5.01 (dd, 1 H, $J_{4,5}$ 4.2 Hz, H-4), 3.67 (dd, 1 H, H-5), 3.46 (d, 2 H, $J_{5,6}$ 5.6, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.0 (C-1), 146.4 (C-2), 115.8 (C-3), 79.1 (C-4), 71.4 (C-5), 62.4 (C-6). Anal. Calcd for $C_7H_{10}O_5$: C, 48.27%; H, 5.75%. Found: C, 48.35%; H, 5.76%.

2-O-Butyl-3-deoxy-D-erythro-*hex-2-enono-1,4-lactone* (**14**).—From D-glucono-1,5-lactone, NaH (0.16 g, 6.74 mM, 1.2 equiv) and BuBr (1.2 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether and EtOAc), **14** was isolated as a solid (0.63 g, 52%); mp 46–48 °C; $[\alpha]_D$ −34.7° (*c* 1, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.46 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 4 Hz, H-4), 3.67 (m, 1 H, H-5), 3.45 (d, 2 H, $J_{5,6}$ 5.5, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.2 (C-1), 145.4 (C-2), 115.9 (C-3), 79.0 (C-4), 71.4 (C-5), 62.4 (C-6). Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55%; H, 7.41%. Found: C, 55.26%; H, 7.33%.

3-Deoxy-2-O-octyl-D-erythro-*hex-2-enono-1,4-lactone* (**16**).—From D-glucono-1,5-lactone, NaH (0.16 g, 6.74 mM, 1.2 equiv) and octyl bromide (1.93 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether), **18** was isolated as a solid

(0.55 g, 36%); mp 58–60 °C; $[\alpha]_D$ −62.3° (*c* 1, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.46 (d, 1 H, $J_{3,4}$ 1.9 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 3.5 Hz, H-4), 3.66 (m, 1 H, H-5), 3.46 (m, 2 H, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.2 (C-1), 145.6 (C-2), 115.9 (C-3), 79.0 (C-4), 71.4 (C-5), 62.4 (C-6). Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.76%; H, 8.82%. Found: C, 61.70%; H, 8.90%.

*3-Deoxy-2-*O*-dodecyl-*D-erythro-*hex-2-enono-1,4-lactone* (**18**).—From D-glucono-1,5-lactone, NaH (0.16 g, 6.74 mM, 1.2 equiv) and dodecyl bromide (2.7 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether), **18** was isolated as a solid (0.64 g, 35%); mp 72–73 °C; $[\alpha]_D$ −21.4° (*c* 1.03, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.46 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 4.2 Hz, H-4), 3.65 (m, 1 H, H-5), 3.45 (m, 2 H, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.1 (C-1), 145.4 (C-2), 115.8 (C-3), 79.0 (C-4), 71.4 (C-5), 62.4 (C-6). Anal. Calcd for $C_{18}H_{32}O_5$: C, 65.85%; H, 9.76%. Found: C, 65.80%; H, 9.80%.

*3-Deoxy-2-*O*-hexadecyl-*D-erythro-*hex-2-enono-1,4-lactone* (**20**).—From D-glucono-1,5-lactone, NaH (0.16 g, 6.74 mM, 1.2 equiv) and hexadecyl bromide (3.36 mL, 11 mM, 2 equiv) in Me_2SO (50 mL) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether), **20** was isolated as a solid (0.84 g, 39%); mp 79.5–81 °C; $[\alpha]_D$ −22.8° (*c* 1, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.44 (s, 1 H, H-3), 4.99 (d, 1 H, $J_{4,5}$ 2.4 Hz, H-4), 3.64 (m, 1 H, H-5), 3.46 (d, 2 H, $J_{5,6}$ 5.2, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.0 (C-1), 145.5 (C-2), 115.7 (C-3), 78.8 (C-4), 71.5 (C-5), 62.3 (C-6). Anal. Calcd for $C_{22}H_{40}O_5$: C, 68.75%; H, 10.42%. Found: C, 68.64%; H, 10.58%.

*2-*O*-Butyl-3-deoxy-*D-threo-*hex-2-enono-1,4-lactone* (**22**).—From D-galactono-1,4-lactone, NaH (0.40 g, 16.85 mM, 3 equiv) and BuBr (1.2 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether and EtOAc), **22** was isolated as a solid (0.35 g, 29%); mp 104–106 °C; $[\alpha]_D$ −14.1° (*c* 0.45, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.39 (d, 1 H, $J_{3,4}$ 2 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 4 Hz, H-4), 3.56 (m, 1 H, H-5), 3.45 (d, 2 H, $J_{5,6}$ 5.5, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.4 (C-1), 145.1 (C-2), 116.6 (C-3), 78.8 (C-4), 71.2 (C-5), 62.2 (C-6). Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55%; H, 7.41%. Found: C, 55.29%; H, 7.20%.

*3-Deoxy-2-*O*-dodecyl-*D-threo-*hex-2-enono-1,4-lactone* (**24**).—From D-galactono-1,4-lactone with NaH (0.26 g, 11 mM, 2 equiv) and dodecyl bromide (2.7 mL, 11 mM, 2 equiv) as described in the general procedure. After purification by chromatography (3:7 EtOAc–petroleum ether), **24** was isolated as a solid (0.33 g, 18%); mp 121–123 °C; $[\alpha]_D$ −33.2° (*c* 0.7, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 6.38 (d, 1 H, $J_{3,4}$ 1.7 Hz, H-3), 5.00 (dd, 1 H, $J_{4,5}$ 4.2 Hz, H-4), 3.55 (m, 1 H, H-5), 3.45 (m, 2 H, H-6–6′); ^{13}C NMR (Me_2SO-d_6): δ 167.4 (C-1), 145.1 (C-2), 116.5 (C-3), 78.8 (C-4), 71.3 (C-5), 62.2 (C-6). Anal. Calcd for $C_{18}H_{32}O_5$: C, 65.85%; H, 9.76%. Found: C, 65.91%; H, 9.85%.

*3-Deoxy-2-O-(2,3,4,6-tetra-O-acetyl-D-glucopyranosyl)-*D-erythro-*hex-2-enono-1,4-lactone* (**26**).—From D-glucono-1,5-lactone (0.4 g, 2.25 mM), NaH (0.11 g, 4.5 mM, 2 equiv) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (1.85 g, 4.5 mM, 2 equiv) in Me_2SO (20 mL) as described in the general procedure. After purification by chromatography (EtOAc), **26** was isolated as a syrup (0.33 *g*, 30% $\alpha/\beta = 16/9$). Anal. Calcd for $C_{20}H_{26}O_{14}$: C, 48.98%; H, 5.30%. Found: C, 49.00%; H, 5.33%. α-anomer: ^{1}H NMR (Me_2SO-d_6): δ 6.79 (d, 1 H, $J_{3,4}$ 1.1 Hz, H-3), 5.34 (m, 2 H, *J* 9.5 Hz), 5.00 (m, 2H), 4.20 (m, 1 H, $J_{5,6}$ 5.0 Hz, H-5), 3.66 (m, 1 H, H-5′), 3.45 (d, 2 H, H-6 and H-6′), 5.45 (d, 1 H, *J*1′,2′ 7.8 Hz, H-1′); ^{13}C NMR (Me_2SO-d_6): δ 166.4 (C-1), 142.7 (C-2), 122.9 (C-3), 78.9 (C-4), 71.2 (C-5), 62.3 (C-6), 98.0 (C-1′), 70.2, 70.8, 71.7 (C-2′, C-3′, C-4′), 71.2 (C-5′), 61.5 (C-6′); β-anomer: ^{13}C NMR (Me_2SO-d_6): δ 166.9 (C-1), 143.2 (C-2), 121.5 (C-3), 78.0 (C-4), 74.3 (C-5), 62.6 (C-6), 100.5 (C-1′), 71.0 (C-2′), 70.4 (C-3′), 68.7 (C-4′), 68.1 (C-5′), 61.6 (C-6′).

General procedure for hydrogenolysis.—The 2-*O*-benzyl-3-deoxy-hex-2-enono-1,4-lactone (150 mg, 0.6 mM) was stirred with cyclohexene (2.43 mL, 24 mM, 40 equiv) and Pd/C 10% (210 mg, 3:1 substrate–catalyst) in anhyd MeOH (12 mL) under argon atmosphere at 70 °C. When no more starting material was detected by TLC, the catalyst was removed by filtration. The filtrate was concd to give the unprotected butenolide.

*3-Deoxy-*D*-erythro-hex-2-enono-1,4-lactone* (**2**).—From **1**, syrup (96 mg, 100%); $[\alpha]_D$ −15.4° (*c* 1.6, MeOH); ^{1}H NMR (CD_3OD): δ 6.30 (s, 1 H, H-3), 4.97 (d, 1 H, $J_{4,5}$ 4.9 Hz, H-4), 3.74 (m, 1 H, H-5), 3.65 (d, 2 H, $J_{5,6}$ 4, H-6–6′); ^{13}C NMR (CD_3OD): δ 172.5 (C-1), 146.0 (C-2), 118.7 (C-3), 81.4 (C-4), 74.7 (C-5), 65.0 (C-6). Anal. Calcd for $C_6H_8O_5$: C, 45.00%; H, 5.00%. Found: C, 44.92%; H, 5.02%.

3 - Deoxy - L - threo - *hex - 2 - enono - 1, 4 - lactone* (**5**).—From **4**, syrup (90 mg, 94%); $[\alpha]_D$ −3.5° (*c* 0.9, MeOH); ^{1}H NMR (CD_3OD): δ 6.20 (s, 1 H, H-3), 5.05 (d, 1 H, $J_{4,5}$ 4.6 Hz, H-4), 3.80 (m, 1 H, H-5), 3.67 (d, 2 H, $J_{5,6}$ 4.2, H-6–6′); ^{13}C NMR (CD_3OD): δ 172.7 (C-1), 146.0 (C-2), 118.6 (C-3), 81.7 (C-4), 74.4 (C-5), 65.0 (C-6). Anal. Calcd for $C_6H_8O_5$: C, 45.00%; H, 5.00%. Found: C, 44.95%; H, 5.05%.

3 - Deoxy - L - erythro - *hex - 2 - enono - 1, 4 - lactone* (**7**).—From **6**, syrup (93 mg, 97%); $[\alpha]_D$ +19.2° (*c* 0.9, MeOH); ^{1}H NMR (CD_3OD): δ 6.30 (s, 1 H, H-3), 4.97 (d, 1 H, $J_{4,5}$ 4.9 Hz, H-4), 3.74 (m, 1 H, H-5), 3.64 (d, 2 H, $J_{5,6}$ 3.9, H-6–6′); ^{13}C NMR (CD_3OD): δ 172.5 (C-1), 146.0 (C-2), 118.5 (C-3), 81.4 (C-4), 74.7 (C-5), 65.0 (C-6). Anal. Calcd for $C_6H_8O_5$: C, 45.00%; H, 5.00%. Found: C, 44.95%; H, 5.08%.

General procedure for hydrogenation.—The 2-*O*-alkyl-3-deoxy-hex- or pent-2-enono-1,4-lactones (200 mg) was stirred with ammonium formate (2 equiv) and Pd/C 10% (3:1 substrate–catalyst) in anhyd MeOH (14 mL) under argon atmosphere at 70 °C. When no starting material was detected by TLC, the catalyst was removed by filtration. The filtrate was concd to give the unprotected butenolide.

3-Deoxy-D-arabino-*hexono-1,4-lactone* (**3**).—From **1**, syrup (116 mg, 90%); $[\alpha]_D$ −7.0° (*c* 1, H_2O); ^{1}H NMR (Me_2SO-d_6): δ 4.44 (dd, 1 H, $J_{2,3}$ 8.4, $J_{2,3'}$ 10.7 Hz, H-2), 2.35 (m, 1 H, $J_{3,3'}$ 12.1 Hz, H-3), 1.99 (m, 1 H, H-3′), 4.38 (m, 1 H, $J_{3,4}$ 5.5 Hz, H-4), 3.69 (m, 1 H, $J_{4,5}$ 9.8 Hz, H-5), 3.34 (m, 2 H, $J_{5,6}$ 5.7, H-6 and H-6′); ^{13}C NMR (Me_2SO-d_6): δ 176.9 (C-1), 67.2 (C-2), 30.8 (C-3), 75.8 (C-4), 70.7 (C-5), 61.9 (C-6). Anal. Calcd for $C_6H_{10}O_5$: C, 44.44%; H, 6.17%. Found: C, 44.38%; H, 6.22%.

3-Deoxy-L-xylo-*hexono-1,4-lactone* (**8**).—From **4**, syrup (127 mg, 98%); $[\alpha]_D$ +35.0° (*c* 1, H_2O), lit. +44.8° (*c* 1.5, H_2O) [8]; ^{1}H NMR (CD_3OD): δ 4.60 (dd, 1 H, $J_{2,3}$ 8.5, $J_{2,3'}$ 10.8 Hz, H-2), 2.56 (m, 1 H, $J_{3,3'}$ 12.4 Hz, H-3), 2.13 (m, 1 H, $J_{3',4}$ 11 Hz, H-3′), 4.50 (m, 1 H, $J_{3,4}$ 5.5 Hz, H-4), 3.70 (m, 3 H, H-5, H-6 and H-6′); ^{13}C NMR (CD_3OD): δ 180.0 (C-1), 70.2 (C-2), 35.0 (C-3), 79.0 (C-4), 74.6 (C-5), 64.7 (C-6). Anal. Calcd for $C_6H_{10}O_5$: C, 44.44%; H, 6.17%. Found: C, 44.40%; H, 6.25%.

3-Deoxy-L-arabino-*hexono-1,4-lactone* (**9**).—From **6**, syrup (124 mg, 96%); $[\alpha]_D$ +4.0° (*c* 1.2, H_2O); ^{1}H NMR (Me_2SO-d_6): δ 4.42 (dd, 1 H, $J_{2,3}$ 8.6, $J_{2,3'}$ 10.2 Hz, H-2), 2.35 (m, 1 H, H-3), 1.99 (m, 1 H, H-3′), 4.36 (m, 1 H, H-4), 3.69 (m, 1 H, H-5), 3.34 (d, 2 H, $J_{5,6}$ 5.8, H-6 and H-6′); ^{13}C NMR (Me_2SO-d_6): δ 176.9 (C-1), 67.1 (C-2), 30.8 (C-3), 75.8 (C-4), 70.7 (C-5), 61.8 (C-6). Anal. Calcd for $C_6H_{10}O_5$: C, 44.44%; H, 6.17%. Found: C, 44.48%; H, 6.25%.

3-Deoxy-D-threo-*pentono-1,4-lactone* (**11**).—From **10**, syrup (120 mg, 100%); $[\alpha]_D$ +11.4° (*c* 1.3, MeOH); ^{1}H NMR (CD_3OD): δ 4.69 (dd, 1 H, $J_{2,3}$ 8.6, $J_{2,3'}$ 10.8 Hz, H-2), 2.57 (m, 1 H, $J_{3,3'}$ 12.4 Hz, H-3), 2.05 (m, 1 H, H-3′), 4.49 (m, 1 H, $J_{3,4}$ 5.7 Hz, H-4), 3.80 (m, 2 H, H-5 and H-5′); ^{13}C NMR (CD_3OD): δ 180.2 (C-1), 70.3 (C-2), 34.6 (C-3), 79.8 (C-4), 64.9 (C-5). Anal. Calcd for $C_5H_8O_4$: C, 45.45%; H, 6.06%. Found: C, 45.52%; H, 6.16%.

3-Deoxy-2-O-methyl-D-arabino-*hexono-1,4-lactone* (**13**).—From **12**, syrup (182 mg, 90%); $[\alpha]_D$ +5.6° (*c* 0.8, MeOH); ^{1}H NMR (CD_3OD): δ 4.34 (dd, 1 H, $J_{2,3}$ 8.6, $J_{2,3'}$ 10.3 Hz, H-2), 2.61 (m, 1 H, $J_{3,3'}$ 12.4 Hz, H-3), 2.15 (m, 1 H, H-3′), 4.50 (m, 1 H, $J_{3,4}$ 5.9 Hz, H-4), 3.85 (m, 1 H, $J_{4,5}$ 5.8 Hz, H-5), 3.50 (m, 2 H, H-6 and H-6′); ^{13}C NMR (CD_3OD): δ 177.0 (C-1), 77.4 (C-2), 30.5 (C-3), 79.2 (C-4), 73.0 (C-5), 63.6 (C-6). Anal. Calcd for $C_7H_{12}O_5$: C, 47.73%; H, 6.82%. Found: C, 47.75%; H, 6.85%.

2-O-Butyl-3-deoxy-D-arabino-*hexono-1,4-lactone* (**15**).—From **14**, syrup (201 mg, 100%); $[\alpha]_D$ −8.6° (*c* 1.3, MeOH); ^{1}H NMR (CD_3OD): δ 4.40 (dd, 1 H, $J_{2,3}$ 8.5, $J_{2,3'}$ 11 Hz, H-2), 2.59 (m, 1 H, $J_{3,3'}$ 12.2 Hz, H-3), 2.15 (m, 1 H, $J_{3',4}$ 10.2 Hz, H-3′), 4.52 (m, 1 H, $J_{3,4}$ 5.9 Hz, H-4), 3.83 (m, 1 H, H-5), 3.58 (m, 2 H, H-6 and H-6′); ^{13}C NMR (CD_3OD): δ 178.3 (C-1), 77.1 (C-2), 32.0 (C-3), 79.1 (C-4), 74.0 (C-5), 64.6 (C-6). Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.04%; H, 8.26%. Found: C, 55.14%; H, 8.30%.

3-Deoxy-2-O-octyl-D-arabino-*hexono-1,4-lactone* (**17**).—From **16**, syrup (201 mg, 100%); $[\alpha]_D$ −48.4° (*c* 1, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 4.39 (dd, 1 H, $J_{2,3}$ 8.7, $J_{2,3'}$ 10.9 Hz, H-2), 2.43 (m, 1 H, $J_{3,3'}$ 12.1 Hz, H-3), 2.00 (m, 1 H, $J_{3',4}$ 11.5 Hz, H-3′), 4.43 (m, 1 H, $J_{3,4}$ 5.8 Hz, H-4), 3.69 (m, 1 H, H-5), 3.32 (m, 2 H, H-6 and H-6′); ^{13}C NMR (Me_2SO-d_6): δ 174.8 (C-1), 74.2 (C-2), 28.5 (C-3), 76.2 (C-4), 70.5 (C-5), 61.8 (C-6). Anal. Calcd for $C_{14}H_{26}O_5$: C, 61.31%; H, 9.49%. Found: C, 61.40%; H, 9.55%.

3-Deoxy-2-O-dodecyl-D-arabino-*hexono-1,4-lactone* (**19**).—From **18**, syrup (181 mg, 90%); $[\alpha]_D$ −23.3° (*c* 1, MeOH); ^{1}H NMR (CD_3OD): δ 4.38 (dd, 1 H, $J_{2,3}$ 8.5, $J_{2,3'}$ 10.2 Hz, H-2), 2.57 (m, 1 H, $J_{3,3'}$ 12.4 Hz, H-3), 2.16 (m, 1 H, $J_{3',4}$ 9.7 Hz, H-3′), 4.48 (m, 1 H, $J_{3,4}$ 5.8 Hz, H-4), 3.84 (m, 1 H, $J_{4,5}$ 5.4 Hz, H-5), 3.57 (d, 2 H, $J_{5,6}$ 5.5 Hz, H-6 and H-6′); ^{13}C NMR (CD_3OD): δ 178.1 (C-1), 77.1 (C-2), 32.1 (C-3), 79.1 (C-4), 74.1 (C-5), 64.6 (C-6). Anal. Calcd

for $C_{18}H_{34}O_5$: C, 65.45%; H, 10.30%. Found: C, 65.40%; H, 10.40%.

3-Deoxy-2-O-hexadecyl-D-arabino-hexono-1,4-lactone (**21**).—From **20**, syrup (201 mg, 100%); $[\alpha]_D$ −14.7° (*c* 1, MeOH); ^{1}H NMR (CD_3OD): δ 4.19 (dd, 1 H, $J_{2,3}$ 8.3, $J_{2,3'}$ 9.8 Hz, H-2), 2.56 (m, 1 H, $J_{3,3'}$12.8 Hz, H-3), 2.20 (m, 1 H, $J_{3',4}$ 9.5 Hz, H-3'), 4.38 (m, 1 H, $J_{3,4}$ 6.1 Hz, H-4), 3.50–4.00 (m, 3 H, H-5, H-6 and H-6'); ^{13}C NMR (CD_3OD): δ 175.2 (C-1), 74.6 (C-2), 30.6 (C-3), 76.3 (C-4), 71.9 (C-5), 62.5 (C-6). Anal. Calcd for $C_{22}H_{42}O_5$: C, 68.39%; H, 10.88%. Found: C, 68.30%; H, 10.92%.

2-O-Butyl-3-deoxy-D-xylo-hexono-1,4-lactone (**23**).—From **22**, syrup (184 mg, 91%); $[\alpha]_D$ −23.2° (*c* 1.1, MeOH); ^{1}H NMR (CD_3OD): δ 4.42 (dd, 1 H, $J_{2,3}$ 8.5, $J_{2,3'}$ 11 Hz, H-2), 2.19 (m, 1 H, $J_{3,3'}$ 12.2 Hz, H-3), 2.15 (m, 1 H, $J_{3',4}$ 10.2 Hz, H-3'), 4.52 (m, 1 H, $J_{3,4}$ 5.9 Hz, H-4), 3.83 (m, 1 H, H-5), 3.58 (m, 2 H, H-6 and H-6'); ^{13}C NMR (CD_3OD): δ 178.3 (C-1), 77.1 (C-2), 33.0 (C-3), 79.1 (C-4), 74.5 (C-5), 67.6 (C-6). Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.04%; H, 8.26%. Found: C, 55.14%; H, 8.35%.

3-Deoxy-2-O-dodecyl-D-xylo-hexono-1,4-lactone (**25**).—From **24**, syrup (201 mg, 100%); $[\alpha]_D$ −10.0° (*c* 1, MeOH); ^{1}H NMR (CD_3OD): δ 4.32 (dd, 1 H, $J_{2,3}$ 8.5, $J_{2,3'}$ 10.4 Hz, H-2), 2.48 (m, 1 H, $J_{3,3'}$ 12.6 Hz, H-3), 2.05 (m, 1 H, $J_{3',4}$ 9.3 Hz, H-3'), 4.43 (m, 1 H, $J_{3,4}$ 5.7 Hz, H-4), 3.74 (m, 1 H, H-5), 3.50 (m, 2 H, H-6 and H-6'); ^{13}C NMR (CD_3OD): δ 176.8 (C-1), 75.6 (C-2), 30.0 (C-3), 77.6 (C-4), 72.9 (C-5), 63.0 (C-6). Anal. Calcd for $C_{18}H_{34}O_5$: C, 65.45%; H, 10.30%. Found: C, 65.40%; H, 10.37%.

3-Deoxy-2-O-(2,3,4,6-tetra-O-acetyl-D-glucopyranosyl)-D-arabino-hexono-1,4-lactone (**27**).—From **26**, syrup (0.2 g, 100% $\alpha/\beta = 16/9$). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78%; H, 5.69%. Found: C, 48.80%; H, 5.72%. α-anomer: ^{1}H NMR (Me_2SO-d_6): δ 4.70 (t, 1 H, $J_{2,3}$ 9, $J_{2,3'}$ 10.2 Hz, H-2), 2.42 (m, 1 H, $J_{3,4}$ 9.7 Hz, H-3), 2.10 (m, 1 H, $J_{3',4}$ 4.1 Hz, H-3'), 4.45 (m, 1 H, $J_{4,5}$ 4.1 Hz, H-4), 3.70 (m, 1 H, H-5), 3.40 (m, 2 H, H-6 and H-6'), 5.06 (d, 1 H, $J_{1',2'}$ 8.1 Hz, H-1'), 4.78 (dd, 1 H, $J_{2',3'}$ 9.5 Hz, H-2'), 5.31 (t, 1 H, $J_{3',4'}$ 9.5 Hz, H-3'), 4.91 (t, 1 H, $J_{4',5'}$ 9.5 Hz, H-4'), 4.00 (m, 1 H, H-5'); ^{13}C NMR (Me_2SO-d_6): δ 173.4 (C-1), 74.1 (C-2), 29.7 (C-3), 76.3 (C-4), 70.5 (C-5), 61.9 (C-6), 99.8 (C-1'), 70.7 (C-2'), 71.9 (C-3'), 68.2 (C-4'), 70.7 (C-5'), 61.6 (C-6'); β-anomer: ^{13}C NMR (Me_2SO-d_6): δ 173.4 (C-1), 74.6 (C-2), 30.0 (C-3), 76.4 (C-4), 70.6 (C-5), 61.9 (C-6), 101.8 (C-1'), 70.9, 70.7 (C-2', C-5'), 73.2 (C-3'), 68.6 (C-4'), 61.9 (C-6').

References

[1] O. Moradei, C. Du Mortier, O.J. Varela, and R.M. De Lederkremer, *J. Carbohydr. Chem.*, 10 (1991) 469–479.

[2] O.J. Varela, A.F. Cirelli, and R.M. De Lederkremer, *Carbohydr. Res.*, 70 (1979) 27–35.

[3] A.G.M. Barrett and H.G. Sheth, *J. Chem. Soc., Chem. Commun.*, (1982) 170–171.

[4] O.J. Varela, A.F. Cirelli, and R.M. De Lederkremer, *Carbohydr. Res.*, 100 (1982) 424–430.

[5] R. M. De Lederkremer, M. I. Litter, and L. F. Sala, *Carbohydr. Res.*, 36 (1974) 185–187.

[6] L. F. Sala, A. F. Cirelli, and R. M. De Lederkremer, *Carbohydr. Res.*, 78 (1980) 61–66.

[7] O. J. Varela, A. P. Nin, and R. M. De Lederkremer, *Tetrahedron Lett.*, 35 (1994) 9359–9362.

[8] K. Bock, I. Lundt, and C. Pedersen, *Acta Chem. Scand.*, B35 (1981) 155–162.

[9] E.J. Enholm and S. Jiang, *Heterocycles*, 34 (1992) 2247–2252.

[10] C. Choquet-Farnier, I. Stasik, D. Beaupère, and R. Uzan, *Carbohydr. Lett.*, 2 (1996) 91–96.

[11] D. Beaupère, I. Boutbaiba, A. wadouachi, C. Fréchou, G. Demailly, and R. Uzan, *New J. Chem.*, 16 (1992) 405–411.

[12] D. Beaupère, P. Bauer, and R. Uzan, *Can. J. Chem.*, 57, 2, (1979) 218–221.

[13] W. Timpe, K. Dax, N. Wolf, and H. Weidmann, *Carbohydr. Res.*, 39 (1975) 53–60.

[14] S. J. Eitelman and M.S. Feather, *Carbohydr. Res.*, 77 (1979) 213–217.

[15] H. Weidmann, W. Timpe, and N. Wolf, *Carbohydr. Res.*, 25 (1972) 67–70.