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Practical synthesis of 2,6-dideoxy-D-*lyxo*-hexose ("2-deoxy-D-fucose") from D-galactose

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Abstract

2,6-Dideoxy-D-*lyxo*-hexose was prepared efficiently from D-galactose in eight steps (25% overall yield). The synthesis is amenable to multigram scale-up. © 1998 Elsevier Science Ltd. All rights reserved

Keywords: 2-Deoxy-D-fucose; Synthesis; D-Galactose; D-Fucose; Oliose

1. Introduction

2,6-Dideoxy-D-*lyxo*-hexose (**1**, 2-deoxy-D-fucose, oliose) and its methyl ethers occur as glycosides in natural products; for example the olivomycin antitumor-antibiotics [1–7], the cardenolide glycoside adigoside [8], and polyketide glycosides, phenelfamycins [9]. Sugar **1** is not commercially available, despite the desirability for its incorporation into natural product syntheses. Syntheses have been reported for DL-**1** [10], and **1** [11–13], but in general they involve starting materials or reagents that are not amenable to large-scale preparation. For example, the Roush synthesis, beginning with 6-hepten-3-yn-2-ol, required kinetic resolution by Sharpless asymmetric epoxidation and gave **1** in seven steps (overall yield, 18–20%) [12]. Recently, we reported a short synthesis of the 2-deoxy-L-fucose derivative, *ent*-**2**, from L-fucose (3 steps, 59% yield) [14] and now required the D- form **2** for natural product synthesis. While the common naturally occurring form of fucose is L- (derived from kelp polysaccharide [15]), D-fucose is rare and prohibitively expensive as a starting material for preparation of **2**.[1] We describe here a convenient preparation of **1** from D-galactose (**3**, ~$80/kg) that takes place by two-step protection of C-1,3,4 OH groups, sequential deoxygenation of the 2,6-OH groups, and deprotection (Scheme 1). The procedure is economical, amenable to multigram scale-up and proceeds through the useful differentially-protected 2-deoxy-D-fucose derivative, **2**.

2. Results and discussion

Conversion of D-galactose (**3**) into the benzyl glycopyranoside **4** (8:1 α:β anomers) was achieved in two steps (BnOH, HCl [16]; 2,2-dimethoxypropane, *p*-TSA [17], 69% overall yield, Scheme 1 (for ^{1}H NMR data, see Table 1). Deoxygenation of the C-6 hydroxyl could be effected by standard methods (selective 6-*O*-tosylation followed by

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[1] L- and D-Fucose are priced at $350/500 g and $4500/100 g, respectively (Pfanstiehl Laboratories, Inc.).

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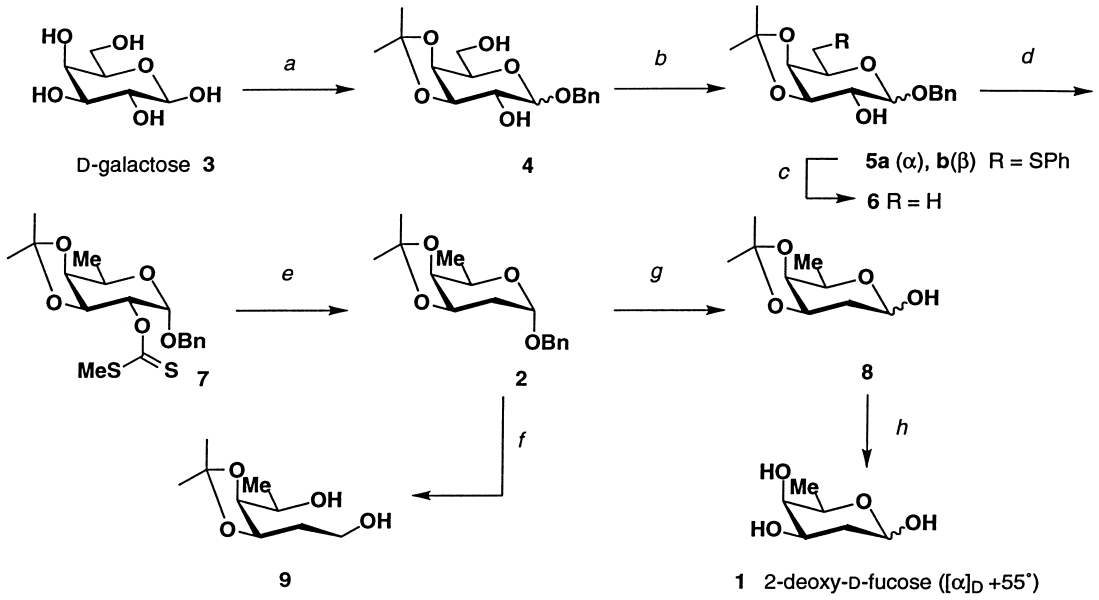

Scheme 1. (a), i BnOH, HCl $_4$, 72%, ii 2,2-dimethoxypropane, *p*-TSA, then Et_3N, MeOH: H_2O, 96%; (b), PhSSPh, *n*-Bu_3P, THF, Δ, 86% (73% α anomer); (c), Ra-Ni, EtOH, Δ, 91%; (d), NaH, CS_2, CH_3I, imidazole, THF, 96%; (e), H_3PO_2, Et_3N, AIBN Δ, diox, 77%; (f), Na, NH_3 (l), THF, −33, 92%; (g), Ca, NH_3 (l), THF, −33, 70%; (h), Dowex 50X (H^+), THF-H_2O, 90%.

Table 1
^{1}H NMR data of compounds **1**, **2**, **6**–**8**

Compound	300 MHz ^{1}H NMR, $CDCl_3$ (α-pyranose): ppm (mult., *J* Hz)						
	i-Pr	H-1	H-2	H-3	H-4	H-5	H-6
1[a]	—	5.34 (bd, 3.5)	1.81 (bdd, 14.0, 5.5) 1.87 (ddd, 14.0, 12.0, 3.5)	4.07 (ddd, 12.0, 5.5, 3.5)	3.68 (bd, 3.5)	4.12 (bq, 6.5)	1.19 (d, 6.5)
2	1.34 (s) 1.49 (s)	5.02 (dd, 6.3, 5.1)	1.80 (ddd, 14.9, 6.3, 4.0) 2.22 (ddd, 14.9, 5.1, 4.9)	4.48 (ddd, 7.1, 4.9, 4.0)	3.98 (dd, 7.1, 2.0)	3.92 (qd, 6.5, 2.0)	1.26 (d, 6.5)
6	1.36 (s) 1.52 (s)	4.94 (d, 3.9)	3.82 (ddd, 7.0[b], 6.5, 3.9)	4.23 (dd, 6.5, 6.0)	4.06 (dd, 6.0, 2.2)	4.16 (qd 6.7, 2.2)	1.31 (d, 6.7)
7	1.36 (s) 1.54 (s)	5.17 (d, 3.6)	5.76 (dd, 8.1, 3.6)	4.55 (dd, (8.1, 5.2)	4.13 (dd, 5.2, 2.5)	4.21 (qd 6.6, 2.5)	1.37 (d, 6.6)
8	1.35 (s) 1.48 (s)	5.34 (ddd, 7.1, 5.3)	1.72 (ddd, 15.1, 7.1, 3.5) 2.25 (ddd, 15.1, 5.3, 4.4)	4.46 (ddd, 7.2, 4.4, 3.5)	3.96 (dd, 7.2, 2.0)	3.84 (qd, 6.3, 2.0)	1.26 (d, 6.3)

[a] Recorded in D_2O, 500 MHz, mixture of pyranose and furanose anomers, δ given for α-pyranose.
[b] Coupling to OH.

iodide displacement and catalytic hydrogenolysis) [18], however, attempts to remove both C-2 and C-6 hydroxyl groups simultaneously using this method gave poor yields due to sluggish rates of displacement reactions at the more-hindered C-2 position. It was found that C-2,6 deoxygenation was more conveniently adapted to large-scale throughput (~50 g) by stepwise reductive cleavage. Compound **4** was converted into the anomeric 6-*S*-phenyl-6-thio glycosides **5a**,**b** (PhSSPh, *n*-Bu_3P, THF, reflux, 86%, 5:1 ratio, respectively) from which the major α anomer **5a** could be isolated by fractional crystallization and chromatography (73%). We have carried out the latter transformation on scales of up to ~70 g without difficulty. Although the **5a**,**b** mixture was successfully converted into **2**, it was more convenient to carry through with crystalline **5a**. Compound **5a** was desulfurized with Raney-Ni (EtOH, reflux, 91%) to give the D-fucose derivative **6**. Conversion of **6** into the corresponding 2-xanthate ester **7** (NaH, CS_2, cat. imidazole, then MeI, 96%) and subsequent reduction was achieved by the Barton–McCombie reaction, using buffered hypophosphorous acid (AIBN, H_3PO_2, aqueous, Et_3N, dioxane, reflux) [19] to afford **2** in 77% yield from **7**. The use of the inexpensive, aqueous soluble hydrogen donor H_3PO_2 gave an improved yield over standard

reducing conditions (*n*-Bu_3SnH in refluxing toluene) and avoided the difficult and often tedious removal of Sn byproducts associated with stannane reductions [19].

Deprotection of the 1-*O*-benzyl group of **2** proved to be difficult without incurring over-reduction. Attempts at debenzylation by catalytic hydrogenolysis (Pearlman's catalyst, $Pd(OH)_2$–C, EtOH, 1 or 4 atm; Pd-C, EtOH, 1–4 atm; Pd-C, NH_4HCOO–MeOH) were sluggish or gave variable, low yields of **8**, perhaps due to poisoning of catalyst by trace sulfur impurities in **2**. Heating the substrate in the presence of Raney-Ni (EtOH, reflux) prior to attempted debenzylation improved the yield of **8** only slightly, while dissolving alkali metal reduction (Li° or Na° in liquid ammonia, −33 °C) gave the over-reduced alditol **9** (92%). While debenzylation of benzyl hexopyranosides with Na°–NH_3 has been reported [20], the 2-deoxy sugar **8** appeared to be particularly sensitive to overreduction. We were pleased to find that replacement of Na° with Ca° (5 equiv, NH_3 (*l*), −33°, 0.75 h) allowed efficient cleavage of the *O*-Bn group to afford **8** (4.5:1 α:β anomers) in good yield (70%), with little over-reduction. Although of Ca°-NH_3(*l*) has been used for reductive removal of primary *O*-Bn ethers [21], to our knowledge, this is the first application to debenzylation of anomeric 1-*O*-Bn sugar derivatives.

Completion of the synthesis was achieved by hydrolysis of the acetonide group in **8** (Dowex 50X2, H^+ form, THF–H_2O) to give pure 2,6-dideoxy-D-*lyxo*-hexopyranose (**1**, 90%, $[\alpha]_D$ +55°, *c* 0.61, H_2O, equil).[2] The ^1H and ^{13}C NMR spectra of **1** (D_2O) were in excellent agreement with published values [10] [12] and confirmed that **1** exists mainly in the pyranose form (~90%, α:β anomers 1:1.2 ratio) with about 10% of the furanose tautomers.

In summary, we have completed an efficient synthesis of **1** from galactose in eight steps, with a 25% overall yield (21% from **5a**) and an average yield per step of 85%. The synthesis is amenable to large-scale throughput using relatively inexpensive reagents. Finally, efficient hydrogenolytic cleavage of the benzyl glycoside **2** in high yield with Ca° in liquid NH_3 allows debenzylation without over-reduction and demonstrates the latter as a useful alternative when Na°–NH_3 (*l*) and catalytic hydrogenation are unsuitable.

3. Experimental

General procedures.—All solvents were dried and distilled from glass prior to use. In particular, THF and 1,4-dioxane were dried and distilled from Na°–benzophenone ketyl. Melting points are uncorrected. Optical rotations were measured on a Jasco DIP 370 polarimeter and ^1H NMR and ^{13}C NMR spectra were recorded on a General Electric QE 300 (300 MHz and 75 MHz, respectively) or GE Omega 500 NMR spectrometers (500 and 125 MHz respectively). Unless otherwise stated, chemical shifts are referenced as follows. ^1H; δ 0.00 ppm, (Me_4Si in $CDCl_3$ or sodium 4,4-dimethy-4-silapentanoate in D_2O), and ^{13}C; δ 77.00 ppm for the center peak of $CDCl_3$ or δ 66.5 ppm for 1,4-dioxane in D_2O. ^{13}C multiplicities (CH_3, CH_2, CH and C) were deduced from DEPT experiments. Mass spectra were obtained on several instruments at the University of California, Riverside, Mass Spectrometry facility and elemental analyses were provided by Midwest Microlabs (Indianapolis, IN). Chromatography was carried out on silica gel (43–63 μm, EM Merck).

*Benzyl 6-deoxy-3,4-*O*-isopropylidene-6-*S*-phenyl-6-thio-*D*-galactopyranoside* (**5**).—Compound **4** [23] (31.43 g, 0.10 mol) in THF (300 mL) was added to a solution of tri-*n*-butylphosphine (64 mL, 0.26 mol) and diphenyl disulfide (48.03 g, 0.26 mol) in THF at 0 °C. After stirring at room temperature for 27.5 h, the solvent was remove in vacuo to give a yellow oil that was purified by vacuum flash chromatography (silica gel; hexane to 3:7 ethyl acetate–hexane) to give a white solid (35.17 g, 86%). The α anomer **5a** was purified by crystallization (EtOAc–hexane) and silica gel chromatography (73%), mp 103–104 °C; $[\alpha]_D$ +80.6° (*c* 5.03, $CHCl_3$); R_f 0.35 (1:1 EtOAc–hexane); UV (MeCN) 257 (ε 8767), 328 nm (ε 49); ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 3 H), 1.49 (s, 3 H), 2.45 (bs, 1 H), 3.24 (m, 2 H, H-6), 3.83 (m, 1 H), 4.15 (m, 1 H), 4.23 (m, 2 H), 4.48 (d, 1 H, *J* 11.5 Hz, CH_2Ph), 4.74 (d, 1 H, *J* 11.5 Hz, CH_2Ph), 4.94 (d, 1 H, *J* 3.8 Hz, H-1), 7.29 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 25.7 (CH_3), 27.5 (CH_3), 34.2 (CH_2), 67.3 (CH), 69.0 (CH), 69.4 (CH_2), 73.6 (CH), 75.8 (CH), 96.4 (CH), 109.5 (C), 126.1 (CH), 127.9 (CH), 128.2 (2×CH), 128.4 (2×CH), 129.0 (2×CH), 129.1 (2×CH), 136.0 (C),

[2] Lit. values $[\alpha]_D$ +48.8°, *c* 1.0, H_2O, equil) [12], +55.5° (no solvent given) [11], +51° (*c* 0.9, H_2O) [3]. For *ent*-**1**, $[\alpha]_D$ −51.5° (*c*, 1.0, H_2O, equil) [22].

136.8 (C); HREIMS found m/z 402.1505 (M^+), $C_{22}H_{26}O_5S$ requires 402.1501; Anal. Calcd for $C_{22}H_{26}O_5S$: C, 65.65; H, 6.52; S, 7.95. Found: C, 65.57; H, 6.42; S, 7.97; β anomer (**5b**) R_f 0.31 (1:1 EtOAc–hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 3 H), 1.51 (s, 3 H), 2.24 (bs, 1 H, OH), 3.34 (dd, 1 H, J 13.4, 6.7 Hz, H-6), 3.38 (dd, 1 H, J 13.4, 6.7 Hz, H-6), 3.60 (dd, 1 H, J 8.5, 7.2 Hz, H-2), 3.79 (ddd, 1 H, J 6.7, 6.7, 2.1 Hz, H-5), 4.00 (dd, 1 H, J 7.2, 5.5 Hz, H-3), 4.16 (d, 1 H, J 8.5 Hz, H-1), 4.19 (dd, 1 H, J 5.5, 2.1 Hz, H-4), 4.58 (d, 1 H, J 11.6 Hz, CH_2Ph), 4.88 (d, 1 H, J 11.6 Hz, CH_2Ph), 7.34 (m, 10 H).

*Benzyl 6-deoxy-3,4-*O*-isopropylidene-6-*D*-galactopyranoside* (**6**).—Raney nickel (W-2, Acros, aqueous suspension) was resuspended and decanted from absolute EtOH (3×) before use. Portions of the Raney Ni–EtOH suspension were added to a stirred solution of benzyl 6-deoxy-3,4-*O*-isopropylidene-6-*S*-phenyl-6-thio-α-D-galactopyranoside (**5**, 23.78 g, 59.2 mmol) in absolute EtOH (200 mL) at reflux over a period of 7 h until the reduction was complete (TLC). The suspension was cooled, filtered through Celite, the filter pad washed with EtOH and combined filtrates concentrated in vacuo to a yellow oil (17.2 g). The crude material was purified by column chromatography (4.5 cm×15 cm, 2:3 to 3:7 EtOAc–hexane) to give **6** as a clear oil (15.79 g, 91%). R_f 0.62 (EtOAc); HRCIMS found m/z 295.1546 (MH^+), $C_{16}H_{22}O_5$ requires 295.1545; α anomer: ^{1}H NMR (see Table 1). ^{13}C NMR ($CDCl_3$) δ 16.0 (CH_3), 25.7 (CH_3), 27.5 (CH_3), 64.0 (CH), 69.2 (CH), 69.5 (CH_2), 75.5 (CH), 75.9 (CH), 96.9 (CH), 108.9 (C), 127.7 (CH), 128.2 (CH), 137.3 (C); β anomer: ^{13}C NMR ($CDCl_3$) δ 16.5 (CH_3), 26.3 (CH_3), 28.2 (CH_3), 69.3 (CH), 70.7 (CH_2), 73.7 (CH), 76.4 (CH), 79.0 (CH), 101.2 (CH), 109.8 (C), 127.9 (CH), 128.2 (CH), 128.4 (CH), 137.2 (C).

*Benzyl 3,4-*O*-isopropylidene-2-*O*-[(*S*-methylthio)-thiocarbonyl]-α-D-galactopyranoside* (**7**).—Benzyl 3,4-*O*-isopropylidene-6-deoxy-6-phenylthio-α-D-galactopyranoside (**6**, 3.493 g, 11.9 mmol) was dissolved in THF (30 mL) and added to hexane-washed NaH (0.53 g–80% dispersion in oil, 17.7 mmol) in THF (30 mL). Imidazole (0.0122 g, 0.18 mmol) was added, and then after 2 h, CS_2 (3.0 mL, 49.9 mmol) was added. After another 2 h, MeI (3.0 mL, 48.2 mmol) was added. Forty-five min later the mixture was poured into 10 mL of H_2O. The aqueous layer was extracted three times with CH_2Cl_2, dried through $MgSO_4$, and evaporated in vacuo to give **7** as a yellow oil (4.3774 g, 96%). α anomer: mp 67–68 °C; ^{1}H NMR (see Table 1): ^{13}C NMR ($CDCl_3$) δ 16.0 (CH_3), 18.7 (CH_3), 26.3 (CH_3), 27.8 (CH_3), 63.6 (CH), 69.8 (CH_2), 73.2 (CH), 76.3 (CH), 80.0 (CH), 94.7 (CH), 109.2 (C), 127.4 (2×CH), 127.6 (CH), 128.2 (2×CH), 137.2 (C), 215.8 (C); β anomer: ^{13}C NMR ($CDCl_3$) δ 16.4, 19.2, 26.3, 27.5, 68.8, 69.7, 76.5, 76.9, 80.9, 98.4, 110.2, 127.3, 127.5, 128.2, 137.0, 215.7. HRCIMS found m/z 385.1150 (MH^+), $C_{18}H_{25}O_5S_2$ requires 385.1177; Anal. Calcd for $C_{18}H_{24}O_5S_2$: C, 56.23; H, 6.29; S, 16.68. Found: C, 55.92; H, 6.25; S, 16.51.

*Benzyl 2-deoxy-3,4-*O*-isopropylidene-α-D-lyxo-hexo-pyranoside* (**2**).—Benzyl 3,4-*O*-isopropylidene-2-*O*-[(*S*-methylthio)thiocarbonyl]-α-D-galactopyranoside (**7**, 1.5160 g, 3.95 mmol) was dissolved in 1,4-dioxane (20 mL). Freshly distilled Et_3N (5.4 mL, 38.7 mmol) was added, and the solution was deoxygenated by passage of a fine stream of N_2 for 10 min. Hypophosphorous acid (2.0 mL of a 50% aqueous solution, 19.3 mmol) was deoxygenated separately and then added to the above solution. An aliquot of degassed AIBN (0.1 eq, in 1,4-dioxane) was added to the solution, and the flask was immersed in a 100 °C oil bath. After 1 h, TLC indicated that the starting material had been consumed. The reaction was cooled, and H_2O (15 mL) was added. The aqueous layer was extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated in vacuo to a yellow oil. The crude material was purified by column chromatography (silica gel; 4.5×25 cm; 1:19 to 2:3 EtOAc–hexane) to give the product **2** as a yellow oil (0.8501 g, 77%); α anomer: $[\alpha]_D$ +80.2° (c 1.0, $CHCl_3$); R_f 0.45 (3:7 EtOAc–hexane); ^{1}H NMR (see Table 1); ^{13}C NMR ($CDCl_3$) δ 16.0 (CH_3), 25.3 (CH_3), 26.7 (CH_3), 30.5 (CH_2), 64.5 (CH), 68.9 (CH_2), 70.6 (CH), 75.1 (CH), 95.7 (CH), 108.6 (C), 127.4 (CH), 127.6 (2×CH), 128.3 (2×CH), 138.2 (C); HREIMS found m/z 278.1524 (M^+), $C_{16}H_{22}O_4$ requires 278.1518. β anomer: $[\alpha]_D$ −41.3° (c 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 16.9 (CH_3), 26.4 (CH_3), 28.2 (CH_3), 35.3 (CH_2), 68.8 (CH), 69.9 (CH_2), 72.3 (CH), 74.0 (CH), 98.0 (CH), 109.1 (C), 127.6 (CH), 127.9 (CH), 128.2 (CH), 137.4 (C).

*2,6-Dideoxy-3,4-*O*-isopropylidene-D-lyxo-hexose* (**8**).—Calcium turnings (0.0806 g, 2.01 mmol) were added to anhydrous liquid NH_3 (200 mL, distilled from $NaNH_2$). A solution of benzyl 2-deoxy-3,4-*O*-isopropylidene-α-D-*lyxo*-hexopyranoside (**2**, 0.1121 g, 0.40 mmol) in THF (1–0 mL) was added

to the blue solution. After 40 min, reaction quenched by addition of solid NH_4Cl. The mixture was diluted with THF and stirred while immersed in a warm water bath until the NH_3 had evaporated. Filtration through $MgSO_4$ and concentration in vacuo gave a yellow oil (0.1135 g). Column chromatography (1.5×15 cm; 3:7 EtOAc–hexane) gave **8** as a clear oil (52.5 mg; 70%) consisting of a mixture of anomers (4.5:1 α:β). $[\alpha]_D$ +10.3° (*c* 3.5, $CHCl_3$); R_f 0.20 (1:1 EtOAc–hexane); IR (NaCl, neat) 3440 (OH), 1460 cm^{-1}; α anomer: ^1H NMR, (see Table 1); ^{13}C NMR ($CDCl_3$) δ 16.1 (CH_3), 25.1 (CH_3), 26.5 (CH_3), 30.8 (CH_2), 64.9 (CH), 70.6 (CH), 75.1 (CH), 90.4 (CH), 108.7 (C), β anomer δ 16.5 (CH_3), 25.1 (CH_3), 26.5 (CH_3), 33.8 (CH_2), 68.3 (CH), 72.0 (CH), 74.9 (CH), 93.2 (CH), 108.7 (C); HRCIMS found *m*/*z* 188.1284 [$(M+NH_4^+-H_2O)^+$], $C_9H_{18}O_3N$ requires 188.1287.

2,6-Dideoxy-3,4-O-*isopropylidene*-D-lyxo-*hexitol* (**9**).—Hexane-washed lithium (0.270 g, 38.9 mmol) was added to anhydrous liquid NH_3 (300 mL, distilled from $NaNH_2$). A solution of benzyl 2-deoxy-3,4-*O*-isopropylidene-α-D-*lyxo*-hexopyranoside (**2**, 0.9707 g, 3.48 mmol) in 20 mL THF was added and after 40 min the reaction was quenched by addition of solid NH_4Cl. The mixture was diluted with THF and stirred while the flask was immersed in a warm water bath until the NH_3 had evaporated. Filtration of the mixture through $MgSO_4$ and concentration in vacuo gave a yellow oil (0.8303 g). Column chromatography (4.5×18 cm; 1:1 EtOAc–hexane to EtOAc) gave **9** as a clear oil (0.6077 g; 92%); $[\alpha]_D$ +16.9° (*c* 0.55, $CHCl_3$); R_f 0.09 (1:1 EtOAc–hexane); IR (NaCl, neat) 3420 (OH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (d, 3 H, *J* 6.2 Hz, H-6), 1.38 (s, 3 H), 1.50 (s, 3 H), 1.69 (m, 1 H, H-2), 1.90 (m, 1 H, H-2), 2.59 (bs, 2 H, OH), 3.82 (m, 3 H), 3.90 (dd, 1 H, *J* 6.3, 5.9 Hz), 4.33 (ddd, 1 H, *J* 10.9, 5.9, 2.8 Hz); ^{13}C NMR ($CDCl_3$) δ 19.6 (CH_3), 25.4 (CH_3), 27.8 (CH_3), 31.9 (CH_2), 60.6 (CH_2), 65.6 (CH), 75.5 (CH), 81.6 (CH), 108.3 (C); HRCIMS found *m*/*z* 191.1287 (MH^+), $C_9H_{19}O_4$ requires 191.1283.

2,6-Dideoxy-D-lyxo-*hexose* (**1**).—Dowex 50X2-400 resin (acid washed, H^+ form) was added to a solution of 2,6-dideoxy-3,4-*O*-isopropylidene-D-*lyxo*-hexose (**8**, 40 mg) in THF–H_2O (1:5, 24 mL). After stirring for 1.5 h at 23 °C, the suspension was filtered and the resin washed with hot deionized-water. Volatile solvent was removed by rotary evaporation and the remaining aqueous solution was lyophilized. The residue was dissolved in H_2O and passed through a syringe filter (Nalgene, 0.2 μm, 25 mm cellulose acetate) with subsequent removal of water to afford **1** as clear glass (31.2 mg, 90%); $[\alpha]_D$ +55° (*c* 0.61, H_2O, equil); R_f 0.05 (1:9 EtOH–CH_2Cl_2); ^1H NMR (500 MHz, D_2O) showed a mixture of tautomeric forms: pyranose (90%, α:β 1:1.2) and furanose (10%), δ were identical with literature values [11] [12]; α pyranose; ^1H NMR, (see Table 1); ^{13}C NMR (D_2O, α/β pyranose, only) δ 15.8/16.0 (CH_3), 31.6/34.5 (CH_2), 64.7/66.4 (CH), 68.0/69.4 (CH), 70.4/70.8 (CH), 91.3/93.5 (CH); HRCIMS found *m*/*z* 166.1084 ($M+NH_4^+$), $C_6H_{16}NO_4$ requires 166.1079.

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References

[1] Y.A. Berlin, S.E. Esipov, M.N. Kolosov, and M.M. Shemyakin, *Tetrahedron Lett.*, (1966) 1431–1436.
[2] Y.A. Berlin, G.V. Borisova, S.E. Esipov, M.N. Kolosov, and V.A. Krivoruchko, *Chem. Nat. Comp.*, 5 (1969) 94–98
[3] Y.A. Berlin, O.A. Kiseleva, M.N. Kolosov, V.D. Kuznetsov, E.I. Lupach, I.V. Severtsova, G.M. Smirnova, V.S. Soifer, and I.V. Yartseva, *Chem. Nat. Comp.*, 8 (1974) 525–528.
[4] Y.A. Berlin, E.F. Boldyreva, M.N. Kolosov, G.P. Pronina, V.S. Soifer, and I.V. Yartseva, *Chem. Nat. Comp.*, 8 (1974) 529–537.
[5] Y.A. Berlin, M.N. Kolosov, and I.V. Yartseva, *Chem. Nat. Comp.*, 9 (1975) 504–508.
[6] M. Miyamoto, Y. Kawamatsu, and M. Shinohara, *Tetrahedron*, 22 (1966) 2785–2799.
[7] N.K. Kochetkov and A.I. Usov, *Akad. Nauk USSR*, (1962) 1042–1050.
[8] S. Hoffmann, E. Weiss, and T. Reichstein, *Helv. Chim. Acta*, 49 (1966) 1855–1872.
[9] J.E. Hochlowski, M.H. Buytendorp, D.N. Whittern, A.M. Buko, R.H. Chen, and J.B. McAlpine, *J. Antibiot.*, 41 (1988) 1300–1315.
[10] M. Chmielewski, *Tetrahedron*, 35 (1979) 2067–2070.

[11] K. Bock, I. Lundt, C. Pedersen, and S. Refn, *Acta Chem. Scand.*, B40 (1986) 740–744.
[12] W.R. Roush and R.J. Brown, *J. Org. Chem.*, 48 (1983) 5093–9101.
[13] W.R. Roush and J.A. Straub, *Tetrahedron Lett.*, 27 (1986) 3349–3352.
[14] P.A. Searle, R.K. Richter, and T.F. Molinski, *J. Org. Chem.*, 61 (1996) 4073–4079.
[15] E. Percival, *Methods Carbohydr. Chem.*, 1 (1962) 195–198.
[16] H.G. Fletcher, Jr., *Methods Carbohydr. Chem.*, 2 (1963) 386–389.
[17] G. Catelani, F. Colonna, and A. Marra, *Carbohydr. Res.*, 182 (1988) 297–300.
[18] O.T. Schmidt, *Methods Carbohydr. Chem.*, 1 (1962) 191–194.
[19] D.H.R. Barton, D.O. Jang, and J.C. Jaszberenyi, *J. Org. Chem.*, 58 (1993) 6838–6842.
[20] G.E. Keck and T.T. Wager, *J. Org. Chem.*, 61 (1996) 8366–8367.
[21] K. Kigoshi, M. Ojika, K. Suenaga, T. Mutou, J. Hirano, A. Sakakura, T. Ogawa, M. Nisiwaki, and K. Yamada, *Tetrahedron Lett.*, 35 (1994) 1247–1250.
[22] D. Horton, T.M. Cheung, and W. Weckerle, *Methods Carbohydr. Chem.*, 8 (1980) 201–204.
[23] W. Steffan, C. Vogel, and H. Kristen, *Carbohydr. Res.*, 204 (1990) 109–120.