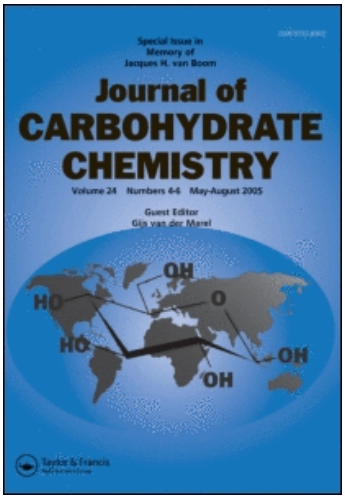

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A Convenient Synthesis of 3,6-Anhydro-2-deoxy-D-glucose [Isoglucal] and Some of Its Derivatives

José A. Serrano[a]; Emilio Román[a]
[a] Departamento de Química Orgánica, Universidad de Extremadura, Badajoz, Spain

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A CONVENIENT SYNTHESIS OF 3,6-ANHYDRO-2-DEOXY-D-GLUCOSE [ISOGLUCAL] AND SOME OF ITS DERIVATIVES

José A. Serrano and Emilio Román*

Departamento de Química Orgánica, Universidad de Extremadura
06071 Badajoz, Spain

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ABSTRACT

The present paper describes a facile synthesis of *isoglucal* (3,6-anhydro-2-deoxy-D-glucose, **3**), starting from the easily available α,β-unsaturated aldehyde (2*E*)-4,6-di-*O*-acetyl-2,3-didehydro-*aldehydo*-D-*erythro*-hex-2-enose (**1**). Compound **3** exists in equilibrium with its corresponding bicyclic forms whose anomeric configurations and ring-sizes have been determined.

INTRODUCTION

Although the synthesis of *C*-glycosyl derivatives has been extensively studied,[1] routes through intramolecular cyclization of α,β-unsaturated aldehydo-sugars are still almost unexplored. In fact, as far as we are aware, the synthesis of *isoglucal* (3,6-anhydro-2-deoxy-D-glucose, **3**) is the only example described to date. The preparation of this compound was originally reported by Bergmann,[2] who started from tri-*O*-acetyl-D-glucal and proposed as the structure of the product, 3,6-anhydro-1-deoxy-D-fructose. Later, Foster *et al.*[3] described the synthesis of 3,6-anhydro-2-deoxy-D-glucose employing a different route. The correct structure for *isoglucal* was proposed by Ferrier and co-workers[4] by comparing the optical rotation and melting point of the *N*-benzyl-*N*-phenylhydrazone of **3** with the data for the products of Bergmann[2] and Foster.[3]

It was considered[4,5] that compound **2** was the intermediate in the formation of the 3,6-anhydride from (2*E*)-4,6-di-*O*-acetyl-2,3-didehydro-*aldehydo*-D-*erythro*-hex-2-enose **1**, by attack of the hydroxymethyl anion at C-6 on the alkenic C-3 carbon. A poor yield was reported due to the presence of by-products.

Now, we are interested in the synthesis of 3,6-anhydro-D-glucofuranosides **10**-**13**, bicyclic systems that are present in several products of biological importance such as herbicides,[6] antitumorals[7] and enzyme inhibitors.[8] Consequently, we have reinvestigated the preparation of 3,6-anhidro-2-deoxy-D-glucose (**3**) and some of its derivatives, starting from the easily available (2*E*)-4,6-di-*O*-acetyl-2,3-didehydro-*aldehydo*-D-*erythro*-hex-2-enose (**1**).[9] The unreported ^{1}H and ^{13}C NMR data from known **3**, **4** and **11**α, as well as from all new compounds are given here.

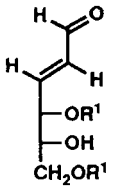
RESULTS AND DISCUSSION

Treatment of (2*E*)-4,6-di-*O*-acetyl-2,3-didehydro-*aldehydo*-D-*erythro*-hex-2-enose (**1**) with methanol-water-triethylamine (5:4:1) at room temperature gave the 3,6-anhydro-2-deoxy-D-glucose (**3**) in 82% yield. In this reaction, compound **1** readily undergoes cyclization by an internal Michael addition, as occurs in similar α,β-unsaturated esters on treatment with alkoxides,[10-13] and also under Wittig reaction conditions for the synthesis of *C*-glycosyl compounds.[10,12,14] Although in those reactions there was preponderant formation of β-anomers, it is noteworthy the cyclization of **1** under mild experimental conditions, as well as the exclusive formation of **3** (α at C-3).

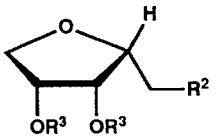
Compound **3** afforded a crystalline (2,4-dinitrophenyl)hydrazone (**4**), whose melting point (157-159 °C) was quite different from that reported by Ferrier[4] (122-124 °C) for this same derivative. At this point we have not been able to explain this difference. Conventional acetylation of **4** yielded the corresponding diacetate **5**.

Reaction of **3** with anhydrous acetone and copper (II) sulfate gave, after column chromatography, the isopropylidene derivative **6**, also characterized as its (2,4-dinitrophenyl)hydrazone **7**. Further elution of the column led to another compound, whose ^{1}H and ^{13}C NMR data supported the hexonic acid structure **8**.[15] Esterification of **8** under alkaline conditions[16] gave an ethyl ester whose ^{13}C NMR data matched that of ethyl 3,6-anhydro-2-deoxy-4,5-*O*-isopropylidene-

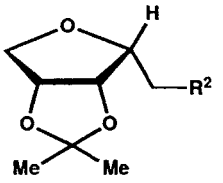
D-*arabino*-hexonate **9**, as described by Buchanan *et al.*[11] These results support the proposed structures for **6-8**. For these compounds, the values of $J_{3,4}$ (3.3-3.6 Hz), $J_{4,5}$ (5.6-6.2 Hz), $J_{5,6}$ (3.5-3.7 Hz), and $J_{6,6'}$ (≈ 0 Hz) were similar to those reported for other *C*-glycoside analogues in the E_o conformation.[11,17]



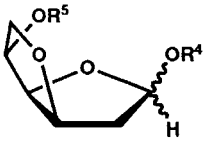
1: R^1 = Ac
2: R^1 = H



3: R^2 = CHO, R^3 = H
4: R^2 = CH=N-NH-[2,4-$(NO_2)_2$-C_6H_4], R^3 = H
5: R^2 = CH=N-NH-[2,4-$(NO_2)_2$-C_6H_4], R^3 = Ac



6: R^2 = CHO
7: R^2 = CH=N-NH-[2,4-$(NO_2)_2$-C_6H_4]
8: R^2 = COOH
9: R^2 = COOEt



10α, **10**β: R^4 = R^5 = H
11α, **11**β: R^4 = Me, R^5 = H
12α, **12**β: R^4 = Me, R^5 = Ac
13α, **13**β: R^4 = R^5 = Ac

As expected,[3,18,19] compound **3** exists in solution as an equilibrium mixture with its corresponding furanose forms **10**α and **10**β. This mixture has $[\alpha]_D^{20}$ +37.5°, in agreement with the literature value (Lit.[4] $[\alpha]_D$ +36.3°). In deuteriochloroform solution (^{1}H and ^{13}C NMR), these bicyclic α and β anomers are in a ratio of 2:1, respectively. Assignment of anomeric configuration for **10**β and the diacetate **13**β is based on the small coupling constants $J_{1,2'}$ and $J_{2',3} \leq$ 2.1 Hz observed, indicating a *trans*-relationship between H-1, H-2' and H-3.[20,21] In the case of methylglycosides **11** and **12**, the values of the coupling constants $J_{1,2'}$ and $J_{2',3}$ did not permit an unequivocal assignment of their anomeric configurations. However, the optical rotation for **11**α ($[\alpha]_D^{20}$ +112°) is very similar to that described[3] for methyl 3,6-anhydro-2-deoxy-α-D-glucofuranoside

($[\alpha]_D^{19}$ +111°). Furthermore, according to Hudson's isorotation rules,[3,22] the α anomers are more dextrorotatory than their β-anomers, thus supporting assignment of anomeric configurations for **11-13**.

Some additional NMR characteristics of compounds **10-13** were also observed. When comparing ^{1}H NMR spectra for each pair of α and β anomers, we observed that the difference in chemical shifts between H-6 and H-6' was greater for **10**α-**13**α than for **10**β-**13**β. Concerning the ring-size of **10-13**, the cyclization between C-1 and C-4 (and not C-5) was demonstrated by the characteristic deshielding[23] for H-5 (*ca.* 0.8-1.0 ppm) and H-4 (*ca.* 0.1-0.4 ppm) on α- and β-acetylation, respectively. Finally, the differences in chemical shifts for C-5 and C-6 in the ^{13}C NMR spectra of each compound and its corresponding acetate were also consistent with the cyclization through C-4.[24]

EXPERIMENTAL

General Procedures. Solvents were evaporated under reduced pressure below 40 °C bath temperature. Melting points were determined with an Electrothermal 8100 apparatus and are uncorrected. Optical rotations were obtained at 20±2 °C with a Perkin-Elmer 241 polarimeter. IR spectra were recorded with a Midac FT-IR spectrophotometer. ^{1}H NMR (200.13 MHz) and ^{13}C NMR (50.33 MHz) were obtained on Bruker AC 200 E instrument with tetramethylsilane as internal reference and deuteriochloroform as solvent. NMR assignments were facilitated by addition of deuterium oxide and decoupling methods. TLC was performed on silica gel 60 GF_{254} (Merck), with visualization of spots by UV light or iodine vapour; solvents were a) chloroform-acetone, 9:1, b) ethyl acetate-ethanol and c) diethyl ether-petroleum ether, 2:1. Elemental analyses were determined by the Servicio de Microanálisis de la Universidad de Extremadura with a Perkin-Elmer 240 C Elemental Analyser.

3,6-Anhydro-2-deoxy-D-glucose (3). A solution of (2*E*)-4,6-di-*O*-acetyl-2,3-dideoxy-*aldehydo*-D-*erythro*-hex-2-enose[9] (**1**, 8.27 g, 35.92 mmol) in methanol-water-triethylamine (5:4:1, 240 mL) was stirred at room temperature while the course of the reaction was monitored by TLC (solvent *a*). After 40 min, the starting material (R_F 0.33) disappeared, and the reaction mixture was decolorized with activated charcoal. The solvents were removed under reduced pressure to a syrup that was chromatographed on a short column of silica gel

(gradient solvent *b*: 9:1 to 3:7), yielding 4.31 g (82%) of a colorless oil. Anomeric mixture (^{1}H NMR): **10**α:**10**β = 2:1: $[\alpha]_D$ +37.5°, $[\alpha]_{578}$ +39°, $[\alpha]_{546}$ +43.5°, $[\alpha]_{436}$ +67°, $[\alpha]_{365}$ +92.5° (*c* 1.21, water). Lit.[4] $[\alpha]_D$ +36.3 (*c* 1.1, water); IR (film) 3366 (OH), 1120, 1081, 1011 (C-O, C-O-C) cm^{-1}; ^{1}H NMR **10**α δ 6.20 (m, 2 H, D_2O exchangeable OH-1,5), 5.49 (br d, 1 H, $J_{1,2}$ ~0 Hz, $J_{1,2'}$ = 4.5 Hz, H-1), 4.62 (m, 1 H, H-3), 4.40 (t, 1 H, $J_{3,4} = J_{4,5}$ = 4.8 Hz, H-4), 4.02 (m, 1 H, H-5), 3.67 (dd, 1 H, $J_{5,6}$ = 6.3 Hz, H-6), 3.33 (t, 1 H, $J_{5,6'} = J_{6,6'}$ = 8.2 Hz, H-6'), 1.91-2.04 (m, 2 H, H-2,2'); **10**β δ 6.20 (m, 2 H, D_2O exchangeable OH-1,5), 5.48 (br d, 1 H, $J_{1,2}$ = 4.5 Hz, $J_{1,2'} \leq 1$ Hz, H-1), 4.49 (m, 2 H, H-3,4), 4.02 (m, 1 H, H-5), 3.73 (dd, 1 H, $J_{5,6}$ = 6.3 Hz, H-6), 3.59 (dd, 1 H, $J_{5,6'}$ = 5.8 Hz, $J_{6,6'}$ = 8.5 Hz, H-6'), 2.09 (dt, 1 H, $J_{2,2'}$ = 14.3 Hz, $J_{2,3}$ = 5.0 Hz, H-2), 1.82 (br d, 1 H, $J_{2',3} \leq 1$ Hz, H-2'); ^{13}C NMR **10**α δ 99.8 (C-1), 81.6 (C-3), 80.4 (C-4), 71.9 (C-5), 70.1 (C-6), 42.4 (C-2); **10**β δ 99.3 (C-1), 83.6 (C-4), 82.0 (C-3), 71.8 (C-6), 71.1 (C-5), 41.3 (C-2).

Treatment of compound **3** with (2,4-dinitrophenyl)hydrazine yielded its crystalline (2,4-dinitrophenyl)hydrazone **4**: mp 157-159 °C (from ethanol-benzene); Lit.[4] mp 122-124 °C; $[\alpha]_D$ +10°, $[\alpha]_{578}$ +11°, $[\alpha]_{546}$ +15° (*c* 0.35, pyridine); IR (KBr) 3437 (OH), 3293 (NH), 1736 (C=N), 1618 (C=C), 1520, 1340 (NO_2) cm^{-1}; ^{1}H NMR δ 11.35 (s, 1H, NH), 8.82 (d, 1H, $J_{3Ar,5Ar}$ = 2.6 Hz, H-3arom), 8.31 (dd, 1H, $J_{5Ar,6Ar}$ = 9.7 Hz, H-5arom), 8.03 (t, 1H, $J_{1,2} = J_{1,2'}$ = 5.4 Hz, H-1), 7.83 (d, 1H, H-6arom), 4.94 (d, 1H, $J_{H,OH}$ = 5.9 Hz, D_2O exchangeable 5-OH), 4.83 (d, 1H, $J_{H,OH}$ = 4.7 Hz, D_2O exchangeable 4-OH), 4.22 (m, 1H, H-5), 4.01 (m, 2H, H-3,4), 3.73 (dd, 1H, $J_{5,6}$ = 6.6 Hz, $J_{6,6'}$ = 8.3 Hz, H-6), 3.53 (dd, 1H, $J_{5,6'}$ = 6.5 Hz, H-6'), 2.62 (t, 2H, $J_{2,3}$ = 5.4 Hz, H-2,2'); ^{13}C NMR δ 153.2 (C-1), 144.6 (C-1arom), 136.4 (C-4arom), 129.6 (C-5arom), 128.5 (C-2arom), 122.9 (C-3arom), 116.3 (C-6arom), 78.3 (C-3), 71.2, 71.1 (C-4,5), 70.6 (C-6), 33.3 (C-2).

Anal. Calcd for $C_{12}H_{14}N_4O_7$: C, 44.17; H, 4.33; N, 17.17. Found: C, 43.78; H, 4.25; N, 17.30.

Compound **4** was acetylated (Ac_2O/Py) to give **5**: mp 148-150 °C (from ethanol-benzene); $[\alpha]_D$ +18°, $[\alpha]_{578}$ +19°, $[\alpha]_{546}$ +24° (*c* 0.70, chloroform); IR (KBr) 3300 (NH), 1746 (C=O), 1618 (C=C, C=N), 1518, 1381 (NO_2); ^{1}H NMR δ 11.08 (s, 1H, NH), 9.08 (d, 1H, $J_{3Ar,5Ar}$ = 2.5 Hz, H-3arom), 8.30 (dd, 1H, $J_{5Ar,6Ar}$ = 9.6 Hz, H-5arom), 7.90 (d, 1H, H-6arom), 7.62 (t, 1H, $J_{1,2} = J_{1,2'}$ = 5.2 Hz, H-1), 5.55 (t, 1H, $J_{3,4} = J_{4,5}$ = 5.1 Hz, H-4), 5.46 (q, 1H, H-5), 4.36 (dt, $J_{2,3}$ = 7.3 Hz, $J_{2',3}$ = 5.1 Hz, H-3), 4.08 (dd, $J_{5,6}$ = 6.2 Hz, $J_{6,6'}$ = 9.9 Hz, H-6), 3.92 (dd, 1H, $J_{5,6'}$ = 5.0

Hz, H-6´), 2.9-2.7 (m, 2H, H-2,2´), 2.15 (s, 3H, 1 OAc), 2.01 (s, 3H, 1 OAc); ^{13}C NMR δ 169.9, 169.7 ($OCOCH_3$), 148.5 (C-1), 144.8 (C-1arom), 137.9 (C-4arom), 129.9 (C-5arom), 128.8 (C-2arom), 123.3 (C-3arom), 116.4 (C-6arom), 76.5 (C-3), 71.9 (C-4,5), 69.4 (C-6), 32.9 (C-2), 20.5 ($OCOCH_3$).

Anal. Calcd for $C_{16}H_{18}N_4O_9$: C, 46.83; H, 4.42; N, 13.65. Found: C, 46.73; H, 4.33; N, 13.55.

3,6-Anhydro-2-deoxy-4,5-*O*-isopropylidene-D-glucose (6). To a solution of 3,6-anhydro-2-deoxy-D-glucose (**3**, 1.0 g, 7.1 mmol) in dry acetone was added anhydrous copper (II) sulfate (9.62 g, 60.27 mmol) and the mixture was stirred at room temperature. After 5 days, TLC (solvent *a*) showed that the reaction had stabilized, with spots at R_F 0.51, 0.32, and 0.15 (starting material). The copper sulfate was filtered and washed on the filter with acetone. The filtrate was concentrated to an oil that was dissolved in chloroform and eluted through a short column of silica gel with a gradient of chloroform and acetone (100:0 to 0:100). Fractions containing compound of R_F 0.51 afforded **6** as an oil (0.3 g, 23%): ^{1}H NMR δ 9.82 (t, 1H, $J_{1,2} = J_{1,2'} = 1.3$ Hz, C*H*O), 4.80 (dd, 1H, $J_{5,6'} = 3.5$ Hz, H-5), 4.71 (dd, 1H, $J_{4,5} = 6.1$ Hz, H-4), 4.00 (d, 1H, $J_{6,6'} = 10.8$ Hz, $J_{5,6} \sim 0$ Hz, H-6), 3.88 (dt, 1H, $J_{3,4} = 3.6$ Hz, H-3), 3,48 (dd, 1H, H-6´), 2.88 (dd, 2H, $J_{2,3} = 6.3$ Hz, H-2,2´), 1.46 and 1.31 (2s, 2x3H, C*Me*$_2$); ^{13}C NMR δ 200.0 (*C*HO), 112.1 (*C*Me$_2$), 81.0, 80.7 (C-4,5), 77.3 (C-3), 72.6 (C-6), 43.0 (C-2), 25.8 and 24.6 (C*Me*$_2$).

The (2,4-dinitrophenyl)hydrazone[25] **7** of **6** had a mp 125-126 °C after recrystallization from methanol-benzene: $[\alpha]_D$ -40°, $[\alpha]_{578}$ -41°, $[\alpha]_{546}$ -42° (*c* 0.5, chloroform); IR (KBr) 3295 (NH), 1615, 1595 (C=N, C=C), 1518, 1323 (NO_2), 1144, 1090 (C-O-C) cm^{-1}; ^{1}H NMR δ 11.08 (s, 1H, NH), 9.10 (d, 1H, $J_{3Ar,5Ar} = 2.5$ Hz, H-3arom), 8.29 (dd, 1H, $J_{5Ar,6Ar} = 9.6$ Hz, H-5arom), 7.92 (d, 1H, H-6arom), 7.66 (t, $J_{1,2} = J_{1,2'} = 5.2$ Hz, H-1), 4.85 (dd, 1H, $J_{4,5} = 5.6$ Hz, $J_{5,6'} = 3.7$ Hz, $J_{5,6} \sim 0$ Hz, H-5), 4.73 (dd, 1H, $J_{3,4} = 3.3$ Hz, H-4), 4.05 (d, 1H, $J_{6,6'} = 10.8$ Hz, H-6), 3.77 (td, 1H, $J_{2,3} = J_{2',3} = 6.5$ Hz, H-3), 3.53 (dd, 1H, H-6´), 2.88 (m, 2H, H-2,2´), 1.52 and 1.36 (2 s, 2x3H, C*Me*$_2$); ^{13}C NMR δ 149.5 (C-1), 145.0 (C-1arom), 137.8 (C-4arom), 129.9 (C-5arom), 128.8 (C-2arom), 123.4 (C-3arom), 116.5 (C-6arom), 112.3 (*C*Me$_2$), 81.1, 80.8 (C-4,5), 79.6 (C-3), 72.7 (C-6), 32.1 (C-2), 26.0 and 24.7 (C*Me*$_2$).

Anal. Calcd for $C_{15}H_{18}N_4O_7$: C, 49.18; H, 4.95; N, 15.29. Found: C, 49.22; H, 4.97; N, 15.00.

The fractions of R_F 0.32 gave 3,6-anhydro-2-deoxy-4,5-*O*-isopropylidene-D-gluconic acid **8** as a syrup (0.33 g, 23%): $[\alpha]_D$ +10°, $[\alpha]_{578}$ +10.5°, $[\alpha]_{546}$ +11.5°, $[\alpha]_{436}$ +17°, $[\alpha]_{365}$ +23° (*c* 0.88, chloroform); IR (film) 3428 (OH), 1730 (C=O), 1212, 1096, 1004 (C-O, C-O-C) cm^{-1}; ^1H NMR δ 10.5 (br s, 1H, COO*H*), 4.80 (dd, 1H, $J_{5,6'}$ = 3.5 Hz, H-5), 4.72 (dd, 1H, $J_{4,5}$ = 6.2 Hz, H-4), 3.99 (d, 1H, $J_{6,6'}$ = 10.8 Hz, $J_{5,6}$ ~ 0 Hz, H-6), 3.87 (td, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 3.50 (dd, 1H, H-6′), 2.80 (d, 2H, $J_{2,3}$ = 6.1 Hz, H-2,2′), 1.48 and 1.33 (2s, 2x3H, C*Me*$_2$); ^{13}C NMR δ 174.3 (*C*OOH), 112.0 (*C*Me$_2$), 80.8, 80.4 (C-4,5), 77.9 (C-3), 72.3 (C-6), 32.2 (C-2), 25.7 and 24.5 (C*Me*$_2$).

Ethyl 3,6-Anhydro-2-deoxy-4,5-*O*-isopropylidene-D-gluconate (9). A solution of 3,6-anhydro-2-deoxy-4,5-*O*-isopropylidene-D-gluconic acid (**8**, 0.098 g, 0.48 mmol), *N,N*-dicyclohexylcarbodiimide (0.080 g, 0.51 mmol), ethanol (0.03 mL, 0.51 mmol), and 4-dimethylaminopyridine (0.006 g, 0.05 mmol) in dichloromethane (2.5 mL) was allowed to stand at room temperature. After 7 h, the *N,N*-dicyclohexyl urea was filtered and the filtrate washed with water (3x15 mL), 5% acetic acid solution (3x15 mL) and again with water (3x15 ml), dried ($MgSO_4$), and the solvent concentrated *in vacuo*. The residue was stirred in ether and more *N,N*-dicyclohexyl urea was removed by filtration. Concentration of the ethereal solution gave the title compound (**9**) as an oil (0.05 g, 51%): $[\alpha]_D$ -10.5°, $[\alpha]_{578}$ -11°, $[\alpha]_{546}$ -13°, $[\alpha]_{436}$ -22°, $[\alpha]_{365}$ -51° (*c* 0.51, chloroform); IR (film) 1737 (C=O), 1212, 1096, 1027 (C-O-C) cm^{-1}; ^1H NMR δ 4.78 (dd, 1H, $J_{5,6'}$ = 3.5 Hz, H-5), 4.70 (dd, 1H, $J_{4,5}$ = 6.1 Hz, H-4), 4.17 (q, 2H, J = 7.1 Hz, CH_2-CH$_3$), 3.99 (d, 1H, $J_{6,6'}$ = 10.8 Hz, $J_{5,6}$ ~ 0 Hz, H-6), 3.85 (td, 1H, $J_{3,4}$ = 3.6 Hz, H-3), 3.49 (dd, 1H, H-6′), 2.77 (d, 2H, $J_{2,3}$ = 7.2 Hz, H-2,2′), 1.47 and 1.32 (2s, 2x3H, C*Me*$_2$), 1.27 (t, 3H, CH$_2$-CH_3); ^{13}C NMR δ 171.1 (*C*OOEt), 112.1 (*C*Me$_2$), 81.0, 80.7 (C-4,5), 78.3 (C-3), 72.6 (C-6), 60.6 (*C*H$_2$-CH$_3$), 33.7 (C-2), 25.9 and 24.8 (C*Me*$_2$), 14.1 (CH$_2$-*C*H$_3$).

Methyl 3,6-Anhydro-2-deoxy-α- and β-D-furanosides (11α and 11β). To a solution of **3** (0.88 g, 6.25 mmol) in methanol (6 mL) was added Dowex 50W-X8 resin (0.6 g), and the suspension was heated at reflux for 24 h. The resin was removed by filtration and washed three times with methanol. The filtrate and washings were combined and concentrated to dryness. Analysis by NMR showed the ratio of α:β anomers in the product mixture to be 2:1. After silica gel chromatography (solvent *c*), appropriate fractions (R_F 0.35) were pooled and concentrated to give **11**α (0.3 g, 40%): $[\alpha]_D$ +112°, $[\alpha]_{578}$ + 117°, $[\alpha]_{546}$ +131.5°,

$[\alpha]_{436}$ +214.5°, $[\alpha]_{365}$ +309° (*c* 2.21, water); Lit.[3] $[\alpha]_D$ +111° (*c* 2.1, water); IR (film) 3438 (OH), 1073 (C-O-C) cm^{-1}; ^1H NMR δ 5.24 (dd, 1H, $J_{1,2}$ = 2.0 Hz, $J_{1,2'}$ = 5.0 Hz, H-1), 4.78 (ddd, 1H, H-3), 4.53 (t, 1H, $J_{3,4} = J_{4,5}$ = 5.2 Hz, H-4), 4.23 (m, 1H, H-5), 3.86 (dd, 1H, $J_{5,6}$ = 6.0 Hz, $J_{6,6'}$ = 8.9 Hz, H-6), 3.56 (dd, 1H, $J_{5,6'}$ = 7.4 Hz, H-6′), 3.42 (d, 1H, $J_{H,OH}$ = 8.1 Hz, D_2O exchangeable 5-OH), 3.37 (s, 3H, OCH_3), 2.26 (ddd, 1H, $J_{2,3}$ = 7.1, $J_{2,2'}$ = 14.2 Hz, H-2), 2.12 (ddd, 1H, $J_{2',3}$ = 3.6 Hz, H-2′); ^{13}C NMR δ 106.6 (C-1), 81.3 (C-3), 80.1 (C-4), 71.2 (C-5), 70.5 (C-6), 54.5 (O*C*H_3), 40.3 (C-2).

The fraction of R_F 0.22 gave **11**β (0.09 g, 10%): $[\alpha]_D$ -80°, $[\alpha]_{578}$ -86°, $[\alpha]_{546}$ -90°, $[\alpha]_{436}$ -254°, $[\alpha]_{365}$ -306° (*c* 0.35, water); IR (film) 3436 (OH), 1070 (C-O-C) cm^{-1}; ^1H NMR δ 5.15 (t, 1H, $J_{1,2} = J_{1,2'}$ = 3.2 Hz, H-1), 4.70 (t, 1H, $J_{3,4} = J_{4,5}$ = 5.6 Hz, H-4), 4.58 (m, 1 H, $J_{2,3} = J_{2',3}$ = 3.4 Hz, H-3), 4.19 (m, 1H, H-5), 3.85 (dd, 1H, $J_{5,6}$ = 5.0 Hz, $J_{6,6'}$ = 9.3 Hz, H-6), 3.75 (dd, 1H, $J_{5,6'}$ = 5.4 Hz, H-6′), 3.46 (s, 3H, OCH_3), 2.98 (d, 1H, $J_{H,OH}$ = 10.1 Hz, D_2O exchangeable 5-OH), 2.2-2.1 (m, 2H, H-2,2′); ^{13}C NMR δ 107.4 (C-1), 84.5 (C-4), 81.6 (C-3), 73.2 (C-6), 71.2 (C-5), 56.1 (O*C*H_3), 40.1 (C-2).

Methyl 5-*O*-Acetyl-3,6-anhydro-2-deoxy-α-D-glucofuranoside (12α). Compound **11**α was acetylated (Ac_2O/pyridine) to give **12**α as a syrup: $[\alpha]_D$ +246°, $[\alpha]_{578}$ +256°, $[\alpha]_{546}$ +289.5°, $[\alpha]_{436}$ +481°, $[\alpha]_{365}$ +730° (*c* 0.46, chloroform); IR (film) 1745 (C=O ester), 1243 (C-O), 1081 (C-O-C ether) cm^{-1}; ^1H NMR δ 5.21 (dd, 1H, $J_{1,2}$ = 2.3 Hz, $J_{1,2'}$ = 4.9 Hz, H-1), 5.05 (ddd, 1H, H-5), 4.79 (ddd, 1H, H-3), 4.69 (t, 1H, $J_{3,4} = J_{4,5}$ = 5.0 Hz, H-4), 3.99 (dd, 1H, $J_{5,6}$ = 6.4 Hz, $J_{6,6'}$ = 9.0 Hz, H-6), 3.73 (dd, 1H, $J_{5,6'}$ = 8.0 Hz, H-6′), 3.34 (s, 3H, OCH_3), 2.23 (ddd, 1H, $J_{2,3}$ = 6.7 Hz, $J_{2,2'}$ = 14.2 Hz, H-2), 2.14 (s, 3H, 1 OAc), 2.11 (ddd, 1H, $J_{2',3}$ = 3.6 Hz, H-2′); ^{13}C NMR δ 170.3 (O*C*OCH$_3$), 106.9 (C-1), 81.8 (C-3), 79.0 (C-4), 73.0 (C-5), 67.7 (C-6), 55.0 (O*C*H_3), 40.6 (C-2), 20.6 (OCO*C*H_3).

Methyl 5-*O*-Acetyl-3,6-anhydro-2-deoxy-β-D-glucofuranoside (12β). Compound **11**β was acetylated (Ac_2O/pyridine) to give **12**β as a syrup: $[\alpha]_D$ +22°, $[\alpha]_{578}$ +24.5°, $[\alpha]_{546}$ +35°, $[\alpha]_{436}$ +96°, $[\alpha]_{365}$ +129° (*c* 0.39, chloroform); IR (film) 1745 (C=O ester), 1243 (C-O), 1081 (C-O-C ether) cm^{-1}; ^1H NMR δ 5.08 (t, $J_{1,2} = J_{1,2'}$ = 2.9 Hz, H-1), 5.03 (td, 1H, H-5), 4.80 (t, 1H, $J_{3,4} = J_{4,5}$ = 5.1 Hz, H-4), 4.74 (m, $J_{2,3} = J_{2',3}$ = 3.0 Hz, H-3), 3.98 (d, 2H, $J_{5,6} = J_{5,6'}$ = 7.2 Hz, H-6,6′), 3.39 (s, 3H, OCH_3), 2.15 (m, 2H, H-2,2′), 2.13 (s, 3H, 1 OAc); ^{13}C NMR δ 170.4 (O*C*OCH$_3$), 106.3 (C-1), 82.0, 81.5 (C-3,4), 73.5 (C-5), 67.8 (C-6), 55.1 (O*C*H_3), 41.2 (C-2), 20.7 (OCO*C*H_3).

1,5-Di-*O*-acetyl-3,6-anhydro-2-deoxy-α- and β-D-Gluco-furanosides (13α and 13β). Compound **3** (0.65 g, 4.45 mmol) was acetylated (Ac_2O/pyridine), yielding the mixture **13**α,β (0.8 g, 78%) as an oil. Analysis by NMR showed the ratio of α:β anomers to be 4.9:1. After column chromatography on silica gel (solvent *c*), appropriate fractions (R_F 0.35) were pooled and concentrated to give **13**α (0.35 g): $[\alpha]_D$ +139°, $[\alpha]_{578}$ +145°, $[\alpha]_{546}$ +164°, $[\alpha]_{436}$ +275°, $[\alpha]_{365}$ +423° (*c* 0.52, chloroform); IR (film) 1745 (C=O ester), 1235, 1104, 1081 (C-O, C-O-C) cm^{-1}; ^1H NMR δ 6.46 (t, $J_{1,2} = J_{1,2'} = 3.9$ Hz, H-1), 5.05 (m, 1H, H-5), 4.9-4.7 (m, 2H, H-3,4), 4.00 (dd, $J_{5,6} = 6.3$ Hz, H-6), 3.76 (dd, $J_{6,6'} = 9.1$ Hz, $J_{5,6'} = 7.3$ Hz, H-6'), 2.33 (m, 2H, H-2,2'), 2.13 (s, 3H, 1 OAc), 2.04 (s, 3H, 1 OAc); ^{13}C NMR δ 169.8, 169.1 ($OCOCH_3$), 99.2 (C-1), 80.6 (C-3,4), 72.4 (C-5), 67.5 (C-6), 39.6 (C-2), 20.5, 20.0 ($OCOCH_3$).

The fractions of R_F 0.17 gave **13**β (0.06 g): $[\alpha]_D$ +55.5°, $[\alpha]_{578}$ +57.5°, $[\alpha]_{546}$ +65°, $[\alpha]_{436}$ +108°, $[\alpha]_{365}$ +163.5° (*c* 0.55, chloroform); IR (film) 1737 (C=O ester), 1251, 1120, 1073 (C-O, C-O-C) cm^{-1}; ^1H NMR δ 6.30 (dd, 1H, $J_{1,2} = 4.0$, $J_{1,2'} = 2.1$ Hz, H-1), 5.04 (td, $J_{5,6} = J_{5,6'} = 7.4$ Hz, H-5), 4.87 (t, 1 H, $J_{3,4} = J_{4,5} = 5.1$ Hz, H-4), 4.77 (td, 1H, $J_{2,3} = 5.1$ Hz, $J_{2',3} = 2.1$ Hz, H-3), 4.04 (d, 1H, $J_{6,6'} \sim 0$ Hz, H-6), 4.03 (d, 1H, H-6'), 2.30 (m, 2H, H-2,2'), 2.09 (s, 3H, 1 OAc), 2.08 (s, 3H, 1 OAc); ^{13}C NMR δ 169.7, 169.5 ($OCOCH_3$), 98.6 (C-1), 82.5 (C-3), 81.2 (C-4), 72.7 (C-5), 68.1 (C-6), 39.6 (C-2), 20.6, 19.9 ($OCOCH_3$).

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