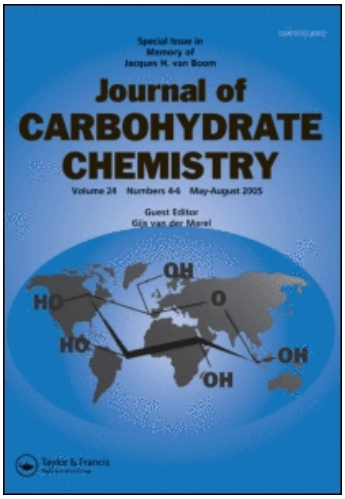

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CONVENIENT SYNTHESIS OF 2-DEOXY-D-GLUCOFURANOSIDES

José Molina Arévalo and Claire Simons*

Medicinal Chemistry Division, Welsh School of Pharmacy,
Cardiff University, Cardiff CF1 3XF, U.K.

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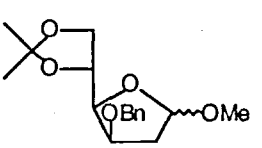
ABSTRACT

Methyl 2-deoxy-D-glucofuranoside has been conveniently prepared starting from 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose, involving the first described deoxygenation at the 2-position.

INTRODUCTION



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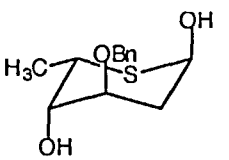
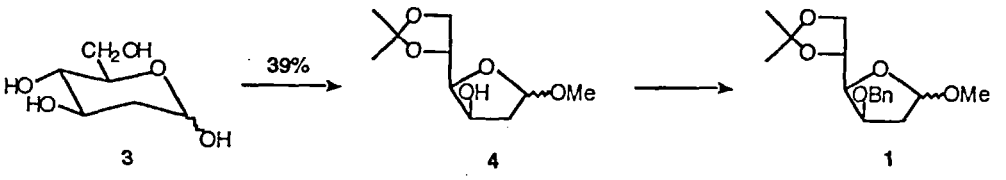


2

This work stemmed from our efforts to prepare 2-deoxy-D-glucofuranosides **1** as useful intermediates in the synthesis of 2,6-dideoxy-5-thio-pyranosides **2**.[1] The well established method[2] for preparing 2-deoxy-glucofuranosides involves the treatment of 2-deoxy-D-glucose **3** with 2,2-dimethoxypropane in the presence of catalytic *p*-TsOH·H_2O to give **4**, followed by modification at the 3-position (Scheme 1).



Scheme 1

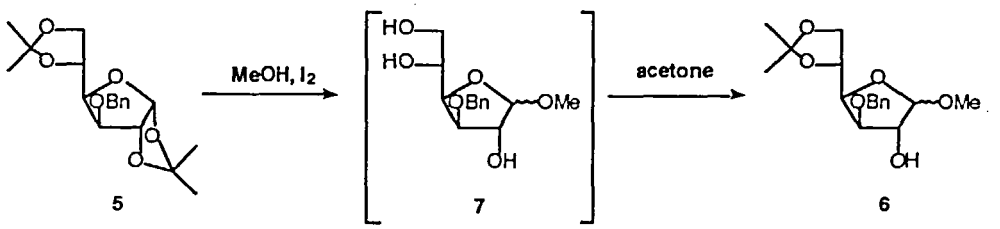
However the cost of **3**, coupled with the low yield of **4** (39%) owing to purification difficulties resulting from the formation of many furanose/pyranose by-products, led us to search for a more convenient, cost-effective synthesis. We describe here a convenient synthesis of 2-deoxy-D-glucofuranosides.

RESULTS AND DISCUSSION

The starting material for the synthesis was the inexpensive 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose which was readily modified to give the 3-*O*-benzyl derivative **5**[3] in quantitative yield. The next step of the synthesis required selective removal of the 1,2-isopropylidene group and methylation at the anomeric position. It has been shown[4] that treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose with 0.5% iodine and methanol at reflux temperatures removes both the 1,2- and 5,6-*O*-isopropylidene groups to give the methyl glycoside. However, treatment of **5** under the same conditions produced the expected methyl glycoside **7** (identified by nmr) in 48% yield and the 5,6-isopropylidene protected compound **6** in 41% yield. When acetone was then added to the I_2/MeOH reaction mixture and heating continued, the percentage of the 5,6-isopropylidene protected compound **6** increased to 71% and **7** decreased to 19% (Scheme 2).

Therefore in a one-pot reaction, in the presence of the soft acid iodine, it is possible to remove the isopropylidene groups of **5**, form the methyl glycoside and reprotect at the 5,6-positions in excellent yield.

Anomeric assignment of compound **6** was determined from molecular modelling calculations (MOPAC, AM1 forcefield), the theoretical H(1)-C(1)-C(2)-H(2) bond angle was calculated as 17.6° for the α-anomer and 119.3° for the β-anomer. By substituting these values into the Karplus-Conroy equation[5] the theoretical $J_{1,2}$ coupling values would



Scheme 2

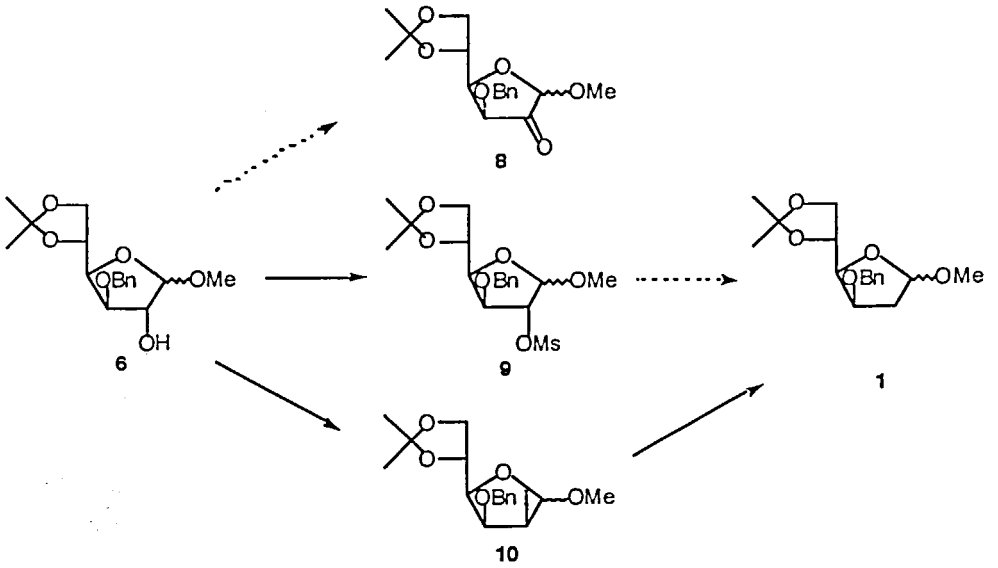
be 7.4 Hz for the α-anomer and 2 Hz for the β-anomer. Based on the observed values, approximately 5 Hz (α) and 0 Hz (β), the α- and β-anomers were assigned.

Although deoxygenation at the 3-position of glucofuranosides has been well described,[6] to the best of our knowledge deoxygenation at the 2-position of glucofuranosides has not been reported in the literature. We made several attempts to deoxygenate at the 2-position, the first route involving oxidation with PDC or TPAP/NMMO or under Swern conditions, to prepare the keto compound **8**, with the aim of then deoxygenating with *t*-butylamine-borane/$AlCl_3$,[7]. However, oxidation failed with either no reaction occurring or complex mixtures were formed.

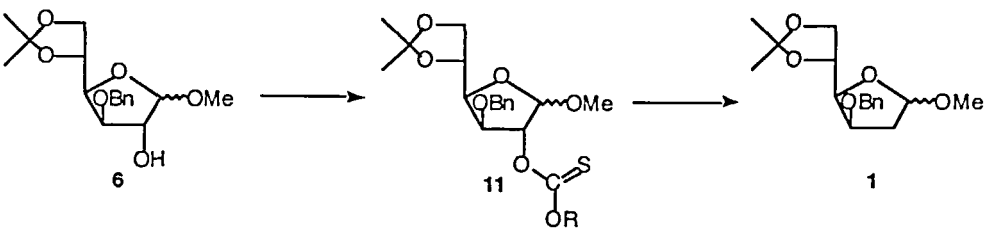
In the second route, the mesylate **9** was prepared in 96% yield, however reaction of **9** with either $LiAlH_4$ or super hydride only produced the starting alcohol **6** (38%) and recovered mesylate (28%). The third route involved preparation of the iodo-compound **10** in a yield of 38% (α:β 9:1 based on $J_{1,2}$ coupling values), by reaction with triiodo-imidazole.[8] Treatment of **10** with $LiAlH_4$ did produce the 2-deoxy sugar **1** but in only 13% yield and only the α-anomer was isolated (Scheme 3).

The final method to prepare **1** was by radical deoxygenation,[9] a method that proved to be very successful. The pentafluorophenoxythiocarbonyl ester (**11**, R = pentafluorophenyl) was prepared in 75% yield. On treatment with tributlytin hydride and AIBN for 30 minutes at 110 °C, the target compound methyl 3-*O*-benzyl-2-deoxy-5,6-*O*-isopropylidene-α/β-glucofuranoside **1** was produced in 68% yield (Scheme 4). The ^1H NMR spectrum of **11** was complicated with diastereoisomers (possibly at C2) of both anomers observed. Presumably the bulky pentafluorophenyl group results in conformational restriction of the sugar allowing observation of individual diastereoisomers by NMR.

The phenoxy and tetrafluorophenoxy thiocarbonyl compounds (**11**, R = phenyl and tetrafluorophenyl respectively) were also prepared, both produced **1** on treatment with tributyltin hydride and AIBN but in lower yields (48 and 52% respectively).



Scheme 3



Scheme 4

CONCLUSION

In this paper, we have described an alternative and more convenient synthesis of 2-deoxy-glucofuranosides involving two novel procedures. The first involves the one-pot synthesis of methyl 3-*O*-benzyl-5,6-*O*-isopropylidene-α/β-glucofuranoside **6**, the second involves the first described deoxygenation at the 2-position of **6** to give the target compound **1**, in an overall yield of 51% from 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**).

EXPERIMENTAL

General methods. ^1H and ^{13}C NMR spectra were recorded with a Brucker Avance DPX300 spectrometer operating at 300 and 75 MHz respectively in $CDCl_3$ unless stated otherwise, with Me_4Si as internal standard. Chemical shifts are expressed in parts per million downfield from TMS. Microanalyses were determined at the department of chemistry, Cardiff University. Flash column chromatography was performed with silica gel 60 (230-400 mesh) (Merck) and TLC were carried out on precoated silica plates (kiesel gel 60 F_{254}, BDH). Melting points were measured with a Gallenkamp Melting Point Apparatus and are reported uncorrected. All the reactions were carried out under nitrogen using anhydrous solvents from Aldrich except for acetone which was obtained from Fisher and dried over 4 Å molecular sieves.

Methyl 3-*O*-Benzyl-5,6-di-*O*-isopropylidene-α,β-D-glucofuranoside (6). A solution of 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5**) (4.01g, 11.45 mmol) in 0.5% w/v iodine/methanol (70 mL) was refluxed (oil bath: 80 °C) for 5 h. The mixture was allowed to cool to room temperature, acetone (35 mL) was added and the new reaction mixture stirred at 70 °C for 10 h. Excess iodine was reduced with aqueous sodium thiosulphate and the mixture was filtered. The filtrate was concentrated and the residue was dissolved into ethyl acetate (200 mL) and washed with water (2 x 50 mL) and brine (40 mL). The aqueous layer was extracted with ethyl acetate (3 x 40 mL) and the organic fractions were combined, dried over $MgSO_4$, filtered and concentrated to give 3.45 g of an oil that was purified by column chromatography (petroleum ether - ethyl acetate 3:1 v/v, then chloroform - methanol from 100:1 to 20:1 v/v) to give 2.65 g (71%) of **6**, with both anomers obtained as pale yellow oils, and 610 mg (19%) of compound **7** with the α-anomer obtained as a white solid (mp 95-96 °C) and the β-anomer as a pale yellow oil. Compound **6**, *α-anomer* : ^1H NMR δ 7.43 (m, 5, Ph), 5.07 (d, $J_{1,2}$ = 4.5 Hz, 1, H-1), 4.72 (dd, $J_{A,B}$ = 11.7 Hz, 2, O-CH_2-Ph), 4.42 (dd, J = 6.0, 12.3 Hz, 1), 4.32 (dd overlapped, J = 5.3 Hz, 1), 4.24 (m, 1), 4.13 (dd, J = 6.4, 8.3 Hz, 1), 4.04 (m, 2), 3.55 (s, 3, OCH_3), 2.95 (bs, 1, OH), 1.50 (s, 3, CH_3), 1.42 (s, 3, CH_3); ^{13}C NMR δ 138.39 (C, Ph), 128.78, 128.32 and 128.10 (CH, Ph), 109.27 (C, CMe_2), 102.61 (CH, C-1), 84.01 (CH), 79.58 (CH), 77.90 (CH), 73.93 (CH), 72.39 (CH_2, CH_2-Ph), 67.03 (CH_2, C-6), 56.32 (CH_3, OCH_3) 27.03 (CH_3), 25.84 (CH_3). Compound **6**, *β-anomer*: ^1H NMR δ 7.40 (m, 5, Ph), 4.84 (s, 1, H-1), 4.67 (dd, $J_{A,B}$ = 12.1 Hz, 2, O-$C\underline{H}_2$-Ph), 4.42 (m, 2), 4.24 (s, 1), 4.12 (m, 2), 3.95 (m, 1), 3.44 (s, 3, OCH_3), 2.45 (bs, ≈1, OH-2), 1.49 (s, 3, CH_3), 1.43 (s, 3, CH_3); ^{13}C NMR δ 138.29 (C, Ph), 128.80 and 128.19 (CH, Ph), 110.19 (C, CMe_2), 109.27 (CH, C-1), 83.25

(CH), 82.51 (CH), 79.37 (CH), 74.47 (CH), 72.72 (CH_2, CH_2-Ph), 67.35 (CH_2, C-6), 56.30 (CH_3, OCH_3), 27.07 (CH_3), 25.91 (CH_3).

Anal. Calcd for α, β mixture $C_{17}H_{24}O_6$ (324.37): C, 62.95; H, 7.46. Found: C, 63.16; H, 7.48.

Compound **7**, *α-anomer*: ^{1}H NMR δ 7.40 (m, 5, Ph), 4.98 (d, $J_{1,2}$ = 4.5 Hz, 1, H-1), 4.90 (d, $J_{A,B}$ = 11.7 Hz, 1, O-CH_A-Ph), 4.63 (d, $J_{A,B}$ = 11.7 Hz, 1, O-CH_B-Ph), 4.32 (*pseudo* t, J = 3.8, 4.2 Hz, 1), 4.18 (m, J = 6.0, 6.4 Hz, 1), 3.98 (m, 1), 3.83 (dd, J = 3.4, 11.7 Hz, 1), 3.70 (dd, J = 5.7, 11.3 Hz,1), 3.72 (bs, 3, OH), 3.51 (s, 3, OCH_3); ^{13}C NMR δ 137.55 (C, Ph), 129.13, 128.61, 128.32 and 128.23 (CH, Ph), 102.10 (CH, C-1), 84.59 (CH), 77.87 (CH), 77.12 (CH), 72.17 (CH_2, CH_2-Ph), 71.22 (CH), 64.41 (CH_2, C-6), 56.09 (CH_3).

Anal. Calcd for $C_{14}H_{20}O_6$ (284.31): C, 59.14; H, 7.09. Found: C, 59.21; H, 7.29.

Compound **7**, *β-Anomer*: ^{1}H NMR δ 7.34 (m, 5, Ph), 4.78 (s, ≈1.5, H-1 overlapped with O-CH_A-Ph), 4.75 (d, $J_{A,B}$ = 11.7 Hz, ≈0.5, O-CH_A-Ph), 4.54 (d, $J_{A,B}$ = 11.7 Hz, 1, O-CH_B-Ph), 4.24 (m, J = 6.8 Hz, 2), 4.10 (dd, J = 2.3, 6.4 Hz, 1), 3.99 (m, 1), 3.79 (m, J = 3.0 Hz, 1), 3.71 (dd, J = 5.3, 11.7 Hz, 1), 3.35 (s, 3, OCH); ^{13}C NMR δ 135.32 (C, Ph), 126.86, 126.24 and 126.13 (CH, Ph), 107.80 (CH, C-1), 82.18 (CH), 77.52 (CH), 76.95 (CH), 70.51 (CH_2, CH_2-Ph), 68.99 (CH), 62.12 (CH_2, C-6), 53.91 (CH_3).

Anal. Calcd for $C_{14}H_{20}O_6$ (284.31): C, 59.14; H, 7.09. Found: C, 59.22; H, 6.89.

Methyl 3-*O*-Benzyl-5,6-di-*O*-isopropylidene-2-*O*-mesyl-α,β-D-gluco-furanoside (9). Mesyl chloride (147 μL, 216.2 mg, 1.89 mmol) was added dropwise to an ice-cooled solution of **6** (278 mg, 0.86 mmol) in dry dichloromethane (5 mL) and dry pyridine (860 μL). The mixture was stirred at 0 °C for 10 min, then at room temperature for 72 h. The reaction mixture was diluted with ethyl acetate (40 mL) and washed with 5% aqueous $NaHCO_3$ (15 mL), water (2 x 15 mL) and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated and the last traces of pyridine removed by azeotroping with toluene. The residue was purified with a precolumn yielding 330 mg (96%) of an α, β mixture (α/β = 1.27) of **9** as an oil which crystallized, on standing at 4 °C, as a white solid. mp 67-69 °C. ^{1}H NMR δ 7.40 (m, 5, Ph), 5.12 (d, $J_{1,2}$ = 0.6, 4.2 Hz, H-1α), 5.06 (s, 0.44, H-1β), 4.99 (s, ≈0.56, H-2α), 4.95 (*pseudo* t, $J_{2,3}$ = 4.2 Hz, $J_{2,1}$ = 4.1 Hz, ≈0.44, H-2β), 4.72 (dd, $J_{A,B}$ = 11.7 Hz, 2, O-CH_2-Ph), 4.36 (m, 2), 4.12 (m, 3), 3.50 (s, ≈1.7, OCH_3α), 3.47 (s, ≈1.3, OCH_3β), 3.08 (s, ≈1.7, SCH_3α), 3.02 (s, ≈1.3, SCH_3β), 1.50 (s, 3, CH_3), 1.42 (s, 3, CH_3); ^{13}C NMR δ 137.62

(C, Ph), 128.89, 128.44 and 128.33 (CH, Ph), 109.62 (C, CαMe$_2$), 109.45 (C, CβMe$_2$), 107.63 (CH, Cβ-1), 101.14 (CαH, C-1), 85.08 (CβH), 82.82 (CβH), 80.97 (CαH), 80.61 (CβH), 78.45 (CαH), 73.98 (CβH), 73.70 (CαH), 73.40 (CH$_2$, CαH$_2$-Ph), 72.96 (CH$_2$, CβH$_2$-Ph), 67.30 (CH$_2$, Cβ-6), 67.02 (CH$_2$, Cα-6), 56.49 (CH$_3$, OCH$_3$), 39.12 (CH$_3$, SCαH$_3$), 38.72 (CH$_3$, SCβH$_3$), 27.12 (CH$_3$), 25.82 (CH$_3$).

Anal. Calcd for $C_{18}H_{26}O_8S$ (402.46): C, 53.72; H, 6.51. Found: C, 53.51; H, 6.62.

Methyl 3-*O*-Benzyl-2-deoxy-2-iodo-5,6-di-*O*-isopropylidene-α,β-D-glucofuranoside (10). Compound **6** (210 mg, 0.90 mmol), triphenylphosphine (354 mg, 1.35 mmol) and triiodoimidazole (301 mg, 0.68 mmol) were refluxed in dry toluene (15 mL) for 3 h, then additional triiodoimidazole (201 mg, 0.45 mmol) and triphenylphosphine (236 mg, 0.90 mmol) were added and the mixture was refluxed overnight. The cold reaction mixture was poured into saturated aqueous $NaHCO_3$ (15 mL) and stirred for 5 min. Iodine was added until the toluene layer remained iodine-coloured and the mixture stirred for a further 10 min. Saturated aqueous $Na_2S_2O_3$ was added to reduce the excess of iodine and both phases were separated. The toluene layer was diluted with more toluene (20 mL) and washed with water (3 x 20 mL), dried ($MgSO_4$), filtered and concentrated to give a yellow oil that was purified by column chromatography (petroleum ether - ethyl acetate from 6:1 to 2:1 v/v) to give 110 mg (39%) of an α, β mixture (ratio ≈9:1) of **10** as a pale yellow oil and 38 mg of an unknown compound. Only the NMR data from the major anomer (alpha) is given: ^{1}H NMR δ 7.25 (m, 5, Ph), 5.23 (d, $J_{1,2}$ = 4.5 Hz, 1, H-1), 4.68 (dd, $J_{A,B}$ =10.6 Hz, 2, O-CH$_2$-Ph), 4.33 (*pseudo* q, J = 6.0, 6.4, 7.2 Hz, 1), 4.10 (m, 3), 3.96 (m, 2), 3.36 (s, 3, OCH$_3$), 1.39 (s, 3, CH$_3$), 1.33 (s, 3, CH$_3$); ^{13}C NMR δ 137.87 (C, Ph), 128.86 (CH, Ph), 128.78 (CH, Ph), 126.27 (CH, Ph), 112.25 (CH, C-1), 109.62 (C, CMe$_2$), 80.60 (CH), 79.45 (CH), 74.58 (CH$_2$-Ph), 73.91 (CH), 67.69 (CH$_2$, C-6), 56.77 (CH$_3$, OCH$_3$), 30.00 (CH, C-2), 27.24 (CH$_3$), 25.88 (CH$_3$).

Anal. Calcd for α, β mixture $C_{17}H_{23}O_5I$ (434.27): C, 47.02; H, 5.34. Found: C, 47.15; H, 5.36.

Methyl 3-*O*-Benzyl-2-*O*-(pentafluorophenoxy)thiocarbonyl-5,6-di-*O*-isopropylidene-α,β-D-glucofuranoside (11). Compound **6** (370 mg, 1.14 mmol) was dissolved in dry acetonitrile (17 mL) and dimethylaminopyridine (349 mg, 2.85 mmol) was added slowly portionwise followed by pentafluorophenyl chlorothionoformate (275 μL, 450 mg, 1.71 mmol). The reaction mixture was stirred at room temperarture for 16 h, then acetonitrile was evaporated and the residue was dissolved in ethyl acetate and filtered through a pad of silica. The filtered solution was

concentrated and the residue purified by circular chromatography (first petroleum ether, then petroleum ether - ethyl acetate from 8:1 to 6:1 v/v) to give 405 mg (64%) of one of the anomers of the title compound and 68 mg (11%) of the other, both as pale yellow oils. Each anomer was a mixture of diastereoisomers (ratio: 3:1). Total yield: 473 mg (75%). For the NMR data the diastereoisomers are distinguished using non-prime (major) and prime (minor) symbols. Indeed, the major diastereomer (non-prime) of anomer 2 was itself another diastereoisomeric mixture (ratio: 2:1), these two diastereomers, are distinguished using left hand side superscript 1 (major) and 2 (minor) in the value of the integral for ^{1}H NMR and in the symbol C, in ^{13}C NMR *Anomer 1*: ^{1}H NMR δ 7.45 (m, 5, Ph), 5.56 (s, 0.25, H'-1), 5.42 (*pseudo* td, J = 3.8 Hz, 0.75, H-2), 5.35 (d, J = 5.2Hz, 0.75, H-1), 5.18 (s, 0.25, H'-2), 4.89 (d, $J'_{A,B}$ = 12.1 Hz, 0.25, O-CH'$_2$-Ph), 4.73 (m, $J_{A,B}$ = 11.7 Hz, 1.75, O-CH$_2$-Ph overlapped with the second doublet of O-CH'$_2$-Ph), 4.49 (m, 2), 4.37 (t, J = 6.0 Hz, 0.75), 4.14 (m, 2.25), 3.51 (s, 0.75, OCH'$_3$), 3.47 (s, 2.25, OCH$_3$), 1.51 (s, 3, CH$_3$), 1.44 (s, 3, CH$_3$); ^{13}C NMR δ 189.72 (C, CS), 188.63 (C, C'S), 135.43 (C, Ph), 126.74, 126.62, 126.29, 126.19, and 126.04 (CH and C'H, Ph), 107.47 (C, CMe$_2$), 107.24 (C, C'Me$_2$), 104.99 (CH, C'-1), 98.31 (CH, C-1), 87.89 (C'H), 86.07 (CH), 81.51 (C'H), 78.53 (CH), 77.76 (C'H), 76.52 (CH), 71.88 (C'H), 71.48 (CH), 71.05 (CH$_2$, CH$_2$-Ph), 70.82 (CH$_2$, C'H$_2$-Ph), 65.13 (CH$_2$, C'-6), 64.82 (CH$_2$, C-6), 54.39 (CH$_3$, OCH$_3$), 54.27 (CH$_3$, OC'H$_3$), 24.84 (CH$_3$), 23.63 (CH$_3$).

Anal. Calcd for $C_{24}H_{23}O_7SF_5$ (550.50): C, 52.36; H, 4.21. Found: C, 52.49; H, 4.28.

Anomer 2: ^{1}H NMR δ 7.40 (m, 5, Ph), 5.57 (s, 0.75, H-1), 5.44 (t, J = 3.4 Hz, 0.25), 5.31 (*pseudo* t, J = 4.5, 6.4 Hz, 0.25), 5.09 (s, ^{2}0.25), 5.06 (s, ^{1}0.50), 4.90 (m, J = 12.4, 12.1 Hz, two doublets from A,B and A',B' system overlapped, 0.75, O-CH$_2$-Ph and O-CH'$_2$-Ph), 4.70 (m, J = 12.1 Hz, 1.75, O-CH$_2$-Ph and O-CH'$_2$-Ph), 4.46 (m, J = 6.0, 6.4 Hz, 1), 4.34 (m, J = 5.7, 6.4, 6.8 Hz, 1), 4.13 (m, 3), 3.50 (s, ^{2}0.75, OCH$_3$), 3.48 (s, ^{1}1.50, OCH$_3$), 3.38 (s, 0.75, OCH'$_3$), 1.49 (s, ^{2}1, CH$_3$), 1.48 (s, ^{1}2, CH$_3$), 1.43 (s, 3, CH'$_3$); ^{13}C NMR δ 193.59 (C, C'S), 192.68 (C, CS), 137.94 (C, Ph), 128.85, 128.74, 128.70, 128.34, 128.32, 128.24, 128.19 and 128.14 (CH and C'H, Ph), 109.53, 109.31 and 109.28 (C, ^{1}CMe$_2$, ^{2}CMe$_2$, and C'Me$_2$), 107.58 (CH, ^{2}C-1), 107.48 (CH, ^{1}C-1), 100.68 (CH, C'-1), 87.91 (CH), 86.26 (C'H), 83.67 (^{2}CH), 83.62 (^{1}CH), 80.91 (C'H), 79.91 (CH), 78.62 (C'H), 74.04 (CH), 73.69 (C'H), 73.08 (CH$_2$, O-C'H$_2$-Ph), 72.65 (CH$_2$, O-^{2}CH$_2$-Ph), 72.61 (CH$_2$, O-^{1}CH$_2$-Ph), 67.39 (CH$_2$, C-6), 66.99 (CH$_2$, C'-6), 56.42 and 56.28 (CH$_3$, OCH$_3$ and OC'H$_3$), 27.07, 27.01 and 25.82 (CH$_3$, ^{1}CH$_3$, ^{2}CH$_3$ and C'H$_3$).

Anal. Calcd for $C_{24}H_{23}O_7SF_5$ (550.50): C, 52.36; H, 4.21. Found: C, 52.54; H, 4.40.

Methyl 3-*O*-Benzyl-2-deoxy-5,6-di-*O*-isopropylidene-α-D-gluco-furanoside (1) from (10). Commercially available 1M lithium aluminium hydride in ether (5.75 mL, 218.2 mg, 5.75 mmol) was carefully added at room temperature with exclusion of moisture, to a solution of **10** (α-anomer, 624 mg, 1.44 mmol) in 1:1 ether/benzene (30 mL). The mixture was then refluxed (oil bath at 78 °C) for 17 h. The reaction was carefully quenched and diluted with ethyl acetate (10 mL and 70 mL respectively), then washed with water (3 x 40 mL) and brine (40 mL). The aqueous layer was extracted (3 x 40 mL) and all the combined organics extracts were dried over $MgSO_4$, filtered and concentrated. The resulting pale yellow oil was purified by circular chromatography (petroleum ether - ethyl acetate, from 15:1 to 10:1 v/v) to give only the α-anomer of the required product **1**. Yield: 58 mg (13%). For analytical data see below.

Methyl 3-*O*-Benzyl-2-deoxy-5,6-di-*O*-isopropylidene-α,β-D-gluco furanoside (1) from (11). Tributhyltin hydride (320 μL, 345 mg, 1.18 mmol) was added to a solution of compound **11** (326 mg 0.59 mmol) in toluene (12 mL), followed by a catalytic amount of AIBN (6 mg). The mixture was then refluxed (oil bath at 110 °C) for 30 min, the toluene was evaporated and the residue purified by circular chromatography (petroleum ether - ethyl acetate, from 8:1 to 4:1 v/v) to give 43 mg (23%) of the α-anomer as a colourless oil that showed identical analytical data to the product (**1**α) obtained from the reaction of **10**α, and 82 mg (45%) of the β-anomer as a colourless oil. Total yield: 125 mg (68%). *α-anomer*: ^{1}H NMR δ 7.38 (m, 5, Ph), 5.20 (m, $J_{1,2''}$ = 3.0 Hz, 1, H-1), 4.60 (dd, *pseudo AB system*, J = 12.1, 12.4 Hz, 2, O-CH_2-Ph), 4.26 (m, 1), 4.18 (m, J = 6.0, 6.4, 7.7 Hz, 1), 4.07 (m, J = 3.0, 3.4 Hz, 2), 3.40 (s, 3, OCH_3), 2.32 (ddd, $J_{2',2''}$= 14.3 Hz, J = 1.9, 5.7 Hz, 1, H-2'), 2.11 (ddd, $J_{2',1}$ =3.0 Hz, $J_{2'',2'}$ = 14.3 Hz, J = 6.0 Hz, 1, H-2''), 1.50 (s, 3, CH_3), 1.45 (s, 3, CH_3); ^{13}C NMR δ 139.08 (C, Ph), 128.75, 128.22 and 127.87 (CH, Ph), 109.33 (C, CMe_2), 104.93 (CH, C-1), 81.40 (CH), 78.67 (CH), 73.76 (CH), 71.97 (CH_2, OCH_2-Ph), 67.50 (CH_2, C-6), 55.70 (CH_3, OCH_3), 40.29 (CH_2, C-2), 27.08 (CH_3), 25.89 (CH_3).

Anal. Calcd for $C_{17}H_{24}O_5$ (308.37): C, 66.21; H, 7.84. Found: C, 66.09; H, 8.11.

β-anomer: ^{1}H NMR δ 7.30 (m, 5, Ph), 5.08 (d, J = 5.7 Hz, 1, H-1), 4.63 (dd, $J_{A,B}$ = 12.1 Hz, 2, O-CH_2-Ph), 4.48 (*pseudo*q, J = 6.0, 6.4 Hz, 1), 4.16 (m, 4), 3.45 (s, 3, OCH_3), 2.20 (m, 2, H-2), 1.50 (s, 3, CH_3), 1.44 (s, 3, CH_3); ^{13}C NMR δ 137.41 (C, Ph), 127.44, 127.04 and 126.81 (CH, Ph), 107.68 (C, CMe_2), 104.16 (CH, C-1),

82.51 (CH), 76.05 (CH), 73.58 (CH), 70.61 (CH_2, OCH_2-Ph), 66.01 (CH_2, C-6), 54.77 (CH_3, OCH_3), 37.34 (CH_2, C-2), 25.81 (CH_3), 24.63 (CH_3).

Anal. Calcd for $C_{17}H_{24}O_5$ (308.37): C, 66.21; H, 7.84. Found: C, 66.04; H, 8.02.

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