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REGIOSELECTIVE ALKYLATION *via* TRIALKYLSTANNYLATION: METHYL α-D-GLUCOPYRANOSIDE*

TOMOYA OGAWA**, YUKIO TAKAHASHI, AND MASANAO MATSUI
The Institute of Physical and Chemical Research, Wako-shi, Saitama, 351 (Japan)
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ABSTRACT

Partial stannylation of methyl α-D-glucopyranoside with $(Bu_3Sn)_2O$, and subsequent alkylation with benzyl bromide, allyl bromide, and trityl chloride, afforded the 2,6-disubstituted derivative as one of the major products in each case.

INTRODUCTION

Partial stannylation of hydroxyl groups with $(Bu_3Sn)_2O$ has been found to provide an efficient approach to the regioselective acylation of methyl hexosides[2]. The stannyl method was also employed for the regioselective benzylation of mannopyranosides, to afford intermediates crucial for the synthesis of branched manno-oligosaccharides of biological importance[3].

Partially protected glucopyranosides bearing benzyl, allyl[4], or trityl groups may be regarded as versatile intermediates for the synthesis of complex, glycan chains involving glucopyranosyl residues. As part of a project on the regioselective transformation of carbohydrates *via* stannylation, we now report the regioselective benzylation, allylation, and tritylation of methyl α-D-glucopyranoside.

RESULTS AND DISCUSSION

It has been reported[2] that stannylation of methyl α-D-glucopyranoside **1** with 1.5 molar equivalents of $(Bu_3Sn)_2O$, and subsequent treatment with benzoyl chloride at room temperature affords methyl 2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside and methyl 2,6-di-*O*-benzoyl-α-D-glucopyranoside (**19**) in 18.4 and 81.4% yield, respectively. Formation of the major product (**19**) and the minor tribenzoate was explained as occurring through the intermediacy of the regioselectively stannylated methyl α-D-glucopyranosides **2** and **6**, respectively.

With the expectation of obtaining partially alkylated D-glucopyranosides, the reaction of partially stannylated methyl α-D-glucopyranosides with benzyl bromide

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**To whom enquiries should be addressed.

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TABLE I

^{13}C CHEMICAL-SHIFTS OF PARTIALLY ALKYLATED METHYL α-D-GLUCOPYRANOSIDES IN $CDCl_3$

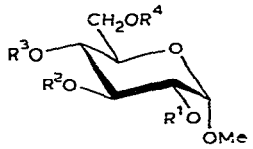
Structure	*Carbon atom*							
	1 ($^1J_{CH}$)	*2*	*3*	*4*	*5*	*6*	*Me*	OCH_2R(*at O-n*)
1 (D_2O)	99.6	71.9	73.6	70.1	71.6	61.2	55.3	
8 (3,6-Bn_2)	99.2 (168.0)	72.4	82.5 (+8.9)[a]	69.9	70.7	69.6 (+8.4)	55.2	73.5 O-6 74.8 O-3
9 (2,6-Bn_2)	97.8 (167.9)	79.2 (+7.3)	73.1	70.0	70.7	69.4 (+8.2)	55.1	73.6 O-6 73.1 O-2
10 (4,6-Bn_2)	99.2 (170.9)	72.5	75.0	77.4 (+7.3)	70.1	68.5 (+7.3)	55.1	73.5 O-6 74.6 O-4
16 (3,4-Bn_2)	99.1 (168.5)	72.8	82.8 (+9.2	77.0 (+6.9)	70.9	61.6	55.1	75.2 O-3 74.7 O-4
11 (6-Bn) (CD_3COCD_3)	100.6 (167.8)	73.2	75.1	72.1	71.5	70.7 (+9.5)	55.2	73.6 O-6
26 2-Bn	97.8 (167.2)	79.3 (+7.4)	73.0	70.5	70.6	62.2	55.3	73.0 O-2
12 (3,6-All_2)	99.3 (168.5)	72.1	82.0 (+8.4)	69.9	70.5	69.4 (+8.2)	55.1	72.4 O-6 73.6 O-3
13 (2,6-All_2)	97.5 (167.2)	78.7 (+6.8)	72.8	69.8	70.6	69.2 (+8.0)	55.1	72.4 O-6 71.8 O-2
14 (6-All)	99.3 (168.9)	71.7	74.2	70.3	70.3	69.2 (+8.0)	55.1	72.4 O-6
21 (3,4,6-Tr_3)	95.6 (157.5)	70.1	79.1[b]	69.8[b]	71.4[b]	61.5	56.9	88.9 88.2 85.5
24 (2,6-Tr_2)	98.4 (169.7)	74.1	72.8[b]	69.3[b]	72.2[b]	64.1	54.5	87.7 86.9

[a]Values in parentheses correspond to the α-effect of alkylation. [b]The assignments are tentative.

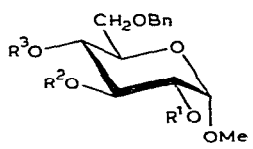
was first examined. Stannylation of **1** with 1.5 molar equivalents of $(Bu_3Sn)_2O$, and subsequent reaction of the partially stannylated intermediates with benzyl bromide at 80–90°, gave the dibenzyl ethers **8**, **9**, and **10**, and the monobenzyl ether **11**, in 4.5, 30.5, 6.0, and 48.6% yield, respectively. The structures of **8**, **9**, **10**, and **11** were assigned by ^{13}C-n.m.r. data (see Table I). Signal assignments for each carbon atom of the substituted methyl α-D-glucopyranosides were based on the chemical shifts reported[5] for the corresponding carbon atoms of **1**. The signals for methylene carbon atoms of the benzyl groups were distinguished by proton, off-resonance decoupling. Carbon atoms bearing a benzyloxy group appeared at lower field due to the α-effect of alkylation[5]; signals for C-6 and C-3 of **8** appeared at δ 69.6 and 82.5, for C-6 and C-2 of **9** at δ 69.4 and 79.2, for C-6 and C-4 of **10** at δ 68.5 and 77.4, and for C-6 of **11** at δ 70.7. These di-*O*-benzyl and mono-*O*-benzyl derivatives had been prepared, in the conventional way, by Küster and Dyong[6] in 1975.

The isolation of the three dibenzyl ethers **8**, **9**, and **10** in the ratios of 3:20:4, together with the 6-*O*-monobenzyl derivative **11**, showed the occurrence of only

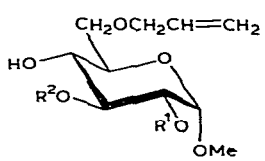
moderate regioselectivity for benzylation, as compared with benzoylation, of partially stannylated intermediates, and indicated the presence of an equilibrium among such partially stannylated intermediates as **2**, **3**, **4**, **5**, **6**, and **7** under the reaction conditions employed. The intermediates **2**, **5**, and **6** may lead to formation of the major product **9**, whereas **3**, **6**, and **7**, and **4**, **5**, and **7**, may lead to production of the two minor products, **8** and **10**, respectively.

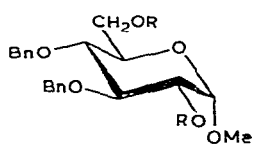


1 $R^1 = R^2 = R^3 = R^4 = H$
2 $R^1 = R^4 = SnBu_3, R^2 = R^3 = H$
3 $R^1 = R^3 = H, R^2 = R^4 = SnBu_3$
4 $R^1 = R^2 = H, R^3 = R^4 = SnBu_3$
5 $R^1 = R^3 = R^4 = SnBu_3, R^2 = H$
6 $R^1 = R^2 = R^4 = SnBu_3, R^3 = H$
7 $R^1 = H, R^2 = R^3 = R^4 = SnBu_3$



8 $R^1 = R^3 = H, R^2 = Bn$
9 $R^1 = Bn, R^2 = R^3 = H$
10 $R^1 = R^2 = H, R^3 = Bn$
11 $R^1 = R^2 = R^3 = H$



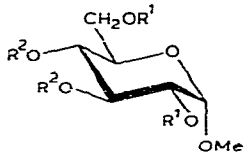


12 $R^1 = H, R^2 = allyl$
13 $R^1 = allyl, R^2 = H$
14 $R^1 = R^2 = H$

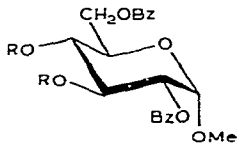
15 R = allyl
16 R = H

The reaction of partially stannylated intermediates with allyl bromide led to isolation of the diallyl ethers **12** and **13** in 8.0 and 41.8% yield, respectively, along with the monoallyl ether **14** in 23% yield. The structures of **12** and **13** were also assigned from ^{13}C-n.m.r. data: signals for C-6 and C-3 of **12** appeared at δ 69.4 and 82.0, whereas those for C-6 and C-2 of **13** appeared at δ 69.2 and 78.7. The β-effect of alkylation was observed for the signal of C-1 of **13**, which was shielded by 2.1 p.p.m. compared with that of **1**, confirming the introduction of an allyl group on O-2 of **13**. The structure of **14** was assigned by the presence of a deshielded signal for C-6 at δ 69.2 in the ^{13}C-n.m.r. spectrum.

The major product, **13**, was transformed into the dibenzyl ether **16** in two steps, namely, benzylation of **13** with NaH–benzyl bromide, and deallylation[7] with 10% Pd–C in EtOH–AcOH–H_2O, in 62% overall yield. The ^{13}C-n.m.r. data for **16** confirmed the structure assigned, by revealing two deshielded signals, at δ 82.8 and 77.0, for C-3 and C-4, respectively.

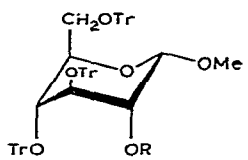


17 R^1 = Bn, R^2 = Me
18 R^1 = H, R^2 = Me

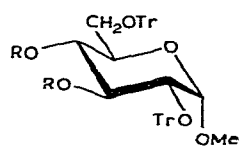


19 R = H
20 R = Me

The structure of the 2,6-dibenzyl ether **9** was confirmed by chemical correlation with authentic methyl 2,6-dibenzoate **19**. Thus, **9** was treated with MeI–NaH to give **17** in 91.4% yield, and **19** was treated with CH_2N_2 in CH_2Cl_2 in the presence of BF_3–ether[8], to give dimethyl ether **20** in 64.3% yield. Hydrogenolysis of **17**, and *O*-debenzoylation of **20**, afforded the same methyl 3,4-di-*O*-methyl-α-D-glucopyranoside (**18**).

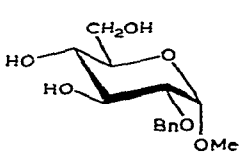


21 R = H
22 R = Ac
23 R = Bn



24 R = H
25 R = Ac

Partial tritylation of **1** *via* stannylated intermediates was also examined. On treatment of partially stannylated **1** with trityl chloride at 65°, the 3,4,6-tritrityl (**21**) and the 2,6-ditrityl ether (**24**) were isolated in 37.3 and 53.6% yield, respectively. The structure of **21** was assigned by chemical transformation into the monobenzyl ether **26** *via* benzylation and hydrolysis. The structure of **26** was determined from the ^{13}C-n.m.r. spectrum, which contained a deshielded signal at δ 79.3 for C-2, and a shielded signal at δ 97.8 for C-1 due to the β-effect of alkylation at O-2. The ^{13}C-n.m.r.



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spectrum of the 3,4,6-tritrityl ether **21** contained three signals for methine carbon atoms of triphenylmethyl groups, at δ 88.9, 88.2, and 85.5, which confirmed the introduction of three trityl groups into **1**. The signal for the anomeric carbon atom appeared at δ 95.6 with $^1J_{CH}$ 157.5 Hz, indicating that the anomeric hydrogen atom was axially oriented. The ^{1}H-n.m.r. spectrum of **21** also revealed a deshielded signal for the axially oriented H-1, at δ 5.02, with w_{hh} 3.5 Hz, compared with the one for the equatorially oriented H-1 of **24**, which appeared at δ 3.88. These chemical and spectral data proved that **21** was the 3,4,6-tri-*O*-trityl derivative of **1**, and that the favored conformation in $CDCl_3$ is $^1C_4$. The $^1J_{CH}$ values of the signals for the anomeric carbon atoms of the acetate **22** (δ 93.8) and the benzyl ether **23** (δ 95.7) were 159.9 and 156.3 Hz, respectively, in agreement with their $^1C_4$ conformation.

The ^{13}C-n.m.r. spectrum of the major product **24** contained two methine signals, at δ 87.7 and 86.9, and the ^{1}H-n.m.r. spectrum of the diacetate **25** showed two deshielded signals, at δ 5.58 and 4.61, both as triplets, with J 9.5 Hz for H-3 and H-4, respectively, thus showing the 2,6-substitution pattern in **24**.

In conclusion, by employing the stannylation–alkylation method, benzyl, allyl, and trityl groups have been selectively introduced at O-2 and O-6 of methyl α-D-glucopyranoside.

EXPERIMENTAL

General. — Melting points were determined with a Yanagimoto micro melting-point apparatus, and are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 141 polarimeter for solutions in $CHCl_3$ at 25°, unless otherwise noted. Column chromatography was performed in columns of Silica Gel Merck (70–230 mesh; E. Merck, Darmstadt, Germany). Thin-layer chromatography was conducted on precoated plates (layer thickness, 0.25 mm; E. Merck, Darmstadt, Germany) of Silica Gel 60 F_{254}. I.r. spectra were recorded with an EPI-G2 Hitachi spectrophotometer, as KBr discs for the crystalline samples, and as neat films for the liquid samples. ^{1}H-N.m.r. spectra were recorded with a Varian HA-100 n.m.r. spectrometer, using tetramethylsilane as the internal standard. ^{13}C-N.m.r. spectra were recorded with a JNM-FX 100FT n.m.r. spectrometer operated at 25.05 MHz. The values of δ_C and δ_H are expressed in p.p.m. downwards from the internal standard for solutions in $CDCl_3$, unless otherwise noted.

*Methyl 3,6-di-*O*-benzyl-α-*D*-glucopyranoside* (**8**), *methyl 2,6-di-*O*-benzyl-α-*D*-glucopyranoside* (**9**), *methyl 4,6-di-*O*-benzyl-α-*D*-glucopyranoside* (**10**), *and methyl 6-*O*-benzyl-α-*D*-glucopyranoside* (**11**). — A mixture of finely powdered **1** (970 mg, 5 mmol) and $(Bu_3Sn)_2O$ (4.5 g, 7.5 mmol) in toluene (50 mL) was stirred under reflux for 14 h with continuous azeotropic removal of water. The clear solution was evaporated *in vacuo*, and a mixture of the residue with benzyl bromide (10 mL) was stirred for 2 days at 80–90° under argon, and evaporated; the residue was chromatographed on SiO_2 (100 g) with 1:1 toluene–EtOAc, to give crude **8** (120 mg), which was rechromatographed on SiO_2 (30 g) with 20:1 CH_2Cl_2–acetone, to give pure[6] **8**

(85 mg, 4.5%), $[\alpha]_D$ +79.2° (*c* 3.50); R_F 0.55 in 1:3 toluene–EtOAc and 0.25 in 20:1 CH_2Cl_2–acetone; δ_H: 7.45–7.30 (s, 10 H, 2 benzyl), 4.96 and 4.76 (AB, *J* 12 Hz, CH_2Ph), 4.75 (d, 1 H, *J* 3 Hz, H-1), 4.58 (s, 2 H, CH_2Ph), and 3.42 (s, 3 H, OMe).

Further elution with 1:3 toluene–EtOAc afforded[6] **9** (571 mg, 30.5%), m.p. 80–82° (iPr_2O), $[\alpha]_D$ +58.7° (*c* 0.73); R_F 0.45 in 1:3 toluene–EtOAc; δ_H: 7.32 (s, 5 H, benzyl), 7.29 (s, 5 H, benzyl), 4.67 (s, 2 H, CH_2Ph), 4.63 (d, 1 H, *J* 4 Hz, H-1), 4.57 (s, 2 H, CH_2Ph), and 3.32 (s, 3 H, OMe).

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.21; H, 7.07.

Further elution with the same solvent afforded[6] **10** (113 mg, 6.0%), m.p. 70–73° (iPr_2O), $[\alpha]_D$ +109.0° (*c* 0.465); R_F 0.30 in 1:3 toluene–EtOAc; δ_H: 7.30 (s, 5 H, benzyl), 7.24 (s, 5 H, benzyl), and 3.38 (s, 3 H, OMe).

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 66.90; H, 6.95.

Further elution, with 10:1 CH_2Cl_2–MeOH, gave **11** (690 mg, 48.6%), m.p. 58–61° (Me_2CO–iPr_2O), $[\alpha]_D$ +104.7° (*c* 0.425); R_F 0.25 in 10:1 CH_2Cl_2–MeOH; δ_H: 7.29 (s, 5 H, benzyl), 4.71 (d, 1 H, *J* 4 Hz, H-1), 4.57 (s, 2 H, CH_2Ph), and 3.37 (s, 3 H, OMe).

Anal. Calc. for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 58.88; H, 7.11.

*Methyl 3,6-di-*O*-allyl-α-*D*-glucopyranoside* (**12**), *methyl 2,6-di-*O*-allyl-α-*D*-glucopyranoside* (**13**), *and methyl 6-*O*-allyl-α-*D*-glucopyranoside* (**14**). — Compound **1** (3.84 g, 20 mmol) was stannylated with $(Bu_3Sn)_2O$ (18 g, 30 mmol) in toluene (100 mL) for 2 h at 140°. The clear solution was evaporated *in vacuo*, and a mixture of the residue with allyl bromide (50 mL) was stirred for 10 days at 80° under argon, cooled, and evaporated *in vacuo*; the residue was chromatographed on SiO_2 (200 g) with 1:3 toluene–EtOAc, to give **12** (425 mg, 8.0%), $[\alpha]_D$ +103.1° (*c* 0.390); R_F 0.47 in 1:3 toluene–EtOAc; δ_H: 6.2–5.7 (m, 2 H, 2 CH_2-C*H*=CH_2), 5.4–5.1 (m, 4 H, 2 -CH=CH_2), 4.75 (d, 1 H, *J* 3 Hz, H-1), 4.4–4.3 (m, 2 H, -CH_2-CH=CH_2), 4.1–4.0 (m, 2 H, -CH_2-CH=CH_2), and 3.44 (s, 3 H, OMe).

Further elution with same solvent afforded **13** (2.265 g, 41.8%), $[\alpha]_D$ +106.5° (*c* 0.755); R_F 0.28 in 1:3 toluene–EtOAc; δ_H: 6.2–5.7 (m, 2 H, 2 -CH_2-C*H*=CH_2), 5.4–5.1 (m, 4 H, 2 -CH_2-CH=CH_2), 4.82 (d, 1 H, *J* 4 Hz, H-1), 4.2–4.0 (m, 4 H, -CH_2-CH=CH_2), and 3.41 (s, 3 H, OMe).

Anal. Calc. for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.79; H, 8.00.

Further elution, with 20:1 CH_2Cl_2–MeOH, gave **14** (1.09 g, 23%), $[\alpha]_D$ +133.0° (*c* 0.87); R_F 0.13 in 20:1 CH_2Cl_2–MeOH; δ_H: 6.1–5.7 (m, 1 H, CH_2-C*H*=CH_2), 5.4–5.1 (m, 2 H, CH_2-CH=CH_2), 4.74 (d, 1 H, *J* 4 Hz, H-1), 4.1–4.0 (m, 2 H, -CH_2-CH=CH_2), and 3.40 (s, 3 H, OMe).

Anal. Calc. for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 50.90; H, 7.77.

*Methyl 2,6-di-*O*-allyl-3,4-di-*O*-benzyl-α-*D*-glucopyranoside* (**15**). — To a solution of **13** (1.577 g, 5.8 mmol) in $HCONMe_2$ (20 mL) was added, portionwise, NaH (50%; 863 mg, 17.4 mmol), and the mixture was stirred for 30 min at 20°. To the cooled mixture was added, dropwise, benzyl bromide (2.1 mL, 17.4 mmol) at −5°. The mixture was stirred for 2 h at −5°, and for 1 h at 20°, and then, to this mixture

was added, dropwise, methanol (2 mL) at 0° (to consume the excess of NaH). Processing, and chromatography on SiO_2 (100 g) with 5:1 toluene–EtOAc, gave **15** (2.6 g, 98%), $[\alpha]_D$ +40.3° (*c* 0.34); R_F 0.70 in 3:1 toluene–EtOAc; δ_H: 7.4–7.2 (m, 10 H, 2 benzyl), 6.2–5.6 (m, 2 H, 2 CH_2-CH=CH_2), 5.4–5.1 (m, 4 H, 2 CH_2-CH=CH_2), 5.0–4.5 (2 AB q, 4 H, 2 CH_2Ph), 4.29 (d, 1 H, *J* 4 Hz, H-1), 4.2–3.9 (m, 4 H, 2 CH_2-CH=CH_2), and 3.40 (s, 3 H, OMe).

Anal. Calc. for $C_{27}H_{34}O_6$: C, 71.34; H, 7.54. Found: C, 71.32; H, 7.53.

*Methyl 3,4-di-*O*-benzyl-α-*D*-glucopyranoside* (**16**). — A mixture of **15** (2.7 g, 5.94 mmol) and 10% Pd–C (0.3 g) in EtOH (20 mL)–AcOH (10 mL)–H_2O (10 mL) was stirred for 68 h at 75°, cooled, filtered (Celite), and the filtrate evaporated *in vacuo*. The residue was chromatographed on SiO_2 (100 g) with 1:1 toluene–EtOAc, to give crystalline **16** (1.40 g, 63.1%)[6,9], m.p. 105–106° (CH_2Cl_2–iPr_2O), $[\alpha]_D$ +101.3° (*c* 0.545); R_F 0.32 in 1:3 toluene–EtOAc; δ_H: 7.28 (bs, 10 H, 2 benzyl), 4.87 and 4.63 (AB q, 2 H, *J* 10 Hz, CH_2Ph), 4.88 (s, 2 H, CH_2Ph), 4.73 (d, 1 H, *J* 3 Hz, H-1), and 3.40 (s, 3 H, OMe).

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.37; H, 7.00. Found: C, 67.19; H, 6.98.

*Methyl 2,6-di-*O*-benzyl-3,4-di-*O*-methyl-α-*D*-glucopyranoside* (**17**). — To a solution of **9** (230 mg, 0.5 mmol) in $HCONMe_2$ (2 mL) was added NaH (50%; 100 mg, 2 mmol, washed with hexane), and the mixture was stirred for 30 min at 15–20°. To this mixture was added MeI (0.5 mL) at −5°, and the mixture was stirred for 2 h at −5 to 0°. Processing, and chromatography on SiO_2 (25 g) with 10:1 toluene–EtOAc, afforded **17** (226 mg, 91.4%), $[\alpha]_D$ +52.0° (*c* 0.535); R_F 0.62 in 3:1 toluene–EtOAc; δ_H: 3.63 (s, 3 H, OMe), 3.44 (s, 3 H, OMe), and 3.32 (s, 3 H, OMe).

Anal. Calc. for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 68.23; H, 7.35.

*Methyl 2,6-di-*O*-benzoyl-3,4-di-*O*-methyl-α-*D*-glucopyranoside* (**20**). — A solution of **19** (160 mg, 0.4 mmol) in CH_2Cl_2 (5 mL) containing 1 drop of BF_3–ether was treated with a solution of CH_2N_2 [prepared from 2 g of $MeN(NO)CONH_2$] in CH_2Cl_2 (20 mL) according to a reported method[8]. Processing, and chromatography on SiO_2 (20 g) with 4:1 toluene–EtOAc, afforded **20** (110 mg, 64.3%), $[\alpha]_D$ +117.5° (*c* 0.435); R_F 0.66 in 3:1 toluene–EtOAc; δ_H: 3.59 (s, 3 H, OMe), 3.58 (s, 3 H, OMe), and 3.37 (s, 3 H, OMe).

Anal. Calc. for $C_{23}H_{26}O_8$: C, 64.17; H, 6.09. Found: C, 64.14; H, 6.14.

*Methyl 3,4-di-*O*-methyl-α-*D*-glucopyranoside* (**18**). — (*A*). A solution of **17** (176 mg) in EtOH (10 mL) was hydrogenolyzed in the presence of 10% Pd–C (100 mg), to give **18**, $[\alpha]_D$ +176.6° (*c* 0.475); R_F 0.12 in 1:3 toluene–EtOAc; δ_H: (3:1 $CDCl_3$–Me_2SO-d_6): 4.69 (d, 1 H, *J* 3 Hz, H-1), 3.64 (s, 3 H, OMe), 3.55 (s, 3 H, OMe), and 3.40 (s, 3 H, OMe).

(*B*). A solution of **20** (60 mg) in MeOH (3 mL)–0.1M NaOMe (0.2 mL) was stirred for 14 h at 55°. Processing, and chromatography on SiO_2 (10 g) with 1:3 toluene–EtOAc, gave **18** (24 mg), which was identified by ^{1}H-n.m.r. spectroscopy with the sample prepared by method (*A*).

*Methyl 3,4,6-tri-*O*-trityl-α-*D*-glucopyranoside* (**21**) *and methyl 2,6-di-*O*-trityl-α-*

D-*glucopyranoside* (**24**). — Compound **1** (4.8 g, 25 mmol) was stannylated with $(Bu_3Sn)_2O$ (23 g, 38 mmol) in toluene (100 mL). The clear solution resulting was stirred in the presence of added TrCl (21 g, 76 mmol) for 36 h at 65°. The mixture was evaporated *in vacuo*, and the residue, in $CHCl_3$ (200 mL), was stirred with[10] aq. KF (20 g in 100 mL) for 5 h at room temperature. Precipitated Bu_3SnF was filtered off, and the filtrate was dried ($MgSO_4$), and evaporated. The residual oil was chromatographed on SiO_2 (550 g) with 20:1:0.2 toluene–EtOAc–Et_3N, to give **21** (8.5 g, 37.3%), $[\alpha]_D$ +1.07° (*c* 0.75); R_F 0.6 in 5:1 toluene–EtOAc; δ_H: 7.3–6.8 (m, 45 H, trityl), 5.02 (bs, 1 H, $w_{h/2}$ 3.5 Hz, H-1), and 3.83 (s, 3 H, OMe).

Anal. Calc. for $C_{64}H_{56}O_6$: C, 83.45; H, 6.13. Found: C, 83.37; H, 6.16.

Further elution, with 10:1:0.1 toluene–EtOAc–Et_3N, afforded **24** (9.0 g, 53.6%), $[\alpha]_D$ +32.8° (*c* 0.90); R_F 0.3 in 5:1 toluene–EtOAc; δ_H: 7.60–7.0 (m, 30 H, trityl), 4.00 (t, 1 H, *J* 9 Hz, H-3), 3.88 (d, 1 H, *J* 3 Hz, H-1), 3.64 (m, 1 H, H-5), 3.36 (q, 1 H, *J* 3,10 Hz, H-2), and 3.28 (s, 3 H, OMe).

Anal. Calc. for $C_{45}H_{42}O_6$: C, 79.62; H, 6.24. Found: C, 79.51; H, 6.25.

*Methyl 2-*O*-acetyl-3,4,6-tri-*O*-trityl-α-*D*-glucopyranoside* (**22**). — Compound **21** (0.5 g) in pyridine (4 mL)–Ac_2O (2 mL)–4-dimethylaminopyridine (0.1 g) was stirred for 1 h at 50°. Processing gave monoacetate **22**, $[\alpha]_D$ −23.6° (*c* 0.50); R_F 0.50 in 10:1 toluene–EtOAc; δ_H: 5.02 (d, 1 H, *J* 3 Hz, H-1), 4.84 (bs, 1 H, w_{hh} 8 Hz, H-2), 3.66 (s, 3 H, OMe), and 2.04 (s, 3 H, OAc); δ_C 93.8 ($^1J_{CH}$ 159.9 Hz, C-1), 88.4, 87.2 and 85.6 (3 methines of 3 trityl), 78.3, 70.7, 68.7, 68.3, 61.9 (C-6), 56.8 (OMe), and 21.1 (Ac).

*Methyl 3,4-di-*O*-acetyl-2,6-di-*O*-trityl-α-*D*-glucopyranoside* (**25**). — Compound **24** (0.7 g) in pyridine (6 mL)–Ac_2O (3 mL) was stirred for 40 h at 15–20°; processing gave diacetate **25**; δ_H: 5.58 (t, 1 H, *J* 9.5 Hz, H-3), 4.61 (t, 1 H, *J* 9.5 Hz, H-4), 4.00 (d, 1 H, *J* 2.4 Hz, H-1), 3.85 (m, 1 H, H-5), 3.52 (q, 1 H, *J* 2.4, 9.5 Hz, H-2), 3.39 (s, 3 H, OMe), 1.85 (s, 3 H, Ac), and 1.76 (s, 3 H, Ac).

*Methyl 2-*O*-benzyl-3,4,6-tri-*O*-trityl-α-*D*-glucopyranoside* (**23**). — Compound **21** (0.30 g) in $HCONMe_2$ (10 mL) was benzylated with benzyl bromide and NaH, to afford **23** (447 mg, 81.4%), $[\alpha]_D$ +20.0° (*c* 0.75); R_F 0.49 in 10:1 toluene–EtOAc; δ_H: 4.92 (d, 1 H, *J* 3.5 Hz, H-1), 3.68 (s, 3 H, OMe); δ_C: 95.7 ($^1J_{CH}$ 156.3 Hz, C-1), 78.3, 75.7, 73.3 (OCH_2Ph), 71.5, 69.5, 61.9 (C-6), and 56.7 (OMe).

Anal. Calc. for $C_{71}H_{62}O_6$: C, 84.36; H, 6.14. Found: C, 84.72; H, 6.18.

*Methyl 2-*O*-benzyl-α-*D*-glucopyranoside* (**26**). — A solution of **23** (182 mg, 0.2 mmol) in 80% aq. AcOH (20 mL) was stirred for 1 h at 80°. Evaporation *in vacuo*, and chromatography of the residue on SiO_2 (25 g) with EtOAc, afforded crystalline **26** (62 mg, 81.3%); m.p. 118.5–120°, $[\alpha]_D$ +85.3° (*c* 0.375); R_F 0.2 in EtOAc; δ_H: 7.36 (s, 5 H, benzyl), 4.67 (d, 1 H, *J* 3 Hz, H-1), 4.68, 4.66, 4.60, and 4.56 (2 H, CH_2Ph), 3.36 (s, 3 H, OMe), 2.70 (bs, 1 H, OH), and 2.12 (bs, 1 H, OH).

Anal. Calc. for $C_{14}H_{20}O_6$: C, 59.16; H, 7.04. Found: C, 58.93; H, 7.06.

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