Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14.
For personal use only.

Synthesis and nuclear magnetic resonance spectra of some partially acylated β-D-glucopyranosides[1]

A. P. TULLOCH AND A. HILL[2]

Prairie Regional Laboratory, National Research Council of Canada, Saskatoon, Saskatchewan

Received February 19, 1968

The synthesis of ten new partially acylated derivatives of methyl β-D-glucopyranoside, all with an acyl group at C-6, is described. The nuclear magnetic resonance spectra of these compounds, and of a number of related derivatives, have been measured using pyridine, acetone-d_6, and deuteriochloroform as solvents. When OH-4 is acylated, the H-6 signals are at higher field (by 0.1–0.3 p.p.m.) than when OH-4 is not acylated, but this effect is not observed when OH-3 is acylated. When a trimethylsilyl ether group is introduced at C-4 the difference between the chemical shifts of the H-6 protons ($\delta A - \delta B$) increases markedly. Estimation of J_{BX} and J_{AX} (where B is the H-6 proton at higher field and X is H-5), from spectra obtained using acetone-d_6 and pyridine as solvents, shows that $J_{BX} < J_{AX}$ when there is an acyl group at C-4 but $J_{BX} > J_{AX}$ when there is no acyl group at C-4.

Canadian Journal of Chemistry, 46, 2485 (1968)

During an investigation of the structure of a partially acylated sophoroside (1), we wished to determine the positions of acyl groups by nuclear magnetic resonance (n.m.r.) spectroscopy. We, therefore, decided to examine the n.m.r. spectra of some methyl β-D-glucopyranoside diesters which would serve as simple model compounds. When we realized that useful correlations between the n.m.r. spectra and the structure of partially acylated glucosides existed, we extended the investigation to a number of related derivatives.

No partially acylated glucosides had been studied in this way though n.m.r. spectra of methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**9**) (2), of β-glucose pentaacetate (3, 4), of 1,3,4,6- and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (5, 6) had been discussed previously.

Synthesis of Partly Acylated Methyl β-D-Glucopyranosides

All four methyl β-D-glucopyranoside triacetates have been synthesized, but only the 3,4,6-triacetate (**6**) (7) was used in the present work. It appears that diacetates other than the 2,3-diacetate, and monoacetates other than the 6-acetate (**3**) (8), have not been prepared before.

The 6-acetate (**3**) was first prepared by Frohwein (8), by partial hydrolysis of the tetraacetate, but the yield was very low. We therefore examined the method used by Hurst and McInnes (9) to synthesize methyl 6-*O*-acetyl-α-D-glucopyranoside, in which a trimethylsilyl group at the 6-position of methyl 2,3,4,6-tetra-*O*-trimethylsilyl-α-D-glucopyranoside is selectively removed, the product acetylated, and the remaining trimethylsilyl groups taken off. When this method was used with β-methyl glucoside, 6-acetate (**3**) and 6-stearate (**4**) were readily prepared.

Methyl 4,6-di-*O*-acetyl-β-D-glucopyranoside (**8**) was prepared by hydrogenolysis of the 4,6-diacetate (**7**), which had been obtained by acetylation of methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside. In addition to the 6-stearate (**4**), above, we also prepared the 6-acetate-4-stearate (**14**) to compare the effects of the long chain stearoyl group with those of the short chain acetyl group. Methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-β-D-glucopyranoside (**12**) was prepared using the trimethylsilyl ether derivative (**10**) as intermediate. Treatment of **12** with stearoyl chloride and hydrogenolysis of the benzyl groups yielded methyl 6-*O*-acetyl-4-*O*-stearoyl-β-D-glucopyranoside (**14**); acetylation gave methyl 2,3,6-tri-*O*-acetyl-4-*O*-stearoyl-β-D-glucopyranoside (**15**).

To compare the effect of an acetate group at C-3 with that of an acetate at C-4 the 3,6-diacetate (**18**) was prepared. Partial acetylation of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (cf. ref. 10) with one mole of acetic anhydride in pyridine, gave a mixture of products which were separated by column chromatography into 3-acetate (22%), 2-acetate (34%), and 2,3-diacetate (15%). A number of other conditions were tried, including the use of acetyl chloride, but all resulted in lower yields of 3-acetate. Methyl 3-*O*-acetyl-β-D-glucopyranoside (**16**) was obtained by removing the benzylidene group with

[1]Issued as NRCC No. 10133.
[2]NRCC Postdoctorate Fellow, 1965–1967.

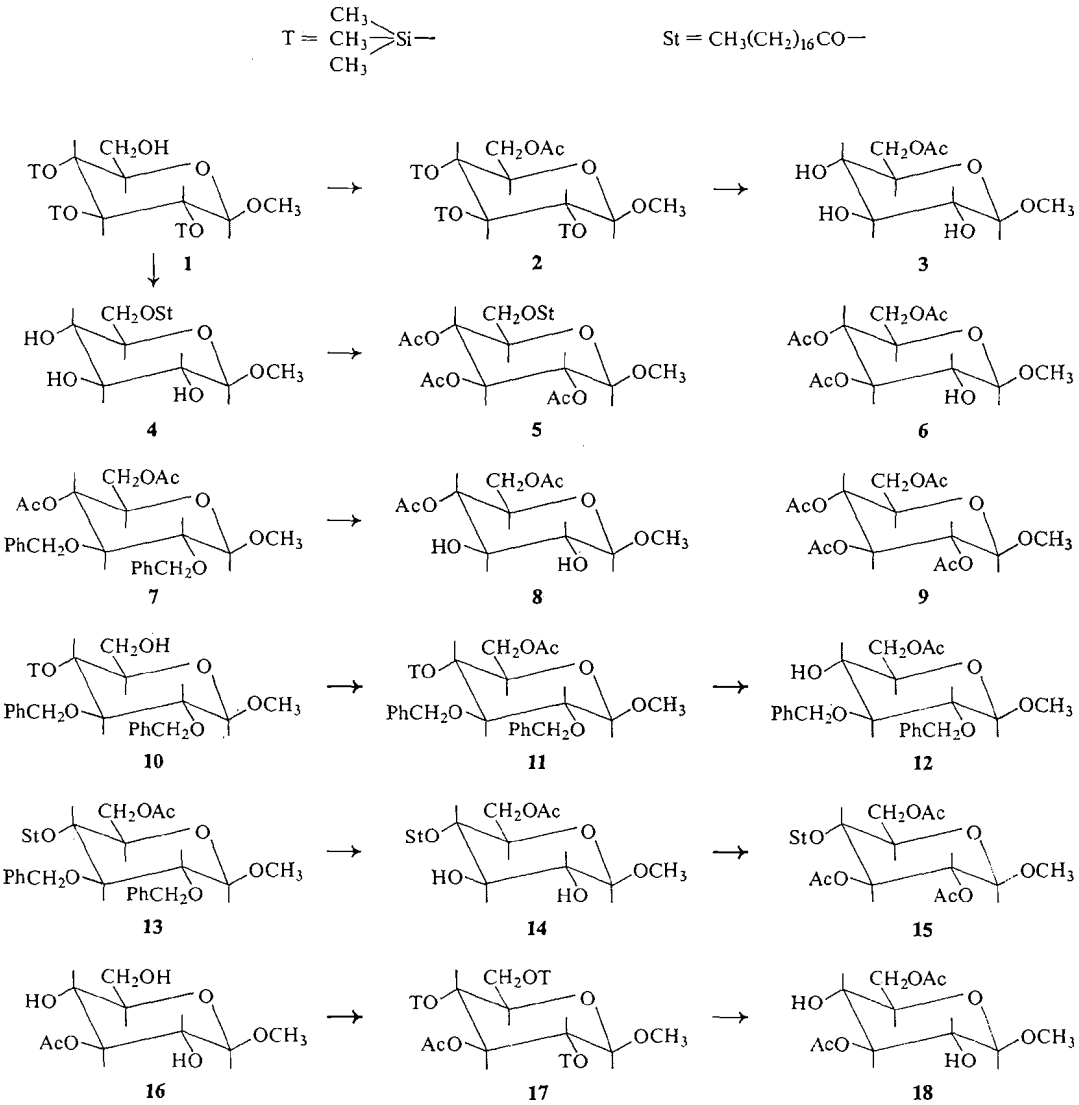
Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

TABLE I

Chemical shifts (in p.p.m.) of acetoxy, H-6, and H-1 protons of β-methyl glucoside derivatives in pyridine, acetone-d_6, and deuteriochloroform

Compound	Acetoxy			H-6			H-1		
	Pyridine	Acetone-d_6	Deuterio-chloroform	Pyridine	Acetone-d_6	Deuterio-chloroform	Pyridine	Acetone-d_6	Deuterio-chloroform
6-*O*-Acetyl (**3**)	1.95	2.03	—	4.79	4.30	—	4.57	4.22	—
6-*O*-Stearoyl (**4**)	—	—	—	4.73	4.29	4.36	4.53	4.18	4.19
4,6-Di-*O*-acetyl (**8**)	2.00, 2.01	1.99, 2.03	2.07, 2.10	4.41	4.10	4.20	4.58	4.24	4.20
3,6-Di-*O*-acetyl (**18**)	1.94, 1.96	2.02, 2.04	2.10, 2.16	4.70	4.30	4.37	4.57	4.28	4.25
6-*O*-Acetyl-4-*O*-stearoyl (**14**)	2.01	1.97	2.06	4.45	4.06	4.14	4.59	4.21	4.20
3,4,6-Tri-*O*-acetyl (**6**)	1.97, 2.01 (2)*	1.96 (2),* 1.98	2.04, 2.07, 2.09	4.40	4.16	4.20	4.60	4.36	4.31
2,3,6-Tri-*O*-acetyl-4-*O*-stearoyl (**15**)	2.00 (2)*, 2.02	1.92,1.96, 2.00	1.97, 2.02, 2.07	4.42	4.15	4.18	4.75	4.60	4.42
2,3,4-Tri-*O*-acetyl-6-*O*-stearoyl (**5**)	1.97, 2.00 (2)*	1.92, 1.97, 1.98	1.97, 1.99, 2.01	4.46	4.20	4.22	4.66	4.61	4.41
2,3,4,6-Tetra-*O*-acetyl (**9**)	1.95, 1.97, 1.99 (2)*	1.93, 1.98 (2),* 2.01	2.00, 2.02, 2.04, 2.08	4.38	4.17	4.19	4.71	4.60	4.42

*Denotes number of coincident signals.



50% acetic acid. Application of the method of Hurst and McInnes (9) to **16** led to the synthesis of the 3,6-diacetate (**18**). The yield was very low, apparently because the presence of the acetate group increased the rate of hydrolysis of the secondary trimethylsilyl groups. The positions of the acyl groups in the new compounds were confirmed by spin decoupling experiments.

Nuclear Magnetic Resonance Spectra

Spectra of all the compounds were recorded using pyridine as solvent, and also, when they were sufficiently soluble, using acetone-d_6 and deuteriochloroform as solvents. We have been concerned with the chemical shifts of the signals due to H-6, H-1 and the acetoxy groups because they can be related to the structure of the compounds under investigation. For the present purpose it was satisfactory to take the center of the H-6 multiplet as the chemical shift of the H-6 protons, except in the case of the trimethylsilyl ether derivatives discussed below.

The chemical shifts of the acetoxy, H-6, and H-1 protons of some β-methyl glucoside derivatives are shown in Table I; those assigned to H-6 will be considered first. The spectra of **3**, **4**, and **18**, compounds, in which OH-4 is not acylated, have H-6 signals at lower field than the spectra

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

of **8**, **14**, and the fully acetylated compounds. The difference in chemical shift of H-6 using pyridine is at least 0.3 p.p.m. and using the other two solvents is 0.1–0.2 p.p.m. The spectra of **3**, **18**, and **8**, shown in Fig. 1, illustrate this observation.

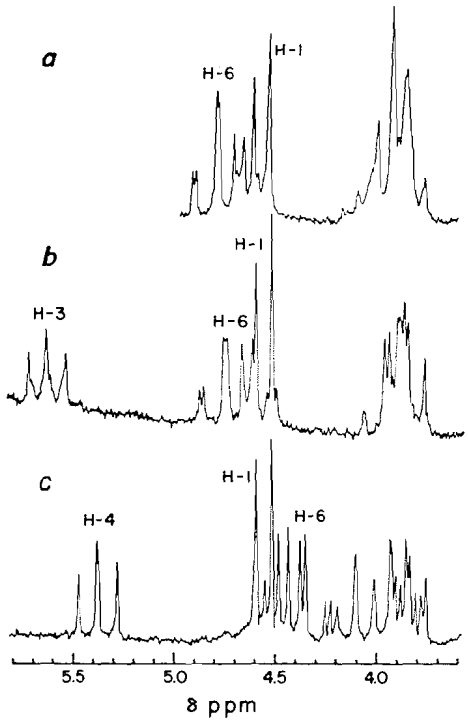


FIG. 1. Nuclear magnetic resonance spectra of: (*a*) methyl 6-*O*-acetyl-β-D-glucopyranoside (**3**); (*b*) methyl 3,6-di-*O*-acetyl-β-D-glucopyranoside (**18**); (*c*) methyl 4,6-di-*O*-acetyl-β-D-glucopyranoside (**8**); in pyridine, (3.5–5.8 p.p.m. region).

The differences in chemical shift are probably the result of interaction between the solvent and OH-4. Pyridine, which could form a hydrogen bond with OH-4, has the greatest effect on the spectra. The deshielding of neighboring protons resulting from complex formation between a hydroxyl group and pyridine has already been noted (11).

Acylation of a hydroxyl group might be expected to have a small deshielding effect on the protons γ to the OH group (see effect of acylation of OH-3 on H-1 in Table I). However, any such deshielding effect resulting from acylation of OH-4 is apparently more than counteracted by the prevention of interaction between OH-4 and the solvent.

TABLE II

Chemical shifts (in p.p.m.) of H-6 protons of β-D-glucopyranoses in pyridine, acetone-d_6, and deuteriochloroform

Compound	H-6		
	Pyridine	Acetone-d_6	Deuteriochloroform
1,2,3,6-Tetra-*O*-acetyl	4.63	4.28	4.36
1,2,4,6-Tetra-*O*-acetyl	4.37	4.12	4.18
1,2,3,4,6-Penta-*O*-acetyl	4.39	4.14	4.09

This effect may be peculiar to H-6 in the glucopyranose ring. However, in the spectrum of methyl 4-hydroxystearate the chemical shift of the methylene protons α to the carboxyl group, which are γ to the OH group, is 2.33 p.p.m. (11), but in the spectrum of methyl 4-acetoxystearate the α methylene signal appears at 2.22 p.p.m. (spectra were taken in carbon tetrachloride).

Table I also shows that the H-1 signal is displaced to lower field when 3 or 4 acyl groups are present. The effect is most noticeable in acetone-d_6 and least noticeable in pyridine. A similar deshielding of H-5 was also observed (using acetone-d_6); the signal appears at about 3.4–3.5 p.p.m. in the spectrum of **3**, but at 3.75–3.90 p.p.m. in the spectra of compounds in which OH-4 is acylated.

Signals due to the acetoxy groups of β-methylglucoside tetraacetate (9), using dimethyl formamide as solvent, were discussed by Barker *et al.* (2) who concluded that the signal at highest field was that of acetate at C-2. This assignment is probably true for spectra using acetone-d_6 and deuteriochloroform since the signal at 1.95–1.97 p.p.m. in the fully acylated compounds is absent from the spectra of those which lack an acetate at C-2. The spectra of the fully acylated compounds (using deuteriochloroform as solvent), except that of **5**, show an acetoxyl signal at relatively low field (2.07–2.09 p.p.m.) which is apparently due to acetate at C-6.

The spectra of β-glucopyranose pentaacetate and of two β-glucopyranose tetraacetates were also examined and the chemical shifts of the H-6 signals are listed in Table II. Here also the absence of an acyl group at C-4 results in the appearance of H-6 at appreciably lower field.

The spectra of some partially acylated deriva-

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

tives containing benzyl and trimethylsilyl groups were then investigated, with the results shown in Table III. Again H-6 is at lower field when OH-4 is not acylated, but H-1 is not affected by acylation of OH-4 when there are benzyl ether groups at C-2 and C-3. The spectra of compounds with a trimethylsilyl group at C-4, **2** and **11**, show an H-6 signal at higher field than do the spectra of the parent compounds, but the displacement is smaller than that shown by spectra of compounds with an acyl group at C-4. However, when the spectra are examined carefully (see Table IV below) the H-6 signal is seen to be more spread out and sometimes (particularly using acetone-d_6) only the high field H-6 proton has been shielded. Thus if the center of the H-6 multiplet is taken as the chemical shift of H-6, only a small displacement seems to have occurred.

The H-6 portion of the spectra of a representative selection of compounds (using acetone-d_6) was next examined in detail. H-6 can be considered as the AB portion of an ABX system (4, 9), where B is the H-6 proton at higher field and X is H-5 and, by the method of Bernstein *et al.* (12), the n.m.r. parameters in Table IV can be determined. In every case J_{AB} is about 12 c.p.s. In the spectra of the four acetylated derivatives $\delta A - \delta B$ is 13.5–16.6 c.p.s., but is much larger in the spectra of the trimethylsilyl ethers **11** and **2**. When $\delta A - \delta B$ becomes larger compared to J_{AB} the appearance of the spectrum changes and the intensities of the outer pairs increase.

Also $J_{BX} < J_{AX}$ when OH-4 is acetylated, but when OH-4 is free, or combined as a trimethylsilyl ether, $J_{BX} > J_{AX}$. Bernstein *et al.* (12) showed that when $J_{AX} + J_{BX}$ is positive and the splitting of the two highfield B pairs is larger than that of the two lowfield A pairs, $J_{BX} > J_{AX}$. Therefore, it can be seen by simple inspection of the spectra whether $J_{BX} > J_{AX}$. The spectra of all the compounds were then examined and in those of compounds with an OH or trimethylsilyl group at C-4, in pyridine solution, $J_{BX} > J_{AX}$; this was also true in acetone-d_6 solution though the spectrum of **12** was insufficiently resolved for measurement of the splitting of the H-6 pairs. In deuteriochloroform solution, $J_{BX} > J_{AX}$ in the spectra of the two trimethylsilyl ether derivatives **2** and **11**; the spectra of **4** and **18** were not well enough resolved; however, in those of **12** and of β-glucose 1,2,3,6-tetraacetate $J_{BX} < J_{AX}$. In the spectra of all the other compounds $J_{BX} < J_{AX}$ no matter which solvent was used.

The observations made here have already been useful in locating acyl groups in naturally occurring sophorosides (1, 13). Nuclear magnetic resonance spectral measurement of partly acylated glucose derivatives before and after conversion to trimethylsilyl ethers should help to locate free hydroxyl groups. Such measurements could be useful in studies of partial esterification of glucosides, and in investigations of migrations of acyl groups.

Experimental

Nuclear magnetic resonance (n.m.r.) spectra were measured at 32 °C using a Varian HA-100 spectrometer. Chemical shifts are in parts per million (p.p.m.) from tetramethylsilane (internal standard). Silicic acid (Bio-Sil A from Bio-Rad Laboratories, Richmond, California) was used for column chromatography. Specific rotations in chloroform solution were measured at 25 °C in a 1 dm cell using a Perkin–Elmer model 141 polarimeter.

Methyl 6-O-Acetyl-β-D-glucopyranoside (3)

Methyl β-D-glucopyranoside (9.6 g) was converted to the tetra-*O*-trimethylsilyl ether (21 g) by the method used with the α anomer (9). The ether was taken up in methanol (100 ml) and cooled to 0 °C; a solution of potassium carbonate (0.055 g) in methanol (12 ml) was added and the mixture kept at 0 °C for 45 min. Acetic acid (0.06 g) was then added and the solution poured into water; the product was extracted with light petroleum and the extract dried over sodium sulfate. Solvent was removed and the residue was crystallized from acetone containing 5% water (50 ml) at −40 °C and then from hexane at −30 °C to give methyl 2,3,4-tri-*O*-trimethylsilyl-β-D-glucopyranoside (**1**), (7.3 g), m.p. 72 °C and $[\alpha]_D$ −8.6° (*c*, 0.5 in chloroform).

Anal. Calcd. for $C_{16}H_{38}O_6Si_3$: C, 46.83; H, 9.27 Found: C, 47.20; H, 9.28.

Acetylation of **1** (6.7 g) with acetic anhydride and pyridine gave **2**, (b.p. 105 °C/0.1 mm), $[\alpha]_D$ −3.4° (*c*, 1.5 in chloroform).

Anal. Calcd. for $C_{18}H_{40}O_7Si_3$: C, 47.75; H, 8.91. Found: C, 47.56; H, 8.77.

Compound **2** was then refluxed for 4 h in methanol–water 4:1 (50 ml), the reagents removed, and the residual gum taken up in ethanol (15 ml) to give **3** (3 g), m.p. 132–134 °C, (lit. (8) gives m.p. 129 °C).

Methyl 6-O-Stearoyl-β-D-glucopyranoside (4)

Compound **1** (3.1 g) was dissolved in a mixture of methylene chloride (10 ml) and pyridine (3 ml) and a solution of stearoyl chloride (2.4 g) in methylene chloride added. After 18 h methylene chloride (15 ml) was added, the solution washed with water and dried over sodium sulfate. Solvent was removed and the trimethylsilyl

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

TABLE III

Chemical shifts (in p.p.m.) of acetoxy, H-6, and H-1 protons of some acylated β-methyl glucoside derivatives containing benzyl and trimethylsilyl groups in pyridine, acetone-d_6, and deuteriochloroform

Compound	Acetoxy			H-6			H-1		
	Pyridine	Acetone-d_6	*Deuterio*-chloroform	Pyridine	Acetone-d_6	*Deuterio*-chloroform	Pyridine	Acetone-d_6	*Deuterio*-chloroform
6-*O*-Acetyl-2,3-di-*O*-benzyl (**12**)	1.93	2.03	2.09	4.65	4.29	4.33	4.52	4.35	4.32
6-*O*-Acetyl-2,3-di-*O*-benzyl-4-*O*-trimethylsilyl (**11**)	2.04	2.06	2.08	4.47	4.24	4.25	4.52	4.38	4.32
6-*O*-Acetyl-2,3-di-*O*-benzyl-4-*O*-stearoyl (**13**)	2.00	1.99	2.04	4.36	4.08	4.13	4.54	4.44	4.30
4,6-Di-*O*-acetyl-2,3-di-*O*-benzyl (7)	1.97	1.96	1.94						
	2.02	2.01	2.06	4.35	4.10	4.14	4.53	4.43	4.32
6-*O*-Acetyl-2,3,4-tri-*O*-trimethylsilyl (**2**)	2.02	2.04	2.09	4.46	4.18	4.22	4.25	4.14	4.06

TABLE IV

Nuclear magnetic resonance parameters (in c.p.s.) of H-6 protons of some partially acylated β-methyl glucosides in acetone-d_6

Compound	J_{AB}	δA−δB	J_{AX}	J_{BX}
6-*O*-Acetyl (**3**)	12.0	16.6	1.45	5.05
3,6-Di-*O*-acetyl (**18**)	12.0	13.5	1.76	5.24
4,6-Di-*O*-acetyl (**8**)	12.0	15.6	5.90	2.40
4,6-Di-*O*-Acetyl-2,3-di-*O*-benzyl (7)	12.0	14.8	5.60	2.10
6-*O*-Acetyl-2,3-di-*O*-benzyl-4-*O*-trimethylsilyl (**11**)	11.5	25.15	1.98	4.52
6-*O*-Acetyl-2,3,4-tri-*O*-trimethylsilyl (**2**)	12.0	33.95	1.70	4.90

groups were taken off as before. Product (**4**) (2 g) crystallized from acetone and had m.p. 102–103 °C and $[\alpha]_D$ −35.9° (*c*, 1.6 in chloroform).

Anal. Calcd. for $C_{25}H_{48}O_7$: C, 65.18; H, 10.50. Found: C, 65.38; H, 10.52.

*Methyl 2,3,4-Tri-O-acetyl-6-O-stearoyl-*β*-*D*-glucopyranoside (5)*

Compound **4** (1.3 g) was acetylated with acetic anhydride and pyridine giving **5** (1.4 g) which was crystallized from acetone; it melted at 55–57 °C and had $[\alpha]_D$ −5.6° (*c*, 1.8 in chloroform).

Anal. Calcd. for $C_{31}H_{54}O_{10}$: C, 63.45; H, 9.28. Found: C, 63.50; H, 9.30.

*Methyl 4,6-Di-O-acetyl-*β*-*D*-glucopyranoside (8)*

Acetylation of methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside (14) (4 g) yielded **7** (4.1 g), which was crystallized from ether–hexane (1:1). The m.p. was 41–43 °C and $[\alpha]_D$ −17.2° (*c*, 1.3 in chloroform).

Anal. Calcd. for $C_{25}H_{30}O_8$: C, 65.49; H, 6.60. Found: C, 65.40; H, 6.48.

Product **7** (1 g) was hydrogenated twice in glacial acetic acid (10 ml) over 10% palladium charcoal (0.3 g), for 5 h each time, when the benzyl groups were completely removed. The solvent was taken off and the residue crystallized from benzene to give **8** (0.4 g) with m.p. 92–95 °C and $[\alpha]_D$ −40.2° (*c*, 2.0 in chloroform). Nuclear magnetic resonance: H-4 at 4.89 p.p.m. ($CDCl_3$), 4.78 p.p.m. (acetone-d_6) and 5.40 p.p.m. (pyridine). Spin-decoupling experiments were carried out in D_2O as the best resolution of the signals was obtained in this solvent, tetramethylsilane was used as an external standard. Irradiation of H-2 at 3.82 p.p.m. affected H-1 (4.88 p.p.m.) but did not affect H-4 (5.32 p.p.m.), irradiation at the center of H-5 (4.33 p.p.m.) affected H-4 and H-6 (center at 4.70 p.p.m.) and irradiation at H-4 affected H-5 and H-3 (4.17 p.p.m.). The spacings of the affected signals were reduced to about two-thirds of the original and the intensities to about one-fifth.

Anal. Calcd. for $C_{11}H_{18}O_8$: C, 47.48; H, 6.52. Found: C, 47.46; H, 6.57.

*Methyl 6-O-Acetyl-2,3-di-O-benzyl-*β*-*D*-glucopyranoside (12)*

Methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside (25 g) was converted to the syrupy trimethylsilyl ether and the crude product taken up in methanol (65 ml) at 0 °C. A solution of potassium carbonate (0.057 g) in methanol (13 ml) was added and, after 75 min at 0 °C, the methanol was removed at 20 °C and 0.5 mm. The residue was extracted with hexane (100 ml) leaving insoluble methyl 2,3-di-*O*-benzyl-β-D-glucopyranoside (13 g) which had lost both trimethylsilyl groups. Methyl 2,3-di-*O*-benzyl-4-*O*-trimethylsilyl-β-D-glucopyranoside (**10**) (11.7 g) crystallized from the hexane extract and had m.p. 77–79 °C and $[\alpha]_D$ +36.5° (*c*, 5.0 in chloroform).

Anal. Calcd. for $C_{24}H_{34}O_6Si$: C, 64.55; H, 7.67. Found: C, 64.46; H, 7.67.

Compound (**10**) (10 g) was allowed to stand overnight in pyridine (60 ml) and acetic anhydride (30 ml); the reagents were then removed at 30 °C and 1 mm and the product crystallized from hexane (50 ml) giving 6-*O*-acetyl-2,3-di-*O*-benzyl-4-*O*-trimethylsilyl-β-D-glucopyranoside (**11**) (11 g). The melting point was 96–97 °C and $[\alpha]_D$ +34.8° (*c*, 2.6 in chloroform).

Anal. Calcd. for $C_{26}H_{36}O_7Si$: C, 63.91; H, 7.43. Found: C, 63.86; H, 7.36.

Compound (**11**) (10 g) was refluxed overnight with methanol (100 ml) and water (20 ml), after removal of the solvents, crystallization from benzene–hexane 1:1 (100 ml) gave **12** (4.7 g) with m.p. 123–124 °C and $[\alpha]_D$ −22.5° (*c*, 1.9 in chloroform).

Anal. Calcd. for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78. Found: C, 66.22; H, 6.69

*Methyl 6-O-Acetyl-4-O-stearoyl-*β*-*D*-glucopyranoside (14)*

Compound **12** (2.5 g) was dissolved in methylene chloride (10 ml) and pyridine (2 ml), and after addition of stearoyl chloride (2.72 g) in methylene chloride (4 ml), the mixture was left overnight at room temperature. Methylene chloride (20 ml) was added and the solution washed with water; removal of the solvent gave a solid (4.6 g) which crystallized from hexane (20 ml) giving methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-4-*O*-stearoyl-β-D-glucopyranoside (**13**) (3.5 g); m.p. 55–56 °C and $[\alpha]_D$ −7.3° (*c*, 2.1 in chloroform).

Anal. Calcd. for $C_{41}H_{62}O_8$: C, 72.10; H, 9.15. Found: C, 71.80; H, 9.01.

Removal of the benzyl groups from **13** (2 g) by the method used to prepare **8** gave a crude material still containing some monobenzyl derivative. This product was chromatographed on a silicic acid column and the monobenzyl compounds were eluted with hexane–chloroform (1:1); elution with chloroform gave **14** (0.65 g); m.p. 80–82 °C and $[\alpha]_D$ −17.7° (*c*, 3.5 in chloroform) (after crystallization from benzene–hexane (1:1)). Nuclear magnetic resonance: H-4 at 4.88 p.p.m. ($CDCl_3$), 4.82 p.p.m. (acetone-d_6), and 5.45 p.p.m. (pyridine).

Anal. Calcd. for $C_{27}H_{50}O_8$: C, 64.51; H, 10.03. Found: C, 64.31; H, 9.85.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.

Methyl 2,3,6-Tri-O-acetyl-4-O-stearoyl-β-D-glucopyranoside (15)

Compound (**15**), obtained by acetylation of **14**, was crystallized from acetone and had m.p. 60–62 °C and $[\alpha]_D$ −14.7° (*c*, 1.1 in chloroform).

Anal. Calcd. for $C_{31}H_{54}O_{10}$: C, 63.45; H, 9.28. Found: C, 63.45; H, 9.17.

Partial Acetylation of Methyl 4,6-O-Benzylidene-β-D-glucopyranoside

Fractions obtained during partial acetylation experiments were analyzed by thin-layer chromatography (t.l.c.) on silica gel in ether; the products had the following R_f values: 2,3-diacetate, 0.7; 2-acetate, 0.53; 3-acetate, 0.34; starting material, 0.16.

A mixture of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (25 g), pyridine (100 ml), and acetic anhydride (9.1 g) was kept at 25 °C for 6 days when the reagents were removed at 20 °C and 0.2 mm. The gummy product was heated with hexane (25 ml) and chloroform (25 ml) and filtered from starting material (7.6 g); on standing 1.3 g of 2-acetate crystallized from the filtrate. The remaining solution was then applied to a silicic acid column (200 g) and eluted with hexane–chloroform (1:1); 2,3-diacetate (0.95 g) was eluted first, followed by a mixture of diacetate and 2-acetate (2.7 g), then pure 2-acetate (0.54 g), then fractions with increasing proportions of 3-acetate (4.9 g). Elution with chloroform gave fairly pure 3-acetate (1.5 g) and finally unacetylated material (1.6 g). The 2-acetate was much less soluble in hexane–chloroform (1:1) than the 3-acetate or the diacetate, but was much more soluble in ethanol than these two compounds. By crystallization of the above fractions from the appropriate solvents, all three products were almost completely separated. The yields and percentage yields, based on unrecovered starting material, were as follows: 2,3-diacetate, 2.8 g, 15%; 2-acetate, 5.4 g, 34%; 3-acetate, 3.5 g, 22%.

Methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside had m.p. 177–178 °C and $[\alpha]_D$ −87.7° (*c*, 1.6 in chloroform). Nuclear magnetic resonance ($CDCl_3$): H-2 at 4.98 p.p.m. (quartet), H-3 at 5.31 p.p.m. (triplet), H-1 at 4.51 p.p.m.

Anal. Calcd. for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 58.96; H, 5.95.

Methyl 2-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside had m.p. 174–177 °C and $[\alpha]_D$ −74.4° (*c*, 1.7 in chloroform). Nuclear magnetic resonance ($CDCl_3$): H-2 at 4.88 p.p.m. (quartet) and H-1 at 4.35 p.p.m.

Anal. Calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.31; H, 6.19.

Methyl 3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside had m.p. 162–163 °C and $[\alpha]_D$ −55.2° (*c*, 2.1 in chloroform). Nuclear magnetic resonance ($CDCl_3$): H-3 at 5.22 p.p.m. (triplet), H-1 at 4.34 p.p.m.

Anal. Calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.11; H, 6.15.

Methyl 3-O-Acetyl-β-D-glucopyranoside (16)

Methyl 3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside (2.53 g) was refluxed for 10 min with 50% acetic acid (100 ml), the solvent taken off at 80 °C/0.2 mm, and the residue crystallized from acetone giving **16** (1.43 g). The m.p. was 137–139 °C and $[\alpha]_D$ −9.8° (*c*, 3.8 in acetone). Nuclear magnetic resonance (acetone-d_6): H-3 at 4.92 p.p.m., irradiation at 3.30 p.p.m. (H-2) reduced the spacing and intensity of both H-3 and H-1 (4.26 p.p.m.) and irradiation of H-1 changed H-2 to a doublet.

Anal. Calcd. for $C_9H_{16}O_7$: C, 45.76; H, 6.83. Found: C, 45,78; H, 6.80.

Methyl 3,6-Di-O-acetyl-β-D-glucopyranoside (18)

Compound **16** (2 g) was converted to methyl 3-*O*-acetyl-2,4,6-tri-*O*-trimethylsilyl-β-D-glucopyranoside (**17**) as before. The crude product was distilled giving pure **17** (2.4 g), with b.p. 108–111 °C/0.1 mm and $[\alpha]_D$ −1.0° (*c*, 1.0 in chloroform).

Anal. Calcd. for $C_{18}H_{40}O_7Si_3$: C, 47.75; H, 8.91. Found: C, 47.76; H, 8.80.

Compound (**17**) (1.94 g), in methanol (5 ml), was treated with a solution of potassium carbonate (0.012 g) in methanol (60 ml) and the mixture kept at 0 °C for 1 h. After removal of the solvent the residue was extracted with hexane giving a gum (0.28 g), which was acetylated and then refluxed with methanol (20 ml) and water (7 ml) for 4 h. The solvents were removed leaving a viscous syrup (0.24 g), which combined with material from previous preparations (total 0.31 g), was chromatographed on silicic acid and eluted with chloroform containing 5% methanol. After elution of by-products, apparently containing more than one acetate group, **18** (0.12 g) was obtained. It was crystallized from methylene chloride and had m.p. 45–47 °C, but appeared to retain traces of solvent very tenaciously; $[\alpha]_D$ −17.2° (*c*, 1.8 in chloroform).

Anal. Calcd. for $C_{11}H_{18}O_8$: C, 47.48; H, 6.52. Found: C, 46.85; H, 6.35.

Nuclear magnetic resonance (acetone-d_6): H-3 at 4.94 p.p.m., irradiation of H-2 (3.32 p.p.m.) reduced the intensity and spacing of both H-1 and H-3; in $CDCl_3$: H-3 at 4.92 p.p.m.; in pyridine: H-3 at 5.64 p.p.m.

Previously described methods were used to prepare methyl 3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (**6**) (7), 1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranose (15) and 1,2,4,6-tetra-*O*-acetyl-β-D-glucopyranose (16).

Acknowledgments

The authors are indebted to Dr. P. A. J. Gorin for a number of very helpful discussions, to Mr. L. L. Hoffman for experimental assistance, to Mr. M. Mazurek for n.m.r. measurements, and to Mr. W. C. Haid for microanalyses.

1. A. P. Tulloch, A. Hill, and J. F. T. Spencer. Chem. Commun. 584 (1967).
2. S. A. Barker, J. Homer, M. C. Keith, and L. F. Thomas. J. Chem. Soc. 1538 (1963).
3. R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider. J. Am. Chem. Soc. **80**, 6098 (1958).
4. R. U. Lemieux and J. D. Stevens. Can. J. Chem. **43**, 2059 (1965).
5. R. U. Lemieux and A. R. Morgan. Can. J. Chem. **43**, 2190 (1965).
6. O. Arndt. Ann. Chem. **695**, 176 (1966).
7. E. K. Gladding and C. B. Purves. J. Am. Chem. Soc. **66**, 153 (1944).

8. Y. Z. FROHWEIN and J. LEIBOWITZ. Bull. Res. Council Israel, Sect. A, **11**, 330 (1963).
9. D. T. HURST and A. G. MCINNES. Can. J. Chem. **43**, 2004 (1965).
10. R. W. JEANLOZ and D. A. JEANLOZ. J. Am. Chem. Soc. **79**, 2579 (1957).
11. A. P. TULLOCH. J. Am. Oil Chemists' Soc. **43**, 670 (1966).
12. H. J. BERNSTEIN, J. A. POPLE, and W. G. SCHNEIDER. Can. J. Chem. **35**, 65 (1957).
13. A. P. TULLOCH, J. F. T. SPENCER, and M. H. DEINEMA. Can. J. Chem. **46**, 345 (1968).
14. J. C. DENNISON and D. I. MCGILVRAY. J. Chem. Soc. 1616 (1951).
15. W. A. BONNER. J. Am. Chem. Soc. **80**, 3697 (1958).
16. K. FREUDENBERG and E. PLANKENHORN. Ann. Chem. **536**, 257 (1938).

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UTEP LIBRARY - SERIALS on 08/19/14
For personal use only.