Carbohydrate Research, 138 (1985) 55–64
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

DISCRIMINATION BETWEEN THE 2,3- AND THE 2′,3′-HYDROXYL GROUPS OF MALTOSE AND CELLOBIOSE THROUGH THEIR SPECIFIC PROTECTION†

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(Received July 10th, 1984; accepted for publication, September 28th, 1984)

ABSTRACT

1,6-Anhydro-4′,6′-*O*-benzylidene-maltose and -cellobiose were subjected to temporary *O*-protection with a tetraisopropyldisiloxane-1,3-diyl group at the 2′,3′- and the 2,3-positions, giving 1,6-anhydro-4′,6′-*O*-benzylidene-2′,3′-*O*-(tetraisopropyldisiloxane-1,3-diyl)maltose (**15**) and 1,6-anhydro-4′,6′-*O*-benzylidene-2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)cellobiose (**19**), respectively, in 60–64% yield. These were then subjected to various types of *O*-protection of the hydroxyl groups remaining. Treatment of **15** and **19** with acetic anhydride or phenyl isocyanate gave the corresponding diacetyl and dicarbamoyl derivatives in high yield. Benzylation of the maltose derivative **15** was rather difficult, but was finally achieved through a phase-transfer reaction, to give the 2,3-di-*O*-benzyl derivative (**18**) in moderate yield. In the cellobiose series, benzylation of **19** was conducted similarly, giving **22**, and also by employing a modification of the conventional procedure. The silyl groups of **18** and **22** were removed by treatment with tetrabutylammonium fluoride, to afford the corresponding diols in high yield.

INTRODUCTION

Both maltose and cellobiose are disaccharides readily obtainable by enzymic or chemical degradation of starch and cellulose, respectively. To establish the methodology of utilizing these disaccharides as the starting materials for various syntheses, means were sought to broaden the applicability of the parent polysaccharides as new sources. Such methodology must involve regioselective chemical modifications and transformations of these disaccharides, which require efficient discrimination between the monosaccharide constituents, because both disaccharides are composed solely of a D-glucopyranosyl group and a D-glucopyranose residue. In order to satisfy this requirement to some extent, we transformed these disaccharides into the 1,6-anhydro derivatives[2] (**1** and **8**), and employed these as the actual starting materials for several syntheses[1,3–5]. Because the 4′- and 6′-hy-

†Synthetic Studies on Mucopolysaccharides, Part II. For Part I, see ref. 1.
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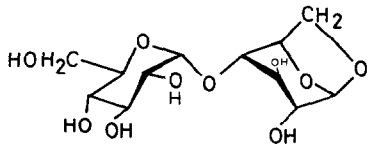

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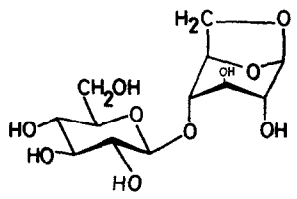

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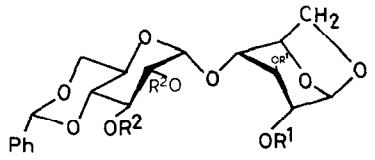
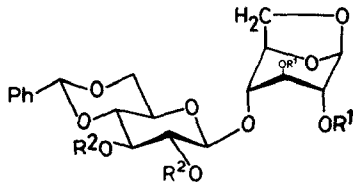


2 $R^1 = R^2 =$ H
3 $R^1 = R^2 =$ Ac
4 R^1 = Ac, R^2 = H
5 R^1 = CONHPh, R^2 = H
6 R^1 = Bn, R^2 = H
7 R^1 = Bn, R^2 = Ac



9 $R^1 = R^2$ = H
10 $R^1 = R^2$ = Ac
11 R^1 = H, R^2 = Ac
12 R^1 = H, R^2 = CONHPh
13 R^1 = H, R^2 = Bn
14 R^1 = Ac, R^2 = Bn

droxyl groups of **1** and **8** are readily masked by *O*-benzylidenation, the problem remaining unsolved concerned the hydroxyl groups at C-2,3 and C-2′,3′.

Herein are described practical procedures for complete discrimination between the 2,3- and the 2′,3′-hydroxyl pairs of **2** and **9** through their specific protection.

RESULTS AND DISCUSSION

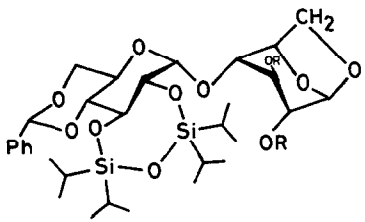
The 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl group[6] has been widely used in nucleoside and monosaccharide chemistry because it can protect two hydroxyl groups simultaneously, and be removed under neutral conditions. To the best of our knowledge, however, it has not been applied to the protection of disaccharide derivatives. We have now found that this silyl group could serve for effective discrimination between the 2,3- and the 2′,3′-hydroxyl pairs of **2** and **9** through temporary protection of one of these pairs, and have established practical procedures for subsequent protection of the remaining hydroxyl pairs with various "persistent" groups.

Treatment of compound **2** (ref. 7) with 1.2 mol. equiv. of 1,3-dichloro-

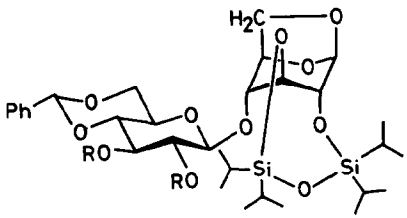
TABLE I

CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (Hz) FOR MALTOSE AND CELLOBIOSE DERIVATIVES

Compounds	*Ac*	*H-2*	*H-3*	*H-2'*	*H-3'*
Maltose series					
3	2.06, 2.09, 2.10, 2.20	4.58 (s)	4.81 (s)	4.88 (dd, *J* 3.91 and 10.0 Hz)	5.65 (t, *J* 10.0 Hz)
16	2.08, 2.11	4.60 (s)	4.89 (s)	3.81 (dd, *J* 3.90 and 10.3 Hz)	4.19 (t, *J* 10.3 Hz)
4	2.13, 2.13	4.67 (s)	5.17 (s)	3.68 (dd, *J* 3.91 and 9.76 Hz)	4.05 (t, *J* 9.76 Hz)
7	1.86, 2.16	3.56 (s)	3.59 (s)	4.81 (dd, *J* 3.91 and 10.0 Hz)	5.59 (t, *J* 10.0 Hz)
Cellobiose series					
10	2.05, 2.07, 2.12, 2.14	4.53 (s)	5.08 (s)	5.07 (dd, *J* 7.81 and 9.28 Hz)	5.33 (t, *J* 9.28 Hz)
20	2.05, 2.09	3.71 (s)	3.74 (s)	4.96 (dd, *J* 7.81 and 9.28 Hz)	5.23 (t, *J* 9.28 Hz)
11	2.08, 2.12	3.81 (s)	3.91 (s)	5.06 (dd, *J* 7.82 and 9.52 Hz)	5.39 (t, *J* 9.52 Hz)
14	2.07, 2.11	4.56 (s)	5.21 (s)	3.56 (t, *J* 8.55 Hz)	3.76 (t, *J* 8.55 Hz)



15 R = H
16 R = Ac
17 R = CONHPh
18 R = Bn



19 R = H
20 R = Ac
21 R = CONHPh
22 R = Bn

1,1,3,3-tetraisopropyldisiloxane in pyridine gave the 2′,3′-cyclic silyl ether (**15**), whereas **9** gave the 2,3-cyclic ether (**19**) under the same treatment. These products, without isolation, were acetylated, for purification and characterization, to afford **16** and **20** in an overall yield of 60–64% from **2** and **9**, respectively. The structures of **16** and **20** were elucidated by comparison of their ^{1}H-n.m.r. spectra with those of the per-*O*-acetylated derivatives **3** (ref. 7) and **10** of **2** and **9**. These data are summarized in Table I. The signals due to H-2′ and H-3′ of **16** appear in the upper field of the chemical shift compared to those of **3**. This reveals that the silyl group attaches to the 2′- and 3′-hydroxyl groups in the maltose derivative **16**. In contrast, in **20**, the signals due to H-2 and H-3 appear in the upper field compared to those of **10**. This shows that the silyl group in the cellobiose derivative **20** attaches to the 2- and 3-hydroxyl groups. Although the disiloxane reagent reacts with different pairs of hydroxyls in **2** and **9**, its selectivity is equally high in the two cases, fulfilling the discrimination between the monosaccharide constituents.

Special care must be taken in further treatment of these disaccharides carrying the silyl group, as this group is highly susceptible to cleavage. For example, *O*-deacetylation of **16** and **20** to afford the original **15** and **19** by the Zemplén procedure failed, because the silyl group underwent solvolysis with sodium methoxide[8], giving multitudinous products. However, treatment of **16** and **20** with 5 mol. equiv. of hydrazine monohydrate in oxolane–methanol afforded the desired diols, **15** and **19** in high yield. *O*-Desilylation of **16** and **20** under the usual anhydrous conditions[9], employing tetrabutylammonium fluoride in oxolane, also failed, giving many products, probably due to acyl migration brought about by attack of the alkoxide

TABLE II

RESULTS OF THE BENZYLATION OF **19**

Entry	*Reagents*	*Solvents*	*Temp. (°)*	*Products*[a]	*Yields (%)*
1	NaH, BnBr	DMF[b]	r.t.[c]	2,3,2′,3′-tetra-*O*-Bn[d]	90
2	BaO, $Ba(OH)_2 \cdot 8\,H_2O$, BnBr	Me_2SO[e]	r.t.	2,3,2′,3′-tetra-*O*-Bn	>90
3	Ag_2O, Bu_4NI, BnBr	THF[f]–DMF	r.t.	2′,3′-di-*O*-Bn 2′-*O*-Bn 3′-*O*-Bn	26 61 13
4	BnOTf[g], 2,4,6-collidine	CH_2Cl_2	−60	2′,3′-di-*O*-Bn 2′-*O*-Bn 3′-*O*-Bn	6 7 10
5	NaH, Bu_4NI, BnBr	THF	r.t.	2′,3′-di-*O*-Bn	82
6	Bu_4NHSO_4, BnBr	toluene 50% aq NaOH	−10	2′,3′-di-*O*-Bn	>90

[a]These structures were elucidated on the basis of the ^{1}H-n.m.r. spectra of their acetate derivatives (*O*-desilylation and acetylation). [b]*N*,*N*-Dimethylformamide. [c]Room temperature. [d]Bn, benzyl derivative. [e]Dimethyl sulfoxide [f]Oxolane. [g]Benzyl triflate

intermediates formed during the *O*-desilylation. In order to scavenge the alkoxide, we employed acetonitrile–water–oxolane as the solvent, and found that the *O*-desilylation of **16** and **20** proceeded satisfactorily, to afford diols **4** and **11** in high yield. Derivatives carrying *N*-phenylcarbamoyl groups, **17** and **21**, were also prepared from **2** and **9** in high yields by successive treatment with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane and phenyl isocyanate in pyridine. In *O*-desilylation of **17** and **21**, anhydrous conditions[9] could be employed, but the yields of the products (**5** and **12**) were not so high. Employment of a protic solvent would probably result in better yields of the products in these cases also.

As the benzyl group is one of the most useful protective groups in carbohydrate chemistry, benzylation of **15** and **19** was next attempted, but it proved unsatisfactory because of the instability of the silyl group under the usual conditions of benzylation. The results of benzylation of the cellobiose derivative **19** are summarized in Table II. The usual procedures (Entries 1 and 2) resulted in a high yield of the 2,3,2′,3′-tetra-*O*-benzyl derivative, whereas, a mixture of mono- and di-*O*-benzyl derivatives was obtained under the conditions given in Entries 3 and 4 (ref. 10).

The desired 2′,3′-di-*O*-benzylation was achieved by two independent procedures. When sodium hydride was added portionwise to a mixture of **19**, benzyl bromide, and tetrabutylammonium iodide[11] in oxolane, the expected 2′,3′-di-*O*-benzyl derivative (**22**) was obtained in 82% yield (Entry 5). The order of adding the reagents is a crucial factor. The other successful, di-*O*-benzylation of **19** was conducted by employing tetrabutylammonium hydrogensulfate[12] as the phase-transfer catalyst, giving **22** in a yield of >90% (Entry 6).

The silyl group of **22** was removed by treatment with tetrabutylammonium fluoride in oxolane[9], giving a high yield of **13**. The structure of **13** was confirmed on the basis of the ^{1}H-n.m.r. spectrum of its diacetate (**14**). In contrast to the successful benzylation in the cellobiose series, the maltose derivative **15** underwent over-benzylation at O-2′-oxygen by use of the same procedure as for Entry 5 in Table II, giving the 2,3,2′-tri-*O*-benzyl derivative in high yield.

However, careful application of the same procedure as in Entry 6 in Table II was successful for the preparation of the 2,3-di-*O*-benzyl derivative (**18**). Thus, **18** and a mono-*O*-benzyl derivative were obtained in 31 and 21% yield, respectively, when **15**, benzyl bromide (a large excess), and tetrabutylammonium hydrogensulfate were vigorously stirred in a mixture of toluene and 50% aqueous sodium hydroxide during 2.3 h at −10°. The mono-*O*-benzyl derivative was also utilizable for the preparation of **18** by employing the same procedure (48% yield). The production of the undesired 2,3,2′-tri-*O*-benzyl derivative was <10%. Treatment of **18** with tetrabutylammonium fluoride gave the diol **6**, which was acetylated to afford **7** for structural elucidation.

In conclusion, procedures for introducing such protecting groups as acetyl, *N*-phenylcarbamoyl, and benzyl onto either O-2,3 or O-2′,3′ of maltose and cellobiose were established. These methodologies will be of great help for the prepara-

tion of biologically interesting compounds having oligosaccharide-related structures[13].

EXPERIMENTAL

General methods. — Melting points were determined with a Yamoto micro melting-point apparatus, and are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 241MC polarimeter. Chromatography was performed in a column 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 a Shimadzu IR-27 spectrophotometer. ^{1}H-N.m.r. spectra were recorded with a JEOL JNM-FX 400 or JNM-GX 400 spectrometer, using tetramethylsilane as the internal standard, for solutions in chloroform-*d*, unless specified otherwise. Solutions were evaporated under diminished pressure, and solvent extracts were dried with magnesium sulfate.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranose (**10**). — A mixture of **8** (19 g, 56 mmol), dimethoxytoluene[14] (9.4 g, 62 mmol), and *p*-toluenesulfonic acid monohydrate (32 mg) in *N,N*-dimethylformamide (120 mL) was placed in a 500-mL, round-bottomed flask; this was then attached to a rotary evaporator, evacuated, lowered into a water-bath at 75–80°, and kept for 1.5 h. After removal of the solvent, acetic anhydride (50 mL) was added to a cooled solution of the residue in pyridine (100 mL) at 0–5°, and the mixture was stirred for 6 h at room temperature. The mixture was evaporated, and the residual syrup was chromatographed on silica gel, with 5:1 (v/v) toluene–ethyl acetate as the eluant, to give **10** (22 g, 68%); m.p. 169–170°, $[\alpha]_D^{26}$ −90° (*c* 0.69, chloroform).

Anal. Calc. for $C_{27}H_{32}O_{24}$: C, 55.87; H, 5.56. Found: C, 55.77; H, 5.56.

1,6-Anhydro-4-O-(4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranose (**9**). — A mixture of **10** (22.0 g, 37.9 mmol) and sodium methoxide (500 mg, 9.3 mmol) in methanol (200 mL) was stirred for 10 h at room temperature. Dowex 50-X8 (H^+) resin was added to the mixture to pH 7.5, the mixture filtered, and the filtrate evaporated. The residue crystallized from methanol–ethyl acetate, to give **9** (14.4 g, 88%); m.p. 140–143°, $[\alpha]_D^{17}$ −31° (*c* 2.20, methanol); δ_H (D_2O) 3.33 (dd, 1 H, *J* 7.82 and 9.28 Hz, H-2′), 3.97 (dd, 1 H, *J* 0.98 and 7.82 Hz, H-6a), 4.23 (dd, 1 H, *J* 4.40 and 10.3 Hz, H-6′a), 4.59 (d, 1 H, *J* 7.82 Hz, H-1′), 5.33 (s, 1 H, H-1), and 5.60 (s, 1 H, benzylidene).

Anal. Calc. for $C_{19}H_{24}O_{10} \cdot H_2O$: C, 53.02; H, 6.09. Found: C, 53.03; H, 5.76.

2,3-Di-O-acetyl-1,6-anhydro-4-O-[4,6-O-benzylidene-2,3-O-(tetraisopropyldisiloxane-1,3-diyl)-α-D-glucopyranosyl]-β-D-glucopyranose (**16**). — 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (920 mg, 2.90 mmol) was added to a cold mixture of **2** (1.0 g, 2.40 mmol) in pyridine (15 mL) at 0–5°; the mixture was stirred for 10

h at room temperature, and then acetic anhydride (5 mL) was added. After being stirred for 6 h at room temperature, the mixture was poured into ice–water, and extracted with ethyl acetate. The extracts were successively washed with cold, dilute sulfuric acid, aqueous sodium hydrogencarbonate, and water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 25:1 (v/v) toluene–ethyl acetate as the eluant, to give **16** (1.07 g, 60%); m.p. 142.5–143°, $[\alpha]_D^{23}$ −13° (*c* 0.94, chloroform).

Anal. Calc. for $C_{35}H_{54}O_{13}Si_2$: C, 56.59; H, 7.37. Found: C, 56.61; H, 7.44.

1,6-Anhydro-2,3-O-(tetraisopropyldisiloxane-1,3-diyl)-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranose (**20**). — Compound **9** (8.54 g, 20.7 mmol) was successively treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (7.84 g, 24.8 mmol) and acetic anhydride (20 mL) as described for the synthesis of **16**, to give **20** (9.72 g, 64%); m.p. 220–225°, $[\alpha]_D^{22}$ −82° (*c* 0.71, chloroform).

Anal. Calc. for $C_{35}H_{54}O_{13}Si_2$: C, 56.59; H, 7.37. Found: C, 56.85; H, 7.33.

1,6-Anhydro-4-O-[4,6-O-benzylidene-2,3-O-tetraisopropyldisiloxane-1,3-diyl)-α-D-glucopyranosyl]-β-D-glucopyranose (**15**). — A mixture of **16** (1.7 g, 2.3 mmol), oxolane (40 mL), methanol (20 mL), and hydrazine monohydrate (694 mg, 13.8 mmol) was stirred for 10 h at room temperature. The mixture was evaporated and the residue was diluted with chloroform–water. The organic layer was washed with water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 9:1 (v/v) chloroform–methanol as the eluant, to give **15** (1.2 g, 80%) as an amorphous powder; $[\alpha]_D^{20}$ +5° (*c* 0.68, chloroform); ν_{max}^{Nujol} 3440 cm^{-1}.

Anal. Calc. for $C_{31}H_{50}O_{11}Si_2$: C, 56.86; H, 7.70. Found: C, 56.77; H, 7.71.

1,6-Anhydro-4-O-(4,6-O-benzylidene-β-D-glucopyranosyl)-2,3-O-(tetraisopropyldisiloxane-1,3-diyl)-β-D-glucopyranose (**19**). — Compound **20** (3.5 g, 4.7 mmol) in oxolane (30 mL) and methanol (10 mL) was treated with hydrazine monohydrate (1.4 g, 28 mmol) as described for the synthesis of **15**, to give **19** (2.9 g, 94%); m.p. 85–87°, $[\alpha]_D^{23}$ −46° (*c* 0.67, chloroform); ν_{max}^{Nujol} 3460 cm^{-1}.

Anal. Calc. for $C_{31}H_{50}O_{11}Si_2$: C, 56.86; H, 7.70. Found: C, 56.89; H, 7.91.

1,6-Anhydro-4-O-[4,6-O-benzylidene-2,3-O-(tetraisopropyldisiloxane-1,3-diyl)-α-D-glucopyranosyl]-2,3-di-O-(N-phenylcarbamoyl)-β-D-glucopyranose (**17**). — 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (5.96 g, 18.9 mmol) was added to a cooled solution of **3** (6.0 g, 14.6 mmol) in pyridine (90 mL) at −10°, and the mixture was stirred for 2 days at room temperature. Phenyl isocyanate (5.48 g, 46 mmol) was added dropwise to the cooled mixture at 0–5°, and the mixture was heated for 1 h at 90°. The excess of the reagent was decomposed by addition of methanol, and the mixture was evaporated. The residue was diluted with ethyl acetate, and the organic layer was successively washed with cold, dilute sulfuric acid, aqueous sodium hydrogencarbonate, and water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 4:1 (v/v) hexane–ethyl acetate as the eluant, to give **17** (7.12 g, 55%); m.p. 126–131°, $[\alpha]_D^{27}$ −13° (*c* 2.60, chloroform); ν_{max}^{KBr} 3350 (NH), 1760 (C=O), and 1530 cm^{-1} (CONH); δ_H 0.85–1.15

(m, 28 H, four isopropyl groups), 3.69 (s, 1 H, H-4), 3.75 (t, 1 H, *J* 10.1 Hz, H-3′), 3.79–3.85 (m, 2 H, H-6b,2′), 4.16–4.26 (m, 2 H, H-4′,5′), 4.72 (d, 1 H, *J* 5.19 Hz, H-5), 4.81 (s, 1 H, H-2), 4.98 (s, 1 H, H-3), 5.19 (d, 1 H, *J* 3.97 Hz, H-1′), 5.56 (s, 1 H, H-1), and 5.59 (s, 1 H, benzylidene).

Anal. Calc. for $C_{45}H_{60}N_2O_{13}Si_2$: C, 60.52; H, 6.77; N, 3.14. Found: C, 60.13; H, 6.72; N, 3.14.

1,6-Anhydro-4-O-[4,6-O-benzylidene-2,3-di-O-(N-phenylcarbamoyl)-β-D-glucopyranosyl]-2,3-O-(tetraisopropyldisiloxane-1,3-diyl)-β-D-glucopyranose (**21**). — Compound **9** (1.40 g, 3.40 mmol) in pyridine (20 mL) was successively treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (1.40 g, 4.42 mmol) and phenyl isocyanate (1.20 g, 10.2 mmol) as described for the synthesis of **17**, to give **21** (1.60 g, 53%); m.p. 128–132°, $[\alpha]_D^{23}$ −53° (*c* 0.69, chloroform); ν_{max}^{KBr} 3300 (NH), 1720 (C=O), and 1525 cm^{-1} (CONH); δ_H 4.36 (dd, 1 H, *J* 4.88 and 10.4 Hz, H-5′), 4.47 (s, 1 H, H-5), 4.78 (d, 1 H, *J* 7.63 Hz, H-1′), 4.99 (t, 1 H, *J* 9.46 Hz, H-2′), 5.25 (s, 1 H, H-1), 5.34 (t, 1 H, *J* 9.46 Hz, H-3′), 5.53 (s, 1 H, benzylidene), 6.81 (s, 1 H, N*H*), and 6.83 (s, 1 H, N*H*).

Anal. Calc. for $C_{45}H_{60}N_2O_{13}Si_2$: C, 60.52; H, 6.77; N, 3.14. Found: C, 60.35; H, 6.77; N, 3.06.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(4,6-O-benzylidene-α-D-glucopyranosyl)-β-D-glucopyranose (**4**). — Tetrabutylammonium fluoride in oxolane (0.7 mL, M solution) was added to a cooled solution of **9** (90 mg, 0.12 mmol) in acetonitrile (1.5 mL) and water (0.1 mL) at 0–5°, and the mixture was stirred for 3 h at room temperature. The mixture was diluted with chloroform, and the organic layer was washed with water, dried, and evaporated. The product (**4**) was purified by preparative t.l.c. (Merck Art 5717, 60 F_{254}) with 50:47:3 (v/v) chloroform–ethyl acetate–methanol, to give an amorphous powder (53 mg, 94%); $[\alpha]_D^{26}$ +48° (*c* 0.54, chloroform).

Anal. Calc. for $C_{23}H_{28}O_{12}$: C, 55.64; H, 5.68. Found: C, 55.43; H, 5.84.

1,6-Anhydro-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranose (**11**). — Compound **20** (76 mg, 0.10 mmol) in acetonitrile (1.5 mL) and water (0.1 mL) was treated with tetrabutylammonium fluoride in oxolane (0.7 mL, M solution) as described for the synthesis of **4**, to give **11** (45 mg, 96%), and the product crystallized from methanol–water; m.p. 194–196° $[\alpha]_D^{27}$ −98° (*c* 0.08, chloroform).

Anal. Calc. for $C_{23}H_{28}O_{12} \cdot H_2O$: C, 53.69; H, 5.88. Found: C, 53.78; H, 5.48.

1,6-Anhydro-4-O-(4,6-O-benzylidene-α-D-glucopyranosyl)-2,3-di-O-(N-phenyl-carbamoyl)-β-D-glucopyranose (**5**). — Tetrabutylammonium fluoride in oxolane (4.5 mL, M solution) was added to a cooled solution of **17** (1.0 g, 1.1 mmol) in oxolane (20 mL) at 0–5°, and the mixture was stirred for 10 h at room temperature. The mixture was evaporated, and the residue was diluted with chloroform. The organic layer was washed with water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 24:1 (v/v) chloroform–2-propanol as the

eluant, to give **5** (110 mg, 16%); m.p. 268–273° (from ethyl acetate), $[\alpha]_D^{27}$ +25° (*c* 0.52, dimethyl sulfoxide); δ_H 4.90 (d, 1 H, *J* 8.79 Hz, H-5), 5.71 (d, 1 H, *J* 3.68 Hz, H-1'), 5.77 (s, 1 H, H-1), and 6.71 (br s, 2 H, 2 N*H*).

Anal. Calc. for $C_{33}H_{34}N_2O_{12} \cdot H_2O$: C, 59.27; H, 5.43; N, 4.18. Found: C, 59.02; H, 5.13; N, 4.12.

*1,6-Anhydro-4-*O*-[4,6-*O*-benzylidene-2,3-di-*O*-(*N*-phenylcarbamoyl)-β-*D*-glucopyranosyl]-β-*D*-glucopyranose* (**12**). — Compound **21** (600 mg, 0.67 mmol) in oxolane (4 mL) was treated with tetrabutylammonium fluoride in oxolane (2 mL, M solution) as described for the synthesis of **5**, to give **12** (180 mg, 41%); m.p. 240–241° (from ethyl acetate–hexane), $[\alpha]_D^{20}$ −41° (*c* 0.65, chloroform); ν_{max}^{KBr} 3400, 3300, 1720 (C=O), and 1530 cm^{-1} (CONH).

Anal. Calc. for $C_{33}H_{34}N_2O_{12}$: C, 60.92; H, 5.27; N, 4.31. Found: C, 60.43; H, 5.28; N, 4.30.

*1,6-Anhydro-2,3-di-*O*-benzyl-4-*O*-[4,6-*O*-benzylidene-2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-α-*D*-glucopyranosyl]-β-*D*-glucopyranose* (**18**). — A solution of **15** (1.0 g, 1.5 mmol) in toluene (10 mL) was added to a cooled mixture of tetrabutylammonium hydrogensulfate (667 mg, 1.96 mmol) and benzyl bromide (9.63 g, 56.3 mmol) in 50% aqueous sodium hydroxide (10 mL) at −10°, and the mixture was vigorously stirred for 2.3 h at −10°. The mixture was diluted with ethyl acetate, washed with water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 40:1 (v/v) toluene–ethyl acetate as the eluant, to give **18** (390 mg, 31%), and the mono-*O*-benzyl (237 mg, 21%), and tri-*O*-benzyl derivative (144 mg, 10%); R_F 0.59, 0.53, and 0.45, respectively, in 9:1 (v/v) benzene–ethyl acetate. For **18**: $[\alpha]_D^{21}$ −20° (*c* 0.62, chloroform).

Anal. Calc. for $C_{45}H_{62}O_{11}Si_2$: C, 64.72; H, 7.48. Found: C, 64.47; H, 7.55.

*1,6-Anhydro-2,3-*O*-(tetraisopropyldisiloxane-1,3-diyl)-4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**22**). — Sodium hydride (110 mg, 50% mineral oil dispersion) was added portionwise to a cooled mixture of **19** (2.92 g, 4.45 mmol), benzyl bromide (8.1 g, 23.6 mmol), and tetrabutylammonium iodide (8.7 g, 23.6 mmol) in oxolane (50 mL) at 0–5°, and the mixture was stirred for 3.5 h at room temperature. The mixture was poured into ice–water, and extracted with ethyl acetate. The extracts were combined, washed with water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 20:1 (v/v) toluene–ethyl acetate as the eluant, to give **22** (3.30 g, 82%) as a syrup; $[\alpha]_D^{23}$ −56° (*c* 0.36, chloroform).

Anal. Calc. for $C_{45}H_{62}O_{11}Si_2$: C, 64.71; H, 7.48. Found: C, 64.57; H, 7.26.

*1,6-Anhydro-2,3-di-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-α-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**6**). — Tetrabutylammonium fluoride in oxolane (10 mL, M solution) was added to a cooled solution of **18** (2.10 g, 2.41 mmol) in oxolane (30 mL) at 0–5°, and the mixture was stirred for 3 h at room temperature. The mixture was evaporated, and the residue was diluted with chloroform. The organic layer was washed with water, dried, and evaporated. The residual syrup was chromatographed on silica gel, with 3:1 (v/v) toluene–ethyl acetate as the eluant, to give **6**

(1.26 g, 88%) as an amorphous powder; $[\alpha]_D^{23}$ +22° (*c* 0.88, chloroform); ν_{max}^{Nujol} 3460 cm^{-1}.

Anal. Calc. for $C_{33}H_{36}O_{10}$: C, 66.88; H, 6.12. Found: C, 66.87; H, 6.21.

1,6-Anhydro-4-O-(2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranose (**20**). — Compound **22** (3.0 g, 3.6 mmol) in oxolane (30 mL) was treated with tetrabutylammonium fluoride in oxolane (10 mL, M solution) as described for the synthesis of **6**, to give **13** (1.9 g, 89%) as an amorphous powder; $[\alpha]_D^{22}$ −56° (*c* 0.59, chloroform).

Anal. Calc. for $C_{33}H_{36}O_{10} \cdot 0.5\ H_2O$: C, 65.88; H, 6.20. Found: C, 65.56; H, 5.99.

1,6-Anhydro-2,3-di-O-benzyl-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranosyl)-β-D-glucopyranose (**7**). — A mixture of **18** (31 mg, 0.05 mmol) in pyridine (1 mL) and acetic anhydride (1 mL) was stirred for 6 h at room temperature. After the usual processing, compound **7** was obtained in quantitative yield; m.p. 137.5–138.5°, $[\alpha]_D^{20}$ +17° (*c* 0.66, chloroform).

Anal. Calc. for $C_{37}H_{40}O_{12}$: C, 65.67; H, 5.96. Found: C, 65.69; H, 5.93.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-benzyl-4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranose (**14**). — Compound **13** (1.0 g, 1.9 mmol) in pyridine (10 mL) was treated with acetic anhydride (5 mL), and after the usual processing, compound **14** was obtained in quantitative yield; m.p. 180–181°, $[\alpha]_D^{17}$ −18° (*c* 0.90, chloroform).

Anal. Calc. for $C_{37}H_{40}O_{12}$: C, 65.67; H, 5.96. Found: C, 65.70; H, 5.93.

ACKNOWLEDGMENTS

We are grateful to Dr. J. Uzawa and Mrs. T. Chijimatsu for recording and measuring the ^1H-n.m.r. spectra, and Dr. H. Homma and his collaborators for the elemental analyses. Also, we thank the Misses Y. Nishimura and Y. Kato for technical assistance.

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