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GLYCOSYLATION OF SUGAR 2,3-DIPHENYL-2-CYCLOPROPEN-1-YL ETHERS. A NEW ROUTE TO OLIGOSACCHARIDES*

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ABSTRACT

The 2,3-diphenyl-2-cyclopropen-1-yl (Ph_2cp) group is proposed for the activation of secondary as well as primary sugar hydroxyl groups in the synthesis of glycosides. Sugar Ph_2cp ethers are easily obtained by the action of 2,3-diphenyl-2-cyclopropen-1-ylium perchlorate on suitably protected sugars in the presence of 2,4,6-trimethylpyridine. Condensation of Ph_2cp ethers with a slight excess of glycosyl bromide and silver perchlorate for 15 min at 50° gave the protected *N*-acetylallolactosamine, *N*-acetyllactosamine, and laminaribiose in 35–50% yields. Protected trisaccharides were obtained in 35% yield.

INTRODUCTION

The formation of 1,2-*trans*-glycosidic bonds in oligosaccharides has been obtained up to now mainly by condensation of a free hydroxyl group of the appropriate sugar derivative with such glycosylating agents as glycosyl halides[2–4] and sugar orthoesters[5]. The yield of these condensations is frequently low; for example, the difficulty of condensation with the hydroxyl group at C-4 [the least reactive of the hydroxyl groups of pyranoses in $^4C_1$ (D) conformation] is well known[6,7]. As oligosaccharides having a (1→4)-linkage are wide-spread in Nature, their synthesis is of importance. One of the possible approaches involves the use of acyclic[6] or 1,6-anhydro derivatives[8–10] .The major disadvantage of this approach is the large number of steps involved in the synthesis of the starting material and the side reactions accompanying the removal of the protecting groups.

Another approach to the glycosylation of hydroxyl groups of low reactivity has been their activation by replacement of the proton with a metal cation or by introduction of special groupings that increase the nucleophilic reactivity of the oxygen atom. Some years ago, Kochetkov *et al.*[11] proposed the use of the *tert*-butyl group for this purpose. Thus, condensation of *tert*-butyl ethers and glycosyl halides in the presence of silver carbonate gave a number of glycosides of aliphatic alcohols and

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hydroxy amino acids. No arguments in favor of the activation by the *tert*-butyl group were forwarded, and it cannot be excluded that, under the drastic reaction conditions employed, the splitting of 2-methylpropene and the formation of the corresponding alcohol took place; thus, the alcohol formed would have interacted with the glycosylating agent. The general application of the *tert*-butyl group for the activation of hydroxyl groups of low reactivity has not, as yet, been demonstrated, and the only known example of its use in oligosaccharide synthesis is that for the preparation of β,β-trehalose [12].

An efficient method of oligosaccharide synthesis based on the condensation of sugar trityl ethers with glycosyl halides in the presence of silver perchlorate was developed by Bredereck *et al.*[13]. The inductive effect of the trityl group increased the nucleophilicity of the oxygen atom of the aglycon. The trityl cation formed possesses high stability (in contrast to the *tert*-butyl cation) and, thus, it is not necessary to introduce a special proton acceptor. The advantage of this method lies in the mildness of the condensation conditions, the stereospecificity, the shortness of the time of the reaction, and also the high yield of products desired. However, the difficulty of tritylating secondary hydroxyl groups of sugars limits this method to the synthesis of oligosaccharides having a (1→6)-glycosidic bond.

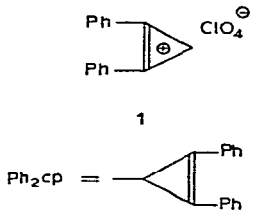
In this connection, we began to search for a new activating group that would be able (a) to etherify secondary as well as primary sugar hydroxyl groups, and (b) to be split off by glycosyl perchlorate to form a stable cation. The 2,3-diphenyl-2-cyclopropen-1-yl (Ph_2cp) group was found to satisfy these conditions.

RESULTS AND DISCUSSION

Since the cyclopropenylium cation possesses an aromatic system, it has high stability, being even more stable than the trityl cation[14,15], but it has not, until now, been used in carbohydrate chemistry.

Sugar Ph_2cp ethers were obtained by treatment of partially protected sugars with 2,3-diphenyl-2-cyclopropen-1-ylium perchlorate[16,17] (**1**) in benzene, acetonitrile, or ethyl acetate solution, in the presence of 2,4,6-trimethylpyridine at room temperature. The reaction was monitored by t.l.c. on neutral alumina, and the Ph_2cp ethers were isolated by column chromatography on the same adsorbent. Thus, the partially protected sugars **2**, **5**, and **7** gave benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-6-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-α-D-glucopyranoside (**3**), benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-α-D-glucopyranoside (**6**), and 3-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**8**), respectively. The spectral data of **3**, **6**, and **8** were in agreement with the postulated structures. The position of the Ph_2cp residue was proved by mild acid hydrolysis, which gave the starting compounds.

The crystalline Ph_2cp ethers **3**, **6**, and **8** were extremely labile under acidic conditions, and they decomposed already during chromatography on silica gel. In contrast, they were stable to such alkali as sodium methoxide or triethylamine in anhydrous methanol, and ammonia in aqueous methanol. Benzyl 2-acetamido-



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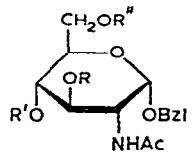
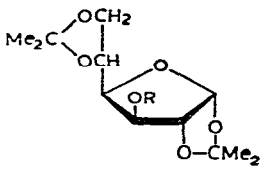
Ph_2cp =



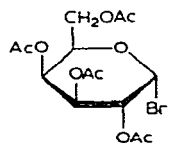
2 R = R′ = Ac, R″ = H
3 R = R′ = Ac, R″ = Ph_2cp
4 R = R′ = H, R″ = Ph_2cp
5 R = R″ = Ac, R′ = H
6 R = R″ = Ac, R′ = Ph_2cp



7 R = H
8 R = Ph_2cp

2-deoxy-6-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-α-D-glucopyranoside (**4**) obtained by *O*-deacetylation of **3** is a crystalline compound possessing a u.v. spectrum typical for Ph_2cp ethers[18]. Acetylation of **4** with acetic anhydride in pyridine at room temperature resulted in partial decomposition and in the formation of a mixture of **3** and benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside.

Compound **3** was selected for testing the usefulness of Ph_2cp ethers in glycoside synthesis. Treatment of **3** with a slight excess of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**9**) in the presence of an equimolar amount of silver perchlorate in benzene solution at 50° gave the known *N*-acetylallolactosamine derivative[19] (**10**) in 50% yield*. The efficiency of the method was examined by synthesizing 2-acetamido-2-deoxy-4-*O*-β-D-galactopyranosyl-D-glucose (*N*-acetyllactosamine, **13**) and 3-*O*-β-D-glucopyranosyl-D-glucose (laminaribiose).



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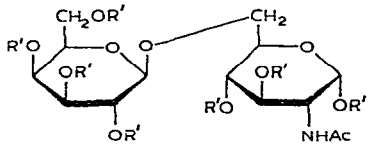
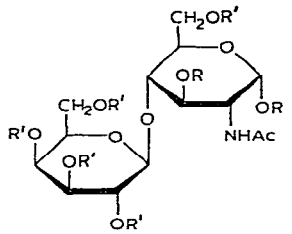


10 R = Bzl, R′ = Ac
11 R = R′ = H



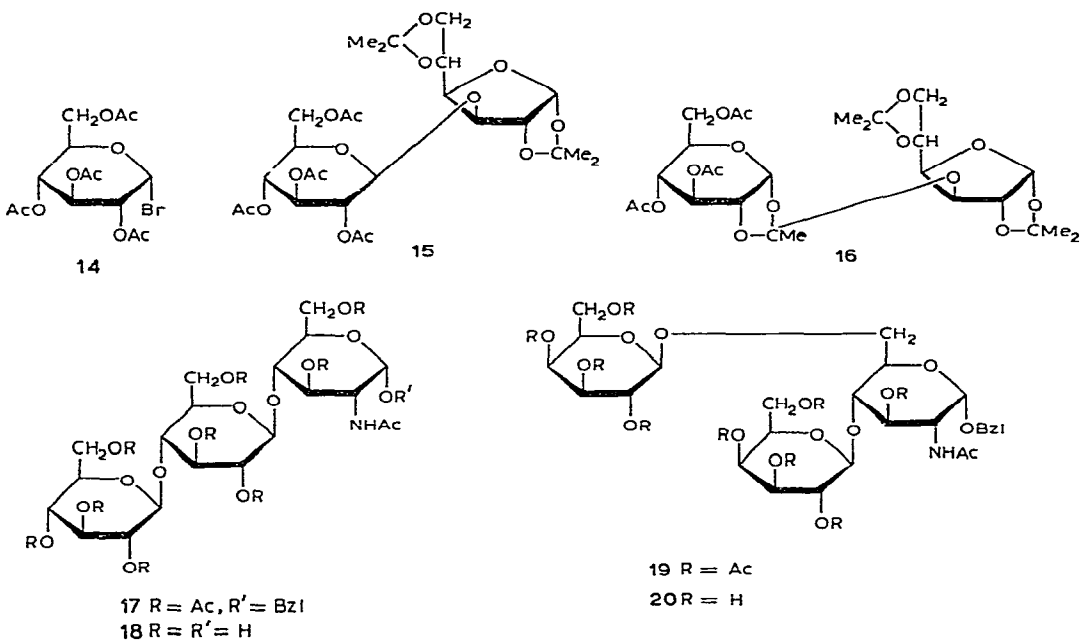
12 R = Bzl, R′ = Ac
13 R = R′ = H

Only two syntheses of *N*-acetyllactosamine involving the direct glycosylation of the equatorial hydroxyl group at C-4 of a 2-acetamido-2-deoxy-D-glucopyranose derivative were known. The synthesis[20] by the Koenigs–Knorr method, starting from 2-acetamido-1,3,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranose, gave only a 4% yield. The condensation[21] of the partially blocked acetate **5** with 3,4,6-tri-*O*-acetyl-1,2-*tert*-butylorthoacetyl-α-D-galactopyranose increased the yield to 19%. The condensation of the Ph_2cp ether **6** and the bromide **9** gave benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyrano-

*Not at room temperature as described in our preliminary communication[1].

side (**12**) in a 35% yield (based on **6**), and the formation of isomeric disaccharides was not observed.

Subsequently, it was found that the condensation could be performed without separation of the Ph_2cp intermediates. Thus, the reaction of **5** with perchlorate **1**, followed by the treatment of the reaction mixture with the bromide **9** and silver perchlorate gave **12** in 42% yield (based on **5**). Under the same conditions, the laminaribiose derivative **15** was obtained in 40% yield from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**7**) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**14**). Previous reports indicated that treatment of **7** by the Koenigs–Knorr method[22–24] and by the orthoester method[25] resulted in the migration of the 5,6-*O*-isopropylidene group and in the formation of the (1→6)-linked disaccharide. In the present synthesis, as well as in the syntheses of oligosaccharides just described, no formation of isomeric disaccharides was observed by paper chromatography after the removal of the protecting groups, which indicates that the condensation is stereospecific.



When **8** was treated with the bromide **14** at room temperature, the orthoester **16** was the major product of the reaction. Structure **16** was proved by n.m.r. spectrometry and by mild acid hydrolysis[26] to give tetra-*O*-acetyl-D-glucose and **7**. Apparently, in the condensation of sugar Ph_2cp ethers with glycosyl halides in the presence of silver perchlorate at room temperature the acyloxonium intermediates give mainly orthoesters, whereas at elevated temperatures oligosaccharides are formed.

This method is also convenient for the synthesis of higher-molecular-weight oligosaccharides. Thus, the condensation of the Ph_2cp ether formed from **5** with octa-*O*-acetyl-α-cellobiosyl bromide gave benzyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranoside (**17**) in 36% yield. The other possible use of this method is in the synthesis of higher-molecular-weight oligosaccharides involving the simultaneous glycosylation of two diphenylcyclopropenyloxy functions. There are only few descriptions of synthesis of branched oligosaccharides[27,28]. A derivative of a branched trisaccharide, benzyl 2-acetamido-3-*O*-acetyl-2-deoxy-4,6-di-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranoside (**19**) was obtained, in 34% yield, starting from benzyl 2-acetamido-3-*O*-acetyl-2-deoxy-α-D-glucopyranoside by treatment with two molar equivalents of perchlorate **1**, and the subsequent action of two molar equivalents of the bromide **9** and silver perchlorate. The *N*-acetyllactosamine derivative and its (1→6)-analog were found to be the by-products of this synthesis and were identified by comparison with authentic samples of **10** and **12**, and **11** and **13** after *O*-deacetylation and hydrogenolysis.

The present method of oligosaccharide synthesis, based on the glycosylation of sugar Ph_2cp ethers, proceeds under mild conditions and is sterically and structurally specific. In none of the syntheses described was the formation of detectable quantity of α-linked oligosaccharides or migration of the protecting groups observed. In contrast to the Bredereck reaction, secondary as well as primary hydroxyl groups can be glycosylated.

EXPERIMENTAL

General. — Melting points were determined with a Boetius apparatus and correspond to corrected melting points. Optical rotations were determined in semi-micro tubes with a Perkin–Elmer Model 141 polarimeter at 20–22°. N.m.r. spectra were recorded with a Varian XL-100 spectrometer with tetramethylsilane as internal standard. I.r. spectra were recorded with a Perkin–Elmer Model 237 spectrophotometer. U.v. spectra were recorded with a Specord spectrophotometer. Mass spectra were recorded with a LKB Model 9000 spectrometer. T.l.c. was performed on alumina (neutral, Woelm, GFR) or on Silica Gel LS 5/40 plates (Lachema, Czechoslovakia), both adsorbents contained ~5% of gypsum. The spots were detected by spraying the plates with 1:4 (v/v) conc. sulfuric acid–methanol and heating at 100–120°. Column chromatography was performed on Silica Gel L 100/160 (Lachema, Czechoslovakia) or on alumina (neutral, Brockmann IV, Reanal, Hungary). Paper chromatography was performed on Filtrak FN1 paper with 5:5:4 (v/v) 2-methylbutanol–pyridine–water. Evaporations were carried out *in vacuo* at a bath temperature below 35°.

*Benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-6-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-α-D-glucopyranoside* (**3**). — 2,4,6-Trimethylpyridine (0.45 ml) and 2,3-diphenyl-2-cyclopropen-1-ylium perchlorate[16,17] (**1**, 0.90 g, 3.1 mmol) were added successively

to a solution of benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-glucopyranoside[29] (**2**, 1.0 g, 2.53 mmol) in dry acetonitrile (10 ml). The mixture was stirred for 15 min at room temperature. The precipitate was removed by filtration and washed with acetonitrile. The combined filtrates were evaporated to dryness, and the residue was chromatographed on a column of alumina. Elution with a gradient of benzene–ether, monitored by t.l.c. on alumina in 3:97 (v/v) methanol–ether, gave chromatographically homogeneous **3** (1.17 g, 80% yield), m.p. 141–142° (from ether); $[\alpha]_D^{20-22}$ +97° (*c* 1, acetone); u.v. data: λ_{max}^{MeCN} 302, 318 nm, and shoulder at 287 nm[18]; i.r. data: ν_{max}^{Nujol} 1800 cm^{-1} (C=C, cyclopropenyl); n.m.r. data (chloroform-*d*): δ 4.6 (s, 1 H, cyclopropenyl) and 7.3–7.9 (m, 10 H, 2 Ph); m.s. data: *m/e* 585 (M^+).

Anal. Calc. for $C_{34}H_{34}NO_8$: C, 69.74; H, 5.68; N, 2.39. Found: C, 69.36; H, 6.01; N, 2.13.

O-Deacetylation of **3** with sodium methoxide or triethylamine in anhydrous methanol or with ammonia in aqueous methanol gave benzyl 2-acetamido-2-deoxy-6-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-α-D-glucopyranoside (**4**), m.p. 152–153° (from methanol); t.l.c. (alumina, 1:4, v/v, methanol–ether): R_3 0.17; u.v. data: λ_{max}^{MeCN} 302, 318 nm, and shoulder at 287 nm.

After acetylation of **4** with acetic anhydride in pyridine, t.l.c. on alumina (1:49, v/v, methanol–ether) showed the presence in the reaction mixture of two compounds identical with **3** and benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside.

*Benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(2,3-diphenyl-2-cyclopropen-1-yl)-α-D-glucopyranoside* (**6**). — This compound was obtained from benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranoside[21] (**5**, 0.79 g, 2.0 mmol), **1** (0.70 g, 2.4 mmol), and 2,4,6-trimethylpyridine (0.5 ml) by the procedure described for **3**; yield 0.72 g (62%). Recrystallized from acetone–ether–light petroleum, **6** had m.p. 170–171°; $[\alpha]_D^{20-22}$ +118° (*c* 1, acetone); i.r. and u.v. spectra of **6** identical with those of **3**; n.m.r. data (chloroform-*d*): δ 4.54 (s, 1 H, cyclopropenyl).

Anal. Calc. for $C_{34}H_{34}NO_8$: C, 69.74; H, 5.86; N, 2.39. Found: C, 69.86; H, 5.71; N, 2.28.

A solution of **6** in methanol was treated with glacial acetic acid, kept for 1 h at room temperature, and neutralized with AV-17 (CO_3^{2-}) anion-exchange resin, which was then removed by filtration. The filtrate was evaporated and the product obtained showed a chromatographic mobility (t.l.c. on silica gel in 1:24, v/v, methanol–ether) and constants identical with those of **5**: m.p. and mixed m.p. 102–103°; $[\alpha]_D^{20-22}$ +80° (*c* 1, chloroform).

3-O-(2,3-Diphenyl-2-cyclopropen-1-yl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**8**). — To a solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**7**, 1.30 g, 5.0 mmol) in dry benzene (30 ml) were added successively 2,4,6-trimethylpyridine (0.80 ml) and **1** (1.75 g, 6.0 mmol). The mixture was stirred for 1 h at room temperature. The precipitate was removed by filtration and washed with benzene. The combined filtrates were evaporated to dryness, and the residue was triturated with several portions of light petroleum. T.l.c. on alumina in 1:2 (v/v) ether–light

petroleum showed that the product contained traces of starting compound **7**. Crude **8** (1.6 g) was obtained in 71% yield and gave an analytical sample after several recrystallizations from heptane, m.p. 92–94°; $[\alpha]_D^{20-22}$ −20° (*c* 0.77, acetone); u.v. data: λ_{max}^{MeCN} 302, 316 nm, and shoulder at 287 nm; i.r. data: ν_{max}^{Nujol} 1808 cm^{-1} (C=C, cyclopropenyl); n.m.r. data (chloroform-*d*): δ 4.54 (s, 1 H, cyclopropenyl) and 7.2–7.9 (m, 10 H, 2 Ph); m.s. data: 450 (M^+).

Anal. Calc. for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 72.20; H, 7.00.

*Benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-α-*D*-glucopyranoside* (**10**). — A solution of silver perchlorate (0.17 g, 0.81 mmol) in dry benzene (4 ml) was added to a warmed (50°), stirred solution of **6** (0.40 g, 0.68 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**9**, 0.34 g, 0.81 mmol) in the same solvent (3 ml). The mixture was stirred for 10 min at 50°. The precipitate was removed by filtration and washed with chloroform. Several drops of pyridine were added and the combined filtrates were evaporated. The syrupy residue was evaporated with 3–4 portions of benzene, treated with acetic anhydride (2.5 ml) in pyridine (3 ml), and kept overnight at room temperature. The acetylated mixture was processed in the usual manner and the residue was chromatographed on a column of silica gel with ether–methanol, the concentration of methanol increasing up to 1.25%; yield of chromatographically homogeneous **10**, identical with an authentic sample[19], 0.25 g (50%); $[\alpha]_D^{20-22}$ +58° (*c* 1, chloroform).

Deacetylation of **10** gave known benzyl 2-acetamido-2-deoxy-6-*O*-β-D-galactopyranosyl-α-D-glucopyranoside[19], m.p. and mixed m.p. 233–235° (from methanol); $[\alpha]_D^{20-22}$ +110° (*c* 1, methanol).

*Benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-α-*D*-glucopyranoside* (**12**). — *A. From* **6**. The synthesis of **12** starting from **6** (0.45 g, 0.77 mmol), bromide **9** (0.40 g, 0.97 mmol), and silver perchlorate (0.20 g, 0.97 mmol) was performed by the procedure just described for **10**. After crystallization from methanol, **12** was obtained in 35% (0.20 g) yield, m.p. 103–104°; $[\alpha]_D^{20-22}$ +65° (*c* 1, chloroform); lit.[21]: m.p. 107–108.5°, $[\alpha]_D^{25}$ +68° (*c* 0.65, chloroform). The i.r. spectrum of **12** was identical with that of an authentic sample.

B. From **5**. 2,4,6-Trimethylpyridine (0.84 ml, 6.3 mmol) and **1** (1.83 g, 6.3 mmol) were added to a solution of **5** (2.4 g, 6.1 mmol) in dry benzene (50 ml). The mixture was stirred for 20 min at 50° and then **9** (2.28 g, 6.1 mmol) and a solution of silver perchlorate (1.24 g, 6.1 mmol) in dry benzene (30 ml) were added successively, and the stirring was continued for 15 min. Pyridine (2 ml) was added, the mixture filtered, and the filter cake washed with chloroform. The filtrate was treated as described for the synthesis of **8**, and **12** (1.9 g, 43% yield, m.p. 103°) was isolated by column chromatography on silica gel.

*1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-α-*D*-glucofuranose* (**15**). — 2,4,6-Trimethylpyridine (0.28 ml, 2.1 mmol) and **1** (0.62 g, 2.1 mmol) were added to a solution of **7** (0.52 g, 2.0 mmol) in dry benzene (15 ml). The mixture was stirred for 15 min at 50°; and then 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**14**, 0.82 g, 2.0 mmol) and a solution of silver perchlorate (0.40 g,

1.92 mmol) in dry benzene (10 ml) were added successively. After the reaction mixture had been stirred for an additional 15-min period at 50°, it was processed as described for the synthesis of **10** and the resulting compound was acetylated. Compound **15** was isolated by column chromatography on silica gel with benzene–chloroform as eluent, the concentration of chloroform increasing up to 80%; yield 0.47 g (40%); after recrystallization from ether–hexane, m.p. 135–136°; $[\alpha]_D^{20-22}$ −19° (*c* 1, chloroform); lit.[25]: m.p. 132–134°, $[\alpha]_D$ −21° (*c* 2.5, chloroform).

*3,4,6-Tri-*O*-acetyl-1,2-*O*-[1-(1,2:5,6-di-*O*-isopropylidene-α-*D*-glucofuranos-3-yloxy)ethylidene]-α-*D*-glucopyranose* (**16**). — To a solution of crude **8** (0.49 g, 1.09 mmol) and **14** (0.29 g, 0.70 mmol) in dry benzene (10 ml) was added a solution of silver perchlorate (0.14 g, 0.70 mmol) in the same solvent (15 ml). The mixture was stirred for 30 min at room temperature and then filtered, and the filter cake was washed with benzene. Several drops of 2,4,6-trimethylpyridine were added, and the filtrate was evaporated to dryness. The orthoester **16** was isolated by column chromatography on alumina with 2:3 (v/v) benzene–chloroform as eluent; yield 0.18 g (44%). After two recrystallizations from ether–light petroleum, m.p. 109–110°; $[\alpha]_D^{20-22}$ −12° (*c* 0.6, chloroform); n.m.r. data (*cf.* Ref. 30) (chloroform-*d*): 5.86 (m, 2 H, H-1 and H-1'), 1.8 (s, 3 H, orthoester Me), and 1.2–1.6 (12 H, 4 Me).

Benzyl O-(*2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-*D*-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-α-*D*-glucopyranoside* (**17**). — The synthesis of **17** starting from **4** (395 mg, 1.0 mmol), **1** (324 mg, 1.1 mmol), 2,4,6-trimethylpyridine (0.15 ml, 1.1 mmol), octa-*O*-acetyl-α-cellobiosyl bromide[31] (700 mg, 1.0 mmol), and silver perchlorate (210 mg, 1.0 mmol) was performed as described for the synthesis of **12** (procedure *B*). Compound **17** was isolated by column chromatography on silica gel with ether–methanol as eluent, the concentration of methanol increasing up to 4%; yield 360 mg (36%); after recrystallization from acetone–ether–hexane, m.p. 179–180°; $[\alpha]^{20-22}$ +35° (*c* 1, chloroform).

Anal. Calc. for $C_{45}H_{59}NO_{25}\cdot H_2O$: C, 52.37; H, 5.96; N, 1.36. Found: C, 52.41; H, 5.90; N, 1.38.

O-Deacetylation of **17** and subsequent hydrogenolysis in the presence of 10% palladium-on-charcoal in aqueous methanol gave amorphous *O*-(β-D-glucopyranosyl)-(1→4)-*O*-(β-D-glucopyranosyl)-(1→4)-2-acetamido-2-deoxy-D-glucose (**18**), $[\alpha]_D^{20-22}$ +30° (*c* 0.29, water); paper chromatography: R_{Gal} 0.42. The enzymic hydrolysis of **18** with β-D-glucosidase from sweet almond afforded D-glucose and 2-acetamido-2-deoxy-D-glucose, which were identified by paper chromatography.

*Benzyl 2-acetamido-2-deoxy-4,6-di-*O*-β-D-galactopyranosyl-α-D-glucopyranoside* (**20**). — The synthesis of the protected trisaccharide **19** starting from benzyl 2-acetamido-3-*O*-acetyl-2-deoxy-α-D-glucopyranoside[32] (0.70 g, 2.0 mmol), perchlorate **1** (1.28 g, 4.4 mmol), 2,4,6-trimethylpyridine (0.58 ml, 4.4 mmol), bromide **9** (1.80 g, 4.4 mmol), and silver perchlorate (0.92 g, 4.7 mmol) was performed by the procedure just described for **12** (procedure *B*). After the acetylation step, the reaction mixture was chromatographed on a column of silica gel with ether–methanol, the concentration of methanol increasing to 4%, to give 0.69 g (34% yield) of amorphous

19, $[\alpha]_D^{20-22}$ +30° (*c* 0.2, chloroform); 0.10 g (13% yield) of **12**, m.p. 101–103° (from methanol), $[\alpha]_D^{20-22}$ +64° (*c* 1, chloroform) (see Ref. 21); and **10** identical with an authentic sample[19]. *O*-Deacetylation of **19** with triethylamine in anhydrous methanol at room temperature gave crystalline **20**, m.p. 160–161° (from methanol–ether), $[\alpha]_D^{20-22}$ +86° (*c* 0.8, water).

Anal. Calc. for $C_{27}H_{41}NO_{16}\cdot H_2O$: C, 49.61; H, 6.67. Found: C, 49.65; H, 6.75.

Hydrogenolysis of **20** in aqueous methanol in the presence of 10% palladium-on-charcoal gave 2-acetamido-2-deoxy-4,6-di-*O*-(β-D-galactopyranosyl)-D-glucose; paper chromatography: R_{Gal} 0.32.

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