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Note

4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl chloride as a glycosyl donor*

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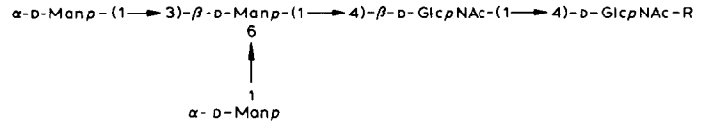
The "core" region of the glycan chain of the *N*-glycoproteins contains the structure **1**, and our laboratory has been concerned with the synthesis of such "lipid intermediates"[2] as **2**. One approach to the synthesis of these compounds involves the initial preparation of a derivative of chitobiose [2-acetamido-4-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2-deoxy-D-glucopyranose], in which only O-4′ is unprotected, and available for mannosylation, and O-1 is protected by a "tempo-



1 R = Asn
2 R = *PP*-Dolichyl

rary"[3] protective goup such as allyl, or a "persistent"[3] group such as benzyl, depending on the structure of the final product. The allyl group has the advantages of offering synthetic versatility and the useful properties of a "chromatographic label"[4], whereas the benzyl group is more readily removed. Benzyl groups are satisfactory for the protection of all other positions. In order to investigate this synthetic route, syntheses of allyl (**14**) and benzyl 2-acetamido-4-*O*-(4-*O*-acetyl-3,6-di-

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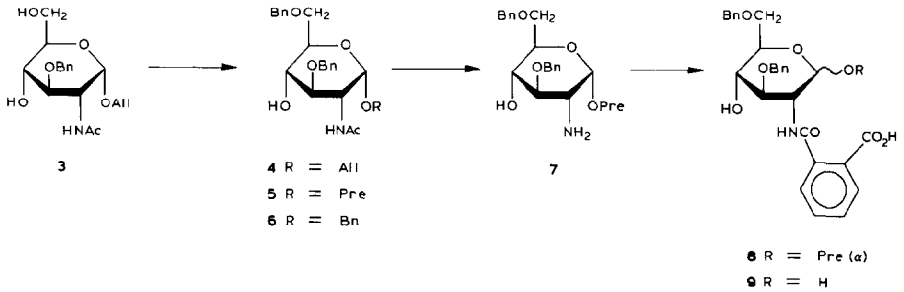
O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**18**) are reported, employing 4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-D-glucopyranosyl chloride (**13**) as the glycosyl donor.

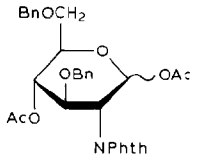
The synthesis of the β-D anomer **17** corresponding to **16**, by use of 2-methyl-(2-acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline[5] as the glycosyl donor, has been reported. Attempts to use this route employing the conditions described by Nashed *et al.*[6], did not, in our hands, yield useful amounts of the desired product, possibly owing to the different anomeric configuration of the acceptor **4**, and an alternative synthesis was investigated.

Lemieux *et al.*[7] reported the efficient synthesis of chitobiose derivatives by use of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide as the glycosyl donor, with silver trifluoromethanesulfonate (triflate) as catalyst. This procedure, as modified by Iversen *et al.*[8] and Paulsen and Lockhoff[9], was satisfactorily used for the synthesis of chitobiose derivatives reported herein, in which both glycosyl donor and acceptor are protected by benzyl groups.

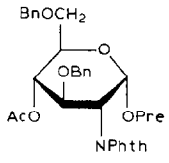


For synthesis of the glycosyl donor **13**, allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**4**) was selected as starting material because of its ease of preparation. It was obtained by selective, partial benzylation of allyl 2-acetamido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**3**), with conventional reagents or *via* the tributylstannylene intermediate[10]. In either instance, it was very readily separated from secondary compounds by liquid chromatography. After isomerization of the allyl group to give **5**, *N*-deacetylation was readily accomplished to yield the amine **7**, which was suitable (without purification) for conversion into the 2-(2-carboxybenzamido) derivative **8**, by treatment with phthalic anhydride[11]. Subsequently the 1-propenyl group was hydrolyzed with mercuric chloride in aqueous acetone[12] to give **9**. Cyclization of the carboxybenzamido group to an *N,N*-phthaloyl group, and concomitant acetylation of O-1 and O-4, were achieved by treatment with acetic anhydride–pyridine, to give **10**. When this compound was treated with the usual bromination reagent (hydrogen bromide in acetic acid at 0°), t.l.c. showed considerable debenzylation, with only traces of the glycosyl bromide being formed. When chlorination was tried instead (hydrogen chloride, hydrogen chloride–acetyl chloride, stannic chloride, chlorotrimethylsilane, or titanium tetra-

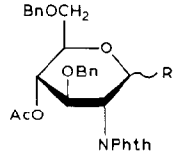
chloride, all in dichloromethane), **10** was recovered unchanged. Therefore, in an alternative approach, **8** was converted into the 4-*O*-acetyl-2-phthalimido derivative **11**, from which the propenyl group was removed conventionally to give **12**. By treatment with chloro-*N,N*-dimethylformamidium chloride (the Vilsmeier reagent)[13,14], **12** was smoothly converted into the glycosyl chloride **13** (mixture of anomers as shown by t.l.c.) containing a trace of the OH-1 compound **12**. Condensation of **4** with **13** in the presence of silver triflate, 2,4,6-trimethylpyridine, and 4A molecular sieve, under a nitrogen atmosphere, and with careful exclusion of moisture, gave disaccharide **14**, isolated by preparative-layer chromatography. Unchanged **4** and **12** (formed by hydrolysis of **13**) were both readily recovered from the chromatogram and could be recycled. Thus, the yield of disaccharide **14**, based on the amount of **4** used in the reaction, was 60%. The identity of **14** was established by i.r., desorptive-chemical-ionization mass (which showed a molecular ion and ions clearly derived from both of the component monosaccharide residues), ^{1}H-, and ^{13}C-n.m.r. spectroscopy, and elemental analysis. When **4** and **13** were coupled in the absence of molecular sieve, at −30°, the yield of desired disaccharide was much lower (10% based on **4** used up), and another, major product was obtained, which was shown to be the 1,4-di-*O*-acetyl compound **10**. Removal of the *N,N*-phthaloyl group from **14** was achieved with hydrazine hydrate[7], after which *N*-acetylation gave a high yield of the di-*N*-acetylchitobiose compound **16**.



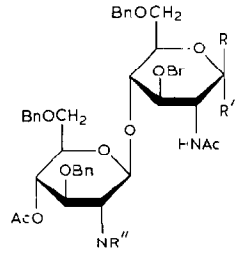
10

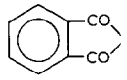


11



12 R = OH
13 R = Cl



Phth = 

All = $CH_2{=}CH{-}CH_2$

Pre = $Me{-}CH{=}CH$

14 R = H, R' = OAll, R'' = Phth
15 R = H, R' = OAll, R'' = H_2
16 R = H, R' = OAll, R'' = H, Ac
17 R = OAll, R' = H, R'' = H, Ac
18 R = H, R' = OBn, R'' = Phth

The coupling of the glycosyl chloride **13** with benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**6**) was performed as for the allyl compound **4**, to give in 40% yield the disaccharide **18**. The lower yield, in this case, probably resulted from a less-efficient chromatographic purification, rather than any difference in the condensation reaction.

EXPERIMENTAL

General methods. — Melting points were determined with a Mettler FP2 hot-stage equipped with a microscope, and correspond to "corrected melting points". Optical rotations were determined in 1-dm, semimicro tubes with a Perkin–Elmer No. 141 polarimeter. I.r. spectra were recorded with a Perkin–Elmer spectrophotometer, Model 237. ^{1}H-N.m.r. spectra were recorded at 500 MHz, and ^{13}C-n.m.r. spectra at 126 MHz, with a Bruker WM 500 spectrometer, with chloroform-*d* as the solvent (containing 1% of tetramethylsilane as the internal standard), at the Northeast Regional N.S.F.–N.M.R. Facility, Yale University, New Haven, CT 06511. The mass spectra were performed with a Finnigan MAT 312 double-focusing mass spectrometer, operated in the chemical-ionization mode, with ammonia as the reagent gas. The cation-exchange resin used was AG 50W-X8 (200–400 mesh; Bio-Rad Laboratories, Richmond, CA 98804). Evaporations were conducted *in vacuo* with the bath temperature kept below 30°. Dichloromethane, acetonitrile, and 1,2-dichloroethane were dried by distillation in the presence of phosphorus pentaoxide and addition of 3A molecular sieve (No. M-9882, Sigma Chemical Co., St. Louis, MO 63178). Dimethyl sulfoxide was dried by distillation *in vacuo* and addition of 4A molecular sieve (No. M-0133, Sigma), and other solvents (where stated) by treatment with molecular sieve followed by addition of calcium hydride (in lump form, Fisher Scientific Co., Pittsburgh, PA 15219). The microanalyses were performed by Dr. W. Manser, CH-8704 Zurich, Switzerland, and by Galbraith Laboratories, Inc., Knoxville, TN 37921.

Chromatographic methods. — T.l.c. and preparative t.l.c. were performed on precoated plates of Silica Gel G, 0.25-mm thick (E. Merck AG, Darmstadt, Germany); for t.l.c., the plates supplied were cut to a length of 6 cm before use, but otherwise were used without pretreatment. All proportions of solvents are v/v. Preparative-layer chromatography (p.l.c.) was performed on precoated Silica Gel F254 PLC plates, 2-mm thick (Merck), or on precoated plates of Silica Gel F254, 0.5-mm thick (Merck). The spray reagent, unless otherwise stated, was 1:1:18 anisaldehyde–sulfuric acid–ethanol[15], and the plates were heated to 125°. Unsaturation was detected by spraying the plates with a solution of 1% potassium permanganate in 2% aqueous sodium hydrogencarbonate. When plates were eluted more than once, they were dried in air between each elution. Column chromatography was performed on silica gel (0.05–0.2 mm, 70–325 mesh, Merck).

Allyl 2-acetamido-3,6-di-O-benzyl-2-deoxy-α-D-glucopyranoside[4] (**4**). — A solution of allyl 2-acetamido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**3**, 6.0 g) in

dry toluene (200 mL) was treated with tributyltin oxide (6 mL, Aldrich Chemical Co., Milwaukee, WI 53201) and boiled under reflux (oil bath, 110°) with continuous removal of water, for 24 h. The resulting suspension was filtered to separate unchanged **4** (3.0 g), the filtrate concentrated to 20 mL, and α-bromotoluene (90 mL) added. The mixture was boiled under reflux for 3 h, and most of the excess α-bromotoluene removed by distillation under diminished pressure, with continuous additions and evaporations of toluene. Examination of the reaction product by t.l.c. (10:1 v/v, chloroform–methanol) revealed one major compound with R_F corresponding to **4**, together with traces of the 3,4-di-*O*-benzyl derivative[4]. Compound **4** was purified by chromatography on silica gel (20:1 chloroform–methanol; Chromatospac Prep 10 preparative-liquid chromatograph; 0.2 MPa). The fractions containing pure **4** according to t.l.c. were combined to give 2.5 g (67% based on **3** consumed) of a product identical with an authentic sample[4] according to t.l.c., mixed m.p., and i.r. spectrum.

1-Propenyl 2-amino-3,6-di-O-benzyl-2-deoxy-α-D-glucopyranoside (**7**). — A solution of 1-propenyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside[5] (**5**, 1.0 g) in methanol (20 mL) was treated with potassium hydroxide (6.5 g), and the mixture stirred at 100° in a sealed tube until t.l.c. (10:1 chloroform–methanol) showed that conversion of **5** (R_F 0.80) into **7** (R_F 0.69) was almost complete. After removal of solvent by distillation, the residue was dissolved in water (10 mL) and the product extracted with ether (3 × 50 mL). The ether extract was washed with water and dried ($MgSO_4$). Evaporation, followed by four additions and evaporations of toluene (5 mL) gave amorphous **7** (0.52 g, 57%), suitable for the next synthetic step without further purification.

For characterization purposes, a 50-mg sample was chromatographed on a p.l.c. plate (0.5-mm thick) with 10:1 (v/v) chloroform–methanol as the solvent. The band containing pure **7** was located by viewing under u.v. light, and **7** was extracted from the silica gel by stirring overnight with 2:1 chloroform–methanol. Filtration through Celite, followed by evaporation, gave amorphous **7**, pure according to t.l.c.; $[\alpha]_D^{25}$ +81° (*c* 1, chloroform); ν_{max}^{KBr} 3375 (OH), 3300 (NH), 1500 (Ph), 625, and 590 cm^{-1} (Ph).

Anal. Calc. for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.48; O, 20.03. Found: C, 69.12; H, 7.23; N, 3.48; O, 20.20.

1-Propenyl 3,6-di-O-benzyl-2-(2-carboxybenzamido)-2-deoxy-α-D-glucopyranoside (**8**). — A stirred solution of **7** (50 mg) in methanol (10 mL) was treated with finely powdered phthalic anhydride (30 mg, added in portions) at room temperature. After the addition was complete, the mixture was stirred at 50–60° until t.l.c. (10:1 chloroform–methanol) showed complete conversion of **7** into **8**, which has a much higher R_F value. The reaction mixture was cooled, the solvent evaporated under a stream of nitrogen, and drying completed *in vacuo* (P_2O_5) to yield amorphous **8** (50 mg, 71%); $[\alpha]_D^{25}$ +67.5° (*c* 1, chloroform); ν_{max}^{film} 3400 (OH), 3500 (NH), 1725 (C=O), 1500 (Ph), 740, and 680 cm^{-1} (Ph).

Anal. Calc. for $C_{31}H_{33}NO_8 \cdot H_2O$: C, 65.82; H, 6.24; N, 2.48. Found: C, 65.85; H, 5.85; N, 2.43.

3,6-Di-O-benzyl-2-(2-carboxybenzamido)-2-deoxy-D-glucose (**9**). — A solution of **8** (0.5 g) in 5:1 acetone–water (5 mL) was stirred at room temperature and treated with mercury dichloride (0.6 g). After 30 min, t.l.c. (10:1 chloroform–methanol) showed complete conversion of **8** into **9**, which had a much lower R_F value, and showed a double spot characteristic of an anomeric mixture. The solvents were evaporated under a stream of nitrogen, and water (10 mL) was added. The precipitated solid was filtered off, washed with water, and dried *in vacuo* (P_2O_5) to give **9** (0.32 g, 100%), m.p. 158.9–159°, $[\alpha]_D^{25}$ +69→+58° (24 h, *c* 1, chloroform); ν_{max}^{KBr} 3375 (OH), 3260 (NH), 1700 (C=O), 1500 (Ph), 725, and 680 cm^{-1} (Ph).

Anal. Calc. for $C_{28}H_{29}NO_8$: C, 66.24; H, 5.76; N, 2.76; O, 25.23. Found: C, 66.22; H, 5.78; N, 2.86; O, 25.25.

1,4-Di-O-acetyl-3,6-di-O-benzyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose (**10**). — A solution of **9** (0.1 g) in 2:1 pyridine–acetic anhydride (10 mL) was stirred overnight at room temperature, diluted with water, and evaporated to dryness. After the addition and evaporation of toluene (3 × 2 mL), the residue was crystallized from methanol, to give **10** (80 mg, 71%) as needles, m.p. 122–123°, $[\alpha]_D^{25}$ +112° (*c* 1, chloroform); ν_{max}^{KBr} 1750 (C=O, Ac), 1720 (Phth), 1500 (Ph), 720, and 680 cm^{-1} (Ph); *m/z* 530 ($M^+ - COCH_3$), 483 ($M^+ - C_6H_5CH_2$), 422, 376, 347, 332, 256, 226, and 91 ($C_6H_5CH_2^+$).

Anal. Calc. for $C_{32}H_{31}NO_9$: C, 67.00; H, 5.80; N, 2.33. Found: C, 66.81; H, 5.62; N, 2.33.

1-Propenyl 4-O-acetyl-3,6-di-O-benzyl-2-deoxy-2-phthalimido-α-D-glucopyranoside (**11**). — A solution of **8** (1.0 g) in pyridine–acetic anhydride (2:1, 10 mL) was stirred for 48 h at room temperature, and then kept for 30 min at 80°. The mixture was diluted with water (2 mL), the solvents were distilled off, and the residue was dried by five additions and evaporations of toluene (2 mL). Examination of the product by t.l.c. (1:1 ethyl acetate–hexane) showed one major compound (R_F 0.87) with minor contaminants, which were removed by p.l.c. on four 2-mm thick plates. The chromatography and extraction of **11** from the silica gel was performed as described for **7**, to give amorphous **11** (0.80 g, 79%), $[\alpha]_D^{25}$ +32.5° (*c* 1, chloroform); ν_{max}^{film} 1750 (C=O, Ac), 1725 (C=O, Phth), 1500 (Ph), 730, 710, and 680 cm^{-1} (Ph).

Anal. Calc. for $C_{33}H_{33}NO_8$: C, 69.34; H, 5.82; N, 2.45; O, 22.39. Found: C, 69.30; H, 5.92; N, 2.60; O, 22.45.

4-O-Acetyl-3,6-di-O-benzyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose (**12**). — A solution of **11** (0.8 g) in 5:1 acetone–water (10 mL) was stirred at room temperature and treated with mercury dichloride (1.6 g). After 30 min, t.l.c. (1:1 ethyl acetate–hexane) showed complete conversion of **11** (R_F 0.87) into **12** (R_F 0.33). The mixture was diluted with a large excess of chloroform and extracted with a saturated aqueous solution of potassium iodide (2 × 10 mL), and the organic layer dried ($MgSO_4$). After evaporation of solvent, the residue was treated with methanol, whereby **12** crystallized on cooling to 4° (0.7 g, 92%), m.p. 156–157°,

$[\alpha]_D^{25}$ +12° (*c* 1, chloroform); ν_{max}^{KBr} 3425 (OH), 1760 (C=O, Ac), 1720 (C=O, Phth), 725, and 680 cm^{-1} (Ph); t.l.c. showed that **12** was a mixture of anomers.

Anal. Calc. for $C_{30}H_{29}NO_8 \cdot 0.5\ H_2O$: C, 66.65; H, 5.59; N, 2.59. Found: C, 66.49; H, 5.41; N, 2.95.

4-O-Acetyl-3,6-di-O-benzyl-2-deoxy-2-phthalimido-α,β-D-glucopyranosyl chloride (**13**). — Compound **12** (0.2 g), thoroughly dried *in vacuo*, was dissolved in 1,2-dichloroethane (2 mL) and the stirred solution treated with chloro-*N,N*-dimethylformamidium chloride[14] (10 mg). After 10 min, the mixture was diluted with a large excess of dry benzene, and the solution filtered through a short column of silica gel and evaporated under a stream of nitrogen. The residue was dried by six additions and evaporations of dry toluene, when t.l.c. (1:1 ethyl acetate–hexane) showed the almost complete conversion of **12** (R_F 0.33) into **13** (R_F 0.56), which appeared as a double spot (mixture of anomers). This t.l.c. showed that **13** was very suitable for use as a glycosyl donor without any further purification.

Allyl 2-acetamido-4-O-(4-O-acetyl-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-3,6-di-O-benzyl-2-deoxy-α-D-glucopyranoside (**14**). — To a stirred mixture of **4** (55 mg, 0.125 mmol), silver triflate (51 mg, 0.20 mmol, Fluka Chemical Co., Hauppauge, NY 11788), 2,4,6-trimethylpyridine (35 mg, 0.29 mmol), molecular sieves 4A (200 mg, activated by heating to ~350° overnight), and dichloromethane (1 mL) was added a solution of **13** (prepared from 100 mg of **12**, 0.185 mmol) in dichloromethane (1 mL). The mixture was stirred overnight, in a nitrogen atmosphere, with exclusion of light and moisture. After dilution with dichloromethane (5 mL), silver salts and molecular sieves were filtered off (Celite), and the filtrate was washed with 3% hydrochloric acid (10 mL), water (10 mL), saturated aqueous sodium hydrogencarbonate (10 mL), and water (10 mL), and dried ($MgSO_4$). Examination of the product by t.l.c. (20:1 chloroform–methanol) showed the disappearance of the glycosyl chloride **13** and the formation of a major compound (**14**, R_F 0.68), together with some **12** (R_F 0.5, formed by hydrolysis of **13**), a byproduct (R_F 0.85) which was shown to be **10** by a comparison of t.l.c., i.r., n.m.r., and mass spectra, and unchanged **4** (R_F 0.3); compounds **4** and **14** containing the allyl group were readily distinguished by their reaction with the potassium permanganate and anisaldehyde spray-reagents[4]. Compounds **4, 12,** and **14** were isolated by p.l.c. on four 0.5-mm thick plates, the bands being detected by viewing under u.v. light, then spraying a narrow zone with the potassium permanganate spray, and finally cutting out a 0.5-cm strip and spraying with the anisaldehyde reagent. The compounds were extracted from the silica gel by stirring overnight with 2:1 chloroform–methanol. Filtration (Celite) and evaporation, followed by addition and evaporation of toluene (3 × 2 mL), gave **4** (18 mg), **12** (31 mg), and **14** (50 mg) (yield of **14** based on the amount of **4** used was 60%), amorphous, $[\alpha]_D^{25}$ +44° (*c* 1, chloroform); ν_{max}^{film} 3400 (NH), 1750 (C=O, Ac), 1710 (C=O, Phth), 1650 (amide 1), 1500 (Ph), 710, and 680 cm^{-1} (Ph); *m/z* 973 ($M + 19^+$), 592, 548, 531 ($C_{30}H_{29}NO_8^+$), 475, 441 ($C_{25}H_{31}NO_6^+$), 365, 291, 233, 168, 105, and 77; ^{1}H-n.m.r. δ 7.72–7.70 [bs, 4 H, $C_6H_4(CO)_2N$], 7.27–6.90 (m, 20 H, Ph-*H*), 5.78–5.71 (o, 1 H,

$CH_2CH{=}CH_2$), 5.31 (d, 1 H, *J* 8.3 Hz, H-1'), 4.79 (d, 1 H, *J* 3.8 Hz, H-1), 4.73–4.34 (m, 8 H, 4 $PhCH_2$), 4.34–3.4 (m, 11 H, OCH_2-CH= and ring protons), 1.94 (s, 3 H, CH_3CO), and 1.84 (s, 3 H, $NHCOCH_3$); ^{13}C-n.m.r.: δ 169.8 (C=O), 128.4, 128.1, (C=C, allyl), 127.9, 127.4 (benzyl), 97.2, 96.5 (C-1, C-1'), 76.9, 76.8 (C-3, C-3'), 73.8, 73.6 (C-4, C-4'), 72.9, 72.8 (C-5, C-5'), 69.6, 68.3 (C-6, C-6'), 56.4, 52.3 (C-2, C-2'), 23.3 (NAc), and 20.9 (OAc).

Anal. Calc. for $C_{55}H_{58}N_2O_{13} \cdot 0.5\ C_7H_8$ (toluene): C, 70.18; H, 6.24; N, 2.80. Found: C, 70.16; H, 6.59; N, 2.86.

*Allyl 2-acetamido-4-*O*-(2-acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**16**). — A solution of **14** (20 mg) in ethanol (5 mL) was treated with hydrazine hydrate (0.2 mL of an 85% solution, Eastman Kodak Co., Rochester, NY 01650), boiled under reflux for 4 h, and then stirred overnight at room temperature, after which t.l.c. (20:1 chloroform–methanol) showed the disappearance of **14** (R_F 0.68). The mixture containing the 2-amino-2-deoxy compound **15** was evaporated to dryness, followed by addition and evaporation of toluene (3 × 0.5 mL). The residue was dissolved in methanol (1 mL) and treated with acetic anhydride (0.5 mL), and the mixture was stirred for 2 h at room temperature. After evaporation of solvents, followed by addition and evaporation of toluene (2 × 0.5 mL), the residue was purified by preparative t.l.c. (0.25-mm thick plate) with 20:1 chloroform–methanol. Compound **16** was located on the plate and extracted by the method described for **14**, to give **16** (14.5 mg, 80%), m.p. 232–233°, $[\alpha]_D^{25}$ +53° (*c* 0.6, chloroform); ν_{max}^{KBr} 3300 (NH), 1750 (C=O, Ac), 1650 (amide I), 1540 (amide II), 725, and 680 cm^{-1} (Ph).

Anal. Calc. for $C_{49}H_{58}N_2O_{12}$: C, 67.88; H, 6.74; N, 3.23; O, 22.14. Found: C, 67.66; H, 7.18; N, 3.09; O, 21.85.

*Benzyl 2-acetamido-4-*O*-(4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-3,6-di-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (**18**). — The condensation of **6** (47 mg, 0.096 mmol) with **13** (prepared from 100 mg of **12**, 0.185 mmol) was performed as described for the preparation of **14**. A similar purification by p.l.c. (except that the potassium permanganate spray-reagent could not be used, making the location of **18** on the chromatogram more difficult) gave **18** (30 mg, 41% based on **6** consumed); $[\alpha]_D^{25}$ +94.6° (*c* 1, chloroform); ν_{max}^{film} 3300 (NH), 1750 (C=O, Ac), 1725 (C=O, Phth), 1650 (amide I), 1500 (Ph), 725, and 680 cm^{-1} (Ph); ^{1}H-n.m.r.: δ 7.71–7.67 [bs, 4 H, $C_6H_4(CO)_2N$], 7.34–7.20 (m, 20 H, 4 C_6H_5), 7.14–6.91 (m, 5 H, C_6H_5), 5.30 (d, 1 H, *J* 8.3 Hz, H-1'), 4.83 (d, 1 H, *J* 3.8 Hz, H-1), 4.64–4.10 (m, 15 H, 5 $PhCH_2$ and ring protons), 3.76–3.35 (m, 7 H, ring protons), 1.89 (s, 3 H, CH_3CO), and 1.74 (s, 3 H, $NHCOCH_3$).

Anal. Calc. for $C_{59}H_{59}N_2O_{13} \cdot 0.5\ H_2O$: C, 69.95; H, 5.97; N, 2.77; O, 21.32. Found: C, 69.90; H, 6.23; N, 2.79; O, 21.01.

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