Preparation of Benzyl Ethers of 1,2-Dideoxy-2'-methyl-α-D-glucopyranoso-[2,1-*d*]-Δ²'-oxazoline for use in Oligosaccharide Synthesis

By **Patrick Rollin** and **Pierre Sinaÿ**,* Laboratoire de Biochimie Structurale, U.E.R. de Sciences Fondamentales et Appliquées, 45045 Orléans Cedex, France

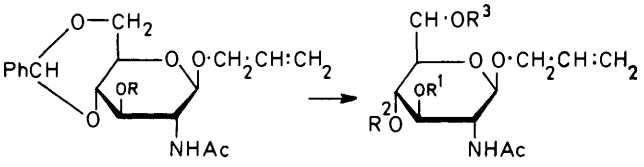
Three benzyl ethers of 1,2-dideoxy-2'-methyl-α-D-glucopyranoso[2,1-*d*]-Δ²'-oxazoline (14) were prepared. High yield β-acetylation of suitably protected derivatives of 2-acetamido-2-deoxy-D-glucopyranose made the use of Matta's method convenient for synthesizing two isomeric acetylated di-*O*-benzyl ethers of (14), and the tri-*O*-benzyl ether was obtained by conventional benzylation of (14). The reactivity of the substituted oxazolines was tested through the preparation of various derivatives of 6-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactopyranose (19).

DURING the past few years, *O*-benzyl systems have been used extensively as 'persistent' blocking groups for syntheses of oligosaccharides.[1] They are stable under appropriate conditions and can be removed with ease. Their use has enabled the 4-hydroxy-groups of benzyl 2-acetamido-2-deoxy-3,6-di-*O*-benzyl-α-D-glucopyranoside [2] and allyl 2-acetamido-2-deoxy-3,6-di-*O*-benzyl-α-D-glucopyranoside [3] to be glycosylated in high yield. We expected that benzyl ethers of 1,2-dideoxy-2'-methyl-α-D-glucopyranoso[2,1-*d*]-Δ²'-oxazoline would be valuable intermediates in the synthesis of oligosaccharides containing internal β-*N*-acetylglucosaminyl linkages. This article describes their preparation.

Among the various methods [4] published for synthesizing the oxazoline (13) the mild iron(III) chloride procedure [4b] is particularly attractive, although a prerequisite is the easy availability of a β-1-*O*-acetyl derivative.

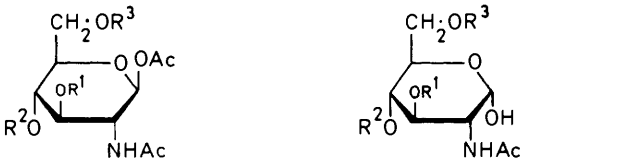
Allyl 2-acetamido-2-deoxy-β-D-glucopyranoside was routinely converted into allyl 2-acetamido-3-*O*-allyl-2-deoxy-β-D-glucopyranoside (4), which was then benzylated and de-*O*-allylated by potassium t-butoxide in dimethyl sulphoxide [5] to give 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranose (9) in crystalline form. The key step of the synthesis was the conversion into the β-acetate (11). Inch and Fletcher [6] suggested that warm pyridine *in the presence of pyridine hydrochloride* may favour the formation of a β-anomer. Indeed, when this procedure was applied, 1,3-di-*O*-acetyl-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranose (11) was isolated in pure and crystalline form in 86% yield after silica gel column chromatography; thus this compound is easily available from the starting material (1). All the other classical methods of acetylation mainly gave the α-anomer. The mechanism of this reaction is unknown. Compound (11) was then easily converted into the syrupy oxazoline (16) (72%) by using iron(III) chloride.[4b] Another possible way of obtaining this oxazoline (16) from the diol (9) is to convert it into the α-acetate and then into 3-*O*-acetyl-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl chloride. This last reaction proved difficult in our hands and the described procedure appears to be the method of choice.

4-*O*-Acetyl-3,6-di-*O*-benzyl-1,2-dideoxy-2'-methyl-α-D-glucopyranoso[2,1-*d*]-Δ²'-oxazoline (17) was prepared following an analogous route. Allyl 2-acetamido-2-deoxy-β-D-glucopyranoside was transformed into allyl 2-acetamido-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside (6) in a routine way. Selective benzylation of this diol



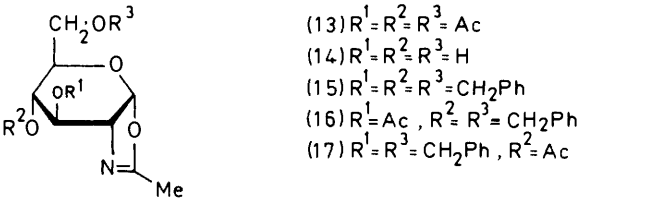
(1) R = H
(2) R = $CH_2CH{:}CH_2$
(3) R = CH_2Ph

(4) $R^1 = CH_2CH{:}CH_2$, $R^2 = R^3 = H$
(5) $R^1 = CH_2CH{:}CH_2$, $R^2 = R^3 = CH_2Ph$
(6) $R^1 = CH_2Ph$, $R^2 = R^3 = H$
(7) $R^1 = R^3 = CH_2Ph$, $R^2 = H$
(8) $R^1 = R^2 = R^3 = CH_2Ph$



(11) $R^1 = Ac$, $R^2 = R^3 = CH_2Ph$
(12) $R^1 = R^3 = CH_2Ph$, $R^2 = Ac$

(9) $R^1 = H$, $R^2 = R^3 = CH_2Ph$
(10) $R^1 = R^3 = CH_2Ph$, $R^2 = H$



(13) $R^1 = R^2 = R^3 = Ac$
(14) $R^1 = R^2 = R^3 = H$
(15) $R^1 = R^2 = R^3 = CH_2Ph$
(16) $R^1 = Ac$, $R^2 = R^3 = CH_2Ph$
(17) $R^1 = R^3 = CH_2Ph$, $R^2 = Ac$

[1] (*a*) P. J. Pfäffli, S. H. Hixson, and L. Anderson, *Carbohydrate Res.*, 1972, **23**, 195; (*b*) P. A. Gent and R. Gigg, *J.C.S. Perkin I*, 1974, 1446; (*c*) J. C. Jacquinet and P. Sinaÿ, *J. Org. Chem.*, 1977, **42**, 720.

[2] J. C. Jacquinet and P. Sinaÿ, *Tetrahedron*, 1976, **32**, 1693.

[3] C. D. Warren and R. W. Jeanloz, *Carbohydrate Res.*, 1977, **53**, 67.

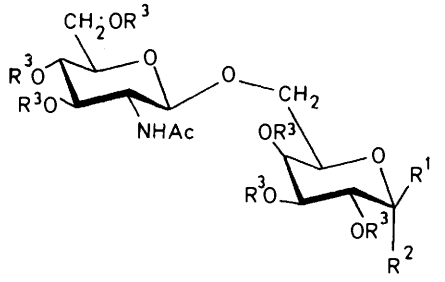
[4] (*a*) A. Ya. Khorlin, M. L. Shul'man, S. E. Zurabyan, I. M. Privalova, and Yu. L. Kopaevich, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1968, 2094; (*b*) K. L. Matta and O. P. Bahl, *Carbohydrate Res.*, 1972, **21**, 460; (*c*) R. U. Lemieux and H. Driguez, *J. Amer. Chem. Soc.*, 1975, **97**, 4063.

[5] J. Gigg and R. Gigg, *J. Chem. Soc.* (*C*), 1966, 82.

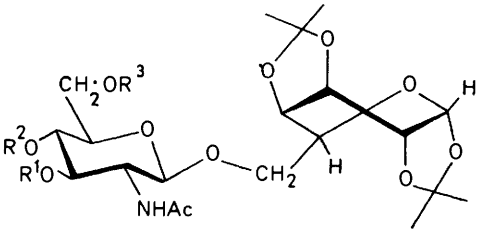
[6] T. D. Inch and H. G. Fletcher, jun., *J. Org. Chem.*, 1966, **31**, 1810.

gave allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (7), which was obtained in crystalline form after purification on a silica gel column (yield 51%). De-*O*-allylation by potassium t-butoxide in dimethyl sulphoxide gave 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranose (10) in crystalline form (84%). Acetylation in warm pyridine and in the presence of pyridine hydrochloride selectively gave the β-acetate (12) (85%), which was easily transformed into the syrupy oxazoline (70%) using iron(III) chloride.

Finally, 3,4,6-tri-*O*-acetyl-1,2-dideoxy-2′-methyl-D-glucopyranoso[2,1-*d*]-Δ^2-oxazoline [4b] (13) was de-*O*-acetylated (sodium methoxide in methanol) and benzylated



(18) R^1 = O·CH_2Ph, R^2 = H, R^3 = CH_2Ph
(19) R^1, R^2 = H, OH; R^3 = H



(20) R^1 = R^2 = R^3 = CH_2Ph
(21) R^1 = R^3 = CH_2Ph, R^2 = H
(22) R^1 = R^2 = R^3 = Ac
(23) R^1 = R^2 = R^3 = H

by the action of sodium hydride and benzyl bromide in *NN*-dimethylformamide to give 3,4,6-tri-O-benzyl-1,2-dideoxy-2′-methyl-α-D-glucopyranoso[2,1-*d*]-$\Delta^{2'}$-oxazoline (15) as a pure syrup [50% from (13)], which could not be induced to crystallise.

The possibility of using benzylated oxazolines for disaccharide synthesis was then demonstrated through the preparation of various derivatives of 6-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactose (19).

The oxazoline (15) was first condensed with benzyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside following a classical procedure [7] to give the disaccharide (18) (73%) in crystalline form. This was transformed in one step (hydrogenolysis over Pd–C in acetic acid) into free 6-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactose (19).[7,8] The oxazoline (17) was then condensed with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose to give a protected disaccharide which was de-*O*-acetylated; the disaccharide (21) was then obtained in crystalline form (62%). In an independent route, this disaccharide (21) was prepared by selective benzylation of 6-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (23). A by-product of this reaction was the fully benzylated disaccharide (20), which has been prepared for comparison from the oxazoline (15). Finally, the disaccharide (22) used after de-*O*-acetylation for the selective benzylation was obtained after condensation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with the oxazoline (13), according to the method of Antonenko *et al.*[7] The physical properties we observed are completely different from those reported in ref. 7 and close to those given by Llewellyn and Williams.[9]

These results show that the benzylated oxazolines may be used as glycosylating agents for disaccharide syntheses. The alcohol (21) can presumably be glycosylated in turn to give various trisaccharides.

EXPERIMENTAL

M.p.s were determined for samples in capillary tubes with a Büchi apparatus. Optical rotations were measured at 22—25 °C with a Perkin-Elmer 141 polarimeter. I.r. spectra were recorded with a JOUAN-JASCO IRA-1 spectrometer. ^{1}H N.m.r. spectra were obtained for solutions in $CDCl_3$ (Me_4Si as internal standard) unless otherwise stated. G.l.c. of per-*O*-(trimethylsilyl) derivatives was performed with a flame ionization detector [3.40 m Pyrex column of 4% OV 17 on GasChrom Q (80—100 mesh); temperature programme 10 °C min^{-1} from 200 to 300 °C; t_R given relative to per-*O*-(trimethylsilyl)trehalose]. Purity of products was determined by t.l.c. on silica gel 60 F 254 (Merck). Components were located by spraying with 50% sulphuric acid in ethanol and heating. Column chromatography was performed on silica gel Merck 60 (powder 0.063—0.200 mm) used without pretreatment. Elemental analyses were obtained from the Service Central de Microanalyse du Centre National de la Recherche Scientifique.

Allyl 2-Acetamido-4,6,-O-benzylidene-2-deoxy-β-D-glucopyranoside (1).[10]—A mixture of allyl 2-acetamido-2-deoxy-β-D-glucopyranoside [11] (20 g) and benzaldehyde (270 ml) was stirred vigorously at room temperature with zinc chloride (21 g). After 12 h, di-isopropyl ether (300 ml) and saturated aqueous ammonium chloride (5 ml) were added with stirring. The product was filtered off and washed with water and di-isopropyl ether to give crude material (1) (18 g, 67%), directly used after drying for the next step. Recrystallisation of a portion from methanol–water gave *needles*, m.p. 262—264°; $[\alpha]_D$ −90° (*c* 1 in pyridine);

[7] T. S. Antonenko, S. E. Zurabyan, and A. Ya. Khorlin, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1970, 2766.
[8] (*a*) R. Kuhn and W. Kirschenlohr, *Chem. Ber.*, 1954, **87**, 684; (*b*) P. F. Lloyd and G. P. Roberts, *J. Chem. Soc.* (*C*), 1965, 3910.
[9] J. W. Llewellyn and J. M. Williams, *J.C.S. Perkin I*, 1975, 1428.
[10] This compound was prepared for the first time in our laboratory by Mr. Gaydell Sall dit Cau (Thesis, Université de Paris-Sud, Orsay, 1973).
[11] R. T. Lee and Y. C. Lee, *Carbohydrate Res.*, 1974, **37**, 193.

$\nu_{max.}$ (Nujol) 3 440 (OH), 3 300 (NH), 1 620 (amide I), 1 560 (amide II), and 685 cm^{-1} (Ph); δ [$(CD_3)_2SO$] 1.85 (3 H, s, NH*Ac*), 4.58 (1 H, d, $J_{1,2}$ 9 Hz, H-1), 5.63 (1 H, s, PhC*H*), 5.7—6.1 (1 H, m, OCH_2·C*H*:CH_2), 7.42 (5 H, s, Ph), and 7.85 (1 H, d, $J_{NH,2}$ 8 Hz, NH) (Found: C, 62.2; H, 6.6; N, 4.0. $C_{18}H_{23}NO_6$ requires C, 61.9; H, 6.6; N, 4.0%).

Allyl 2-*Acetamido*-3-O-*allyl*-4,6,-O-*benzylidene*-2-*deoxy*-β-D-*glucopyranoside* (2).—A suspension of compound (1) (3.5 g), barium oxide (6.7 g), and barium hydroxide octahydrate (2 g) in dry *NN*-dimethylformamide (65 ml) was stirred vigorously for 4 h in the presence of allyl bromide (1.7 ml, 2 equiv.). After dilution with chloroform (500 ml), aqueous 50% acetic acid (100 ml) was added. The chloroform layer was washed with aqueous sodium hydrogen carbonate and water, dried (K_2CO_3), and evaporated to give *compound* (2) (3.7 g, 95%), which was recrystallised from methanol; m.p. 264—266°; $[\alpha]_D$ −71.5° (*c* 1.14 in pyridine); $\nu_{max.}$ (Nujol) 3 300 (NH), 1 660 (amide I), 1 570 (amide II), and 755 and 695 cm^{-1} (Ph) (Found: C, 64.7; H, 6.9; N, 3.7. $C_{21}H_{27}NO_6$ requires C, 64.8; H, 7.0; N, 3.6%).

Allyl 2-*Acetamido*-3-O-*allyl*-2-*deoxy*-β-D-*glucopyranoside* (4).—A mixture of allyl 2-acetamido-3-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (2) (7.9 g) and 50% acetic acid (400 ml) was stirred for 24 h at 50 °C. Evaporation, followed by several additions and evaporations of water, then of dry toluene, gave a pure solid (98%), which was recrystallised from acetone–hexane to give *compound* (4), m.p. 187—188.5°; $[\alpha]_D$ −35.5° (*c* 1.13 in MeOH); $\nu_{max.}$ (KBr) 3 400 (OH), 1 640 (amide I), and 1 545 cm^{-1} (amide II); δ [$(CD_3)_2SO$] 1.81 (3 H, s, NH*Ac*), 4.40 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1), and 7.82 (1 H, d, $J_{NH,2}$ 8.5 Hz, NH) (Found: C, 55.7; H, 7.6; N, 4.8. $C_{14}H_{23}NO_6$ requires C, 55.8; H, 7.7; N, 4.7%).

Allyl 2-*Acetamido*-3-O-*allyl*-4,6-*di*-O-*benzyl*-2-*deoxy*-β-D-*glucopyranoside* (5).—A suspension of compound (4) (10.3 g), barium oxide (15.6 g), and barium hydroxide octahydrate (5.2 g) in dry *NN*-dimethylformamide (260 ml) was stirred vigorously for 24 h in the presence of α-bromotoluene (16.3 ml, 4 equiv.). The same treatment as reported for the preparation of compound (2) gave *compound* (5), which was recrystallised from ethyl acetate–ether (yield 11 g, 67%); m.p. 146—147°; $[\alpha]_D$ +8.7° (*c* 1.24 in $CHCl_3$); $\nu_{max.}$ (Nujol) 3 300 (NH), 1 650 (amide I), 1 560 (amide II), and 740 and 695 cm^{-1} (Ph) (Found: C, 69.7; H, 7.2; N, 2.9. $C_{28}H_{35}NO_6$ requires C, 69.8; H, 7.3; N, 2.9%).

2-*Acetamido*-4,6-*di*-O-*benzyl*-2-*deoxy*-α-D-*glucopyranose* (9).—Allyl 2-acetamido-3-*O*-allyl-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (5) (4.2 g) was converted into the prop-1-enyl ether by the action of potassium t-butoxide in dimethyl sulphoxide.[5] The residue was hydrolysed in acetone (150 ml) containing M-hydrochloric acid (16 ml) under reflux for 1.5 h. After cooling, the solution was neutralised with Dowex 1-X 8 resin and evaporated. The residue was crystallised from ethyl acetate to give *compound* (9) (2.6 g, 75%), m.p. 199—201°; $[\alpha]_D$ +63° ⟶ +60° (*c* 0.93 in methanol); $\nu_{max.}$ (Nujol) 3 330 (NH), 1 630 (amide I), 1 560 (amide II), and 735 and 695 cm^{-1} (Ph); δ [$(CD_3)_2SO$] 1.88 (3 H, s, NH*Ac*), 6.58 (1 H, d, $J_{OH,1}$ 5.5 Hz, anomeric OH), 7.32 and 7.35 (10 H, 2 s, Ph), and 7.68 (1 H, d, $J_{NH,2}$ 8 Hz, NH) (Found: C, 65.9; H, 6.7; N, 3.6. $C_{22}H_{27}NO_6$ requires C, 65.8; H, 6.8; N, 3.5%).

2-*Acetamido*-1,3-*di*-O-*acetyl*-4,6-*di*-O-*benzyl*-2-*deoxy*-β-D-*glucopyranose* (11).—A solution of 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranose (9) (853 mg) in dry pyridine (10 ml) containing anhydrous pyridine hydrochloride (300 mg) was heated at 100 °C for 1 h. Acetic anhydride (0.5 ml) was then added to the hot solution, which was finally left for 12 h at room temperature. The pyridine was evaporated off and the residue was chromatographed on silica gel (25 g); elution with chloroform–acetone (19 : 1) gave pure *compound* (11) (860 mg, 86%), which was recrystallised from ethyl acetate–ether; m.p. 153—155°; $[\alpha]_D$ −8.8° (*c* 1.67 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 320 (NH), 1 760 and 1 740 (OAc), 1 660 (amide I), 1 555 (amide II), and 745 and 695 cm^{-1} (Ph); δ 1.89 (3 H, s, NH*Ac*), 1.96 and 2.09 (6 H, 2 s, OAc), 3.85 (1 H, t, $J_{3,4} = J_{4,5}$ = 8 Hz, H-4), 5.15 (1 H, q, $J_{2,3}$ 9 Hz, H-3), 5.65 (1 H, d, $J_{1,2}$ 8.5 Hz, H-1), 6.15 (1 H, d, $J_{NH,2}$ 9.5 Hz, NH), and 7.0—7.4 (10 H, m, Ph) (Found: C, 64.3; H, 6.5; N, 2.7; O, 26.1. $C_{26}H_{31}NO_8$ requires C, 64.3; H, 6.4; N, 2.9; O, 26.4%).

3-O-*Acetyl*-4,6-*di*-O-*benzyl*-1,2-*dideoxy*-2′-*methyl*-α-D-*glucopyranoso*[2,1-d]-$\Delta^{2'}$-*oxazoline* (16).—A solution of 2-acetamido-1,3-di-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranose (11) (206 mg) in dichloromethane (10 ml) was treated with anhydrous iron(III) chloride (85 mg) and the reaction was allowed to proceed for 20 h at room temperature. The mixture was washed with water, dried (Na_2SO_4), and evaporated to dryness, giving a syrup containing some starting material. It was chromatographed on silica gel (20 g); elution with chloroform–acetone (9 : 1) gave *compound* (16) (130 mg, 72%) as a syrup, $[\alpha]_D$ +59° (*c* 1 in $CHCl_3$); $\nu_{max.}$ (film) 1 750 (OAc), 1 675 (C=N), and 740 and 695 cm^{-1} (Ph); δ (CCl_4) 1.95 (3 H, s, OAc), 1.97 (3 H, d, $J_{Me,2}$ 2 Hz, Me), 3.2—3.5 (3 H, m, H-5 and H-6), 5.30 (1 H, d, $J_{2,3}$ 3 Hz, H-3), 5.85 (1 H, d, $J_{1,2}$ 8 Hz, H-1), and 7.21 and 7.23 (10 H, 2 s, Ph) (Found: C, 67.3; H, 6.3; N, 3.2; O, 22.5. $C_{24}H_{27}NO_6$ requires C, 67.7; H, 6.4; N, 3.3; O, 22.6%).

Allyl 2-*Acetamido*-3-*O*-*benzyl*-4,6-O-*benzylidene*-2-*deoxy*-β-D-*glucopyranoside* (3).[10]—A suspension of allyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (1) (17.7 g), barium oxide (43.5 g), and barium hydroxide octahydrate (12.8 g) in dry *NN*-dimethylformamide (380 ml) was stirred vigorously for 12 h in the presence of α-bromotoluene (13 ml, 2 equiv.). Treatment similar to that described for the synthesis of (2) gave *compound* (3) (20.5 g, 92%), m.p. 261—262° (from ethanol); $[\alpha]_D$ −59° (*c* 1.1 in *NN*-dimethylformamide); $\nu_{max.}$ (Nujol) 3 280 (NH), 1 650 (amide I), and 1 550 cm^{-1} (amide II) (Found: C, 68.3; H, 6.7; N, 3.2. $C_{25}H_{29}NO_6$ requires C, 68.3; H, 6.7; N, 3.2%).

Allyl 2-*Acetamido*-3-*O*-*benzyl*-2-*deoxy*-β-D-*glucopyranoside* (6).—Compound (3) (15.8 g) underwent hydrolysis under the same conditions as reported for compound (2) to give *compound* (6) (11.2 g, 89%), m.p. 188—189° (from acetone); $[\alpha]_D$ −11.4° (*c* 1.17 in MeOH); $\nu_{max.}$ (KBr) 3 320 (OH), 1 655 (amide I), 1 560 (amide II), and 730 and 692 cm^{-1} (Ph); δ [$(CD_3)_2SO$] 1.80 (3 H, s, NH*Ac*), 4.43 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1), 7.32 (5 H, s, Ph), and 7.90 (1 H, d, $J_{NH,2}$ 8 Hz, NH) (Found: C, 61.4; H, 7.2; N, 3.9. $C_{18}H_{25}NO_6$ requires C, 61.5; H, 7.2; N, 4.0%).

Allyl 2-*Acetamido*-3,6-*di*-O-*benzyl*-2-*deoxy*-β-D-*glucopyranoside* (7).—A suspension of allyl 2-acetamido-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside (6) (3.5 g), barium oxide (7 g), and barium hydroxide octahydrate (1.8 g) in *NN*-dimethylformamide (30 ml) was stirred vigorously for 3 h in the presence of α-bromotoluene (1.4 ml, 1.2 equiv.). After the usual work-up, the residue was chromatographed on silica gel (75 g); elution with chloroform–acetone (9 : 1)

gave *compound* (7) (2.2 g, 51%), m.p. 140—142° (from ethyl acetate–hexane); $[\alpha]_D$ −4.3° (*c* 1.86 in MeOH); $\nu_{max.}$ (KBr) 3 440 (OH), 3 300 (NH), 1 660 (amide I), 1 560 (amide II), and 725 and 690 cm^{-1} (Ph); δ 1.90 (3 H, s, NH*Ac*), 3.0br (1 H, s, OH), 5.82 (1 H, d, $J_{NH,2}$ 8 Hz, NH), and 7.36 (10 H, s, Ph) (Found: C, 67.9; H, 6.9; N, 3.1. $C_{25}H_{31}NO_6$ requires C, 68.0; H, 7.1; N, 3.2%).

*Allyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-*D*-glucopyranoside* (8) [10] was isolated from the column as a by-product (30%), m.p. 150—151° (from methanol), $[\alpha]_D$ +8.3° (*c* 1 in $CHCl_3$); $\nu_{max.}$ (Nujol) 3 290 (NH), 1 650 (amide I), and 1 550 cm^{-1} (amide II) (Found: C, 72.5; H, 7.2; N, 2.7. $C_{32}H_{37}NO_6$ requires C, 72.3; H, 7.0; N, 2.6%).

*2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-*α*-*D*-glucopyranose* (10).—Allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (7) (1 g) was deallylated as previously described for the preparation of (9), leading to *compound* (10) (0.8 g, 84%), m.p. 165—166° (from acetone–ether); $[\alpha]_D$ +55° → +53.5° (*c* 1.42 in MeOH); $\nu_{max.}$ (KBr) 3 420 (OH), 3 320 (NH), 1 640 (amide I), 1 540 (amide II), and 730 and 690 cm^{-1} (Ph); δ [$(CD_3)_2SO$–D_2O] 1.84 (3 H, s, NH*Ac*), 4.52 (2 H, s, CH_2Ph), 4.75 (2 H, q, AB, *J* 12 Hz, CH_2Ph), 4.95 (1 H, d, $J_{1,2}$ 3.5 Hz, H-1), and 7.32 and 7.35 (10 H, 2 s, Ph) (Found: C, 65.6; H, 6.8; N, 3.3; O, 23.9. $C_{22}H_{27}NO_6$ requires C, 65.8; H, 6.8; N, 3.5; O, 23.9%).

*2-Acetamido-1,4-di-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-*β*-*D*-glucopyranose* (12).—A solution of 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranose (10) (627 mg) in dry pyridine (10 ml) containing anhydrous pyridine hydrochloride (250 mg) was acetylated with acetic anhydride (0.5 ml) as for the preparation of compound (11). The residue was chromatographed on silica gel; elution with chloroform–acetone (19 : 1) gave *compound* (12) (640 mg, 85%), which was recrystallised from ethyl acetate–hexane; m.p. 167—169°; $[\alpha]_D$ +43.7° (*c* 1.22 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 320 (NH), 1 750 (OAc), 1 660 (amide I), 1 550 (amide II), and 730 and 695 cm^{-1} (Ph); δ 1.85 (3 H, s, NH*Ac*) 1.90 and 2.08 (6 H, 2 s, OAc), 4.50 and 4.62 (4 H, 2 s, CH_2Ph), 5.18 (1 H, t, $J_{3,4} = J_{4,5}$ = 8 Hz, H-4), 5.75 (1 H, d, $J_{NH,2}$ 8 Hz, NH), 5.90 (1 H, d, $J_{1,2}$ 8 Hz, H-1), and 7.32 (10 H, s, Ph) (Found: C, 64.5; H, 6.6; N, 2.8; O, 26.3. $C_{26}H_{31}NO_8$ requires C, 64.3; H, 6.4; N, 2.9; O, 26.4%).

*4-O-Acetyl-3,6-di-*O*-benzyl-1,2-dideoxy-2′-methyl-*α*-D-glucopyranoso*[2,1-d]-Δ$^{2'}$-*oxazoline* (17).—2-Acetamido-1,4-di-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranose (12) (327 mg) was transformed into the syrupy *oxazoline* (17) (200 mg, 70%) as for the preparation of (16); $[\alpha]_D$ −4.9° (*c* 1.54 in $CHCl_3$); $\nu_{max.}$ (film) 1 750 (OAc), 1 672 (C=N), and 740 and 695 cm^{-1} (Ph); δ (CCl_4) 1.92 (3 H, s, OAc), 1.95 (3 H, d, $J_{Me,2}$ 2 Hz, Me), 4.48 (2 H, s, CH_2Ph), 4.70 (2 H, q, AB, *J* 12 Hz, CH_2Ph), 5.85 (1 H, d, $J_{1,2}$ 8 Hz, H-1), and 7.25 (10 H, s, Ph) (Found: C, 67.3; H, 6.4; N, 3.1; O, 22.8. $C_{24}H_{27}NO_6$ requires C, 67.7; H, 6.4; N, 3.3; O, 22.6%).

*3,4,6-Tri-*O*-benzyl-1,2-dideoxy-2′-methyl-*α*-D-glucopyranoso*[2,1-d]-Δ$^{2'}$-*oxazoline* (15).—A solution of 3,4,6-tri-*O*-acetyl-1,2-dideoxy-2′-methyl-α-D-glucopyranoso[2,1-d]-Δ$^{2'}$-oxazoline (13) [4b] (891 mg) in dry methanol (20 ml) was *O*-deacetylated at room temperature for 3 h after addition of 2 drops of dry concentrated methanolic sodium methoxide. The methanol was evaporated off and the residue of 1,2-dideoxy-2′-methyl-α-D-glucopyranoso[2,1-*d*]-Δ$^{2'}$-oxazoline (14) [4a] (526 mg, 95%) was immediately benzylated; δ (C_5D_5N–D_2O) 2.05 (3 H, d, $J_{Me,2}$ 1.8 Hz, Me) and 6.35 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1).

Sodium hydride (0.47 g of a 50% oil suspension) was slowly added to a solution of compound (14) in dry *NN*-dimethylformamide (10 ml) and α-bromotoluene (1.1 ml, 3.5 equiv.) and the mixture was stirred for 2 h. The product was isolated in the usual way as a syrup, which was chromatographed on alumina (50 g). . *Compound* (15) was eluted with ether (containing 0.2% of triethylamine) as a syrup [647 mg, 50% from (13)], which could not be induced to crystallise; $[\alpha]_D$ +33.5° (*c* 2.23 in $CHCl_3$); $\nu_{max.}$ (film) 1 665 (C=N) and 730 and 692 cm^{-1} (Ph); δ 2.02 (3 H, d, $J_{Me,2}$ 2.2 Hz, Me), 6.05 (1 H, d, $J_{1,2}$ 7.5 Hz, H-1), and 7.27, 7.32, and 7.37 (15 H, 3 s, Ph) (Found: C, 73.7; H, 6.9; N, 3.1; O, 17.2. $C_{29}H_{31}NO_5$ requires C, 73.6; H, 6.6; N, 3.0; O, 16.9%).

*Benzyl-6-O-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-*β*-D-galactopyranoside* (18).—A solution of the oxazoline (15) (310 mg) in benzene (10 ml) was added dropwise to a stirred mixture of benzyl 2,3,4-tri-*O*-benzyl-β-D-galactopyranoside [12] (295 mg), toluene-*p*-sulphonic acid (10 mg), and powdered molecular sieves (4 Å; 100 mg) in dry benzene (5 ml) at 70 °C. After 20 h, the suspension was cooled, neutralised with triethylamine, diluted with chloroform, washed with water, and evaporated. The residue was chromatographed on silica gel (50 g); elution with chloroform gave *compound* (18) (405 mg, 73%), which was recrystallised from ethyl acetate; m.p. 182—184°; $[\alpha]_D$ −8° (*c* 1.12 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 300 (NH), 1 665 (amide I), 1 570 (amide II), and 730 and 695 cm^{-1} (Ph) (Found: C, 74.5; H, 6.7; N, 1.3; O, 17.3. $C_{63}H_{67}NO_{11}$ requires C, 74.6; H, 6.7; N, 1.4; O, 17.3%).

*6-O-(2-Acetamido-2-deoxy-*β*-D-glucopyranosyl)-D-galactose* (19).—A solution of the protected disaccharide (18) (140 mg) in acetic acid (10 ml) was hydrogenolysed over Pd–C (10%; 100 mg) for 36 h. The mixture was filtered and evaporated to dryness to give *compound* (19) (46 mg, 88%) as an amorphous powder, $[\alpha]_D$ +9.3° (*c* 0.63 in H_2O) [lit.,[8a] +9.2° (*c* 0.65 in H_2O); lit.,[7] +10° (*c* 1.55 in H_2O); lit.,[8b] +9.9° (*c* 0.10 in H_2O)] (Found: C, 41.9; H, 6.6; N, 3.3; O, 48.5. $C_{14}H_{25}NO_{11},H_2O$ requires C, 41.9; H, 6.6; N, 3.5; O, 47.8%). This compound gave a single peak on g.l.c. after reduction with sodium borohydride (t_R 1.29).

*6-O-(2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose* (20).— 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (186 mg) was glycosylated as for the synthesis of (18). The residue was purified on silica gel (50 g); elution with chloroform–acetone (19 : 1) gave *compound* (20) (365 mg, 70%), which was recrystallised from ether–hexane; m.p. 122—123°, $[\alpha]_D$ −35° (*c* 1 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 320 (NH), 1 660 (amide I), 1 550 (amide II), and 740 and 695 cm^{-1} (Ph); δ 1.32, 1.45, and 1.53 (12 H, 3 s, Me), 1.91 (3 H, s, NH*Ac*), 5.55 (1 H, d, $J_{1,2}$ 7 Hz, H-1 of Gal), 5.65 (1 H, d, $J_{NH,2}$ 8 Hz, NH), and 7.30, 7.33, and 7.35 (15 H, 3 s, Ph) (Found: C, 67.0; H, 7.0; N, 1.8; O, 23.9. $C_{41}H_{51}NO_{11}$ requires C, 67.1; H, 7.0; N, 1.9; O, 24.0%).

*6-O-(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose* (21).— 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (260 mg) was glycosylated with the oxazoline (17) (460 mg) as previously described. The syrupy residue was dissolved in dry methanol (10 ml) containing a few drops of saturated methanolic sodium methoxide. After 12 h, the solution was concentrated to a syrup. Chromatography on silica

[12] A. Lipták, I. Jodál, and P. Nánási, *Carbohydrate Res.*, 1975, **44**, 1.

gel (25 g), with chloroform–acetone (17 : 3) as eluant, gave the *disaccharide* (21) (430 mg, 62%), m.p. 156—157° (from ethyl acetate–hexane); $[\alpha]_D$ −54° (*c* 1.34 in $CHCl_3$); $\nu_{max.}$ (Nujol) 3 540 (OH), 3 340 (NH), 1 660 (amide I), 1 540 (amide II), and 730 and 692 cm^{-1} (Ph); δ 1.30, 1.42, and 1.50 (12 H, 3 s, Me), 1.91 (3 H, s, NH*Ac*), 3.08br (1 H, s, OH), 5.50 (1 H, d, $J_{1,2}$ 5 Hz, H-1 of Gal), 5.80 (1 H, d, $J_{NH,2}$ 8 Hz, NH), and 7.32 (10 H, s, Ph) (Found: C, 63.4; H, 7.0; N, 2.2; O, 27.0 $C_{34}H_{45}NO_{11}$ requires C, 63.4; H, 7.0; N, 2.2; O, 27.3%).

6-O-(2-*Acetamido*-3,4,6-*tri*-O-*acetyl*-2-*deoxy*-β-D-*glucopyranosyl*)-1,2:3,4-*di*-O-*isopropylidene*-α-D-*galactopyranose* (22).—This *compound* was prepared from the oxazoline (13) as previously described [7] (yield 75%); m.p. 99—102° (from ether); $[\alpha]_D$ −66° (*c* 1.11 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 340 (NH), 1 750 (C=O of ester), 1 660 (amide I), and 1 550 cm^{-1} (amide II); δ 1.36 (6 H, s, Me_2C), 1.47 and 1.53 (3 H each, s, Me_2C), 1.99, 2.02, 2.04, and 2.11 (3 H each, s, MeCO), 4.78 (1 H, d, $J_{1,2}$ 8 Hz, H-1 of GNAc), 5.59 (1 H, d, *J* 5 Hz, H-1 of Gal) and 5.88 (1 H, d, *J* 8 Hz, CONH), {lit.,[9] m.p. 105—107° (from ether) or 117—119° (from ether–pentane), $[\alpha]_D$ −56.5° ($CHCl_3$); lit.,[7] m.p. 198° (from propan-2-ol), $[\alpha]_D$ +85° (*c* 0.54 in MeOH)}.

6-O-(2-*Acetamido*-2-*deoxy*-β-D-*glucopyranosyl*)-1,2:3,4-*di*-O-*isopropylidene*-α-D-*galactopyranose* (23).—*O*-Deacetylation of the disaccharide (22) (sodium methoxide) gave the *disaccharide* (23) (95%), m.p. 200—202° (from propan-2-ol), $[\alpha]_D$ −61° (*c* 1.78 in MeOH) (Found: C, 51.6; H, 7.2; N, 3.3; O, 38.1. $C_{20}H_{33}NO_{11}$ requires C, 51.8; H, 7.2; N, 3.0; O, 38.0%).

Selective Benzylation of 6-O-(2-*Acetamido*-2-*deoxy*-β-D-*glucopyranosyl*)-1,2:3,4-*di*-O-*isopropylidene*-α-D-*galactopyranose* (23).—A suspension of the disaccharide (23) (1.76 g), barium oxide (2.82 g), and barium hydroxide octahydrate (0.67 g) in *NN*-dimethylformamide (20 ml) was stirred for 4 days in the presence of α-bromotoluene (0.9 ml, 2 equiv.). The mixture was diluted with chloroform (100 ml), filtered, and evaporated. The residue was chromatographed on silica gel (100 g), with chloroform–ethanol (15 : 1) as eluant, to give 6-O-(2-*acetamido*-3,4,6-*tri*-O-*benzyl*-2-*deoxy*-β-D-*glucopyranosyl*)-1,2:3,4-*di*-O-*isopropylidene*-α-D-*galactopyranose* (20) (0.56 g, 20%), and 6-O-(2-*acetamido*-3,6-*di*-O-*benzyl*-2-*deoxy*-β-D-*glucopyranosyl*)-1,2:3,4-*di*-O-*isopropylidene*-α-D-*galactopyranose* (21) (0.99 g, 40%), identical with the compounds previously prepared.

[7/1056 *Received*, 20*th June*, 1977]