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PROTECTED GLYCOSIDES AND DISACCHARIDES OF 2-AMINO-2-DEOXY-D-GLUCOPYRANOSE BY FERRIC CHLORIDE-CATALYZED COUPLING

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ABSTRACT

The ferric chloride-catalyzed glycosylation of hydroxy compounds by protected 2-acylamino-2-deoxy-β-D-glucopyranose 1-acetates is described. In addition to known glycosides from the reaction of alcohols with 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**3**), allyl (and other alkyl) β-glycosides were obtained from the *N*-benzoyl, *N*-phenoxyacetyl, *N*-methoxyacetyl, *N*-chloroacetyl, and *N*-phthaloyl congeners of **3**. The latter compounds, except for the *N*-phthaloyl derivative, gave oxazolines in the absence of an alcoholic reactant. Compound **3** and the related *N*-benzoyl, *N*-chloroacetyl, *N*-acetyl-3,4,6-tri-*O*-benzyl, and *N*-acetyl-4-*O*-acetyl-3,6-di-*O*-benzyl derivatives were coupled to one or more protected sugars to form protected, β-linked disaccharides. Coupling at the 6-positions of acceptors proceeded smoothly and gave 67–80% yields. For successful coupling at positions 3 and 4, long reaction times and multiple additions of glycosyl donor were required, and yields ranged from 60% to as low as 30%. 1,3,4,6-Tetra-*O*-acetyl-2-(chloroacetamido)-2-deoxy-β-D-glucopyranose appeared to be the most reactive glycosyl donor in this series. The reaction of 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline (derived from **3**) with allyl alcohol was catalyzed by ferric chloride, and oxazolines were detected as intermediates in some of the glycosylations of protected sugars.

INTRODUCTION

2-Acylamino-2-deoxy-β-D-glucopyranose 1-acetates have been used as sources of glycosyl units in synthesis since 1972, when Matta and Bahl[1] published a procedure for their conversion into oxazoline derivatives that function as glycosyl donors. The conversion reaction, discovered by Bach and Fletcher, involves treatment of the 1-acetate with anhydrous ferric chloride in dichloromethane[1]. Some years later, we studied the effect of adding simple alcohols or partially protected

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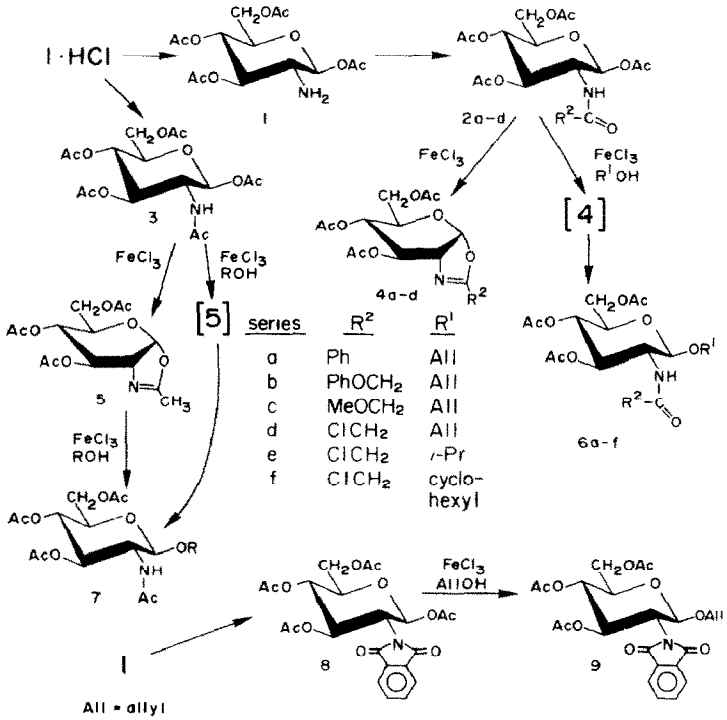
sugars to the reaction mixture and, as described in preliminary communications[2,3], obtained glycosides of 2-acylamino-2-deoxy-β-D-glucopyranoses in generally good yields. As this "direct" glycosylation procedure has found substantial use, in our own laboratories[4] and elsewhere, publication of a full report seemed desirable.

RESULTS AND DISCUSSION

Our initial studies (Scheme 1) of the direct glycosylation were conducted with the well-known 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**3**), prepared from the hydrochloride of the tetra-acetate **1**. These intermediates were described many years ago by Bergmann and Zervas[5]. On reaction with allyl, benzyl, isopropyl, and *tert*-butyl alcohols in the presence of ferric chloride, compound **3** gave the known allyl, benzyl, isopropyl, and *tert*-butyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosides (**7**). The yields (isolated) of the first three products were >80%; that of the *tert*-butyl glycoside was 55%. Thus, the ferric chloride procedure constitutes a facile preparation of the simple β-glycosides of 2-acetamido-2-deoxy-D-glucose. It is now our method of choice, despite the somewhat lengthy synthesis required to obtain the starting material.

The next series of experiments was done with analogs of **3** in which the *N*-acyl group was varied, in order to assess the effect of changes in the electronic character of the R-portion of the *N*-acyl group on the coupling capability of the oxazolines



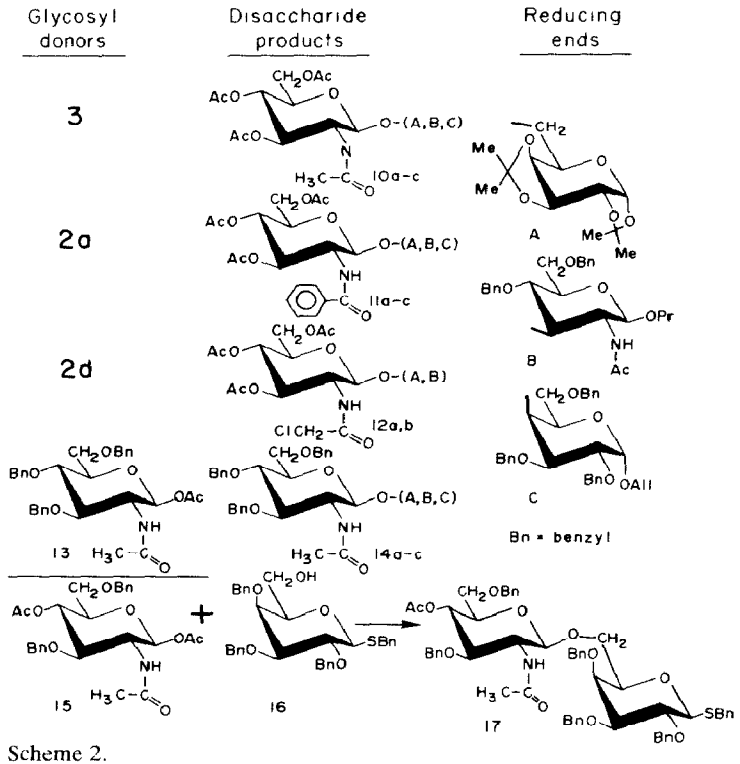
Scheme 1.

formed from the compounds by ring closure. The high reactivity of the phenyloxazoline **4a** toward simple alcohols has been noted[6–8], and the effect of *p*-substitution on the rate of the reaction of **4a** with chloride ion has been studied by Osawa[7]. In the present work, the analogs of **3** examined were the known *N*-benzoyl (**2a**) and *N*-chloroacetyl (**2d**) compounds, and their *N*-phenoxyacetyl (**2b**) and *N*-methoxyacetyl (**2c**) congeners, obtained by treating **1** with the corresponding acid chlorides. As expected, ferric chloride in the absence of an alcohol smoothly catalyzed the conversion of **2a** into **4a**. The phenoxyacetyl derivative **2b** likewise furnished a stable oxazoline (**4b**) in high yield, but the *N*-methoxyacetyl and *N*-chloroacetyl derivatives (**2c,d**) gave low yields of oxazolines (**4c,d**) that were quite labile.

On reaction with allyl alcohol under the conditions used for the preparation of the simple glycosides **7** (overnight, room temperature), compounds **2a–d** gave the corresponding allyl glycosides **6a–d** in high yield. The chloroacetyl derivative **2d** also coupled smoothly with 2-propanol and cyclohexanol to form the isopropyl glycoside **6e** and the cyclohexyl glycoside **6f**. The reaction of the *N*-phthaloyl compound **8** with allyl alcohol was rapid (1 h, room temperature), and the allyl β-glycoside **9** could be isolated in 89% yield.

Since the reaction of the 1-acetates **3** and **2a–d** with alcohols occurs under the same conditions as those used for the formation of oxazolines from these acetates, it is reasonable to suppose that oxazolines (**5,4**) are intermediates in the glycosidation process. The reaction mixtures that furnished the simple glycosides of structures **6** and **7** were therefore monitored by t.l.c., but no oxazoline intermediates could be detected. However, the appearance and then disappearance of oxazolines was noted during the glycosylation of bulkier, less reactive alcohols (partially blocked sugars–see next section). Moreover, the oxazoline (**5**) corresponding to **3** was rapidly converted into the allyl glycoside **7** (R=All) under our standard conditions. These results are consistent with the hypothesis that when oxazolines are capable of forming they are the active glycosylating agents in the direct synthesis. However, the ability of the *N*-phthaloyl compound **8** to undergo the reaction shows that oxazoline formation is not mechanistically obligatory. In this case, the glycosylating species presumably resembles that resulting from the action of silver salts on the corresponding *N*-phthaloyl glycosyl halides[9]. It might be expected that other electrophilic reagents would serve for the activation of **8**, and, indeed, the use of trimethylsilyl trifluoromethanesulfonate[10] and boron trifluoride etherate[11] to promote glycosylation by 2-deoxy-2-phthalimidoglycopyranose 1-acetates has recently been described. Glycosylation by the oxazoline **5** can also be catalyzed by trimethylsilyl trifluoromethanesulfonate[10].

Disaccharides. — To explore the potential of the direct glycosylation procedure in oligosaccharide synthesis, compounds **3** (*N*-acetyl), **2a** (*N*-benzoyl), and **2d** (*N*-chloroacetyl) were used as glycosyl donors. In addition, the fully *O*-benzylated (at positions 3, 4, and 6) β-1-acetate **13** and its partially *O*-benzylated congener **15** were prepared. Each of the donors **3, 2a,** and **13** was coupled to protected sugar



Scheme 2.

derivatives (see Scheme 2) having, respectively, a free 6-OH (1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, **A**-OH), a free 3-OH (propyl 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside, **B**-OH), and a free 4-OH (allyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside, **C**-OH). The *N*-chloroacetyl donor **2d** was tested with the first two of these acceptors. Also, compound **15** was coupled to the benzyl thiogalactoside **16**, which has its 6-OH free and, like **B**-OH and **C**-OH, carries *O*-benzyl protecting groups. Acceptors **16**, **B**-OH, and **C**-OH are typical of the "standardized intermediates" used in the Wisconsin laboratory as building blocks for oligosaccharides.

In coupling the various glycosyl donors to acceptors having free primary hydroxyl groups (**A**-OH, **16**), the same conditions were used as for simple alcohols (room temperature, overnight), but smaller relative proportions of glycosyl acceptor were employed (1.2–2 molar equivalents). It was noted that the reaction of the *N*-chloroacetyl donor **2d** with **A**-OH was complete in 3 h. The yields of disaccharide products (**10a, 11a, 12a, 14a,** and **17**), isolated by column chromatography, ranged from 67 to 80%, based on glycosyl *donor*.

When the phenyloxazoline **4a** was used as a glycosyl donor in place of the *N*-benzoyl compound **2a**, in reaction with **A**-OH, disaccharide **11a** was again formed in excellent yield. Similarly, the oxazoline corresponding to **15** coupled smoothly with **16** to furnish disaccharide **17** (83%).

In acceptors **B**-OH and **C**-OH, the free hydroxyl groups are secondary and hence substantially less reactive than the primary hydroxyl groups of **A**-OH and **16**. Glycosylations of **B**-OH and **C**-OH were therefore carried out at 35°. To facilitate maximal conversion of the acceptors, reactions were prolonged for 2–3 days, and second or even third portions of donor and catalyst were added at intervals of ~24 h. The initial portion of donor was 0.5–1 molar equivalent, and the total donor used was two equivalents, with respect to glycosyl acceptor. The yields, based on *acceptor,* were 60% in couplings to **B**-OH and 30–45% in couplings to **C**-OH. Exceptions to this protocol were two couplings to **B**-OH where single additions of glycosyl donor sufficed. The donors were **2d** (*N*-chloroacetyl, molar ratio 1:1, yield of disaccharide 60%) and **13** (donor–acceptor 1:1.5, 62% yield based on donor).

The ^{1}H-n.m.r. spectra of the foregoing products generally showed resonances characteristic of both the donor and acceptor moieties, and a doublet for H-1′ in the range δ 4.70–5.05. When the latter signal was visible, the value of $J_{1',2'}$ was 8.1–8.8 Hz, leading to the conclusion that all of the compounds were β-linked. The interconversion of certain of the products, as necessary, then confirmed this conclusion. Thus, replacement of the *N*-benzoyl group of **11b** and **11c** by *N*-acetyl[12] gave **10b** and **10c**, respectively. Compound **12b** (*N*-chloroacetyl) was also converted into **10b**. The *O*-benzylated products **14b** and **17** were debenzylated, and the deblocked disaccharides examined. The identity of **14c** was established by its independent synthesis from **10c**, by successive *O*-deacetylation and benzylation.

Conclusions. — The work described here demonstrates the facile preparation of β-glycosides of 2-amino-2-deoxy-D-glucose by the reaction of alcohols with *O*-protected 2-acylamino-2-deoxy-β-D-glucose 1-acetates in the presence of anhydrous ferric chloride. The reaction appears to proceed, to some extent at least, *via* oxazoline intermediates. Partly protected sugars are suitable as alcoholic components if they are sufficiently reactive to couple well with oxazolines by standard procedures involving catalysis by protonic acids[13]. No α-linked products were detected from any of the coupling reactions, but since the procedure emphasized the isolation of the primary product, minor proportions of α anomers may have escaped detection. In any event, if the procedure is not completely stereospecific, it is at least highly stereoselective.

Our results provide some indication that the reactivities of a 2-acylamino-2-deoxyglucose 1-acetate, and the oxazoline derived from it, can be usefully altered by modifying the electronic character of the *N*-acyl group. In particular, the *N*-chloroacetyl compound **2d** had enhanced reactivity, and thus the *N*-chloroacetyl derivatives may be superior glycosylating agents. If an *N*-substituent other than acetyl is required, chloroacetyl is an attractive possibility, because it can be readily converted into acetyl by reduction with tributyltin hydride.

EXPERIMENTAL

General methods. — The instrumental and chromatographic procedures

employed were those previously listed[14]. ^{1}H-N.m.r. spectra "for the record" were determined at 270 MHz, with decoupling as required. Samples were dissolved in $CDCl_3$ (internal Me_4Si) except as otherwise specified. Chromatography on silica gel (E. Merck Kieselgel 60, 0.063–0.200 mm) was accomplished with mixtures of chloroform (major component) and acetone or methanol. Elemental analyses were done at the Galbraith Laboratories, Inc., Knoxville, TN 37821.

Starting materials. — 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride[5] (**1** · HCl) was converted into the free base[5] **1** as needed. 2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose[5] (**3**) was obtained from **1** · HCl by treatment with acetic anhydride in pyridine at room temperature. Treatment[5] of **1** with benzoyl chloride gave crystalline 1,3,4,6-tetra-*O*-acetyl-2-benzamido-2-deoxy-β-D-glucopyranose (**2a**), which was used without further purification and had m.p. 236° (dec.), $[\alpha]_D^{25}$ +35° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.7–7.2 (m, 5 H, Ph), 6.53 (d, 1 H, *J* ~9 Hz, NH), 5.73 (d, 1 H, *J* ~8.6 Hz, H-1), 2.08, 2.07, and 1.98 (3 s, 12 H, 4 Ac).

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-(phenoxyacetamido)-β-D-glucopyranose (**2b**). — A solution of **1** from **1** · HCl (1.0 g) in dry pyridine (5.4 mL) was stirred at 0°, and phenoxyacetyl chloride (0.5 g) was added. Stirring was continued for 2 h, then the solution was poured into ice–water, and the crystalline product (1.26 g, quantitative) was collected. After recrystallization from ethanol–dichloromethane, **2b** had m.p. 208–209°, $[\alpha]_D^{25}$ +29°, $[\alpha]_{436}^{25}$ +60° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.4–6.5 (m, 6 H, Ph and NH), 5.73 (d, 1 H, *J* ~8.4 Hz, H-1), 2.07, 2.04, 2.02, and 1.93 (4 s, 12 H, 4 Ac).

Anal. Calc. for $C_{22}H_{27}NO_{11}$ (481.85): C, 54.88; H, 5.65; N, 2.91. Found: C, 54.99; H, 5.62; N, 2.79.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-(methoxyacetamido)-β-D-glucopyranose (**2c**). — A solution of the free base from **1** · HCl (1.0 g) in dry pyridine (5.4 mL) was treated with methoxyacetyl chloride (0.26 g) overnight at 0° and then poured into ice–water, and the product was recovered by conventional chloroform extraction. The recrystallized product **2c** (0.82 g, 75%) had m.p. 187–188°, $[\alpha]_D^{25}$ +5°, $[\alpha]_{436}^{25}$ +11° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 6.53 (d, 1 H, *J* ~9 Hz, NH), 5.72 (d, 1 H, *J* ~8.5 Hz, H-1), 3.8 (s, 2 H, -$COCH_2$-), and 3.33 (s, 3 H, OMe).

Anal. Calc. for $C_{17}H_{25}NO_{11}$ (419.38): C, 48.69; H, 6.01; N, 3.34. Found: C, 48.48; H, 5.67; N, 3.21.

1,3,4,6-Tetra-O-acetyl-2-(chloroacetamido)-2-deoxy-β-D-glucopyranose (**2d**). — Compound **1** · HCl (5 g) was converted into the free base, and a solution in chloroform (25 mL) plus 2,6-dimethylpyridine (2.5 mL) at −10° was treated with chloroacetyl chloride (1.15 mL). The mixture was stirred for 1 h at 0°, and the product was isolated by conventional chloroform extraction and crystallized from ethanol–hexane to give **2d** (5 g, 91%), m.p. 171–172°, $[\alpha]_D^{25}$ +12°, $[\alpha]_{436}^{25}$ +23° (*c* 0.5, chloroform); lit.[5] m.p. 165–166°. ^{1}H-N.m.r. data (60 MHz): δ 6.67 (d, 1 H, *J* ~8 Hz, NH), 5.75 (d, 1 H, *J* ~8.4 Hz, H-1), and 3.93 (s, 2 H, $COCH_2Cl$).

Reaction of **2a–d** *with ferric chloride in the absence of alcohols. Formation of*

oxazolines **4a–d**. — Each of the β-1-acetates **2a–d** was treated with anhydrous ferric chloride in dry dichloromethane as described below for the preparation of alkyl glycosides. The chloroform solutions obtained by working-up the reaction mixtures were concentrated to dryness, and the amounts of oxazoline in the residues were estimated by 60-MHz ^{1}H-n.m.r. spectroscopy using the integrated intensities of the signals for H-1 in the range δ 6.2–6.0 ($J_{1,2}$ ~7.4 Hz).

Compound **2a** was completely converted into syrupy[8] 2-phenyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline[6] (**4a**). ^{1}H-N.m.r. data[8]: δ 8.0–7.3 (m, 5 H, Ph), 6.17 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 5.41 (t, 1 H, H-3), 4.96 (ddd, 1 H, $J_{3,4}$ 2.2, $J_{4,5}$ 8.8 Hz, H-4), 4.37 (ddd, 1 H, $J_{2,3}$ 2.6, $J_{2,4}$ 1.1 Hz, H-2), 4.15 (m, 2 H, H-6,6'), 3.65 (quintet, 1 H, $J_{5,6} = J_{5,6'}$ = 4.4 Hz, H-5), 2.13, 2.07, and 2.01 (3 s, 9 H, 3 Ac).

In the product from the cyclization of **2b**, the presence of 80% of 2-(phenoxymethyl)-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline (**4b**) could be inferred from the n.m.r. analysis [δ 6.07 (H-1)].

According to their n.m.r. spectra, the products from **2c** and **2d** were mixtures of unchanged starting-material, the respective oxazolines **4c** [δ 6.0 (H-1), ~40%] and **4d** [δ 6.03 (H-1), ~50%], and decomposition products. Efforts to increase the degree of conversion by prolonging the reaction times, with or without the addition of more ferric chloride, led to the destruction of the oxazolines.

*Alkyl 3,4,6-tri-*O*-acetyl-2-acylamino-2-deoxy-β-*D*-glucopyranosides*. — To anhydrous ferric chloride (125 mg, 0.77 mmol) were added dichloromethane (4 mL, dried over molecular sieves) and anhydrous calcium sulfate (200 mg), and the mixture was stirred for 10 min (if the ferric chloride is sufficiently dry, pretreatment with anhydrous calcium sulfate may be unnecessary). The β-acetate **3** (200 mg, 0.51 mmol) and the alcohol (2–10 mol) were then added, and stirring was continued overnight at room temperature. In some reactions, tetramethylurea (~60 μL) was included, but this was unnecessary with simple alcohols. The mixture was poured into ice-cold, aqueous sodium hydrogencarbonate, diluted with a little chloroform, and stirred until the organic phase became colorless (for a large-scale reaction, the ordinary extraction procedure is effective). The mixture was filtered through Celite, and the product was isolated conventionally from the organic phase and then crystallized from ethanol. Specific examples are given in a prelimiary communication[2].

With acetates **2a–d** as donors, essentially the same procedure was followed, with 10 mol of alcohol. In some reactions, the anhydrous calcium sulfate was omitted.

*Allyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside*[14] (**7**, *R* = *All*). — To a solution (see above) of ferric chloride (50 mg) in dichloromethane (1 mL) were added a solution of oxazoline[1] **5** (100 mg) in dichloromethane (1 mL) and then allyl alcohol (0.1 mL). The mixture was stirred for 2 h at room temperature. Almost all of the **5** had then reacted (t.l.c.), and further stirring led to the formation of some decomposition products. Work-up gave 80% of **7** (R = All).

*Allyl 3,4,6-tri-*O*-acetyl-2-benzamido-2-deoxy-β-*D*-glucopyranoside* (**6a**). — A

mixture of ferric chloride (540 mg), dichloromethane (20 mL), **2a** (1.0 g), and allyl alcohol (1.5 mL) was processed as described above. The product was crystallized from ethanol to give **6a** (85%), m.p. 240° (dec.), $[\alpha]_D^{25}$ +22°, $[\alpha]_{436}^{25}$ +46° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.73–7.35 (m, 5 H, Ph), 6.42 (d, 1 H, *J* 8.8 Hz, NH), 5.79 (m, 1 H, -CH=), 5.3–5.1 (m, 2 H, $=CH_2$), 5.44 and 5.14 (2 t, 2 H, *J* ~10 Hz, H-3,4), 4.79 (d, 1 H, *J* 8.5 Hz, H-1), 3.77 (m, 1 H, H-5), 2.11, 2.04, and 1.98 (3 s, 9 H, 3 Ac).

Anal. Calc. for $C_{22}H_{27}NO_9$ (449.46): C, 58.79; H, 6.06; N, 3.12. Found: C, 58.92; H, 6.04; N, 3.05.

*Allyl 3,4,6-tri-O-acetyl-2-deoxy-2-(phenoxyacetamido)-β-*D*-glucopyranoside* (**6b**). — The direct glycosylation of allyl alcohol by **2b**, according to the procedure used for the benzamido analog **6a**, gave **6b** (78%), m.p. 160–161°, $[\alpha]_D^{25}$ +19°, $[\alpha]_{436}^{25}$ +41° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.4–6.8 (m, 5 H, Ph), 6.69 (d, 1 H, *J* 8.8 Hz, NH), 5.80 (m, 1 H, -CH=), 5.26 and 5.18 (2 m, 2 H, $=CH_2$), 5.40 (dd, 1 H, *J* 10.3, 9.2 Hz, H-3 or 4), 5.08 (t, 1 H, *J* 9.2 Hz, H-3 or 4), 4.80 (d, 1 H, *J* 8.5 Hz, H-1), 4.28 and 4.14 (2 dd, 2 H, H-6,6'), 4.32–4.06 (m, 2 H, $-OCH_2CH=$), 3.93 (m, 1 H, H-2), 3.73 (m, 1 H, H-5), 2.08, 2.02, and 1.93 (3 s, 9 H, 3 Ac).

Anal. Calc. for $C_{23}H_{29}NO_{10}$ (479.48): C, 57.61; H, 6.10; N, 2.92. Found: C, 57.49; H, 5.94; N, 2.78.

*Allyl 3,4,6-tri-O-acetyl-2-deoxy-2-(methoxyacetamido)-β-*D*-glucopyranoside* (**6c**). — Obtained (80%) from **2c**, **6c** had m.p. 176–177°, $[\alpha]_D^{25}$ −11°, $[\alpha]_{436}^{25}$ −19° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 6.56 (d, 1 H, *J* 8.8 Hz, NH), 5.85 (m, 1 H, -CH=), 5.35 (dd, 1 H, *J* 10.7, 9.2 Hz, H-3), 5.27–5.19 (m, 2 H, $=CH_2$), 5.08 (dd, 1 H, *J* 9.9, 9.2 Hz, H-4), 4.77 (d, 1 H, *J* 8.1 Hz, H-1), 3.70 (m, 1 H, H-5), 3.39 (s, 3 H, OMe), 2.09, 2.03, and 2.02 (3 s, 9 H, 3 Ac).

Anal. Calc. for $C_{18}H_{27}NO_{10}$ (417.41): C, 51.79; H, 6.52; N, 3.36. Found: C, 51.61; H, 6.46; N, 3.20.

*Allyl 3,4,6-tri-O-acetyl-2-(chloroacetamido)-2-deoxy-β-*D*-glucopyranoside* (**6d**). — Obtained (86%) from **2d**, **6d** had m.p. 166–167°, $[\alpha]_D^{25}$ −9°, $[\alpha]_{436}^{25}$ −17° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 6.63 (d, 1 H, *J* 8.5 Hz, NH), 5.87 (m, 1 H, -CH=), 5.37 (dd, 1 H, *J* 10.7, 9.2 Hz, H-3), 5.28–5.22 (m, 2 H, $=CH_2$), 5.09 (~t, 1 H, H-4), 4.78 (d, 1 H, *J* 8.1 Hz, H-1), 4.01 (q_{AB}, 2 H, $COCH_2Cl$), 3.90 (m, 1 H, H-2), and 3.75 (m, 1 H, H-5).

Anal. Calc. for $C_{17}H_{24}ClNO_9$ (421.83): C, 48.41; H, 5.74; Cl, 8.40; N, 3.32. Found: C, 48.04; H, 5.61; Cl, 8.18; N, 3.20.

*Isopropyl 3,4,6-tri-O-acetyl-2-(chloroacetamido)-2-deoxy-β-*D*-glucopyranoside* (**6e**). — Obtained (90%) from **2d** and 2-propanol, **6e** had m.p. 192–193° (from ethanol), $[\alpha]_D^{25}$ −7°, $[\alpha]_{436}^{25}$ −15° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 4.88 (d, 1 H, *J* 8.1 Hz, H-1), 4.0 (q_{AB}, 2 H, $-COCH_2Cl$), 3.92 (m, 1 H, $-OCHMe_2$), 1.23, and 1.13 (2 d, 6 H, *J* 6.3 Hz, $-OCHMe_2$).

Anal. Calc. for $C_{17}H_{26}ClNO_9$ (423.85): C, 48.17; H, 6.18; Cl, 8.36; N, 3.30. Found: C, 48.26; H, 6.08; Cl, 7.86; N, 3.29.

*Cyclohexyl 3,4,6-tri-O-acetyl-2-(chloroacetamido)-2-deoxy-β-*D*-glucopyrano-*

side (**6f**). — Obtained (86%) from **2d** and cyclohexanol, **6f** had m.p. 208° (from ethanol), $[\alpha]_D^{25}$ −10°, $[\alpha]_{436}^{25}$ −24° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 6.59 (d, 1 H, *J* 8.1 Hz, NH), 4.91 (d, 1 H, *J* 8.5 Hz, H-1), 4.0 (q_{AB}, 2 H, $COCH_2Cl$), and 2.1–1.1 (m, 10 H, C_6H_{10}).

Anal. Calc. for $C_{20}H_{30}ClNO_9$ (463.91): C, 51.78; H, 6.52; N, 3.02. Found: C, 51.75; H, 6.09; N, 3.01.

*1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranose* (**8**). — Prepared from **1** (20 g) by the procedure of Akiya and Osawa[15], **8** had m.p. 77–82° (from ethanol) (lit.[15] m.p. 92–95°) and contained alcohol of solvation. When crystallized from ethyl acetate–hexane, **8** had m.p. 100–103°, $[\alpha]_D^{25}$ +68°, $[\alpha]_{436}^{25}$ +155° (*c* 0.5, chloroform); lit.[9] m.p. 90–94°, $[\alpha]_D^{22}$ +65.5°. ^{1}H-N.m.r. data: δ 7.83 and 7.72 (m, 4 H, aromatic protons), 6.52 (d, 1 H, H-1), 5.89 (dd, 1 H, H-3), 5.22 (dd, 1 H, $J_{4,5}$ 9.9, $J_{3,4}$ 9.2 Hz, H-4), 4.47 (dd, 1 H, $J_{2,3}$ 10.7, $J_{1,2}$ 8.8 Hz, H-2), 4.37 and 4.15 (2 dd, 2 H, J_{gem} 12.5, $J_{5,6}$ 4.41 and 2.21 Hz, H-6,6′), 4.03 (m, 1 H, H-5), 2.11, 2.04, 2.0, and 1.86 (4 s, 12 H, 4 Ac).

*Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**9**). — A mixture of anhydrous ferric chloride (8.42 g), dichloromethane (200 mL, dried over molecular sieves), and allyl alcohol (4.8 mL, ~2 mol, optimal for this preparation) was stirred for 5 min, and a solution of **8** (16.5 g) in dichloromethane (130 mL) was added. Stirring was continued for 1 h at room temperature and then the mixture was poured into ice-cold, aqueous sodium hydrogencarbonate. After the addition of chloroform and mixing, the organic layer was filtered through Celite, and the filtrate and washings were combined, washed with dilute aqueous sodium hydrogencarbonate and then water, dried, and concentrated. Crystallization of the residue from ethanol–hexane gave **9** (89%), m.p. 109–110°, $[\alpha]_D^{25}$ +37°, $[\alpha]_{436}^{25}$ +91° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.8–7.7 (m, 4 H, aromatic protons), 5.80 (dd, 1 H, H-3), 5.67 (m, 1 H, -CH=), 5.42 (d, 1 H, *J* 8.5 Hz, H-1), 5.19 (dd, 1 H, H-4), 5.14–5.08 (q_{AB}, 2 H, $=CH_2$), 4.36 (dd, 1 H, *J* 10.7 and 8.5 Hz, H-2), 4.02–4.18 (m, 2 H, $-OCH_2CH=$), 3.84 (m, 1 H, H-5), 2.12, 2.02, and 1.86 (3 s, 9 H, 3 Ac).

Anal. Calc. for $C_{23}H_{25}NO_{10}$ (475.45): C, 58.10; H, 5.30; N, 2.95. Found: C, 58.02; H, 5.29; N, 2.81.

Coupling to protected sugars. — The procedure was essentially that used for simple alcohols, with modifications as described in the Discussion. To further illustrate the modifications, full details are given for the first three examples that follow. Details are omitted for the remaining couplings, but each has an analogy in the early examples. Tetramethylurea was added to several of the reaction mixtures, but only when the glycosyl acceptor was acid labile (**A**-OH) did it have a beneficial effect.

*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* (**10a**). — A mixture of anhydrous ferric chloride (185 mg), dichloromethane (3 mL), and anhydrous calcium sulfate (300 mg) was stirred for 5–10 min. 2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-

glucopyranose (**3**; 300 mg, 0.77 mmol), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**A**-OH; 241 mg, 0.93 mmol), and tetramethylurea (92 μL) in dichloromethane (3 mL) were then added. Stirring was continued overnight at room temperature, and the mixture was processed as described above. After purification by column chromatography and crystallization from ether–dichloromethane, **10a** was obtained (67% based on **3**); m.p. 105–107°, $[\alpha]_D^{25}$ −67°, $[\alpha]_{436}^{25}$ −134° (*c* 0.5, chloroform); lit.[16] m.p. 99–102°, $[\alpha]_D$ −66°.

Propyl 2-acetamido-3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-4,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**10b**). — *(a) By direct coupling.* Anhydrous ferric chloride (63 mg) and anhydrous calcium sulfate (100 mg) were stirred in dichloromethane (2 mL). The glycosyl donor **3** (100 mg, 0.26 mmol), propyl 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside[17] (**B**-OH; 113 mg, 0.25 mmol), and tetramethylurea (31 μL) were added. The mixture was stirred overnight at 35°, and more anhydrous ferric chloride (63 mg), **3** (100 mg), and tetramethylurea (31 μL) were added. Stirring was again continued overnight and the mixture was processed. The residue was purified by column chromatography to give **10b** as an amorphous solid (120 mg, 61% based on **B**-OH), $[\alpha]_D^{25}$ −31°, $[\alpha]_{436}^{25}$ −65° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.4–7.2 (m, 10 H, 2 Ph), 6.52 and 6.16 (2 d, 2 H, *J* 8.0, 8.6 Hz, 2 NH), 5.29 and 5.08 (2 t, 2 H, H-3′,4′), 5.0 (d, 1 H, *J* 8.1 Hz, H-1′), 2.04, 2.01, 1.99, and 1.91 (4 s, 15 H, 5 Ac), 1.57 (m, 2 H, -OCH-CH_2CH$_3$), and 0.92 (t, 3 H, -OCH-CH$_2$CH_3).

Anal. Calc. for $C_{39}H_{52}N_2O_{14}$ (772.85): C, 60.61; H, 6.78; N, 3.62. Found: C, 60.55; H, 6.89; N, 3.51.

(b) By acyl exchange. A mixture of **11b** (50 mg), anhydrous sodium acetate (3 mg), acetic anhydride (0.6 mL), and acetic acid (0.15 mL) was heated for 24 h under reflux[12]. Water (0.11 mL) was then added and heating was continued for 1 h. The mixture was concentrated to dryness and the product was subjected to column chromatography to give **10b** (60%) identical with the product obtained in *(a)*.

Allyl 4-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-galactopyranoside (**10c**). — *(a) By direct coupling.* A mixture of anhydrous ferric chloride (125 mg), dichloromethane (4 mL), anhydrous calcium sulfate (200 mg), allyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside[18] (**C**-OH; 504 mg, 1.03 mmol), **3** (200 mg, 0.51 mmol), and tetramethylurea (62 μL) was stirred overnight at 35°. The same amounts of **3**, ferric chloride, and tetramethylurea were again added, and stirring was continued for another 24 h. Since the acceptor was still present, more reagents (double the previous amounts) were added, and stirring was continued for a third 24-h period. The crude product was subjected to column chromatography to give **10c** (350 mg, 42% based on **C**-OH). Recrystallization from ethyl acetate–hexane gave material with m.p. 142–143°, $[\alpha]_D^{25}$ +41°, $[\alpha]_{436}^{25}$ +77° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.4–7.2 (m, 15 H, 3 Ph), 5.9 (m, 1 H, -CH=), 5.7 (d, 1 H, *J* 8.3 Hz, NH), 5.3–5.1 (m, 2 H, =CH$_2$), 2.02, 2.01, 1.97, and 1.53 (4 s, 12 H, 4 Ac).

Anal. Calc. for $C_{44}H_{53}NO_{14}$ (819.90): C, 64.46; H, 6.52; N, 1.71. Found: C, 64.45; H, 6.44; N, 1.71.

(b) By acyl exchange. Compound **10c**, obtained from **11c** as described for the conversion **11b**→**10b**, was identical with the product obtained in *(a)*.

1,2:3,4-Di-O-isopropylidene-6-O-(3,4,6-tri-O-acetyl-2-benzamido-2-deoxy-β-D-glucopyranosyl)-α-D-galactopyranose (**11a**). — *(a) From the acetate* **2a**. Compound **11a**, obtained (70–80% based on the donor) by the reaction of **2a** with **A**-OH (1.2–2 mol) (see the preparation of **10a**), had m.p. 198–199° (from dichloromethane), $[\alpha]_D^{25}$ −44°, $[\alpha]_{436}^{25}$ −89° (*c* 0.5, chloroform); lit.[19] m.p. 200–201°, $[\alpha]_D^{25}$ −47°. ^{1}H-N.m.r. data: δ 7.75–7.33 (m, 5 H, Ph), 6.39 (d, 1 H, *J* ~9 Hz, NH), 5.42 (d, 1 H, *J* 4.8 Hz, H-1), 5.34 and 5.15 (2 t, 2 H, *J* ~10 Hz, H-3′,4′), 4.89 (d, 1 H, *J* 8.5 Hz, H-1′), 2.17, 2.03, and 1.95 (3 s, 9 H, 3 Ac), 1.41, 1.27, 1.13, and 0.92 (4 s, 12 H, 2 CMe_2).

Anal. Calc. for $C_{31}H_{41}NO_{14}$ (651.66): C, 57.14; H, 6.34; N, 2.15. Found: C, 57.15; H, 6.08; N, 2.12.

(b) From the oxazoline **4a**. The coupling of 2-phenyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline (**4a**) to **A**-OH (2 mol) in the presence of anhydrous ferric chloride (0.5 mol) in dichloromethane gave **11a** (82% based on **4a**).

Propyl 2-acetamido-4,6-di-O-benzyl-2-deoxy-3-O-(3,4,6-tri-O-acetyl-2-benzamido-2-deoxy-β-D-glucopyranosyl)-β-D-glucopyranoside (**11b**). — The direct glycosylation of **B**-OH by **2a** (2 mol), which was added in portions as described for **10b**, was continued for 2 nights at 35°. The product was subjected to column chromatography to give amorphous **11b** (60% based on **B**-OH), $[\alpha]_D^{25}$ −18°, $[\alpha]_{436}^{25}$ −39° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.83–7.24 (m, 15 H, 3 Ph), 6.83 (d, 1 H, *J* 8.1 Hz, NHBz), 5.84 (d, 1 H, *J* 8.1 Hz, NHAc), 5.36 and 5.17 (2 t, 2 H, *J* ~10 Hz, H-3′,4′), 5.06 (d, 1 H, *J* 8.1 Hz, H-1′), 4.64 (d, 1 H, *J* 6.6 Hz, H-1), 2.02, 1.99, 1.97, and 1.93 (4 s, 12 H, 4 Ac), 1.43 (m, 2 H, $OCH_2CH_2CH_3$), and 0.78 (t, 3 H, $OCH_2CH_2CH_3$).

Anal. Calc. for $C_{44}H_{54}N_2O_{14}$ (834.92): C, 63.30; H, 6.52; N, 3.36. Found: C, 63.42; H, 6.67; N, 3.27.

Allyl 2,3,6-tri-O-benzyl-4-O-(3,4,6-tri-O-acetyl-2-benzamido-2-deoxy-β-D-glucopyranosyl)-α-D-galactopyranoside (**11c**). — Compound **C**-OH was coupled with **2a** (2 mol) as described for **10c**, to give **11c** (30%), $[\alpha]_D^{25}$ +46°, $[\alpha]_{436}^{25}$ +95° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.8–7.0 (m, 20 H, 4 Ph), 6.63 (d, 1 H, *J* 8.4 Hz, NH), 4.90 (d, 1 H, *J* 8.8 Hz, H-1′), 4.65 (d, 1 H, *J* 2.9 Hz, H-1), 3.52 (dd, 1 H, H-2), 2.06, and 1.90 (2 s, 9 H, 3 Ac).

Anal. Calc. for $C_{49}H_{55}NO_{14}$ (881.97): C, 66.73; H, 6.29; N, 1.59. Found: C, 66.31; H, 6.34; N, 1.45.

1,2:3,4-Di-O-isopropylidene-6-O-[3,4,6-tri-O-acetyl-2-(chloroacetamido)-2-deoxy-β-D-glucopyranosyl]-α-D-galactopyranose (**12a**). — Compound **A**-OH (1.2 mol) was glycosylated with **2d** as described for the synthesis of **10a** and **11a**. The reaction, which was almost complete after 3 h, gave amorphous **12a** (80% based on

2d), $[\alpha]_D^{25}$ −42°, $[\alpha]_{436}^{25}$ −83° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 6.56 (d, 1 H, *J* 8.8 Hz, NH), 5.50 (d, 1 H, *J* 5.2 Hz, H-1), 5.32 and 5.09 (t, dd, 2 H, H-3',4'), 4.76 (d, 1 H, *J* 8.1 Hz, H-1'), 2.03 and 2.09 (2 s, 9 H, 3 Ac), 1.50, 1.43, and 1.32 (3 s, 12 H, 2 CMe_2).

Anal. Calc. for $C_{26}H_{38}ClNO_{14}$ (624.04): C, 50.04; H, 6.14; N, 2.24. Found: C, 49.85; H, 5.88; N, 2.12.

Propyl 2-acetamido-4,6-di-O-benzyl-2-deoxy-3-O-[3,4,6-tri-O-acetyl-2-(chloroacetamido)-2-deoxy-β-D-glucopyranosyl]-β-D-glucopyranoside (**12b**). — The coupling of **2d** to **B**-OH (1 mol) was conducted overnight at 35° to give **12b** (60%), m.p. 176–177°, $[\alpha]_D^{25}$ −25°, $[\alpha]_{436}^{25}$ −52° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.5–7.3 (m, 10 H, 2 Ph), 6.81 (d, 1 H, *J* 8.8 Hz, N*H*$COCH_2Cl$), 5.88 (d, 1 H, *J* 8.1 Hz, N*H*Ac), 5.35 (~t, 1 H, *J* 9.6 Hz, H-3'), 5.09 (~t, 1 H, *J* 9.6 Hz, H-4'), 5.05 (d, 1 H, *J* 8.1 Hz, H-1'), 4.69 (d, 1 H, *J* 7.4 Hz, H-1), 2.02, 2.01, and 1.96 (3 s, 12 H, 4 Ac), 1.57 (m, 2 H, $OCH_2CH_2CH_3$), and 0.89 (t, 3 H, $OCH_2CH_2CH_3$).

Anal. Calc. for $C_{39}H_{51}ClN_2O_{14}$ (807.29): C, 58.02; H, 6.37; Cl, 4.39; N, 3.47. Found: C, 58.04; H, 5.95; Cl, 4.01; N, 3.42.

Compound **12b** (100 mg) was suspended in dry benzene (1 mL), and 2,2'-azobisisobutyronitrile (AIBN) (5.5 mg) and tributyltin hydride (39 μL) were added. The mixture was boiled under reflux for 3 h under nitrogen, and then concentrated. The residue was subjected to column chromatography to afford amorphous **10b** (70%).

2-Acetamido-1-O-acetyl-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranose (**13**). — Allyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside[20], prepared by benzylation[21] of the *O*-unsubstituted allyl glycoside[14], was treated with potassium *tert*-butoxide in methyl sulfoxide[22] to give the 1-propenyl glycoside. The 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose obtained by mild acidic hydrolysis of the propenyl glycoside was acetylated[16] with acetic anhydride in the presence of pyridine hydrochloride. Crystallization of the product from ethyl acetate–ether afforded **13** (80%), m.p. 159–162°, $[\alpha]_D^{25}$ +34°, $[\alpha]_{436}^{25}$ +64° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.3–7.2 (m, 15 H, 3 Ph), 5.6 (d, 1 H, *J* 8 Hz, H-1), 5.3 (d, 1 H, *J* 8 Hz, NH), 4.9–3.5 (m, 12 H, OCH_2Ph), 2.02, and 1.76 (2 s, 6 H, 2 Ac).

Anal. Calc. for $C_{31}H_{35}NO_7$ (533.62): C, 69.78; H, 6.61; N, 2.62. Found: C, 69.55; H, 6.64; N, 2.52.

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 (**14a**). — The coupling of **A**-OH with **13** (1.2–2 mol) by the standard procedure gave amorphous **14a** (80% based on acceptor), $[\alpha]_D^{25}$ −29°, $[\alpha]_{436}^{25}$ −58° (*c* 0.5, chloroform); lit.[16] m.p. 122–123°, $[\alpha]_D$ −35°. ^{1}H-N.m.r. data: δ 7.33–7.2 (m, 15 H, 3 Ph), 5.71 (d, 1 H, *J* 8.5 Hz, NH), 5.49 (d, 1 H, *J* 5.2 Hz, H-1), 4.70 (d, 1 H, *J* 8.1 Hz, H-1'), 1.88 (s, 3 H, Ac), 1.51, 1.42, and 1.30 (3 s, 12 H, 2 CMe_2).

Propyl 2-acetamido-3-O-(2-acetamido-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranosyl)-4,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**14b**). — The β-acetate

13 (200 mg, 0.37 mmol) was coupled to 250 mg (0.56 mmol) of **B**-OH by reaction overnight at 35°. The product was subjected to column chromatography (4:1 chloroform–acetone) to afford **14b** (62% based on **13**). Recrystallization from ethyl acetate gave material of m.p. 173–175°, $[\alpha]_D^{25}$ −1°, $[\alpha]_{436}^{25}$ −6° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.3–7.2 (m, 25 H, 5 Ph), 5.9 and 6.1 (2 d, 2 H, *J* 8.8 Hz, NH), 1.93 (s, 6 H, 2 Ac), 1.57 (m, 2 H, $OCH_2CH_2CH_3$), and 0.86 (t, 3 H, $OCH_2CH_2CH_3$).

Anal. Calc. for $C_{54}H_{64}N_2O_{11}$ (917.11): C, 70.72; H, 7.03; N, 3.05. Found: C, 70.68; H, 6.98; N, 3.04.

For *O*-debenzylation, a mixture of **14b** (30 mg), 14:1 ethanol–water (4 mL), and 10% Pd-C (5 mg) was stirred for 2 days at room temperature under hydrogen at atmospheric pressure. The mixture was filtered through Celite and concentrated to dryness, and the residue was subjected to four cycles of dissolution in D_2O and concentration to dryness. ^{1}H-N.m.r. data (D_2O, internal TSP): at 20°, δ 4.58 (d, 1 H, *J* 7.4 Hz, H-1′) and 4.47 (d, 1 H, *J* 7.0 Hz, H-1); at 60°, δ 4.62 (d, 1 H, *J* 8.1 Hz, H-1′), and 4.49 (d, 1 H, *J* 8.1 Hz, H-1).

Allyl 4-O-(2-acetamido-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-galactopyranoside (**14c**). — *(a) By direct coupling.* The reaction of **13** (2 mol) with **C**-OH was conducted in dry benzene. Otherwise, the protocol was as already given for the synthesis of **10c**. Compound **14c** was obtained as a syrup (45% based on **C**-OH), $[\alpha]_D^{25}$ +42°, $[\alpha]_{436}^{25}$ +81° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.4–7.15 (m, 30 H, 6 Ph), 5.89 (m, 1 H, -CH=), 5.69 (d, 1 H, *J* 8.1 Hz, NH), 5.39–5.29 (m, 2 H, $=CH_2$), and 1.58 (s, 3 H, Ac).

Anal. Calc. for $C_{59}H_{65}NO_{11}$ (964.17): C, 73.50; H, 6.80; N, 1.45. Found: C, 73.19; H, 6.81; N, 1.29.

(b) From **10c**. A sample (50 mg) of **10c** was *O*-deacetylated and then *O*-benzylated[21] to give **14c** (49 mg, 83%), identical with the product in *(a)*.

Benzyl 6-O-(2-acetamido-4-O-acetyl-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-1-thio-β-D-galactopyranoside (**17**). — *(a) From the 1-acetate* **15**. 1-Propenyl 2-acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside[14] was subjected to mild acid hydrolysis, and the resulting free sugar was converted[16] into the β-1-acetate **15**. Compound **15** was coupled to 1.2 mol of benzyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside[13] (**16**), as described for the synthesis of **10a**, to give **17** (80% based on **15**). Recrystallization from methanol gave material of m.p. 178–179°, $[\alpha]_D^{25}$ −21°, $[\alpha]_{436}^{25}$ −42° (*c* 0.5, chloroform). ^{1}H-N.m.r. data: δ 7.3–7.2 (m, 30 H, 6 Ph), 5.50 (d, 1 H, *J* 7.4 Hz, NH), 5.04 (t, 1 H, *J* 9.6 Hz, H-4′), 4.84 (d, 1 H, *J* 8.1 Hz, H-1′), 4.24 (d, 1 H, *J* 9.6 Hz, H-1), 1.89, and 1.79 (2 s, 6 H, 2 Ac).

Anal. Calc. for $C_{58}H_{63}NO_{11}S$ (982.20): C, 70.93; H, 6.47; N, 1.43; S, 3.26. Found: C, 71.27; H, 6.35; N, 1.43; S, 3.36.

(b) From the oxazoline. A mixture of anhydrous ferric chloride (31 mg), dichloromethane (1 mL), and anhydrous calcium sulfate (200 mg) was stirred for 5–10 min. A solution of 2-methyl-(4-*O*-acetyl-3,6-di-*O*-benzyl-1,2-dideoxy-α-D-glu-

copyrano)[2,1-*d*]-2-oxazoline (163 mg, prepared from the corresponding 1-propenyl glycoside[14]) in dichloromethane (2 mL) and the glycosyl acceptor (**16**, 250 mg) were then added. The mixture was stirred overnight at room temperature and processed. The product was subjected to column chromatography to give **17** (314 mg, 83% based on the oxazoline).

Deprotection of **17**. — *O*-Deacetylation of **17** (100 mg) was conducted with methanolic sodium methoxide. Neutralization with ion-exchange (H^+) resin and concentration gave a residue which was treated[23] with methyl iodide (1.7 mL) in acetone (6.7 mL) containing water (1.7 mL). The mixture was stirred overnight at 50° and then extracted with chloroform. The extract was dried and concentrated, and the syrupy residue was subjected to column chromatography to remove minor contaminants. The resulting 6-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzyl-D-galactose was dissolved in 14:1 ethanol–water (12 mL) and hydrogenolyzed over 10% Pd/C (15 mg) until t.l.c. showed the presence of a single product. The mixture was filtered (Celite) and concentrated to dryness to yield 6-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactose as an amorphous solid, $[\alpha]_D^{25}$ +9°, $[\alpha]_{436}^{25}$ +12° (*c* 1, water, equil.); lit.[24] $[\alpha]_D$ +9° to +9.9°.

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