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Potential HIV protease inhibitors: Preparation of di-*N*-alkylated 2-, 6-, and 2,6-aminodeoxy-derivatives of D-glucose by direct displacement and by a novel reductive-alkylation procedure

Jiaqiang Cai [a], Bruce E. Davison [a,*], C. Robin Ganellin [a], Suvit Thaisrivongs [b], Keith S. Wibley [a]

[a] *Department of Chemistry, Christopher Ingold Laboratories, University College London, 20 Gordon Street, London WC1H 0AJ, England, UK*

[b] *Pharmacia and Upjohn, Inc., Kalamazoo, MI 49001, USA*

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Abstract

Glucose derivatives carrying branched lipophilic groups at the 2-, 6-, and 2,6-positions were required for biological testing as inhibitors of the protease produced by the human immunodeficiency virus. The synthesis of (*N*-benzyl-*N*-ethyl)-2-, 6- and 2,6-diaminodeoxy-D-glucose derivatives is described. The 2-*tert*-amino group was introduced by a two-step reductive alkylation procedure. The novel tertiary aminosugar, 2,6-di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-D-glucose, was made via direct substitution of the sulphonate group in allyl 2-acetamido-2-deoxy-6-*O*-tosyl-D-glucopyranoside with *N*-benzylethylamine. © 1997 Elsevier Science Ltd.

Keywords: Reductive alkylation; Sulphonate displacement; (*N*-Benzyl-*N*-ethyl)-aminodeoxyglucose derivatives; *N*,6-*O*-Dibenzyl-*N*-ethyl-D-glucosamine; Allyl 2-(*N*-benzyl-*N*-ethyl)amino-2-deoxy-α-D-glucopyranoside; 2,6-Di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-D-glucose

1. Introduction

The threat posed by the human immunodeficiency virus (HIV) has led to an intensive search for effective chemotherapeutic intervention for controlling acquired immunodeficiency syndrome (AIDS) [1]. The virally-encoded proteinase of the *pol* gene, HIV protease, has been a major target for drug design [2] but most inhibitors have been peptides which are not very effective in vivo [3]. The identification at Upjohn Laboratories of 4-hydroxypyran-2-ones as inhibitors [4] led us to consider other oxygen-containing non-peptides such as sugar derivatives. It has previously been noted that carbohydrates may inhibit enzymes by functioning as peptidomimetics [5–8]. Molecular modelling of the active site of HIV pro-

* Corresponding author. Fax: +1-171-3807463.

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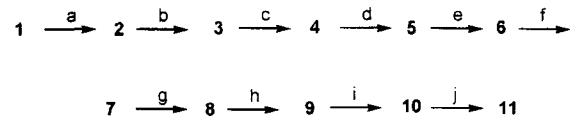
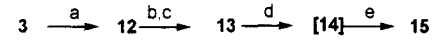


Scheme 1. a: Allyl alcohol–BF_3OEt_2 (cat.), 95 °C, 5 h; b: $PhCH(OMe)_2$–TsOH(cat.)–DMF, 75% on **1**; c: TEA–PhCOCl, 53%; d: $NaBH_3CN$–THF–Et_2O–HCl then C_5H_5N–PhOCl, 50%; e: NaOH–MeOH–H_2O, reflux, 4 h, 62%; f: NaOH (1 M), 110 °C, 15 h; g: PhCHO–C_6H_6 (remove H_2O azeotropically) then $NaBH_4$–MeOH, 0 °C, 55%; h: $NaBH_4$–CH_3CO_2H, 90%; i: *t*-BuOK–Me_2SO, 100 °C, 2 h, 90%; j: Me_2CO–H_2O(10:1)–HCl(2 M), reflux, 6 h, 72%.

tease for inhibitor design is well established [9] and hydroxyethylamine is a very important structural unit in some inhibitors [10]. Our modelling suggested that glucose derivatives with amino groups bearing hydrophobic substituents at the 2-, 6-, and 2,6-positions and which are β to a hydroxy group should be well accommodated and, in particular, *N*-benzyl-*N*-ethyl-D-glucosamine derivatives were predicted to have strong bonding interactions at the active site of the protease. [1] This paper reports the synthesis of such compounds (**11**, **15**, **23**, Schemes 1–3).

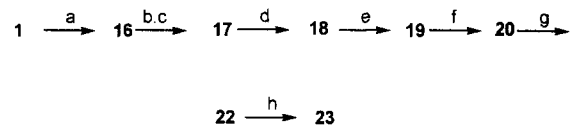
2. Results and discussion

Previously reported preparations of alkylated D-glucosamine derivatives include the direct reduction of the amido function [11] and the alkylation or oxazolidination of acylamino-D-glucosamine derivatives followed by reduction of the amido function [12,13]. These methods either require complete protection of hydroxy groups or are limited to formation of *N*-methylated products. To overcome these limitations a new two-step reductive-alkylation method was applied to appropriate glucosamine derivatives for the preparation of the title compounds. The synthetic



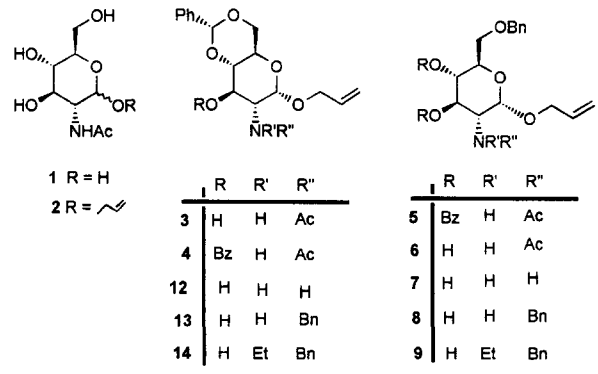
Scheme 2. a: NaOH(1 M), 110 °C, 6 d, 100%; b: PhCHO–C_6H_6 (remove H_2O azeotropically); c: $NaBH_4$–MeOH–THF, 0 °C, 77%; d: $NaBH_4$–CH_3CO_2H; e: CH_3CO_2H–H_2O (5:3), 80 °C, 69% on **13**.

[1] Molecular modelling was carried out using the SYBYL package v 6.03 (Tripos Associates, Inc., St. Louis, MO, USA) and co-ordinates taken from the Brookhaven Protein Data Bank derived from X-ray crystallographic determination (J. Erikson et al., *Science*, 249 (1990) 527).



Scheme 3. a: Allyl alcohol–BF_3OEt_2 (cat.), 95 °C, 5 h; b: TsCl–C_5H_5N, 85% on **1** as anomeric mixture; c: BnEtNH, 140–160 °C, 16 h, 58%; d: NaOH (2 M), 110 °C, 15 h, 90%; e: PhCHO–C_6H_6 (remove H_2O azeotropically) then $NaBH_4$–MeOH, 0 °C, 47%; f: $NaBH_4$–CH_3CO_2H, 90%; g: *t*-BuOK–Me_2SO, 100 °C, 2 H; h: HCl (1 M), 80 °C, 2 h, 72% on **20**.

route to the requisite 2-(*N*-benzyl-*N*-ethyl)amino-deoxyglucose derivative is shown in Scheme 1 above.

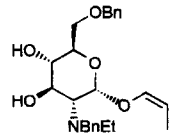


	R	R'	R"
3	H	H	Ac
4	Bz	H	Ac
12	H	H	H
13	H	H	Bn
14	H	Et	Bn

	R	R'	R"
5	Bz	H	Ac
6	H	H	Ac
7	H	H	H
8	H	H	Bn
9	H	Et	Bn

The preparation of allyl 2-acetamido-2-deoxy-α,β-D-glucopyranoside (**2**) and of the α-anomer of the corresponding 4,6-*O*-benzylidene product (**3**) from *N*-acetyl-D-glucosamine (**1**) has been described [14]. In our hands the synthesis of (**3**) from (**1**) was improved from 49% of a 10:1 (α:β) anomeric mixture to 75% pure α-anomer by using the method described by Holder and Fraser-Reid [15] for making methyl 4,6-*O*-benzylidene-α-D-glucopyranoside. Benzoylation of compound (**3**) to yield the ester (**4**) followed by a selective reductive acetal ring opening [16], gave the 6-*O*-benzyl derivative which was purified as its benzoylated product (**5**). Methanolic aqueous sodium hydroxide readily removed the ester groups to give allyl 2-acetamido-6-*O*-benzyl-2-deoxy-α-D-glucopyranoside (**6**), hydrolysis of which gave the corresponding amino derivative (**7**). The introduction of both the *N*-ethyl and *N*-benzyl groups was achieved by means of successive reductive alkylation using sodium borohydride, the first reported use of such reactions for the synthesis of differentially disubstituted aminosugars. Thus reaction of (**7**) with benzaldehyde under Dean and Stark conditions yielded the imine, which was reduced in situ with sodium borohydride in methanol at 0 °C [17], to give

the benzylamine derivative (**8**). The *N*-ethyl group was introduced by a similar reaction using sodium borohydride-acetic acid, to afford (**9**) in 90% yield. Removal of the allyl group was effected by the isomerisation-hydrolysis method developed by Gigg et al. [18,19] to yield the required final product *N*,6-O-dibenzyl-*N*-ethyl-D-glucosamine (**11**). The same two-step reductive dialkylation procedure was used (Scheme 2) on the 4,6-*O*-benzylidene derivative (**12**), which was obtained in quantitative yield by hydrolysis of (**3**). Reductive benzylation of (**12**) provided the benzylamine product (**13**), and the subsequent reductive ethylation gave the dialkylamine (**14**) which on hydrolysis yielded the required 2-(*N*-benzyl-*N*-ethyl)aminodeoxyglucoside (**15**).



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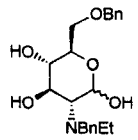

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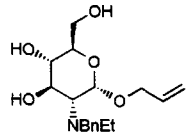

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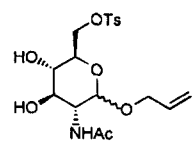
The reductive alkylation procedure was not effective for the synthesis of allyl 2-acetamido-6-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-D-glucoside since the S_N2 substitution of the *p*-toluenesulphonyl group in allyl 2-acetamido-2-deoxy-6-*O*-*p*-toluenesulphonyl-α,β-D-glucopyranoside (**16**) by benzylamine did not furnish the requisite 6-benzylamino intermediate. Instead the 6-*O*-tosyl-glucoside (**16**), obtained in two steps from *N*-acetyl-D-glucosamine (**1**) in 85% yield, was subjected to a one-step direct sulphonate substitution with *N*-benzyl-ethylamine as solvent and reagent to yield the pure trialkylamine derivative (**17**) in 58% yield (Scheme 3).

Hitherto 2,6-dialkylamino-2,6-dideoxy-D-glucose derivatives have not been described, although the unsubstituted analogue, 2,6-diamino-2,6-dideoxy-D-glucose, has been prepared on a large scale [20–23]. The synthetic route to 2,6-di(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-D-glucose is shown in Scheme 3. Hydrolysis of (**17**) gave allyl 2-amino-6-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-D-glucopyran-oside (**18**), which was subjected to reductive benzylation to give the benzylamino derivative (**19**) in good yield. The reductive ethylation was carried out as described above to afford the expected allyl 2,6-di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-D-glucopyran-oside (**20**), also characterised as its oxalate salt (**21**). Removal of the allyl group via the prop-2-enyl glycoside (**22**) gave 72% of 2,6-di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-D-glucose (**23**), the target molecule.



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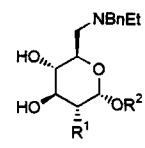

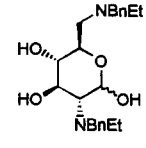

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	R^1	R^2
17	NHAc	
18	NH_2	
19	NHBn	
20	NBnEt	
22	NBnEt	

The work described herein demonstrates that the direct displacement reaction of sulphonates by secondary amines provides a facile route to 6-dialkylamino-hexose derivatives, while successive reductive alkylation procedures afford a versatile method for introduction of the dialkylamino-functionality at the ring carbon positions.

3. Experimental

General methods.—All melting points were determined using a Reichert hot stage microscope or an Electrothermal open capillary melting point apparatus and are uncorrected. Thin layer chromatography was carried out on Merck Kieselgel 60 F254 plates, visualised at 254 nm then stained with potassium permanganate solution or vanillin solution or concentrated H_2SO_4 in ethanol followed by heating. The ^1H NMR spectra were recorded on a Varian XL-200 NMR or a Varian VXR-400 NMR spectrometer. IR spectra were recorded on a Perkin–Elmer 1605 FTIR or a Nicolet 205 FTIR spectrometer from thin film on KBr discs unless otherwise indicated. HPLC was carried out on a Kromasil C18 5 mm reverse phase column using a Shimadzu LC-9A pump, Shimadzu C-R6A Chromatopac integrator and Pye Unicam UV detector at 254 nm. Mass spectra (EI, FAB and ZAB-SE) were carried out on a VG ZAB/SE spectrometer. Optical rotations were determined on an Optical Activity Ltd automatic polarimeter. Microanalyses were carried out in the Microanalysis Service Department of University College London. All solvents and chemicals were obtained from Aldrich, Lancaster, BDH or Fluka and used without further purification.

Allyl 2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (3).—Boron trifluoride etherate (5 mL) was added to *N*-acetyl-D-glucosamine (**1**) (40 g)

in allyl alcohol (400 mL), and the mixture was heated at 95 °C for 5 h. The solvent was removed by evaporation, the last traces of allyl alcohol being removed by co-evaporation with DMF (50 mL). The residue was dissolved in DMF (150 mL), and tosic acid (4 g) and α,α-dimethoxytoluene (41 g) were added. The mixture was heated at 60–80 °C for 2 h, the DMF was removed under vacuum, the residue was treated with 3% $NaHCO_3$ (500 mL) and stirred at 80 °C for 1 h. The product was collected by filtration and washed successively with H_2O (2 L), toluene (300 mL) and hexane (500 mL), and dried under vacuum (0.1 mm Hg) at 60 °C to give the title glycoside (**3**) (47 g; 75%): mp 233–235 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.06 (s, 3 H, CH_3CO), 3.60 (dd, 1 H, $J_1 = J_2$ 9.2 Hz, C4–H), 3.76 (dd, 1 H, J_1 10.3, J_2 10.1 Hz, C6–H_{ax}), 3.85 (ddd, 1 H, J_1 4.3, $J_2 = J_3$ 9.3 Hz, C5–H), 3.94 (dd, 1 H, J_1 9.8, J_2 9.6 Hz, C3–H), 4.00 (dd, 1 H, J_1 6.3, J_2 12.8 Hz, CH_2 at allyl), 4.19–4.29 (m, 3 H, C2–H, C6–H_{eq}, CH_2 at allyl), 4.88 (d, 1 H, J 3.7 Hz, C1–H), 5.25 (dd, 1 H, J_1 1.3, J_2 10.4 Hz, $=CH_2$), 5.31 (dd, 1 H, J_1 1.5, J_2 17.2 Hz, $=CH_2$), 5.56 (s, 1 H, benzylidene CH), 5.89–5.94 (m, 2 H, CH=, NH), 7.34–7.40 (m, 3 H, Ar), 7.49–7.52 (m, 2 H, Ar).

Allyl 2-acetamido-3-O-benzoyl-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (**4**).—The allyl glucoside (**3**) (17.5 g) was suspended in $CHCl_3$ (250 mL), Et_3N (15.2 g) was added, followed by slow addition of PhCOCl (14 g). The mixture was heated under reflux for 2 h. The organic layer was washed with H_2O (2 × 500 mL) and 5% $NaHCO_3$ (2 × 200 mL), dried over Na_2SO_4, evaporated, and the residue recrystallised from toluene–hexane to give the 3-benzoate (**4**) (12.1 g, 53%); mp 193–196 °C. $[\alpha]_D^{20}$ +25°(*c* 1.0, CH_2Cl_2); IR (neat); ν 3302(m), 2867(w), 1722(s), 1656(s), 1602(w), 1540(m), 1452(w), 1379(m), 1268(s), 1092(s), 1053(m), 994(m),758(m), 712(m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.87 (s, 3 H, CH_3), 3.83 (dd, 1 H, J_1 10.3, J_2 10.2 Hz, C4–H), 3.89 (dd, 1 H, J_1 9.5, J_2 9.5 Hz, C6–H_{ax}), 4.00–4.06 (m, 2 H, C5–H, CH_2 at allyl), 4.25 (ddt, 1 H, J_t 1.4, J_2 5.3, J_3 12.9 Hz, CH_2 at allyl), 4.33 (dd, 1 H, J_1 4.8, J_2 10.4 Hz, C6–H_{eq}), 4.54 (ddd, 1 H, J_1 3.7, J_2 9.6, J_3 10.5 Hz, C2–H), 4.95 (d, 1 H, J 3.7 Hz, C1–H), 5.27 (dd, 1 H, J_1 1.4, J_2 10.3 Hz, $=CH_2$), 5.34 (dd, 1 H, J_1 1.6, J_2 17.3 Hz, $=CH_2$), 5.57 (s, 1 H, benzylidene CH), 5.62 (dd, 1 H, J_1 10.4, J_2 9.6 Hz, C3–H), 5.86–5.97 (m, 2 H, CH=, NH), 7.30–7.33 (m, 3 H, Ph), 7.41–7.45 (m, 4 H, Bz + Ph), 7.56 (t, 1 H, J 7.4 Hz, Bz), 8.03 (dd, 2 H, J_1 1.4, J_2 8.5 Hz, Bz).

Allyl 2-acetamido-6-O-benzyl-2-deoxy-3,4-O-dibenzoyl-α-D-glucopyranoside (**5**).—Dried 3 A molecular sieves (12 g) and sodium cyanoborohydride (14.2 g) were added to the benzoate (**4**) (11.33 g) in THF (120 mL). The mixture was cooled to 0 °C, Et_2O saturated with HCl was added and the mixture stirred until 10 minutes after gas release had ceased. Water (50 mL) and CH_2Cl_2 (300 mL) were added, the molecular sieves filtered off, and the organic layer separated, dried over Na_2SO_4 and evaporated. The residue was redissolved in CH_2Cl_2 (250 mL), pyridine (25 mL) was added, followed by slow addition of PhCOCl (12.5 mL). Stirring was continued for 2 h. After normal work-up, the crude product was chromatographed on silica gel (1:1, petrol:EtOAc) to give the dibenzoate (**5**) (7 g, 50%). $[\alpha]_D^{20}$ +20° (*c* 0.40, CH_2Cl_2); IR (neat); ν 3292(br), 1728(s), 1713(s), 1682(s), 1651(s), 1600(m), 1451(s), 1108(s), 1026(s), 708(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.87 (s, 3 H, $COCH_3$), 3.38–3.45 (m, 1 H, C5–H), 3.64–3.70 (m, 1 H, C6–H), 4.05–4.35 (m, 3 H, CH_2 allyl, C6–H(1)), 4.50 (d, 1 H, J 12.1 Hz, CH_2Ph), 4.56 (d, 1 H, J 12.1 Hz, CH_2Ph), 4.50–4.65 (m, 1 H, C2–H, overlap), 5.31 (d, 1 H, J 3.6 Hz, C1–H), 5.28 (dd, 1 H, J_1 1.1, J_2 10.4 Hz, $=CH_2$), 5.36 (dd, 1 H, J_1 1.3, J_2 17.4 Hz, $=CH_2$), 5.60 (dd, 1 H, J_1 9.7, J_2 9.6 Hz, C4–H), 5.67 (dd, 1 H, J_1 10.5, J_2 9.5 Hz, C3–H), 5.90–5.97 (m, 2 H, NH, –CH=), 7.15–7.25 (m, 5 H, Ph), 7.32–7.45 (m, 4 H, Bz), 7.47–7.52 (m, 2 H, Bz), 7.89 (dd, 2 H, J_1 1.4, J_2 8.5 Hz, Bz), 7.93 (dd, 2 H, J_1 1.7, J_2 8.4 Hz, Bz). MS FAB: (*m/z*) 561(M + 2, 0.44), 560(M + 1, 0.31), 503(2.2), 105(100), 91(59). Anal. Calcd for $C_{32}H_{33}NO_8$: C, 68.08; H, 5.94; N, 2.50. Found: C, 67.71; H, 6.09; N, 2.53.

Allyl 2-acetamido-6-O-benzyl-2-deoxy-α-D-glucopyranoside (**6**).—Sodium hydroxide (4 g) and H_2O (25 mL) were added to the dibenzoate (**5**) (11.5 g) in MeOH (150 mL), and the mixture was heated under reflux for 4 h. Methanol was removed in vacuo, H_2O (100 mL) was added and mixture heated to obtain a clear solution. Cooling to room temperature caused crystallisation. Filtration yielded the dihydroxy derivative (**6**) as white crystals (4.5 g, 62.3%); mp 180–181.5 °C. $[\alpha]_D^{20}$ +119° (*c* 1.0, MeOH); IR (Nujol); ν 3292(m), 3200–3600(br), 1468(s), 1638(s), 1547(s), 1462(s), 1454(s), 1376(s), 1063, 1042 cm^{-1}; ^{1}H NMR (CD_3OD, 200 MHz): δ 1.98 (s, 3 H, CH_3CO), 3.39 (dd, 1 H, J_1 9.4, J_2 9.2 Hz, C4–H), 3.6–3.8 (m, 5 H, C2, C3, C5, C6–H), 3.8–4.1 (2 dd, 2 H, overlap, CH_2 at allyl(1), C6–H), 4.19 (dd, 1 H, J_1 5.1, J_2 13.1 Hz, CH_2 at allyl(1)), 4.58 (s, 2 H,

CH_2Ph), 4.82 (d, 1 H, J 3.6 Hz, C1–H), 5.17 (dd, 1 H, J_1 1.2, J_2 10.5 Hz, $=CH_2$), 5.30 (dd, 1 H, J_1 1.6, J_2 17.3 Hz, $=CH_2$), 5.92 (m, 1 H, –CH=), 7.2–7.5 (m, 5 H, Ph), (4.89 (H_2O), no NH visible); MS. FAB: (m/z) 352(MH, 10), 294(10), 154(15), 136(15), 91(100). Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.51; H, 7.14; N, 3.99.

Allyl 2-amino-6-O-benzyl-2-deoxy-α-D-glucopyranoside (**7**).—The glycoside (**6**) (6.8 g) in 1 M NaOH (100 mL) was heated under reflux at 110 °C for 15 h, the mixture extracted with $CHCl_3$ (3 × 100 mL), and the extracts dried over K_2CO_3. Evaporation of the solvent gave the free amine (**7**) as an oil (5.7 g, 95.2%); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.1–2.8 (br, 4 H, OH, NH_2, H_2O), 3.4–3.8 (m, 6 H, C2, C3, C4, C5, C6–H), 3.95 (ddt, 1 H, J_1 1.1, J_2 6.0, J_3 13.0 Hz, CH_2 at allyl(1)), 4.18 (dd, 1 H, J_1 5.2, J_2 12.8 Hz, CH_2 at allyl(1)), 4.53 (d, 1 H, J 12.3 Hz, CH_2Ph), 4.61(d, 1 H, J 12.1 Hz, CH_2Ph), 4.78 (d, 1 H, J 2.6 Hz, C1–H), 5.16 (d, 1 H, J 10.3 Hz, $=CH_2$), 5.26 (d, 1 H, J 17.3 Hz, $=CH_2$), 5.82–5.96 (m, 1 H, –CH=), 7.24–7.37 (m, 5 H, Ph).

Allyl 6-O-benzyl-2-benzylamino-2-deoxy-α-D-glucopyranoside (**8**).—The amine (**7**) (5.7 g) and PhCHO (2.35 g) in benzene (250 mL) were heated under reflux with azeotropic water removal. After removal of all solvent, the residue was dissolved in methanol (50 mL), sodium borohydride (4 g) was added portionwise at 0 °C during 30 minutes with stirring and the mixture stirred for a further hour. Sodium carbonate (10%, 50 mL) was added, the solution extracted with $CHCl_3$ (3 × 100 mL), the extracts dried over K_2CO_3, and evaporated. The crude product was chromatographed on silica gel (3:1, EtOAc:petrol) to give the benzylamino derivative (**8**) (4.0 g, 55%); mp 72.3–73 °C; $[\alpha]_D^{20}$ +93°(c 1.0, MeOH); IR (Nujol): ν 3200(br), 1459.2(s), 1375(m), 1096(s), 1084(s), 1063(s), 1027(s), 736(s), 697(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.30 (br, 3 H, OH, NH), 2.62 (dd, 1 H, J_1 3.5, J_2 9.8 Hz, C2–H), 3.55–3.69 (m, 2 H, C4–H, C5–H), 3.69–3.73 (m, 3 H, C3–H, C6–H), 3.79 (d, 1 H, J 13.4 Hz, NCH_2Ph), 3.86 (d, 1 H, J 13.1 Hz, NCH_2Ph), 3.87 (dd, 1 H, J_1 6.3, J_2 12.8 Hz, CH_2 at allyl(1)), 4.15 (ddt, 1 H, J_t 1.6, J_2 5.1, J_3 12.8 Hz, CH_2 at allyl(1)), 4.56 (d, 1 H, J 12.1 Hz, CH_2Ph), 4.63 (d, 1 H, J 12.1 Hz, CH_2Ph), 4.83 (d, 1 H, J 3.4 Hz, C1–H), 5.21 (dd, 1 H, J_1 1.3, J_2 10.3 Hz, $=CH_2$), 5.28 (dd, 1 H, J_1 1.6, J_2 17.2 Hz, $=CH_2$), 5.85–5.92 (m, 1 H, –CH=), 7.26–7.35 (m, 10 H, 2 × Ph); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 51.77, 61.58, 68.32, 69.49, 70.13, 71.47, 72.64, 73.56 (C2–C6, 2 × CH_2Ph, CH_2 at allyl), 95.62(C1), 117.66, 127.35, 127.67(2), 128.14, 128.42, 128.61, 133.83, 138.06, 140.18 ($CH=CH_2$, 2 × Ph); MS FAB: (m/z) 400(MH^+, 88), 154(30), 136(35), 91(100). Anal. Calcd for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32; N, 3.51. Found: C, 68.95; H, 7.45; N, 3.49.

Allyl 6-O-benzyl-2-(N-benzyl-N-ethyl)amino-2-deoxy-α-D-glucopyranoside (**9**).—Sodium borohydride (8 g) was added portionwise during 1.5 h to a stirred solution of the benzylamino-glucoside (**8**) (1.0 g) in acetic acid (50 mL) and stirring continued for 1.5 h. After standing overnight, the reaction mixture was neutralised with 10% Na_2CO_3, extracted with $CHCl_3$, the extracts dried over K_2CO_3, and evaporated to give the dialkylamine (**9**) (1.11 g, 90%); $[\alpha]_D^{20}$ +86°(c 0.50, MeOH); IR (neat): ν 3480(br,s), 3028(m), 2921(s), 1647(w), 1603(w), 1495(m), 1453(s), 1362(m), 1140(s), 1098(s), 1027(s), 930(m), 736(s), 698(s) cm^{-1}. MS FAB: (m/z) 428(MH, 9.7), 386(6.8), 91(100); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.04(t, 3 H, J 7.2 Hz, CH_3), 2.64–2.90 (m, 3 H, CH_2Me, C2–H), 3.60–3.81 (m, 5 H, C3, C4, C5, C6–H), 3.97–4.03 (m, 2 H, CH_2 at allyl(1), $NCH_2Ph(1)$), 4.10 (d, 1 H, J 14.3 Hz, $NCH_2Ph(1)$), 4.22 (ddt, 1 H, J_t 1.5, J_2 5.2, J_3 13.0 Hz, CH_2 at allyl(1)), 4.57 (d, 1 H, J 12.2 Hz, $CH_2Ph(1)$), 4.63 (d, 1 H, J 12.1 Hz, $CH_2Ph(1)$), 5.05 (d, 1 H, J 3.1 Hz, C1–H), 5.20 (dd, 1 H, J_1 1.6, J_2 10.4 Hz, $=CH_2$), 5.31 (dd, 1 H, J_1 1.7, J_2 17.2 Hz, $=CH_2$), 5.89–5.97 (m, 1 H, –CH=), 7.24–7.36 (m, 10 H, 2 × Ph); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.36(CH_3), 44.84 (CH_2Me), 54.37, 62.85, 68.24, 68.93, 69.63, 69.85, 73.08, 73.58 (C2–C6, 2 × CH_2Ph, CH_2 at allyl), 96.33(C1), 117.30, 127.05, 127.70, 128.36, 128.43, 128.48, 128.52, 133.93, 138.06, 140.17 ($CH=CH_2$, 2 × Ph); high resolution MS FAB: (m/z) 450.2253 [$(M + Na)^+$; calcd for $C_{25}H_{33}NO_5Na$: M, 450.2256].

Propenyl 6-O-benzyl-2-(N-benzyl-N-ethyl)amino-2-deoxy-α-D-glucopyranoside (**10**).—Potassium t-butoxide (1.0 g) was added to the allyl glycoside (**9**) (0.8 g) in Me_2SO (20 mL) and the mixture heated at 100 °C for 2 h. Water (50 mL) was added, the mixture was extracted with Et_2O (3 × 20 mL), the extracts dried over Na_2SO_4 and evaporated to yield the crude product which was purified by chromatography on silica gel (1:1 petrol:EtOAc) to give the *title compound* (**10**) in over 90% yield; IR (neat): ν 3418(br,s), 3029(w), 2923(s), 2862(s), 1672(s), 1603(w), 1495(m), 1454(s), 1252(m), 1139(s), 1043(s), 738(s), 698(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400

MHz): δ 1.06 (t, 3 H, J 7.1 Hz, CH_3(Et)), 1.58 (minor isomer 5%, dd, J_1 1.6, J_2 6.9 Hz, CH_3C=), 1.61 (main isomer, dd, J_1 1.8, J_2 6.8 Hz, CH_3C=), 2.68–2.90 (m, 3 H, CH_2Me, C2–H), 3.64–3.77 (m, 5 H, C4, C5, C6–H, $NCH_2Ph(1)$), 4.07 (dd, 1 H, J_1 8.2, J_2 10.9 Hz, C3–H), 4.13 (d, 1 H, J 14.3 Hz, $NCH_2Ph(1)$), 4.55 (d, 1 H, J 12.1 Hz, CH_2Ph), 4.60 (q, 1 H, J 6.8 Hz, =CHMe), 4.63 (d, 1 H, J 12.2 Hz, CH_2Ph), 5.21 (d, 1 H, J 3.1 Hz, C1–H), 6.17 (dd, 1 H, J_1 1.8, J_2 6.2 Hz, O–CH=), 7.26–7.28 (m, 10 H, 2 × Ph); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 9.59 (CH_3) (12.5), 14.36 ($CH_{3'}$), 44.77, 54.26(54.17), 62.54(62.50), 68.83(68.77), 69.30(69.37), 70.18(70.10), 72.80, 73.56(73.53) (C2–C6, 2 × CH_2Ph, CH_2Me), 97.19(96.75)(C1), 103.82(104.8), 127.13, 127.74, 127.77(2), 128.45, 128.53(2), 137.94(140.016), 141.48(142.587). MS FAB: (m/z) 428(MH, 20.4), 370(13.4), 91(100). HPLC(C–18, 60MeOH:40water:0.1TFA, UV-254 nm, 1 mL min^{-1}): 6.74′(82.9%), 7.78′(13.3%); high resolution MS FAB: (m/z) 450.2253 $(M + Na)^+$; calcd for $C_{25}H_{33}NO_5Na$: M, 450.2256.

N,6-O-Dibenzyl-N-ethyl-D-glucosamine (**11**).—The propenyl glycoside (**10**) (0.55 g) in 2 M HCl (10 mL) and Me_2CO (50 mL) was heated under reflux for 6 h. After evaporation, 5% Na_2CO_3 (50 mL) was added and the mixture extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and evaporated to yield the crude product which was chromatographed on silica gel (70:30, EtOAc:petrol) to give the title compound (**11**) (0.36 g, 72%); $[\alpha]_D^{20}$ +36°(c 0.50, MeOH); T.l.c. R_f (silica gel, Et_2O) 0.52, 0.44; IR (neat): ν 3393(br), 3029(m), 2963(s), 2920(s), 2870(s), 1496(s), 1454(s), 1368(s), 1313(s), 1208(m), 1047(s), 738(s), 699(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.07 (t, 3 H, J 7.2 Hz, CH_3), 2.53 (dd, 0.65 H, J_1 8.4, J_2 9.8 Hz, C2–H, β-isomer), 2.75–2.92 (m, 3.35 H, CH_2Me, C2–H α-isomer, OH), 3.4–3.6 (m, 3.5 H), 3.6–3.85 (m, 3.5 H), 3.9–4.2 (m, 2 H) (C3, C4, C5, C6, NCH_2Ph, 2 × OH together for above three multiplets), 4.53–4.62 (m, 2 H, CH_2Ph), 4.88 (d, 0.65 H, J 8.3 Hz, C1–H β-isomer), 5.45 (d, 0.35 H, J 2.6 Hz, C1–H, α-isomer), 7.26–7.35 (m, 10 H, 2 × Ph); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.14(14.58), 44.54(44.93), 54.36(54.79), 62.71(64.44), 68.44(69.80), 70.08(70.17), 71.84(72.53), 73.30(73.69), 73.72(74.56) (4 × CH_2, C2–C5, CH_3), 95.75(91.39)(C1), 127.29, 127.90(2), 128.51, 128.56, 129.01, 137.70, 139.54 (2 × Ph); MS FAB: (m/z) 388(MH, 55), 154(25), 136(30), 91(100). Anal. Calcd for $C_{22}H_{29}NO_5$: C, 68.20; H, 7.54; N, 3.61. Found: C, 68.56; H, 7.80; N, 3.28. HPLC (C-18, 60 MeOH:40 H_2O:0.1 TFA, UV-254 nm, 1 mL min^{-1}): 3.72′(100%).

Allyl 2-amino-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (**12**).—The acetamido derivative (**3**) (17.5 g) suspended in 2 M NaOH (200 mL) was heated under reflux at 110 °C for 6 days. The reaction mixture was extracted with $CHCl_3$, the extracts were dried and evaporated to give the amine (**12**) (16 g, 100%); $[\alpha]_D^{20}$ +94°(c 1.0, MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.80 (dd, 1 H, J_1 3.7, J_2 9.7 Hz, C2–H), 3.48 (dd, 1 H, J_1 9.3, J_2 9.3 Hz, C3–H), 3.74 (dd, 1 H, J_1 10.3, J_2 10.2 Hz, C6–H_{ax}), 3.76 (dd, 1 H, J_1 9.5, J_2 9.3 Hz, C4–H), 3.87 (ddd, 1 H, J_1 4.8, J_2 9.5, J_3 9.9 Hz, C5–H), 4.02 (ddt, 1 H, J_t 1.3, J_2 6.1 J_3 12.9 Hz, CH_2 at allyl(1)), 4.22 (ddt, 1 H, J_t 1.4, J_2 5.2, J_3 12.8 Hz, CH_2 at allyl(1)), 4.27 (dd, 1 H, J_1 4.8, J_2 10.2 Hz, C6–H_{eq}), 4.85 (d, 1 H, J 3.7 Hz, C1–H), 5.23 (dd, 1 H, J_1 1.5, J_2 10.4 Hz, =CH_2), 5.32 (dd, 1 H, J_1 1.6, J_2 17.3 Hz, =CH_2), 5.55 (s, 1 H, benzylidene CH), 5.88–5.98 (ddd, 1 H, –CH=), 7.35–7.41 (m, 3 H, Ph), 7.50 (dd, 2 H, J_1 2.0, J_2 7.8 Hz, Ph); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 56.70, 62.80, 68.69, 69.09, 71.83, 82.10, 99.45, 101.93, 117.71, 126.33, 128.36, 129.24, 133.73, 137.23.

Allyl 2-benzylamino-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (**13**).—The amine (**12**) (4.7 g) and PhCHO (1.9 g) in benzene (200 mL) were heated under reflux with azeotropic water removal. The solution was evaporated in vacuo, the residue dissolved in MeOH (40 mL) and THF (20 mL) and the solution cooled to 0 °C. Sodium borohydride (4 g) was added portionwise and the mixture stirred for 6 h. Water (200 mL) was added, the mixture extracted with CH_2Cl_2, the extracts dried over K_2CO_3 and evaporated to yield the crude product, which was chromatographed on silica gel (2.5:1 petrol:EtOAc). The title compound (**13**) was obtained as an oil which slowly solidified on standing (77%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.71 (dd, 1 H, J_1 3.6, J_2 9.9 Hz, C2–H), 3.56 (dd, 1 H, J_1 9.3, J_2 9.3 Hz, C4–H), 3.70–3.93 (m, 6 H, CH_2 at allyl(1), C6–H(1), C3, C5–H, NCH_2Ph), 4.18 (ddt, 1 H, J_t 1.5, J_2 5.2, J_3 12.8 Hz, CH_2 at allyl(1)), 4.25 (dd, 1 H, J_1 4.6, J_2 9.9 Hz, C6–H_{eq}), 4.83 (d, 1 H, J 3.5 Hz, C1–H), 5.26 (dd, 1 H, J_1 1.4, J_2 10.3 Hz, =CH_2), 5.33 (dd, 1 H, J_1 1.6, J_2 17.2 Hz, =CH_2), 5.56 (s, 1 H, benzylidene CH), 5.87–5.94 (m, 1 H, –CH=), 7.27–7.39 (m, 8 H, Ph), 7.49–7.53 (m, 2 H, Ph).

Allyl 2-(N-benzyl-N-ethyl)amino-2-deoxy-α-D-glucopyranoside (**15**).—Sodium borohydride (10 g) was added portionwise during 1 h. to the benzylamino–

glucoside (**13**) (6 g) in AcOH (150 mL) and the mixture heated at 80 °C for 2 h. The mixture was neutralised with NaOH, extracted with $CHCl_3$, the extracts were dried over Na_2SO_4 and evaporated to yield the crude intermediate. This was added to a mixture of AcOH (50 mL) and H_2O (30 mL) and the solution heated at 80 °C for 8 h. Evaporation to dryness, addition of the residue to 4 M NaOH (15 mL), extraction with $CHCl_3$, and drying and evaporation of the extracts gave the crude product. Chromatography on silica gel (EtOAc) gave the pure *N*-ethyl derivative (**15**) (3.5 g, 69%); $[\alpha]_D^{20}$ +114° (*c* 0.5, MeOH); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.03 (t, 3 H, *J* 7.2 Hz, CH_3), 2.64 (dq, 1 H, J_q 6.9, J_d 13.6 Hz, CHMe), 2.75 (dd, 1 H, J_1 2.9, J_2 10.9 Hz, C2–H), 2.87 (dq, 1 H, J_d 13.7, J_q 7.3 Hz, CHMe), 3.49–3.72 (m, 3 H, NCHPh, C4, C5–H), 3.81 (d, 2 H, *J* 3.3 Hz, C6–H_2), 3.91–4.25 (m, 4 H, OCH_2 at allyl, C3–H, NCHPh), 5.00 (d, 1 H, *J* 2.9 Hz, C1–H), 5.12 (dd, 1 H, J_1 1.3, J_2 10.5 Hz, $=CH_2$), 5.29 (dd, 1 H, J_1 1.6, J_2 17.2 Hz, $=CH_2$), 5.81–5.99 (m, 1 H, –CH=), 7.2–7.4 (m, 5 H, Ph); MS FAB: (*m/z*) 338(MH, 41.8), 296(11), 280(10), 177(12), 91(100). Anal. Calcd for $C_{18}H_{27}NO_5$: C, 64.07; H, 8.07; N, 4.15. Found: C, 63.74; H, 8.33; N, 3.90.

*Allyl 2-acetamido-6-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-*D*-glucopyranoside* (**17**).—*N*-Acetylglucosamine (**3**) (50 g) and boron trifluoride etherate (5 mL) in allyl alcohol (500 mL) was heated at 95 °C, the excess allyl alcohol was removed under vacuum, and the residue dried by co-evaporation with toluene (4 × 50 mL). The residue was dissolved in anhydrous pyridine (250 mL) and added dropwise at 0 °C to a solution of TsCl (60 g) in CH_2Cl_2 (150 mL) during 1 h. The reaction mixture was allowed to stand overnight, $CHCl_3$ (400 mL) was added and the solution washed successively with cold H_2O (3 × 200 mL), 3 M hydrochloric acid (3 × 400 mL), H_2O (200 mL) again, and finally dried over anhydrous $MgSO_4$. The solvent was removed in vacuo to give allyl 2-acetamido-2-deoxy-6-*O*-*p*-toluenesulphonyl-α,β-D-glucopyranoside (**16**) as a solid (79 g, 85% based on *N*-acetylglucosamine). The 6-*O*-tosyl-glucoside (**16**) (34 g) in *N*-benzylethylamine (75 mL) was heated at 140–160 °C for 16 h. Excess *N*-benzylethylamine was removed under vacuum, $CHCl_3$ (200 mL) was added, and the resultant solution washed with 10% K_2CO_3, dried over anhydrous magnesium sulphate, and evaporated. Chromatography of the crude product on silica gel (10:1, EtOAc:methanol) gave the (*N*-benzyl-*N*-ethyl)amino-glucoside (**17**) (18 g, 58%); mp 133–134 °C; $[\alpha]_D^{20}$ +103° (*c* 1.0, MeOH); IR (KBr): ν 3478(m, sharp, NH), 3313(s), 1648(s), 1550(s), 1453(m), 1313(s), 1129(m), 1104(s), 1054(s), 1030(m), 742(s), 701(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.11 (t, 3 H, *J* 7.2 Hz, CH_3), 2.03 (s, 3 H, CH_3CO), 2.43 (dq, 1 H, J_d 12.9, J_q 7.0 Hz, CHMe), 2.66 (dd, 1 H, J_1 4.3, J_2 12.7 Hz, C6–H(1)), 2.71 (qu, 1 H, *J* 7.3 Hz, CHMe), 2.80 (dd, 1 H, J_1 10.1, J_2 12.7 Hz, C6–H(1)), 3.37 (t, 1 H, *J* 9.0 Hz, C4–H), 3.37 (d, 1 H, *J* 13.1 Hz, NCH_2Ph(1)), 3.67–3.76 (m, 2 H, C3, C5–H), 3.88 (d, 1 H, *J* 13.1 Hz, NCH_2Ph(1)), 3.96 (ddt, 1 H, J_t 1.3, J_2 6.2, J_3 13.0 Hz, CH_2 at allyl(1)), 4.04 (ddd, 1 H, J_1 3.7, J_2 8.7, J_3 10.5 Hz, C2–H), 4.13 (ddt, 1 H, J_t 1.4, J_2 5.3, J_3 13.0 Hz, CH_2 at allyl(1)), 4.80 (d, 1 H, *J* 3.8 Hz, C1–H), 5.21 (dd, 1 H, J_1 1.3, J_2 10.4 Hz, $=CH_2$), 5.28 (dd, 1 H, J_1 1.6, J_2 17.2 Hz, $=CH_2$), 5.86–5.93 (m, 2 H, –CH=, NH), 7.27–7.36 (m, 5 H, Ph); MS FAB: (*m/z*) 379(MH, 100), 148(50), 91(96). Anal. Calcd for $C_{20}H_{30}N_2O_5$: C, 63.47; H, 7.99; N, 7.40%. Found: C, 63.35; H, 7.93; N, 7.21.

*Allyl 2-benzylamino-6-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-*D*-glucopyranoside* (**19**).—The acetamido compound (**17**) (10 g) was treated as described for **12** to give the deacetylated product (**18**) (8 g). The free 2-amino-glucoside (**18**) (7.2 g) was treated as described for **8** to give the crude title compound (9.2 g). Of this, 1.4 g was chromatographed on silica gel to give the benzylamino compound (**19**) (0.65 g, 47%); mp 90–92 °C; $[\alpha]_D^{20}$ +77°(*c* 1.0, MeOH); IR (KBr) ν 3230(s), 1453(s), 1152(s), 1110(s), 1090(s), 1081(s), 995(s), 732(s), 697(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12(t, 3 H, *J* 7.1 Hz, CH_3), 2.40 (dq, 1 H, J_d 12.9, J_q 7.0 Hz, CHMe), 2.55–2.65 (m, 2 H), 2.70–2.81 (m, 2 H) (2.55–2.81, 4 H, CHMe, C6–H, C2–H), 3.33 (d, 1 H, *J* 13.3 Hz, NCHPh at C6), 3.38 (dd, 1 H, J_1 2.0, J_2 8.9 Hz, CH_2 at allyl(1)), 3.62 (dd, 1 H, J_1 10.4, J_2 8.8 Hz, C4–H), 3.66–3.73 (m, 1 H, C5–H), 3.77–3.93 (m, 4 H, NCH_2Ph at C2, NCHPh at C6, C3–H), 4.10 (m, 1 H, CH_2 at allyl(1)), 4.73 (d, 1 H, *J* 3.2 Hz, C1–H), 5.22 (dd, 1 H, J_1 1.6, J_2 10.3 Hz, $=CH_2$), 5.30 (dd, 1 H, J_1 1.7, J_2 17.4 Hz, $=CH_2$), 5.85–5.91 (m, 1 H, –CH=), 7.24–7.35 (m, 10 H, 2 × Ph); MS FAB: (*m/z*) 427(MH^+, 20), 148(45), 91(100). Anal. Calcd for $C_{25}H_{34}N_2O_4$: C, 70.40; H, 8.03; N, 6.57. Found: C, 70.19; H, 7.87; N, 6.54.

*Allyl 2,6-di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-*D*-glucopyranoside* (**20**).—The benzylamino-glucoside (**19**) (3.62 g) was treated as described for **9** except that NaOH was used for neutralisation. The crude product was chromatographed on silica gel

(2:1, EtOAc:petrol) to give the ditertiary amine (**20**) (3.79 g, 98%); $[\alpha]_D^{20}$ +71° (*c* 1.0, MeOH); IR (neat): ν 3415(br), 3027(m), 1648(w), 1602(w), 1494(m), 1452(s), 1041(s), 733(s), 679(s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.02 (t, 3 H, *J* 7.1 Hz, CH_3), 1.11 (t, 3 H, *J* 7.0 Hz, $CH_{3'}$), 2.39 (dq, 1 H, J_d 13.1, J_q 7.0 Hz, CHMe), 2.60–2.90 (m, 6 H, C2–H, CH_2Me, CHMe, C6–H2), 3.34 (d, 1 H, *J* 13.0 Hz, NCHPh at C6), 3.40 (dd, 1 H, J_1 8.7, J_2 8.9 Hz, C4–H), 3.71 (d, 1 H, *J* 14.3 Hz, NCHPh at C2), 3.77 (ddd, 1 H, J_1 4.1, J_2 10.2, J_3 9.5 Hz, C5–H), 3.92 (d, 1 H, *J* 13.2 Hz, NCHPh at C6), 3.98 (dd, 1 H, J_1 6.0, J_2 13.1 Hz, CH_2 at allyl(1)), 4.05 (d, 1 H, *J* 14.0 Hz, NCHPh at C2), 4.06 (dd, 1 H, J_1 8.5, J_2 10.5 Hz, C3–H), 4.16 (ddt, 1 H, J_1 1.4, J_2 5.3, J_3 13.0 Hz, CH_2 at allyl(1)), 4.90 (d, 1 H, *J* 3.1 Hz, C1–H), 5.20 (dd, 1 H, J_1 1.5, J_2 10.4 Hz, $=CH_2$), 5.31 (dd, 1 H, J_1 1.7, J_2 17.2 Hz, $=CH_2$), 5.89–5.95 (m, 1 H, –CH=), 7.22–7.39 (m, 10 H, 2 × Ph). Anal. Calcd for $C_{27}H_{38}N_2O_4$: C, 71.34; H, 8.43; N, 6.16. Found: C, 71.04; H, 8.34; N, 6.38.

*Allyl 2,6-di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-*D*-glucopyranoside oxalate* (**21**).—Oxalic acid (0.22 g) dissolved in MeOH (1 mL) was added to the ditertiary amine (**20**) (0.6 g) in Et_2O (10 mL). The solution was evaporated to dryness in vacuo, THF (6 mL) was added and the mixture heated until solution was complete. The solution was cooled to room temperature, stored in the refrigerator for 10 h, evaporated to dryness, Et_2O (15 mL) was added and the precipitated white solid was collected by filtration. Drying in the vacuum oven gave white crystals of the *oxalate salt* (**21**); mp 97–100 °C; IR (KBr): ν 3350(s), 1719(m), 1703(m), 1616(s), 1457(s), 1404(s), 1280(s), 1217(s), 1051(s), 1029(s), 722(s) cm^{-1}; ^1H NMR (Me_2SO-d_6, 200 MHz): δ 0.92 (t, 3 H, CH_3), 1.12 (t, 3 H, CH_3), 2.55–3.10 (m, 7 H, C2–H, 2 × CH_2Me, C6–H2), 3.18 (d, 1 H, *J* 14.0 Hz, NCHPh at C6), 3.65–4.30 (m, 8 H, CH_2 at allyl, C3, C4, C5–H, NCH_2Ph at C2, NCHPh), 4.72 (d, 1 H, *J* 3.5 Hz, C1–H), 5.14 (d, 1 H, *J* 10.5 Hz, $=CH_2$), 5.28 (d, 1 H, *J* 17.2 Hz, $=CH_2$), 5.8–6.0 (m, 1 H, –CH=), 7.1–7.5 (m, 10 H, 2 × Ph), 8–10 (br, 2.5 H, H^+). MS FAB: (*m/z*) 455(MH, 4), 91(100). Anal. Calcd for $C_{27}H_{38}N_2O_4.2.9C_2H_2O_4$ C, 55.04; H, 6.17; N, 3.91. Found: C, 55.06; H, 6.31; N, 4.00.

*Propenyl 2,6-di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α-*D*-glucopyranoside* (**22**).—Potassium *t*-butoxide (2.8 g) was added to a solution of the allyl glycoside (**20**) (1.0 g) in Me_2SO (20 mL) and the mixture heated at 120 °C for 24 h. The solution was cooled to room temperature, H_2O (100 mL) and Et_2O (100 mL) were added. The organic layer was separated and the aqueous layer extracted with Et_2O (2 × 50 mL). The combined Et_2O extracts were dried over anhydrous K_2CO_3 and evaporated to dryness to yield the crude product. Chromatography on silica gel (1:1, EtOAc:petrol) gave the title propenyl α-D-glucopyranoside (**22**) (0.8 g, 80%); ^1H NMR ($CDCl_3$, 400 MHz): δ 1.03 (t, 3 H, *J* 7.1 Hz, CH_3), 1.10 (t, 3 H, *J* 7.1 Hz, CH_3), 1.61 (dd, 3 H, J_1 1.7, J_2 6.8 Hz, $=CCH_3$), 2.38 (dq, 1 H, J_d 13.0, J_q 6.9 Hz, CHMe), 2.60–2.91 (m, 6 H, CH_2Me, CHMe, C2–H, C6–H2), 3.13 (1 H, OH), 3.32 (d, 1 H, *J* 13.1 Hz, NCHPh), 3.42 (dd, 1 H, J_1 8.4, J_2 9.2 Hz, C4–H), 3.72 (d, 1 H, *J* 14.1 Hz, NCHPh at C2), 3.78 (ddd, 1 H, J_1 3.7, J_2 10.3, J_3 9.4 Hz, C5–H), 3.91 (d, 1 H, *J* 13.0 Hz, NCHPh at C6), 4.08 (d, 1 H, *J* 14.3 Hz, NCHPh at C-2), 4.14 (dd, 1 H, J_1 8.4, J_2 10.9 Hz, C3–H), 4.60 (qu, 1 H, *J* 6.8 Hz, –C=CHMe), 5.0 (d, 1 H, *J* 3.0 Hz, C1–H), 6.12 (dd, 1 H, J_1 1.8, J_2 6.3 Hz, OCH=), 7.2–7.5 (m, 10 H, 2 × Ph); MS FAB: (*m/z*) 455(MH, 12.8), 454(M^+, 1.7), 453(M–H, 6.6), 217(9.8), 148(36), 91(100).

*2,6-Di-(*N*-benzyl-*N*-ethyl)amino-2,6-dideoxy-α,β-*D*-glucose* (**23**).—The propenyl glucoside (**22**) (0.6 g) in 1 M HCl (50 mL) was heated at 80 °C for 2 h, then at 60 °C overnight. The solution was neutralized with 4 M NaOH, extracted with Et_2O, the extracts dried over Na_2SO_4, evaporated, and the residue chromatographed on silica gel (7:1, EtOAc:petrol) to give the 2,6-di-(*N*-benzyl-*N*-ethyl)amino-glucose derivative (**23**) (0.49 g, 90%); mp 49–52 °C; $[\alpha]_D^{20}$ +18° (*c* 1.0, MeOH); IR (KBr): ν 3300(s), 3028(w), 2969(m), 1453(s), 1375(s), 1154(s), 1146(s), 1093(s), 1045(s), 741(s), 700(s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.02–1.13 (m, 6 H, 2 × CH_3)(of these, main anomer, 1.066 (t, *J* 7.1 Hz), 1.11 (t, *J* 7.4 Hz)), 2.34–2.90 (m, 7 H, 2 × CH_2Me, C2–H, C6–H2), 3.19 (1 H, OH), 3.29–3.50 (m, 3 H, C4, C5, NCHPh), 3.70–4.30 (m, 5 H, NCH_2Ph, NCHPh, C3–H, OH), 4.76 (d, 0.74 H, *J* 8.1 Hz, C1–H, β-anomer), 5.28 (d, 0.26 H, *J* 3.1 Hz, C1–H, α-anomer), 7.20–7.45 (m, 10 H, 2 × Ph). MS FAB: (*m/z*) 415(MH, 20), 148(25), 91(100). Anal. Calcd for $C_{24}H_{34}N_2O_4$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.47; H, 8.17; N, 6.61.

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