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Note

Stereospecific synthesis of *C*-(2-amino-2-deoxy-β-D-glucosyl) compounds by Wittig-type olefination of D-glucosamine derivatives

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C-Glycosyl compounds represent a class of products used as chiral synthons[1] and as potential glycosidase inhibitors[2]. A number of methods have been devised for their synthesis[3], but despite the biological importance of D-glucosamine, few *C*-glycosyl derivatives of this carbohydrate have been synthesized.

α-*C*-glycosyl compounds have been obtained selectively from protected 2-acetamido-2-deoxy-D-glucose by a Wittig-type reaction and subsequent cyclization[4]. Other selective reactions include the reaction of mercuric cyanide with tri-*O*-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranosyl bromide, to obtain selectively the β-D-glycosyl cyanide, described by Myers et al.[5]; Carcano et al.[6] have prepared 2-amino-2-deoxy-α-D-glucopyranosylmethane from a protected D-arabinofuranosylbenzylamine, the key-step being vinylation with subsequent mercuri-cyclization. Grondin et al.[7] recently presented an original alternative by synthesizing selectively α-D-glucosaminylalkanes from C-1 alkyl glycals. Several authors have reported difficulties in glucosaminylalkane synthesis and, except for the synthesis of Myers et al.[5], the few stereoselective syntheses have concerned the α anomer. We decided, therefore, to apply to D-glucosamine some syntheses of *C*-glycosyl compounds previously described with other carbohydrates and leading stereospecifically to the β anomer.

The first is a Wittig–Horner–Emmons type reaction of the sodium salt of phosphonate **1** on unprotected monosaccharides. Davidson et al.[8] have observed that such a reaction with D-glucose led to the two anomers of the *C*-glucofuranosyl derivative; these are converted into the thermodynamically more stable β-*C*-glucopyranosyl derivative by treatment with base. The second reaction is a Wittig-type

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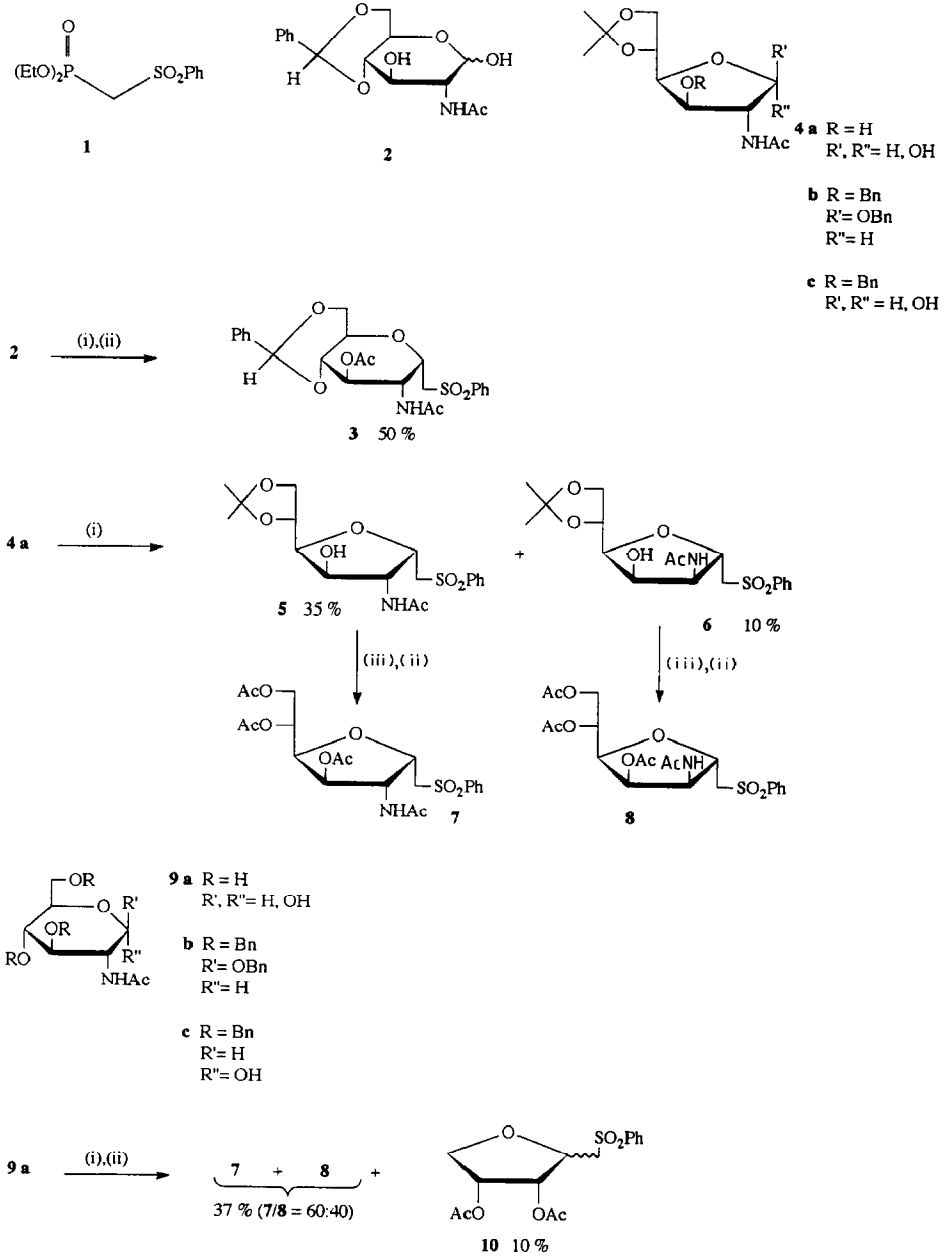
reaction that we have just reported[9], in which 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose reacted with methyl bromoacetate, tributylphosphine, and zinc to give stereospecifically the β-*C*-glucosyl derivative.

Reaction of the sodium salt of **1** with 2-acetamido-4,6-*O*-benzylidene-2-deoxy-D-glucose (**2**) gave solely the *C*-α-glycosyl compound **3** in a yield of 50%. 2-Acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucose (**4a**) reacted with **1** to give the *C*-α-glucofuranosyl derivative **5** (35%), and also the *C*-α-mannofuranosyl derivative **6** (10%). The stereochemistry of these products was determined from NMR characteristics of the acetylated derivatives **7** ($J_{1,2}$ 4.0, $J_{2,3}$ 0 Hz) and **8** ($J_{1,2}$ 10.2, $J_{2,3}$ 4.1 Hz)[10], obtained respectively by acid hydrolysis and acetylation of compounds **5** and **6**.

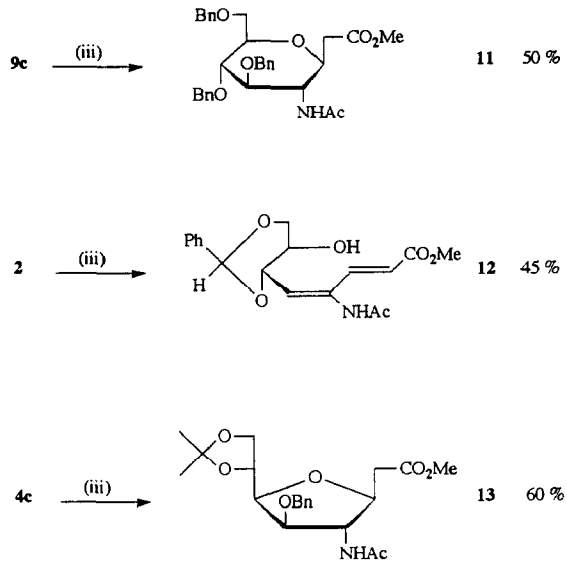
When treated with the sodium salt of **1**, 2-acetamido-2-deoxy-D-glucose (**9a**) gave a complex mixture. The main products were identified, after acetylation, as the *C*-glucofuranosyl and *C*-mannofuranosyl derivatives **7** and **8** (37%, inseparable mixture; ratio, 6:4), and **10** (10%) the result of condensation after a retroaldol reaction[11]. All further basic treatments of the reaction mixture led to more complex mixtures.

We then studied the behaviour of several pyranose and furanose derivatives of 2-acetamido-2-deoxy-D-glucose towards the Wittig-type reaction in the presence of zinc. The substrates for these reactions were prepared as follows. The synthesis of 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (**9c**) was described by Harrison and Fletcher[12]; they effected benzylation of **9a** in the presence of barium oxide and barium hydroxide to give **9b**, followed by acid hydrolysis of the anomeric benzyloxy group. During the hydrolysis, however, deprotection of the amine occurred, so acetylation followed by *O*-deacetylation was necessary to obtain **9c**. We performed this anomeric deprotection by selective hydrogenolysis. A recent preliminary communication of Bieg and Szeja[13] has described regioselective hydrogenolysis of equatorial benzyl glycosides, using a catalytic Pd–Al_2O_3 hydrogen-transfer system with ammonium formate as the hydrogen donor; we have observed similar results with a Pd–C catalyst. The benzyl glycoside **9b**, treated with a Pd–C–ammonium formate system, led to the glycopyranose **9c** in 74% yield. Benzylation of 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucose (**4a**) in the presence of BaO–$Ba(OH)_2$ gave the benzyl glycoside **4b** in a yield of 40%. The acid-labile isopropylidene group in **4b** precludes the use of acid hydrolysis to remove the anomeric benzyloxy group. Regioselective hydrogenolysis of **4b**, however, using the catalytic Pd–C hydrogen-transfer system, gave the glycofuranose **4c** (60%). The 2-acetamido-2-deoxyglucopyranoses **9c** and **2** and the 2-acetamido-2-deoxyglucofuranose **4c** were treated with methyl bromoacetate, tributylphosphine, and zinc. Compound **9c** led stereospecifically to the *C*-β-glycosyl derivative **11** in a yield of 50%. However, reaction with 2-acetamido-4,6-*O*-benzylidene-2-deoxy-D-glucose (**2**) gave only the diene **12** (45%); the Wittig-type reaction occurred, but was followed by elimination of water. The Wittig-type reaction with glycofuranose **4c** led stereospecifically to the *C*-β-glycofuranosyl derivative **13** in a yield of 60%.



(i) sodium salt of **1**, pyridine
(ii) Ac_2O / pyridine
(iii) Amberlyst 15(H^+), EtOH

Scheme 1.



(iii) $BrCH_2CO_2Me$ /Zn / nBu_3P

Scheme 2.

In conclusion, the Wittig–Horner–Emmons reaction with the sodium salt of the phosphonate-sulphone **1** is not a suitable method for *C*-glycosylation using unprotected 2-acetamido-2-deoxy-D-glucose. Performed on furanoid derivatives of D-glucosamine, this reaction was accompanied by some epimerization at C-2, but pyranoid derivatives gave stereospecifically the *C*-α-glycosyl derivatives of glucosamine. The Wittig-type reaction using methyl bromoacetate and tributylphosphine in the presence of zinc led stereospecifically to the *C*-β-glycofuranosyl or -glycopyranosyl derivatives from 2-acetamido-2-deoxy-D-glucose. This method is therefore useful for the synthesis of *C*-(2-amino-2-deoxy-β-D-glucosyl) compounds.

EXPERIMENTAL

General methods.—Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were measured with a Jobin–Yvon polarimeter at 20°C. TLC was performed on Silica Gel $60F_{254}$ Merck (230 mesh). Column chromatography was performed on Silica Gel 35–70 μm (400–200 mesh) Amicon. ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker WB 300 spectrometer with $CDCl_3$ as deuterated solvent. Elemental analysis were performed by the Laboratoire Central d'Analyses du C.N.R.S. (Vernaison, France).

Diethyl phenylsulfonylmethylphosphonate (**1**).—3-Chloroperoxybenzoïc acid (1.0 g, 5.8 mmol) was added to a stirred solution of diethyl phenylthiometh-

ylphosphonate[14] (0.5 g, 1.9 mmol) in CH_2Cl_2 (40 mL). The mixture was stirred at room temperature (4 h), washed with aq NaOH (0.1 M, 60 mL) and water (20 mL), dried with sodium sulfate, and concentrated in vacuo. Chromatographic purification on silica gel in 5:5 hexane–EtOAc afforded diethyl phenylsulfonylmethylphosphonate (79% yield) as a colourless syrup. ^{13}C NMR δ 16.00, 15.93 (CH_3), 53.24 (d, J 136.6 Hz, PCH_2), 63.12, 63.04 (OCH_2), 133.89, 128.93, 128.03 [*C*H(Ar)], 139.91 (C-ipso). Anal. Calcd for $C_{11}H_{17}O_5PS$: C, 45.20; H, 5.82; P, 10.6; S, 10.95. Found: C, 45.30; H, 5.50; P, 10.20; S, 11.00.

General procedures.—(A) Wittig–Horner–Emmons reaction with **1**. To a stirred solution of **1** (1.228 g, 4.2 mmol) in anhyd THF (50 mL) under Ar and cooled at 0°C was added dropwise a solution of sodium bis(trimethylsilyl)amide (0.767 g, 4.2 mmol) in anhyd THF (15 mL). The solution was stirred during 30 min, and then concentrated in vacuo. To the white crystals was added a solution of the aldose (3.2 mmol) in anhyd pyridine (20 mL). The solution was then stirred under Ar at 45°C during 48 h. Then Ac_2O (1.6 mL) was added at room temperature, and the solution was stirred overnight. After concentration in vacuo, the residue was dissolved in CH_2Cl_2. The organic layer was washed three times with M HCl (100 mL) and then with aq Na_2CO_3 (60 mL), dried with sodium sulfate, and concentrated in vacuo. Chromatographic purification on silica gel afforded the products.

(B) Wittig-type reaction in the presence of zinc. To a solution of aldose and acid-washed zinc dust[15] (20 equiv) in anhyd benzene (8 mL for 1 g of aldose) were added, at room temperature, tributylphosphine (5 equiv) and methyl bromoacetate (5 equiv). The mixture was heated at reflux and the reaction monitored by TLC. When the reaction ended, the mixture was concentrated and chromatographic purification on silica gel afforded the products.

(2-Acetamido-3-O-acetyl-4,6-O-benzylidene-2-deoxy-α-D-glucopyranosyl)methyl phenyl sulfone (**3**).—Obtained from 2-acetamido-4,6-*O*-benzylidene-2-deoxy-D-glucose[16] (**2**) by procedure *A*. Chromatographic purification on silica gel in 19:1 and then 72:1 $CHCl_3$–acetone afforded **3** (50%) as white crystals; mp 206–208°C; $[\alpha]_D$ +51° (*c* 0.1, $CHCl_3$); R_f 0.21 (9:1 $CHCl_3$–acetone). ^1H NMR: δ 1.9, 2.1 (2 s, 6 H, 2 CH_3), 3.4 (m, 4 H, H-5, 6a,6b,1′), 3.65 (t, 1 H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4), 3.85 (dd, 1 H, $J_{1'a,1'b}$ 10.7, $J_{1'a,1}$ 3.9 Hz, H-1′a), 4.40 (m, 1 H, $J_{1,2}$ 6.3 Hz, H-2), 4.75 (m, 1 H, H-1), 5.10 (dd, 1 H, $J_{3,4}$ 9.4, $J_{2,3}$ 11.0 Hz, H-3), 5.40 (s, 1 H, PhC*H*), 6.30 (d, 1 H, $J_{NH,2}$ 7.9 Hz, NH), 7.40–8.00 (m, 10H, Ar-H). ^{13}C NMR δ 20.85, 22.96 (CH_3), 51.98 (C-2), 52.16 (C-1′), 64.68 (C-5), 68.33 (C-6), 69.47 (C-3), 70.84 (C-1), 79.24 (C-4), 101.40 (*C*HPh), 126.02, 128.17, 128.33, 129.08, 129.19, 133.90 [CH (Ph)], 136.70, 139.38 (C-ipso), 170.82, 170.00 (C=O). Anal. Calcd for $C_{24}H_{27}NO_8S$: C, 58.89; H, 5.56; N, 2.86; S, 6.5. Found: C, 58.69; H, 5.76; N, 2.72; S, 6.4.

(2-Acetamido-2-deoxy-5,6-O-isopropylidene-α-D-glucofuranosyl)methyl phenyl sulfone (**5**).—Obtained from **4a**[17] by procedure *A*, without the acetylation step. Chromatographic purification on silica gel in 70:1 and then 40:1 $CHCl_3$–MeOH afforded **5** (35%) and **6** (10%); **5** had mp 47–48°C; $[\alpha]_D$ +21° (*c* 0.1, $CHCl_3$); R_f 0.05 (40:1 $CHCl_3$–MeOH). ^1H NMR: δ 1.30, 1.40, 1.95 (3 s, 9 H, CH_3), 3.40 (m,

2H, H-1'a,1'b), 3.55 (m, 1 H, $J_{4,5}$ 5.3 Hz, H-5), 3.85 (m, 2 H, H-4,6b), 4.15 (dd, 1 H, $J_{6a,6b}$ 13.7 Hz, H-6a), 4.20 (d, 1 H, $J_{3,4}$ 8.3 Hz, H-3), 4.35 (d, 1 H, $J_{1,2}$ 3.9, $J_{NH,2}$ 6.7 Hz, H-2), 4.55 (m, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 6.60 (d, 1 H, $J_{NH,2}$ 6.7 Hz, NH), 7.50–8.00 (m, 5H, Ar-H). ^{13}C NMR: δ 22.91, 25.02, 26.67 (CH_3), 56.73 (C-1'), 59.97 (C-2), 66.58 (C-6), 73.34, 73.27 (C-4,5), 75.29 (C-1), 81.30 (C-3), 108.93 (CMe_2), 128.24, 129.09, 133.81 [CH (Ph)], 139.20 (C-ipso), 170.90 (C=O). Anal. Calcd for $C_{18}H_{25}NO_7S$: C, 54.13; H, 6.26; N, 3.50; S, 8.02. Found: C, 54.01; H, 6.02; N, 3.60; S, 7.82.

(2-Acetamido-2-deoxy-5,6-O – isopropylidene-α-D-mannofuranosyl)methyl phenyl sulfone (**6**).—Obtained from **4a**[17] by procedure *A* (10%); mp 140°C; $[\alpha]_D$ +4° (*c* 0.2, $CHCl_3$); R_f 0.11 (40:1 $CHCl_3$–MeOH). ^{1}H NMR; δ 1.20, 1.30, 1.95 (3 s, 9 H, 3 CH_3), 3.45 (m 3 H, H-1'a,1'b,6b), 3.70 (dd, 1 H, $J_{3,4}$ 8.6, $J_{4,5}$ 3.0 Hz, H-4), 3.80 (dd, 1 H, $J_{6a,6b}$ 8.8, $J_{5,6a}$ 6.3 Hz, H-6a), 4.10 (m, 1 H, $J_{4,5}$ 3.0 Hz, H-5), 4.20 (m, 3 H, H-1,2,3), 6.55 (d, 1 H, $J_{NH,2}$ 6.7 Hz, NH), 7.50–8.00 (m, 5 H, Ar-H). ^{13}C NMR: δ 22.93, 25.08, 26.70 (CH_3), 56.66 (C-2), 60.03 (C-1'), 66.74 (C-6), 70.41 (C-5), 72.97 (C-1), 75.45 (C-4), 82.25 (C-3), 109.21 (CMe_2), 128.17, 128.80, 133.51 [CH (Ph)], 139.99 (C-ipso), 171.27 (C=O). Anal. Calcd for $C_{18}H_{25}NO_7S$: C, 54.13; H, 6.26; N, 3.50; S, 8.02. Found: C, 53.89; H, 6.56; N, 3.24; S, 7.80.

(2-Acetamido-3,5,6-tri-O-acetyl-2-deoxy-α-D-glucofuranosyl)methyl phenyl sulfone (**7**).—A solution of *C*-glycosyl compound **5** (0.100 g, 0.25 mmol) in EtOH (10 mL) was stirred with Amberlyst-15 (H^+) wet resin at 40°C during 75 min. The solution was filtered and concentrated in vacuo, and the residue was dissolved in anhyd pyridine (10 mL). Acetic anhydride (1 mL) was added, and the mixture stirred overnight. CH_2Cl_2 (50 mL) was added, and the organic layer was washed with M HCl (150 mL), then satd aq $NaHCO_3$ (30 mL), dried with sodium sulfate, and concentrated in vacuo. Chromatographic purification on silica gel in 4:1 EtOAc–hexane afforded **7** (63%) as white crystals; mp 56°C; $[\alpha]_D$ +16° (*c* 0.1, $CHCl_3$); R_f 0.14 (1:4 hexane–EtOAc). ^{1}H NMR: δ 1.88, 1.90, 1.95, 2.00 (4 s, 12 H, 4 CH_3), 3.4 (d, 2H, $J_{1,1'}$ 5.7 Hz, H-1'), 3.75 (dd, 1 H, $J_{6a,6b}$ 12.1, $J_{5,6b}$ 5.8 Hz, H-6b), 4.20 (dd, 1 H, $J_{3,4}$ 4.1, $J_{4,5}$ 9.1 Hz, H-4), 4.25 (dd, 1 H, $J_{6a,6b}$ 12.1, $J_{5,6a}$ 2.4 Hz, H-6a), 4.45 (dd, 1 H, $J_{NH,2}$ 8.5, $J_{1,2}$ 4.0 Hz, H-2), 4.60 (dd, 1 H, $J_{1,2}$ 4.0, $J_{1,1'}$ 5.7 Hz H-1), 6.05 (m, 1 H, H-5), 5.35 (d, 1 H, $J_{3,4}$ 4.1 Hz, H-3), 6.15 (d, 1 H, $J_{NH,2}$ 8.5 Hz, NH), 7.40–8.00 (m, 5 H, Ar-H). ^{13}C NMR: δ 20.62 ($OCOCH_3$), 22.89 ($NCOCH_3$), 56.61 (C-1'), 57.86 (C-2), 63.30 (C-6), 67.52 (C-5), 74.89 (C-1,3), 77.19 (C-4), 128.17, 129.18, 133.99 [CH (Ph)], 139.39 (C-ipso), 169.07, 169.54, 170.09, 170.55 (C=O). Anal. Calcd for $C_{21}H_{27}NO_{10}S$: C, 51.95; H, 5.56; N, 2.88; S, 6.59. Found: C, 51.60; H, 5.31; N, 2.60; S, 6.50.

(2-Acetamido-3,5,6-tri-O-acetyl-2-deoxy-α-D-mannofuranosyl)methyl phenyl sulfone (**8**).—Obtained in a yield of 60% from compound **6** (0.110 g, 0.275 mmol) by the procedure described for the synthesis of **7** from compound **5**; white crystals; mp 193–194°C; $[\alpha]_D$ +10° (*c* 0.1, $CHCl_3$); R_f 0.15 (1:4 hexane–EtOAc). ^{1}H NMR: δ 1.85, 1.90, 1.95, 2.00 (4 s, 12 H, 4 CH_3), 3.45 (m, 2 H, H-1'a,1'b), 3.50 (dd, 1 H, $J_{4,5}$ 9.9, $J_{3,4}$ 3.6 Hz, H-4), 4.35 (dd, 1 H, $J_{6a,6b}$ 12.2, $J_{5,6a}$ 2.1 Hz, H-6a), 4.40 (m, 1 H,

$J_{1,2}$ 10.2 Hz, H-1), 4.45 (m, 1 H, $J_{2,3}$ 4.1 Hz, H-2), 4.98 (m, 1 H, H-5), 5.45 (dd, 1 H, $J_{2,3}$ 4.1, $J_{3,4}$ 3.6 Hz, H-3) 6.35 (d, 1 H, $J_{NH,2}$ 8.4 Hz, NH), 7.40–8.00 (m, 5 H, Ar-H). ^{13}C NMR: δ 20.56 ($OCOCH_3$), 22.83 ($NCOCH_3$), 55.27 (C-2), 59.83 (C-1′), 62.80 (C-6), 67.50 (C-5), 70.83 (C-3), 75.16 (C-1), 77.69 (C-4), 128.18, 129.01, 133.92 [CH (Ph)], 139.63 (C-ipso), 169.35, 169.67, 170.32, 170.71 (C=O). Anal. Calcd for $C_{21}H_{27}NO_{10}S$; C, 51.95; H, 5.56; N, 2.88; S, 6.59. Found: C, 51.89; H, 5.37; N, 2.47; S, 6.30.

(2,3 Di-O-acetyl-α,β-D-erythrofuranosyl)methyl phenyl sulfone (**10**).—Obtained from **9a** by procedure *A*. Chromatographic purification on silica gel in 19:1 CH_2Cl_2–acetone and then in CH_2Cl_2 afforded an inseparable mixture of **7** and **8** (37%, ratio 6:4, determined by comparison of the ^{13}C NMR spectrum with those of pure samples of **7** and **8**, obtained above by hydrolysis and acetylation on **5** and **6**), and compound **10** (10%) as a syrup; $[\alpha]_D$ +2° (*c* 0.2, $CHCl_3$); R_f 0.68 (9:1 CH_2Cl_2–acetone). ^{13}C NMR: δ 20.36 (CH_3), 56.23 (C-1′α), 58.77 (C-1′β), 69.53 (C-4α), 70.28 (C-4β), 70.89, 74.04, 74.33 (C-1,2,3β), 71.24, 71.67, 73.10 (C-1,2,3α), 127.99 - 133.78 [CH (Ph)], 139.51 (C-ipso α), 139.80 (C-ipso β), 169.21, 169.59 (C=O α), 169.59, 169.77 (C=O β). Anal. Calcd for $C_{15}H_{18}O_7S$: C, 52.62; H, 5.26; S, 9.36. Found: C, 51.98; H, 5.01; S, 9.12.

Benzyl 2-acetamido-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranoside (**9b**).—To a solution of **9a** (10.0 g, 45.2 mmol) and benzyl bromide (70 mL) in DMF (200 mL), stirred at 0°C, were added portionwise BaO (65 g) and then $Ba(OH)_2$ (25 g). The mixture was stirred at 0°C for 5 h, and then for 18 h at room temperature. CH_2Cl_2 (200 mL) was added, and the solution was filtered. The organic phase was washed with water, dried, and concentrated in vacuo. Recrystallization from MeOH afforded white crystals (65%) of **9b**; mp 160–168°C (lit.[12] mp 160–161°C and 170–172°C); $[\alpha]_D$ −12.1° (*c* 1, $CHCl_3$) {lit.[12] $[\alpha]_D$ −12.1° (*c* 1.3, $CHCl_3$)}; R_f 0.82 (19:1 CH_2Cl_2–MeOH). ^{13}C NMR: δ 23.48 (CH_3), 56.36 (C-2), 69.03 (C-16), 70.63, 73.43, 74.45 (4 CH_2Ph), 74.82 (C-3), 78.45 (C-4), 80.47 (C-5), 99.27 (C-1), 127.78–138.42 [CH (Ph)], 170.19 (C=O). Anal. Calcd for $C_{36}H_{39}NO_6$: C, 74.33; H, 6.76; N, 2.41. Found: C, 74.13; H, 6.95; N, 2.49.

2-Acetamido-3,4,6-tri-O-benzyl-2-deoxy-α-D-glucopyranose (**9c**).—Benzyl glycoside **9b** (1.12 g, 19 mmol), Pd–C (0.70 g 0.66 mmol), and ammonium formate (0.3 g, 4.8 mmol) were stirred in anhyd MeOH (60 mL) at 70°C. The reaction was monitored by TLC (19:1 CH_2Cl_2–MeOH). After 16 min, the mixture was filtered and the catalyst washed with hot MeOH. The solution was concentrated in vacuo. Chromatographic purification on silica gel in 60:1 CH_2Cl_2–MeOH, and then recrystallization from MeOH afforded **9c** (74%); mp 218–219°C (lit.[12] mp 218°C); $[\alpha]_D$ +63° (*c* 0.9, pyridine) {lit.[12] $[\alpha]_D$ +63° (*c* 0.9, pyridine)}; R_f 0.30 (70:1 CH_2Cl_2–MeOH). ^{13}C NMR: δ 22.52 (CH_3), 53.16 (C-2), 69.04 (C-6), 69.66 (C-3), 72.23, 73.89 (CH_2Ph), 78.50 (C-4), 79.76 (C-5), 90.91 (C-1), 127.42–128.17 [CH (Ph)], 138.82, 138.76 (C-ipso), 169.15 (C=O). Anal. Calcd for $C_{28}H_{33}NO_6$: C, 70.86; H, 6.77; N, 2.85. Found: C, 70.80; H, 6.82; N, 2.76.

Methyl 2-(2-acetamido-3,4,6-tri-O-benzyl-2-deoxy-β-D-glucopyranosyl)acetate (**11**).

—Obtained from **9c** by procedure *B*. Chromatographic purification on silica gel in 3:2 EtOAc–hexane, followed by a second purification in 19:1 CH_2Cl_2–acetone, afforded **11** in a yield of 50% as white crystals: mp 147–148°C; $[\alpha]_D$ +27.8° (*c* 0.1, $CHCl_3$); R_f 0.27 (6:4 EtOAc–hexane). ^1H NMR: δ 1.75 (s, 3 H, CH_3), 2.55 (d, 2 H, $J_{1,1'}$ 5.9 Hz, H-1'), 3.45 (m, 1 H, H-5), 3.55 (d, 1 H, $J_{3,4}$ 8.9, $J_{2,3}$ 9.9 Hz, H-3), 3.65 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 3.62 (s, 3 H, OCH_3), 3.65 (m, 2 H, H-6a,6b), 3.70 (m, 1 H, $J_{1,2}$ 10.2 Hz, H-1), 3.85 (m, 1 H, $J_{2,3}$ 9.9 Hz, H-2), 4.40–4.90 (3 AB, 6 H, 3 CH_2Ph), 5.45 (d, 1 H, $J_{NH,2}$ 9.1 Hz, NH), 7.00–8.00 (m, 15 H, Ar-H). ^{13}C NMR: δ 23.25 (CH_3), 37.85 (C-1'), 51.65 (OCH_3), 54.48 (C-2), 68.80 (C-6), 72.32, 74.38, 74.79 (*C*H_2Ph), 75.83 (C-1), 78.69 (C-4), 79.22 (C-5), 83.06 (C-3), 127.58–128.48 [CH (Ph)], 138.04, 138.16, 138.37 (C-ipso), 170.24, 172.10 (C=O).Anal. Calcd for $C_{32}H_{37}NO_7$: C, 70.20; H, 6.76; N, 2.56. Found: C, 70.12; H, 6.62; N, 2.41.

(2E,4E)*Methyl 4-acetamido-6,8-O-benzylidene-2,3,4,5-tetradeoxy-*D-erythro-*oct-2,4-dienonate* (**12**).—Obtained from 2-acetamido-2-deoxy-4,6-*O*-benzylidene-D-glucopyranose[16] (**2**) by procedure *B*. Chromatographic purification on silica gel in 50:1 and then 30:1 $CHCl_3$–MeOH afforded **12** (45%); mp 154–156°C; $[\alpha]_D$ −71° (*c* 0.1, $CHCl_3$); R_f 0.35 (19:1 $CHCl_3$–MeOH). ^1H NMR: δ 1.85 (s, 3 H, CH_3), 3.40 (m, 2 H, H-7,8b), 3.45 (s, 3 H, OCH_3), 4.50 (dd, 1 H, $J_{8a,8b}$ 4.1, $J_{7,8a}$ 3.8 Hz, H-8a), 3.95 (dd, 1 H, $J_{6,7}$ 8.0, $J_{5,6}$ 7.0 Hz, H-6), 4.03 (br s, 1 H, OH), 5.25 (s, 1 H, C*H*Ph), 5.65 (d, 1 H, $J_{5,6}$ 7.0 Hz, H-5), 5.70 (d, 1 H, $J_{2,3}$ 15.7 Hz, H-2), 6.95 (d, 1 H, $J_{2,3}$ 15.7 Hz, H-3), 7.20 (m, 5 H, Ar-H), 7.80 (s, 1 H, NH). ^{13}C NMR: δ 23.20 (CH_3), 51.80 (OCH_3), 65.69 (C-6), 71.37 (C-8), 78.09 (C-7), 100.88 (*C*HPh), 119.58 (C-2), 126.07, 128.28, 129.13 {*C*H (Ph)], 131.21 (C-5), 134.47 (C-4), 137.16 (C-ipso), 141.80 (C-3), 166.79, 170.29 (C=O). Anal. Calcd for $C_{18}H_{21}NO_6$: C, 62.24; H, 6.05; N, 4.03. Found: C, 62.13; H, 6.02; N, 3.68.

*Benzyl 2-acetamido-3-O-benzyl-2-deoxy-5,6-O-isopropylidene-β-*D-*glucofuranoside* (**4b**).—To a solution of 2-acetamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose[17] (**4a**) (0.70 g, 2.68 mmol) and benzyl bromide (2.0 mL) in DMF (14 mL), stirred at 0°C, were added portionwise BaO (1.9 g) and then $Ba(OH)_2$ (0.7 g). The mixture was stirred at 0°C for 5 h, and then for 18 h at room temperature. CH_2Cl_2 (150 mL) was added and the solution was filtered. The organic phase was washed with water, dried, and concentrated in vacuo. Chromatographic purification of the residue on silica gel in 7:1 EtOAc–hexane afforded **4b** (40%) as white crystals; mp 140–142°C; $[\alpha]_D$ −65° (*c* 0.1, $CHCl_3$); R_f 0.34 (3:7 hexane–EtOAc). ^1H NMR: δ 1.35, 1.40, 1.90 (3 s, 9 H, $3CH_3$), 3.92 (d, 1 H, $J_{3,4}$ 4.8 Hz, H-3), 4.03 (dd, 1 H, $J_{6a,6b}$ 8.6, $J_{5,6b}$ 6.2 Hz, H-6b), 4.05 (dd, 1 H, $J_{5,6a}$ 5.8, $J_{6a,6b}$ 8.6 Hz, H-6a), 4.32 (t, 1 H, $J_{3,4}$ 4.8, $J_{4,5}$ 5.2 Hz, H-4), 4.35 (m, 1 H, H-5), 4.45 (d, 1 H, $J_{NH,2}$ 7.3 Hz, H-2), 4.45–4.90 (2 AB syst., 4 H, CH_2Ph), 5.05 (s, 1 H, H-1), 6.50 (d, 1 H, $J_{NH,2}$ 7.3 Hz, NH), 7.00–7.50 (m, 10 H, Ar-H). ^{13}C NMR: δ 22.89, 25.23, 26.61 (CH_3), 59.85 (C-2), 66.51 (C-6), 69.43, 71.51 (*C*H_2Ph), 74.26 (C-5), 81.69 (C-4), 82.64 (C-3), 105.88 (C-1), 108.52 (C-iso), 127.39–128.26 [CH (Ph)], 137.41, 138.07 (C-ipso), 170.10 (C=O). Anal. Calcd for $C_{25}H_{31}NO_6$: C, 68.02; H, 7.03; N, 3.17. Found: C, 67.88; H, 7.20; N, 2.93.

2-Acetamido-3-O-benzyl-2-deoxy-5,6-O-isopropylidene-α-D-glucofuranose (**4c**).—Benzyl glycoside **4b** (0.86 g, 1.95 mmol), Pd–C (0.70 g 0.66 mmol), and ammonium formate (0.3 g, 4.8 mmol) were stirred in anhyd MeOH (30 ml) at 70°C. The reaction was monitored by TLC (19:1 $CHCl_2$–MeOH). After 6 min, the mixture was filtered and the catalyst was washed with hot MeOH. The mixture was concentrated in vacuo. Chromatographic purification on silica gel in 60:1 CH_2Cl_2–MeOH afforded the α,β-furanose (60%) (α/β 4:1); mp 105°C; $[\alpha]_D$ −22° (*c* 0.15, $CHCl_3$); R_f 0.30 (30:1 CH_2Cl_2–MeOH). ^{13}C NMR: δ 22.77, 23.10, 25.11, 26.44, 26.59 (CH_3 β and α), 58.04 (C-2α), 59.86 (C-2β), 66.30 (C-6α), 66.89 (C-6β), 71.76 (CH_2Ph α), 72.45 (CH_2Ph β), 73.48 (C-5α), 73.66 (C-5β), 77.54 (C-4α), 81.14 (C-4β), 82.07 (C-3β), 82.78 (C-3α), 94.96 (C-1α), 101.55 (C-1β), 108.58 (CMe_2 α), 108.87 (CMe_2 β), 127.55–128.37 [CH (Ph)], 137.04 (C-ipso β), 138.01 (C-ipso α), 170.50 (C=O α), 170.79 (C=O β).

Recrystallization from MeOH afforded the α anomer **4c**; mp 114–115°C; $[\alpha]_D$ −12° (*c* 0.2, $CHCl_3$). ^1H NMR: δ 1.30, 1.35, 1.95 (3 s, 9 H, $3CH_3$), 3.90 (dd, 1 H, $J_{2,3}$ 2.4, $J_{3,4}$ 4.8 Hz, H-3), 3.95 (m, 2 H, H-6a,6b), 4.20 (dd, 1 H, $J_{3,4}$ 4.8, $J_{4,5}$ 5.6 Hz, H-4), 4.30 (m, 2 H, H-2,5), 4.55 (d, 1 H, *J* 11.9 Hz, C*H*Ph), 4.75 (d, 1 H, *J* 11.9 Hz, C*H*Ph), 5.50 (d, 1 H, $J_{1,2}$ 5.3 Hz, H-1), 5.80 (s, 1 H, OH), 6.50 (d, 1 H, $J_{NH,2}$ 6.8 Hz, NH), 7.00–7.50 (m, 5 H, Ar-H). ^{13}C NMR; δ 23.19, 25.07, 26.42 (CH_3), 58.12 (C-2), 66.20 (C-6), 71.75 (CH_2Ph), 73.53 (C-5), 78.85 (C-4), 82.72 (C-3), 95.01 (C-1), 108.56 (CMe_2), 127.57, 127.77, 128.22 [*C*H (PH)], 137.98 (C-ipso), 170.25 (C=O). Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.50; H, 7.17; N, 3.98. Found: C, 61.22; H, 6.92; N, 3.47.

Methyl 2-(2-acetamido-3-O-benzyl-2-deoxy-5,6-O-isopropylidene-β-D-glucofuranosyl)acetate (**13**).—Obtained from **4c** by procedure *B*. Chromatographic purification on silica gel in 3:2 EtOAc–hexane, followed by a second purification in 100:5:1 EtOAc–hexane–MeOH, afforded **13** as a colourless syrup (60%); $[\alpha]_D$ −12° (*c* 0.1, $CHCl_3$); R_f 0.30 (7:3 EtOAc–hexane). ^1H NMR: δ 1.25, 1.30, 1.90 (3 s, 9 H, 3 CH_3), 2.50 (m, 2 H, H-1'a,1'b), 3.60 (s, 3 H, OCH_3), 3.82 (dd, 1 H, $J_{5,6b}$ 6.4, $J_{6a,6b}$ 8.5 Hz, H-6b), 3.90 (d, 1 H, $J_{3,4}$ 4.2 Hz, H-3), 4.00 (dd, 1 H, $J_{5,6a}$ 6.4, $J_{6a,6b}$ 8.5 Hz, H-6a), 4.08 (dd, 1 H, $J_{3,4}$ 4.2, $J_{4,5}$ 6.4 Hz, H-4), 4.25 (q, 1 H, $J_{4,5} = J_{5,6a} = J_{5,6b} = 6.4$ Hz, H-5), 4.50 (d, 1 H, $J_{NH,2}$ 8.2 Hz, H-2), 4.51 (m, 1 H, H-1), 4.55 (d, 1 H, *J* 11.9 Hz, C*H*Ph), 4.75 (d, 1 H, *J* 11.9 Hz, C*H*Ph), 6.50 (d, 1 H, $J_{NH,2}$ 8.2 Hz, NH), 7.10–7.50 (m, 5 H, Ar-H). ^{13}C NMR: δ 22.14, 24.48, 25.48 (CH_3), 33.64 (C-1), 50.99 (OCH_3), 54.93 (C-2), 65.46 (C-6), 71.15 (CH_2Ph), 72.97 (C-5), 74.33 (C-1), 79.81 (C-4), 82.15 (C-3), 107.52 (C iso), 126.71–127.33 [*C*H (Ph)], 136.71 (C-ipso), 169.10, 170.20 (C=O). Anal. Calcd for $C_{21}H_{29}NO_7$: C, 61.90; H, 71.9; N, 3.43. Found: C, 62.04; H, 7.12; N, 3.20.

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