Pentenyl Mannosides in the Synthesis of *N*-Acylmannopyranosyl Amides: Conformational Analysis of Intermediates

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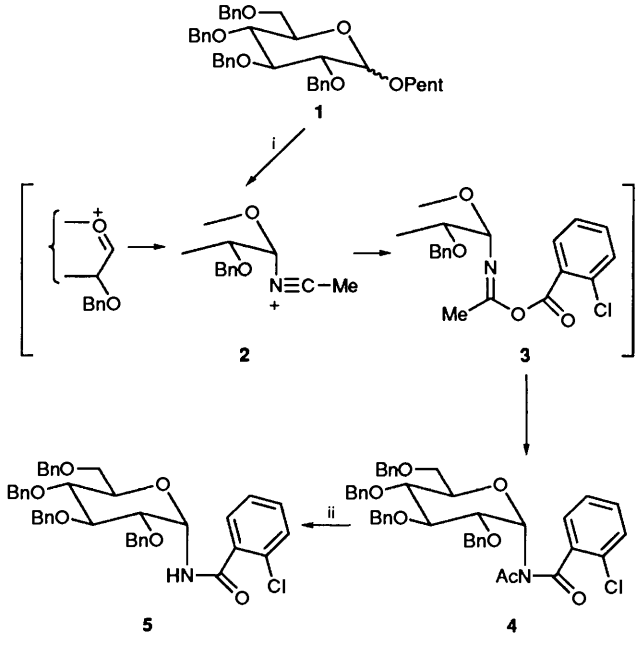
The reaction of a pentenyl mannopyranoside with *N*-bromosuccinimide in the presence of acetonitrile and a carboxylic acid leads to an *N*-acetyl-*N*-acyl-α-D-mannopyranosyl imide, the acetyl group being derived from acetonitrile, and the acyl group from the carboxylic acid. The latter can be aromatic or aliphatic as exemplified with a protected aspartic acid from which an α-mannopyranosyl asparagine is obtained. Chemoselective deacetylation can be effected either with sodium methoxide or piperidine depending on whether the other acyl group is aromatic or aliphatic, respectively. ^{1}H NMR data, conformational and molecular mechanics analyses show that the *N*,*N*-diacyl derivatives exist in a conformation lying between a $B_{2,5}$ boat and a $^1S_5$ twist boat.

We have previously shown that *N*-bromosuccinimide (NBS) induced cleavage of the glycosidic ketal of the perbenzylated pent-4-enyl α,β-D-glucopyranoside **1** in acetonitrile generates stereoselectively axial glucopyranosyl acetonitrilium ions, **2**, that on trapping with 2-chlorobenzoic acid yield, *via* rearrangement of intermediate **3**, the perbenzylated *N*-acetyl-2-chloro-*N*-(α-D-glucopyranosyl)benzamide **4**.[1] Formation of compound **4** represents the kinetic product of the reaction, given the absence of any products resulting from β-acetonitrilium ions which would be favoured by the reverse anomeric effect.[2] We also found that the *N*-acetyl moiety of compound **4** could be cleaved chemoselectively with sodium methoxide to give the perbenzylated 2-chloro-*N*-(α-D-glucopyranosyl)benzamide derivative **5** (Scheme 1). This methodology has been used by us to construct the *N*-(α-D-glucosyl)asparagine linkage found in the nephritogenoside trisaccharide core structure isolated from the glomerular basement membrane of rats.[3] Subsequently, our methodology for the same target has recently been successfully applied to thioglycoside analogues by Sasaki *et al.*[4] Recently the intermediacy of axially orientated nitrilium ions, both as agents for direct glycosylation reactions[5–9] and as for the synthesis of oxazolines through intramolecular trapping by adjacent hydroxy groups,[10] has been documented. We now report our continuing studies on the generation of mannopyranosyl acetonitrilium ions and subsequent trapping with 2-chlorobenzoic acid.



Pent = Pent-4-enyl, Bn = benzyl, Ac = acetyl

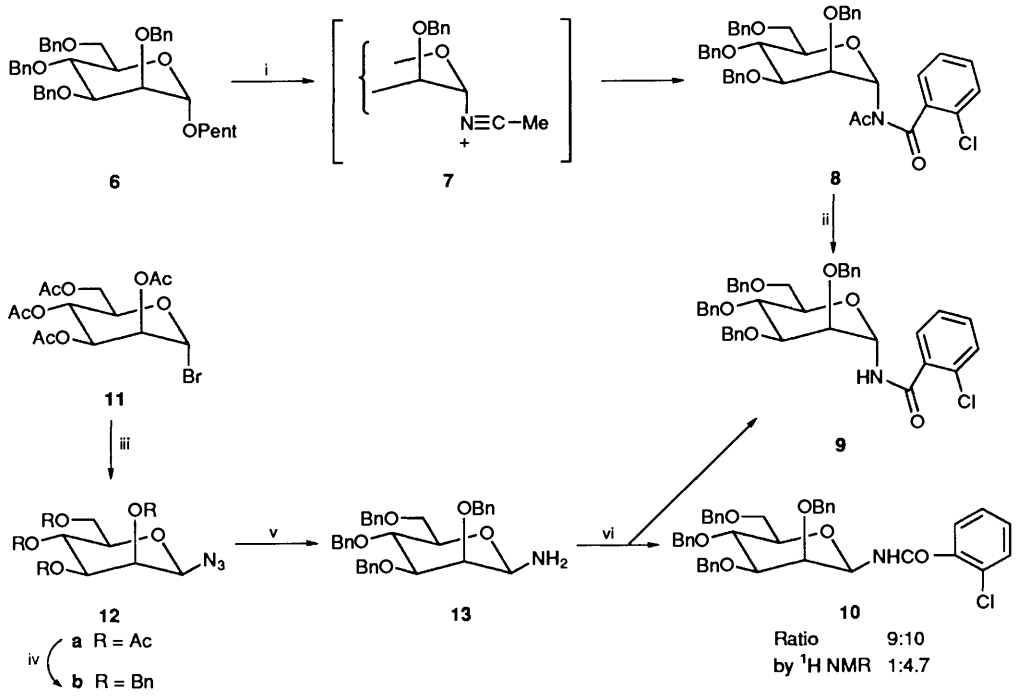
Scheme 1 *Reagents:* i, NBS, 2-chlorobenzoic acid, MeCN; ii, NaOMe

Results and Discussion

Reaction of the perbenzylated pent-4-enyl α-D-mannopyranoside **6**[11] with NBS and 2-chlorobenzoic acid in acetonitrile led to the formation of the perbenzylated *N*-acetyl-2-chloro-*N*-(α-D-mannopyranosyl)benzamide **8** in 61% yield, with no evidence of any β-anomer (Scheme 2). In mannose derivatives described by a $^4C_1$ chair conformation, the size of the coupling constant $J_{1,2}$ is not a reliable criterion for determining the anomeric configuration. However, in the case of compound **8** the magnitude of $J_{1,2}$ 9.0 Hz was indicative of a *trans* diaxial relationship between the protons concerned. Such an alignment between 1-H and 2-H could only arise by having the aglycone in the α orientation with the pyranose ring substantially distorted from the $^4C_1$ chair.

Evidence for the α-D-*manno* configuration for compound **8** was sought by treatment with sodium methoxide, which led to selective *N*-deacetylation and formation of a perbenzylated 2-chlorobenzamide tentatively assigned as compound **9**, in 91% yield (Scheme 2). However, again the value $J_{1,2}$ 3.3 Hz in the ^{1}H NMR spectrum did not provide a clear basis for assigning the α-D configuration in compound **9**. However, the size of the coupling constants of the other protons clearly defined the *manno* skeleton with a $^4C_1$ chair conformation.

Confirmation of the axial orientation of the 2-chlorobenzamide moiety in compound **9** and thus the α-configuration of the imide moiety in compound **8**, was provided by synthesis of the perbenzylated 2-chloro-*N*-(β-D-mannopyranosyl)benzamide **10**, by adaptation of a route developed previously for β-acetamides.[1] Hence, the peracetylated β-D-mannopyranosyl azide **12a** was prepared by treatment of the corresponding mannopyranosyl bromide **11**[12] with sodium azide in hexamethylphosphoric triamide (HMPA), according to the procedure of Györgydeák and Paulsen[13] (Scheme 2). Deacetylation of compound **12a**, followed by benzylation, gave the perbenzylated β-D-mannopyranosyl azide analogue **12b** (66%) (Scheme 2). Catalytic hydrogenation of the azide moiety was achieved chemoselectivity[1] using 10% Pd/C and careful monitoring of the reaction. The resulting amine **13** (95%) was acylated with 2-chlorobenzoyl chloride to afford an inseparable anomeric

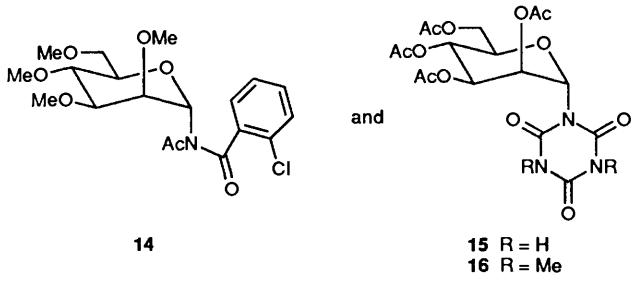


Scheme 2 *Reagents:* i, NBS, 2-chlorobenzoic acid, MeCN; ii, NaOMe; iii, NaN_3, HMPA; iv, NaOMe; then BnBr, NaH; v, Pd/C, H_2; vi, 2-chlorobenzoyl chloride, pyridine, Et_2O

mixture of perbenzylated 2-chloro-*N*-(D-mannopyranosyl)-benzamides in the ratio 4.7:1 by ^1H NMR spectroscopy (Scheme 2). The minor component gave ^1H NMR resonances superposable upon those of compound **9**, while the major component, **10**, gave pyranoid ring-coupling constants in accord with the *manno* configuration in a $^4C_1$ chair conformation. Again, as with compound **9**, the orientation of the 2- chlorobenzamide moiety in compound **10** could not be established solely on the basis of the $J_{1,2}$ value 1.0 Hz. However, the higher up-field resonances recorded for 1-H and 5-H in compound **10** (δ 5.40 and 3.60–3.54, respectively) relative to those of compound **9** (δ 5.95 and 3.84–3.72, respectively) clearly delineated compound **10** as the β-anomer and, by corollary, compound **9** as the α-anomer.

In view of the fact that amine **13** was homogenous judging from its ^1H NMR spectrum, we concluded that anomerization to yield compound **9** had occurred during the acylation step.

To probe the ring conformation of the α-imide **8** we turned to molecular dynamics, choosing *N*-acetyl-2-chloro-*N*-(2,3,4,6-tetra-*O*-methyl-α-D-mannopyranosyl)benzamide **14** as a model. The Concord 3D builder[14] was used to construct the initial structure in a $^4C_1$ chair conformation. Molecular dynamics (DISCOVER,[15] CVFF force field) was then used to sample conformational space of this model compound. The *in vacuo* simulation was carried out at 27 °C for 3 ps and, following clustering, a representative conformation was selected. This conformation was energy-minimized with DISCOVER and used as the input structure for the distance geometry program DEGOM.[16] Torsional constraints derived from proton ^1H NMR ring-coupling constants of compound **8** according to the Karplus equation were applied. A molecular model of the resulting structures suggests that the best fit for compound **14**, and hence compound **8**, is a flexible conformation between $B_{2,5}$ boat and $^1S_5$ skew, in which the α-imide aglycone takes a pseudoequatorial orientation with the *N*-acetyl group carbonyl bisecting protons 2-H and 5-H. Several further features of the ^1H NMR spectrum of compound **8** are in line with such a description. First the significant downfield chemical shifts of 2-H (δ 4.77) and 5-H (δ 4.37–4.32) can be reconciled with the deshielding effect of the bisecting amido residue, and, secondly, difference NOE studies showed an 8% enhancement for 5-H and 7% enhancement for 3-H upon irradiation of 2-H, with no effect on 1-H.



Recently Jochims and co-workers[17] synthesized the per-acetylated 1-(α-D-mannopyranosyl)isocyanuric acid derivatives **15** and **16**, and proposed that they existed in solution as dynamic equilibria of flexible $^OS_2$ skew conformations bearing pseudoequatorial aglycones. In this respect it is worth noting that $^OS_2$ skew, $B_{2,5}$ boat and $^1S_5$ skew are closely related.*

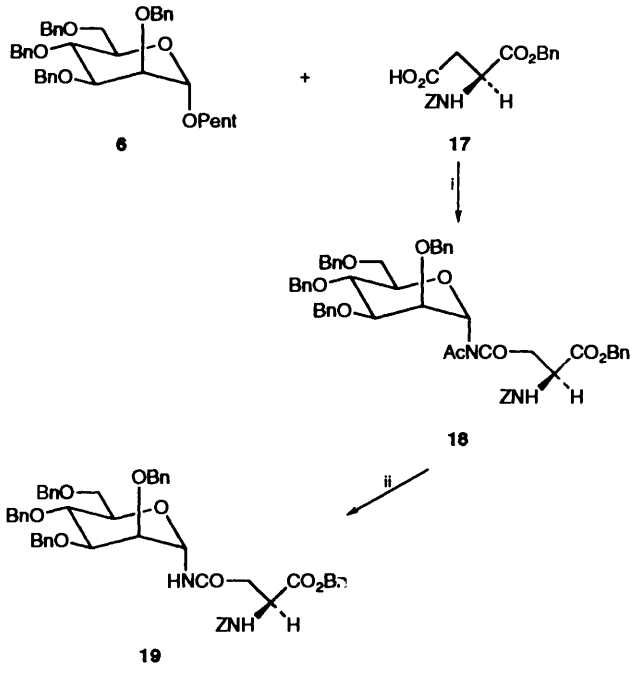
Assuming a similar cascade of events as depicted in Scheme 1 it is interesting to compare the conformation of the α-imide **8**, with the flattened $^4C_1$ chair conformation observed for the *gluco*-α-imide **4**.[1] It is clear in both cases that there is a driving force for the α-linked imide aglycones to adopt pseudoequatorial positions. We proposed in the case of compound **4** that the distortion of the pyranose ring was due largely to the steric bulk of the imide moiety,[1] and we now suggest a similar explanation for compound **8**, given that removal of the *N*-acetyl group of compound **8** results in α-2-chlorobenzamide **9**, assuming a more conventional $^4C_1$ chair *manno* conformation.

The differing degrees of conformational change from the $^4C_1$ chair in *gluco* and *manno* configurations of the α-imides may be attributed to the configuration of the C-2 alkoxy group. In the case of *gluco*-α-imide **4** movement of the axial α-imide aglycone

* Rules for conformation nomenclature for five- and six-membered rings, in monosaccharides and their derivatives, are given in ref. 18.

into a pseudoequatorial position requires going past the equatorial C-2 alkoxy group. Such steric congestion in the *manno*-α-imide **8** is minimized since the C-2 alkoxy group is axial.

Replacement of 2-chlorobenzoic acid with 1-benzyl *N*-benzyloxycarbonyl-L-aspartate **17**[19] trapped the mannopyranosyl acetonitrilium ion to afford stereoselectively the α-linked asparagine imide derivative **18** (68%, Scheme 3). By virtue of the large $J_{1,2}$ coupling constant (9.2 Hz) and low-field chemical shifts of 2-H and 5-H in the ^{1}H NMR spectrum of compound **18** a similar pyranoid ring conformation to that of compound **8** may be assigned.



Scheme 3 *Reagents:* i, NBS, MeCN; ii, piperidine, DMF

In our previous studies directed toward the *N*-(α-D-glucosyl)aspartic linkage in the nephritogenoside trisaccharide core structure,[3] we found that sodium methoxide cleavage of the *N*-acetyl moiety of the α-glucosyl asparagine imide analogue of compound **18** also affected the peptide linkages, and we developed the use of piperidine as the chemoselective reagent of choice.[3] Accordingly, treatment of the α-mannosyl asparagine imide **18** with piperidine in *N*,*N*-dimethylformamide (DMF) for 1 h led exclusively to the *N*-deacetylated glycopeptide **19** (90%, Scheme 3).

Our results show that addition of acetonitrile to the *manno* oxocarbenium ion occurs from the α-face as with its *gluco* counterpart, giving the nitrilium ions **7** (Scheme 2) and **2** (Scheme 1) respectively. It has been shown that use of nitriles as solvent in low-temperature glycosidation reactions of *galacto*[6,7] and *gluco*[5,7,8] donors containing non-participating C-2 substituents can lead to enhanced β-coupling, and in the case of neuramic acid derivatives[9] enhanced α-selectivity. These results are in accord with the kinetic formation of intermediate axial nitrilium ions, that subsequently undergo S_N2 displacement at the anomeric centre. However, with corresponding *manno* donors[8] no such preference is observed. Lack of stereoselectivity may result from a mismatch between kinetic generation of α-mannopyranosyl nitrilium ions and thermodynamic stability of the resulting β-mannopyranosides.

Experimental

Column chromatography was carried out on Kieselgel (230–400 mesh) with the eluent specified in parentheses. All reactions requiring anhydrous conditions were conducted in oven-dried apparatus under a static atmosphere of argon. Organic extracts were dried over Na_2SO_4 and evaporated at aspiration pressure using a rotary evaporator unless otherwise stated. Light petroleum refers to the fraction boiling between 35 and 60 °C. Diethyl ether (referred to as ether), dichloromethane, pyridine, piperidine, methanol, acetonitrile, and DMF were dried and distilled using standard methods.[20] NBS was recrystallized from hot water and dried *in vacuo* over phosphorus pentaoxide. ^{1}H NMR spectra were recorded in deuteriochloroform at 300 MHz with a Varian XL-300 spectrometer. Chemical shifts are reported in δ-values relative to tetramethylsilane, and *J*-values are given in Hz. ^{13}C NMR spectra were recorded in deuteriochloroform at 75 MHz with a Varian XL-300 spectrometer. Chemical shifts are reported in δ-values relative to internal solvent standard (δ_C 77.0). Optical rotations were measured in chloroform solutions using a Perkin-Elmer 241 instrument. $[\alpha]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}. TLC was conducted on precoated Kieselgel 60 °F 254 (Art. 5554; Merck) and spots were visualized using a mixture of ammonium molybdate(VI) tetrahydrate and cerium(IV) sulfate tetrahydrate in 10% aq. sulfuric acid. M.p.s were recorded with a Buchi 510 apparatus and are uncorrected. Elemental combustion analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

Reaction of Pent-4-enyl 2,3,4,6-Tetra-O-benzyl-α-D-mannopyranoside **6** *with NBS and 2-Chlorobenzoic Acid.*—NBS (455 mg, 2.56 mmol) and 2-chlorobenzoic acid (178 mg, 1.14 mmol) was added to a solution of compound **6**[11] (606 mg, 1.00 mmol) in dry acetonitrile (10 cm^3). The reaction flask was wrapped in silver foil and the mixture was stirred under argon at room temperature for 3 h. The resulting green solution was then quenched with 10% aq. sodium thiosulfate (2 cm^3) and the acetonitrile was removed under reduced pressure. The resulting residue was partitioned between water (20 cm^3) and dichloromethane (20 cm^3), the layers were thoroughly stirred and separated, and the aqueous layer was further extracted with dichloromethane (3 × 25 cm^3). The combined organic layers were washed with water (2 × 25 cm^3), and then dried, and the solvent was removed under reduced pressure. Flash chromatography of the residue [light petroleum–ethyl acetate (8:2)] gave *N-acetyl-2-chloro*-N-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)*benzamide* **8** as an oil (435 mg, 61%), $[\alpha]_D^{23}$ +13.8 (*c*, 0.63); δ_H 7.37–7.12 (24 H, ArH), 5.62 (1 H, d, *J* 9.0, 1-H), 4.77 (1 H, dd, J_1 9.0, J_2 2.7, 2-H), 4.55–4.38 (8 H, m, 4 × CH_2Ph), 4.37–4.32 (1 H, m, 5-H), 3.91 (1 H, t, *J* 2.4, 3-H), 3.68 (1 H, dd, J_1 3.9, J_2 3.0, 4-H), 3.57–3.46 (2 H, m, 6-H$_2$) and 2.31 (3 H, s, COMe); δ_C (*inter alia*) 174.15, 171.22 (C=O) and 81.03 (C-1) (Found: C, 71.75; H, 5.9; N, 1.9. $C_{43}H_{42}ClNO_7$ requires C, 71.71; H, 5.88; N, 1.94%).

2-Chloro-N-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)-*benzamide* **9**.—To a solution of compound **8** (200 mg, 0.28 mmol) in dry dichloromethane (4 cm^3) was added dropwise 1.85 mol dm^{-3} sodium methoxide in methanol (0.23 cm^3, 0.43 mmol). The resulting solution was stirred at room temperature under argon for 1 h, then saturated aq. ammonium chloride (5 cm^3), water (20 cm^3) and dichloromethane (25 cm^3) were added. The layers were thoroughly stirred and separated, and the aqueous layer was further extracted with dichloromethane (3 × 25 cm^3). The combined dried extracts were evaporated under reduced pressure and the residue was purified by flash chromatography [light petroleum–ethyl acetate (7:3)] to give the title compound **9** as an oil (171 mg, 91%), $[\alpha]_D^{21}$ +11.0 (*c*, 0.69); δ_H (the 2-chlorobenzamide locants are primed) 7.67 (1 H, dd, J_1 7.1, J_2 1.4, 6′-H), 7.48–7.15 (23 H, m, ArH), 6.69 (1 H, d, *J* 7.5, NH), 5.95 (1 H, dd, J_1 7.4, J_2 3.3, 1-H), 4.81–4.46 (8 H, m, 4 × CH_2Ph),

4.00 (1 H, t, *J* 7.9, 4-H), 3.95 (1 H, t, *J* 3.0, 2-H) and 3.84–3.72 (4 H, m, 3-, 5-H, and 6-H_2); δ_C(*inter alia*) 165.76 (C=O) and 78.03 (C-1) (Found: C, 72.5, H, 6.0; N, 2.0. $C_{41}H_{40}ClNO_6$ requires C, 72.61; H, 5.94; N, 2.07%).

2,3,4,6-*Tetra*-O-*benzyl*-β-D-*mannopyranosyl Azide* **12b**.—To a solution of compound **12a**[13] (480 mg, 1.29 mmol) in dry methanol (15 cm^3) was added 1.84 mol dm^{-3} sodium methoxide in methanol (6 cm^3, 11.04 mmol). The resulting solution was stirred at room temperature under argon for 3 h, then neutralized with Dowex 50W-H^+. After filtration the solvent was removed under reduced pressure and the residue dried over P_2O_5 *in vacuo*. To the residue were added dry DMF (10 cm^3), tetrabutylammonium iodide (100 mg) and sodium hydride (60% dispersion in oil; 204 mg, 5.10 mmol). Benzyl bromide (0.61 cm^3, 5.13 mmol) was then added and the resulting mixture was stirred at room temperature overnight. The bulk of DMF was evaporated off at 0.1 mmHg and the residue was partitioned between water (50 cm^3) and dichloromethane (50 cm^3). The layers were thoroughly stirred and separated, and the aqueous layer was further extracted with dichloromethane (50 cm^3). The combined organic layers were dried, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (dichloromethane) to give the title compound as an oil that slowly solidified to give *compound* **12b** as a solid (480 mg, 66%), m.p. 52–53 °C; $[\alpha]_D^{22}$ −6.2 (*c*, 6.44); δ_H 7.45–7.17 (20 H, m, ArH), 4.95–4.56 (8 H, m, 4 × CH_2Ph), 4.39 (1 H, d, *J* 1.1, 1-H), 3.96 (1 H, t, *J* 9.6, 4-H), 3.88 (1 H, dd, J_1 2.8, J_2 1.2, 2-H), 3.78 (2 H, d, *J* 3.7, 6-H_2) and 3.56–3.52 (2 H, m, 3- and 5-H); δ_C (*inter alia*) 86.49 (C-1) (Found: C, 71.9; H, 6.2; N, 7.4. $C_{34}H_{35}N_3O_5$ requires C, 72.19; H, 6.24; N, 7.43%).

2-*Chloro*-N-(2,3,4,6-*tetra*-O-*benzyl*-α,β-D-*mannopyranosyl*)-*benzamide* **9** *and* **10**.—A solution of azide **12b** (850 mg, 1.50 mmol) in ethanol (15 cm^3) containing 10% Pd/C (200 mg) was hydrogenated at atmospheric pressure and room temperature. After 2 h the mixture was filtered through Celite, which was then thoroughly washed with ethanol (2 × 10 cm^3). The combined filtrates were evaporated under reduced pressure to give 2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranosylamine **13** as a glass (770 mg, 95%), δ_H 7.41–7.12 (20 H, m, ArH), 5.10–4.49 (8 H, m, 4 × CH_2Ph), 4.13 (1 H, d, *J* 0.6, 1-H), 3.92 (1 H, dd, J_1 2.8, J_2 0.7, 2-H), 3.82 (1 H, t, *J* 9.6, 4-H), 3.73 (1 H, dd, J_1 10.4, J_2 1.9, 3-H), 3.64–3.57 (2 H, m, 6-H_2), 3.49–3.43 (1 H, m, 5-H) and 2.05–1.75 (2 H, br s, NH_2).

To a cooled solution (0 °C) of amine **13** in dry ether (20 cm^3) were added 2-chlorobenzoyl chloride (400 mg, 2.29 mmol) and dry pyridine (2 cm^3). The resulting mixture was stirred at 0 °C for a further 0.5 h, after which it was filtered and the white precipitate was collected, and washed with ether (50 cm^3). The combined filtrates were evaporated under reduced pressure and the crude product was purified by flash chromatography (gradient elution with 10–30% ethyl acetate in light petroleum) to give an oil (827 mg, 85%) consisting of β-saccharide **10** and its previously described anomer **9** in 4.7:1 ratio. For compound **10**: δ_H 7.47–7.18 (24 H, ArH), 6.99 (1 H, d, *J* 9.3, NH), 5.40 (1 H, dd, J_1 7.3, J_2 1.0, 1-H), 4.82–4.51 (8 H, m, 4 × CH_2Ph), 4.09 (1 H, t, *J* 9.5, 4-H), 3.96 (1 H, br d, *J* 1.3, 2-H), 3.83–3.74 (3 H, m, 3-H and 6-H_2), 3.60–3.54 (1 H, m, 5-H); δ_C (*inter alia*) 165.63 (C=O) and 83.68 (C-1).

N^4-*Acetyl*-N^2-*benzyloxycarbonyl*-N^4-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)-L-*asparagine Benzyl Ester* **18**.—To a solution of compound **6**[11] (310 mg, 0.51 mmol) in dry acetonitrile (10 cm^3) were added 1-benzyl *N*-benzyloxycarbonyl-L-aspartate **17**[19] (214 mg, 0.60 mmol) and NBS (205 mg, 1.15 mmol). The mixture was stirred in the dark at room temperature under argon for 1 h. The resulting green solution was then quenched with 10% aq. sodium thiosulfate (2 cm^3) and the acetonitrile was removed under reduced pressure. The resulting residue was partitioned between water (20 cm^3) and dichloromethane (20 cm^3), the layers were thoroughly stirred and separated, and the aqueous layer was further extracted with dichloromethane (2 × 25 cm^3). The combined organic layers were washed with water (2 × 25 cm^3), then were dried, and the solvent was removed under reduced pressure. Flash chromatography of the residue [light petroleum–ethyl acetate (3:1)] gave *compound* **18** as an oil (320 mg, 68%), $[\alpha]_D^{22}$ +52.2 (*c*, 0.77); δ_H 7.41–7.12 (30 H, m, ArH), 5.88 (1 H, d, *J* 9.0, N*H*CO_2Bn), 5.73 (1 H, d, *J* 9.2, 1-H), 5.22–5.04 (4 H, m, 2 × CO_2CH_2Ph), 4.76–4.66 (1 H, m, $COCH_2CH$) 4.64–4.26 (10 H, m, 4 × OCH_2Ph, 2- and 5-H), 3.87 (1 H, t, *J* 2.4, 3-H), 3.69–3.52 (4 H, m, 4-H, 6-H_2 and $COCH_AH_BCH$), 3.16 (1 H, dd, J_1 17.8, J_2 3.9, $COCH_AH_B$) and 2.22 (s, 3 H, COMe) (Found: C, 71.4; H, 6.2; N, 3.0. $C_{55}H_{56}N_2O_{11}$ requires C, 71.72; H, 6.13; N, 3.04%).

N^2-*Benzyloxycarbonyl*-N^4-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)-L-*asparagine Benzyl Ester* **19**.—A solution of imide **18** (250 mg, 0.27 mmol) in dry DMF (5 cm^3) and dry piperidine (0.1 cm^3, 1.01 mmol) was stirred under argon for 1 h, then was concentrated at 0.1 mmHg. The residue was partitioned between water (50 cm^3) and chloroform (50 cm^3), the layers were thoroughly stirred and separated, and the aqueous layer was further extracted with chloroform (2 × 25 cm^3). The combined organic layers were washed with water (1 × 50 cm^3), then were dried, and the solvent was removed under reduced pressure. Flash chromatography [light petroleum–ethyl acetate (2:1)] of the residue gave *compound* **19** as an oil (215 mg, 90%), $[\alpha]_D^{22}$ +13.9 (*c*, 0.55); δ_H 7.36–7.13 (30 H, m, ArH), 6.36 (1 H, d, *J* 7.4, N*H*$COCH_2$), 5.96 (1 H, d, *J* 8.4, N*H*CO_2Bn), 5.68 (1 H, dd, J_1 7.3, J_2 4.1, 1-H), 5.19–5.02 (4 H, m, 2 × CO_2CH_2Ph), 4.73–4.46 (9 H, m, 4 × OCH_2Ph, $COCH_2CH$), 3.90 (1 H, t, *J* 7.0, 4-H), 3.79–3.74 (5 H, m, 2-, 3-, 5-H and 6-H_2), 2.87 (1 H, dd, J_1 16.1, J_2 4.2, $COCH_AH_BCH$) and 2.66 (1 H, dd, J_1 15.9, J_2 2.8, $COCH_AH_BCH$) (Found: C, 72.0; H, 6.3; N, 3.2. $C_{53}H_{54}N_2O_{10}$ requires C, 72.42; H, 6.19; N, 3.19%).

Acknowledgements

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