Studies related to carba-pyranoses: a strategy for the synthesis of β-1,3-glycosidically linked aminomonocarba-disaccharides[1]

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Received (in Cambridge, UK) 19th June 2001, Accepted 19th July 2001
First published as an Advance Article on the web 23rd August 2001

The reaction of (*E*)-1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-3-(trimethylsiloxy)buta-1,3-diene **1** and maleic anhydride gives cycloadduct **10** and ketone **12**. Reduction of ketone **13**, formed by acidic hydrolysis of silyl enol ether **10**, with sodium cyanoborohydride in acetic acid gives an 83 : 17 mixture of the γ- and δ-lactone **14** and **15**. γ-Lactone **14** is transformed into the aminomonocarba-disaccharide, 4-acetamido-2,4-dideoxy-3-*O*-(β-D-gluco-pyranosyl)-5a-carba-β-L-*lyxo*-hexopyranose **7**, using a five-step procedure involving the Curtius rearrangement of acyl azide **16**. A similar sequence using γ-lactone **21**, prepared from ketone **12**, gives the protected aminomonocarba-disaccharide, 4-acetamido-1,6-di-*O*-acetyl-2,4-dideoxy-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-5a-carba-β-D-*lyxo*-hexopyranose **8**.

Reaction of cycloadduct **10** with dimethyldioxirane gives acyloin **26**. Acetylation under acidic conditions followed by reduction with sodium cyanoborohydride in acetic acid gives a 75 : 25 mixture of the γ- and δ-lactone **28** and **29**. Using a sequence similar to that employed for the preparation of compounds **7** and **8**, γ-lactone **28** is converted into the fully substituted aminomonocarba-disaccharide, 4-acetamido-1,2,6-tri-*O*-acetyl-4-deoxy-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-5a-carba-β-L-galactopyranose **9**.

Introduction

Over the past few years, we have shown that anomerically linked glycopyranose units can confer a useful degree of facial reactivity on 1-oxybuta-1,3-dienes in cycloaddition reactions.[2–9] For example, the diene **1** displays good *Re*-face reactivity and undergoes highly *endo*-selective Diels–Alder reactions[2,3,5] with cyclic dienophiles of type **2** to give predominantly cycloadducts of type **3**. As well as endeavouring to understand the basis of the stereoinduction, we have sought to employ such cyclo-additions in the assembly of compounds of biological relevance. Within the latter context, asymmetric syntheses of anthracyclinones,[2,5] bostrycins,[6] dehydropiperazic acids[7,8] and 5-arylpentopyranoses[9] have been effected.

In the aforementioned syntheses, the glycopyranose moiety served a 'chiral auxiliary' role, being removed from the pre-target structures by mild acidic hydrolysis. Mindful of the emerging importance of saccharides in medicinal chemistry,[10,11] we have also sought to prepare oligosaccharide-like compounds that retain the glycopyranose unit. Within this framework, monocarba-disaccharides that feature a pyranose entity glycosidically linked to a carba-pyranose moiety have attracted our attention. Such assemblies, which are found in some amino-glycoside antibiotics, *e.g.* validamycin A **4**,[12] have been the subject of relatively few synthetic endeavours.

We planned to use Diels–Alder reactions to construct such monocarba-disaccharides and initially decided to employ the readily available diene **1**.[2,3] In consequence, any targets would feature a β-D-glucopyranosyl unit. Noting that few acetal-linked (1⟶3)-monocarba-disaccharides had been synthesised[13] (examples include compounds **5** and **6**[14]), we decided to prepare further representatives of this group. Earlier,[1] we communicated our initial findings where we synthesised 4-acetamido-2,4-dideoxy-3-*O*-(β-D-glucopyranosyl)-5a-carba-β-L-*lyxo*-hexopyranose **7**. This paper describes those findings in full and extensions to that work which culminated in the syntheses of a relative with the D-*lyxo* configuration, *i.e.* **8**, and a fully substituted monocarba-disaccharide, *i.e.* 4-acetamido-1,2,6-tri-*O*-acetyl-4-deoxy-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-5a-carba-β-L-galactopyranose **9**.

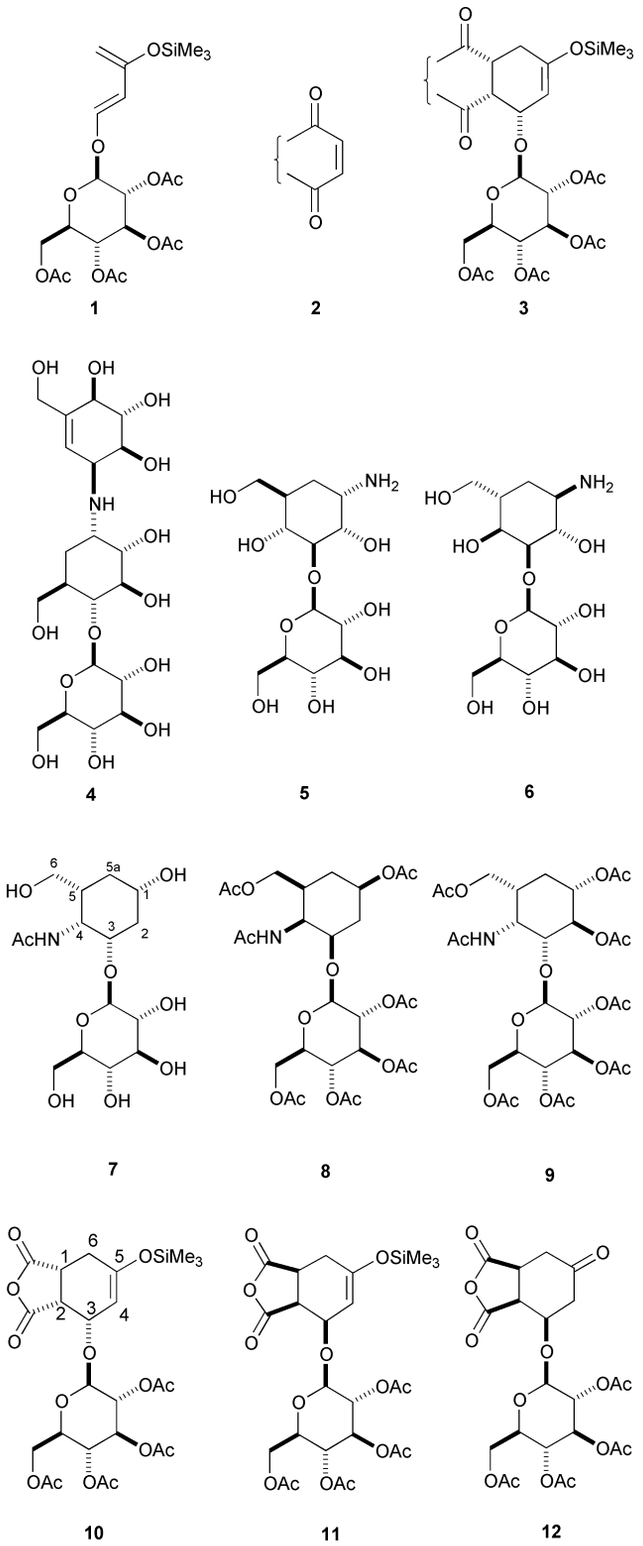
Results and discussion

The strategy employed for the synthesis of (1⟶3)-linked monocarba-disaccharides would require that C-5 of cyclo-adducts, typified by **10**, would become the pseudo-anomeric centre of the carba-pyranose ring. This necessitates that the anhydride carbonyl function at C-1 be selectively reduced to a hydroxymethyl group and that that at C-2 be replaced with heteroatom functionality. With respect to the latter issue, it was envisaged that amino functionality could be introduced with retention of stereochemistry using the Curtius rearrangement of a derived acyl azide. Oxidation of the silyl enol ether group and reduction of the resulting α-hydroxy ketone would serve to install the 1- and 2-hydroxy groups.

In this study, conducted on a ≈50 mmol scale, diene **1** reacted with maleic anhydride in benzene[3] to give a 3 : 1 mixture of the two cycloadducts **10** and **11**. Trituration of the crude product with diethyl ether afforded cycloadduct **10** in 59% yield. Careful crystallisation of the residue obtained from the filtrate gave the previously unreported ketone **12**, formed by adventitious hydrolysis of cycloadduct **11**, in 15% yield.

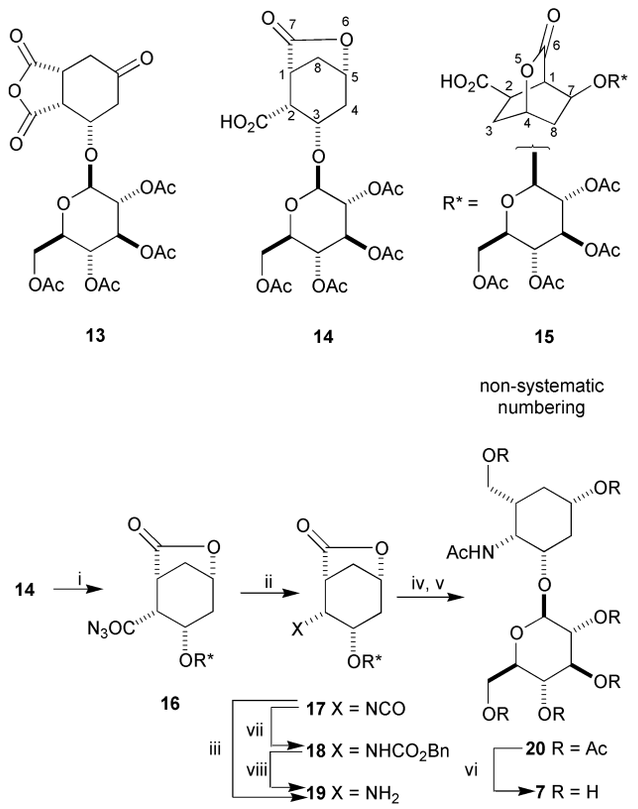
We felt that the critical step in the strategy would be the differentiation of the carbonyl groups of the anhydride. Thus, our initial study employed ketone **13** prepared by the acidic hydrolysis of silyl enol ether **10**.[3] It was inferred from models that reduction of the ketone would produce an intermediary alcohol that could react with the C-1 and/or C-2 anhydride carbonyl group. Gratifyingly, treatment of a solution of ketone **13** in glacial acetic acid with sodium cyanoborohydride resulted in a regioselective opening of the anhydride to afford an 83 : 17 mixture of the γ- and δ-lactone acids **14** and **15** which were isolated in yields of 72 and 7%, respectively. The structures of

 DOI: 10.1039/b105374b



the last-cited compounds were deduced from their analytical and spectroscopic data, with the γ-lactonic acid **14** exhibiting a peak at 1769 cm^{-1} in the IR spectrum attributable to the γ-lactone carbonyl group.

Acyl azide **16** was prepared from the acid **14** under standard conditions in a 90% yield (Scheme 1). A near-quantitative conversion of acyl azide **16** into isocyanate **17** was achieved by heating at reflux in benzene. The retention of stereochemistry at C-2 for the rearrangement was apparent from the strong (5%) NOE enhancement between 2-H and 8-H^{β} (Fig. 1). Hydrolysis of the isocyanate **17** to the amine **19** proved to be problematic. To avoid urea formation, the hydrolysis was best effected under basic conditions using triethylamine in aq. THF to give the



Scheme 1 *Reagents and conditons*: i, $(COCl)_2$, DMF, CH_2Cl_2; then NaN_3, THF (90%); ii, C_6H_6, Δ (98%); iii, NEt_3, aq. THF (35%); iv, $LiAlH_4$, THF, v, Ac_2O, pyr (81% over two steps); vi, IRA-400 (OH^-), MeOH (73%); vii, BnOH, C_6H_6, Δ (94%); viii, 10% Pd–C, EtOH (84%).

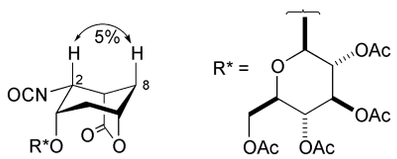


Fig. 1 NOE enhancement for **17**.

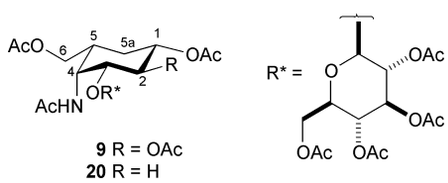


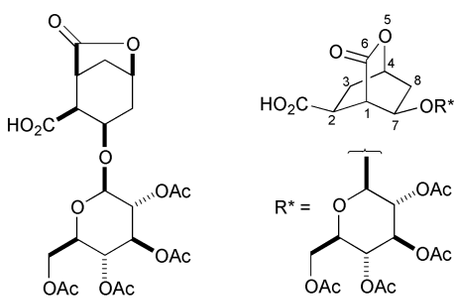
Fig. 2 Solution conformation of carba-pyranoses **9** and **20**.

amine **19** in 35% yield. The sequence was continued with the lithium aluminium hydride reduction of lactone **19** which gave, after subsequent treatment with acetic anhydride and pyridine, the peracetylated 4-amino-2,4-dideoxy-monocarba-disaccharide **20** in 81% yield. The structure and *lyxo*-stereochemistry of the carbocyclic ring of compound **20** was apparent from an analysis of the ^1H NMR spectrum. The pseudo-anomeric proton, 1-H, resonated as an apparent triplet of triplets with coupling constants $J_{1,5a\text{-}ax}$ (11 Hz) and $J_{1,2ax}$ (12 Hz) confirming its axial orientation. Similarly, axial orientations of 3-H and 5-H were apparent from the coupling constants $J_{2ax,3}$ (12 Hz) and $J_{5,5a\text{-}ax}$ (13 Hz). The coupling constants $J_{3,4}$ and $J_{4,5}$, both of 4 Hz, indicated the equatorial disposition of 4-H, thus confirming that the Curtius rearrangement of acyl azide **16** had indeed proceeded with retention of configuration. The analysis of coupling-constant data was also consistent with the carbocyclic ring adopting a $^1C_4$ chair-like conformation (Fig. 2). The final step in the sequence involved deacetylation of compound **20** using IRA-400 (OH^-) resin in methanol; after

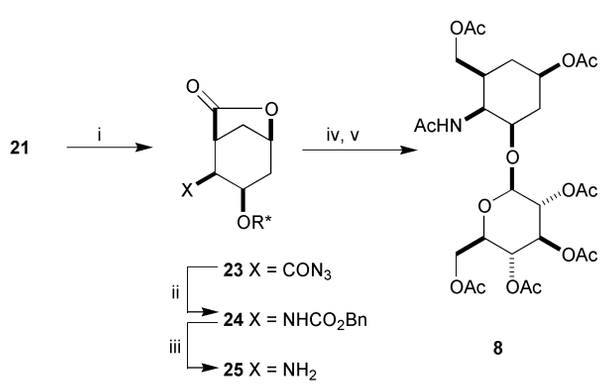
purification by reversed-phase HPLC, the pseudo-disaccharide **7** was isolated in 73% yield. Although the spectral data were consistent with the proposed structure, microanalysis suggested that compound **7** existed as a hydrate. Reacetylation of compound **7** under standard conditions confirmed the structural assignment by furnishing **20** in 81% yield.

The low-yielding step in the **14** → **7** sequence was the hydrolysis of the isocyanate **17**. We believed that this was due to competing hydrolyses of the lactone and ester functions of compound **17** and that the resulting by-products could also be converted into monocarba-disaccharide **7**. Indeed, when the crude reaction product from the hydrolysis was subjected to the reduction, acetylation and deprotection sequence, the monocarba-disaccharide **7** was isolated in an improved overall yield of 56% (*cf.* 21% overall yield for the earlier sequence). An alternative method for the preparation of amine **19** was also pursued. Treatment of isocyanate **17** with benzyl alcohol gave carbamate **18** in 94% yield, catalytic hydrogenolysis of which furnished an 84% yield of amine **19**.

A similar sequence using isomeric ketone **12** allowed the synthesis of a carba-sugar with the opposite stereochemistry at the carbocyclic ring. Sodium cyanoborohydride reduction of ketone **12** gave a 75 : 25 mixture of the lactonic acids **21** and **22**.

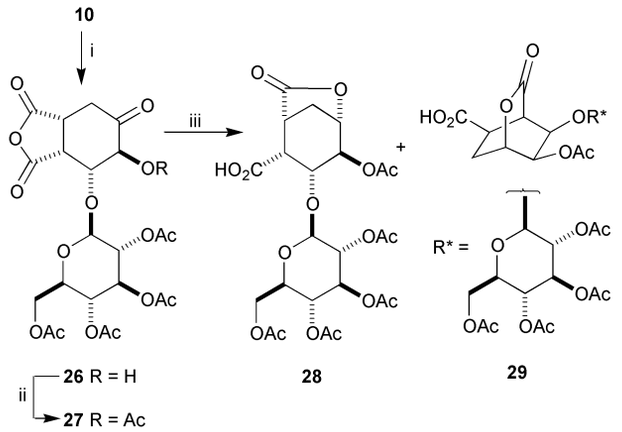


Crystallisation of the mixture gave the major lactonic acid **21** in 58% yield. Treatment of the acid chloride derived from acid **21** with sodium azide gave acyl azide **23** which, on heating in a mixture of benzyl alcohol and benzene, gave the carbamate **24** (Scheme 2). The yield for the two steps was 88%. Hydrogenolysis of benzyl carbamate **24** gave amine **25** (57%), which was then reduced with lithium aluminium hydride and acetylated to give the protected monocarba-disaccharide **8** (63%).



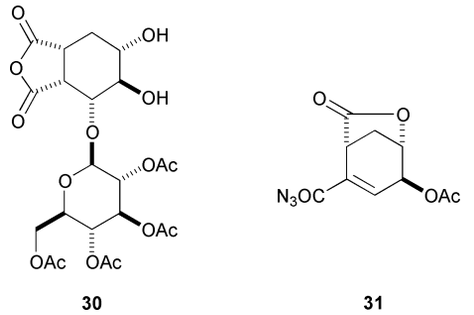
Scheme 2 *Reagents and conditons*: i, $(COCl)_2$, DMF, CH_2Cl_2; then NaN_3, THF (99%); ii, C_6H_6, BnOH, Δ (89%); iii, 10% Pd–C, EtOH (57%); iv, $LiAlH_4$, THF; v, Ac_2O, pyr (63% over two steps).

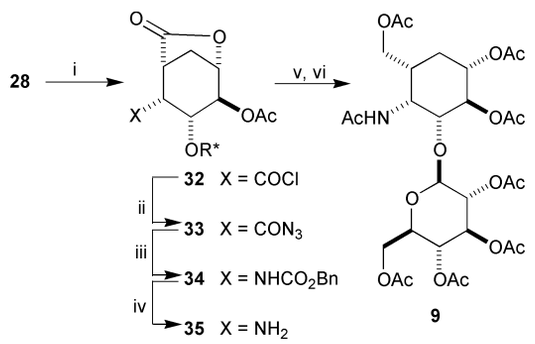
Our attention then focused on hydroxylation at C-4 of the carbocycle to give a fully substituted carba-sugar. This was achieved by treatment of cycloadduct **10** with an acetone solution of dimethyldioxirane (DMDO)[15] (Scheme 3). The acyloin **26** was obtained in 85% yield after crystallisation. The configuration at C-4 could not be determined from NMR data; however, it is reasonable to assume that the oxidant reacted preferentially from the least-hindered face of the enol ether to give the C-4 β-alcohol. The next step in the sequence involved reduction of ketone **26** with sodium cyanoborohydride. Unfortunately, it did not result in the desired lactonisation but instead gave diol **30** (56% yield). This problem was overcome by acetylation of the hydroxy group of **26** under acidic conditions. Sodium cyanoborohydride reduction of the resultant acetoxy ketone **27** gave a 75 : 25 mixture of the lactonic acids **28** and **29** which were isolated in 52 and 9% yield, respectively.



Scheme 3 *Reagents and conditions*: i, DMDO in Me_2CO (85%); ii, Ac_2O, cat $HClO_4$ (84%); iii, $NaBH_3CN$, AcOH (52% for **28**).

Problems were encountered with the formation of the corresponding acyl azide derived from the acid **28**. Using the protocol developed for the formation of compound **16**, the acid **28** gave the unsaturated acyl azide **31** *via* β-elimination of the tetra-*O*-acetyl-D-glucopyranose moiety. This was overcome using a two-step procedure involving initial isolation of acid chloride **32** (Scheme 4) and its subsequent treatment, in





Scheme 4 *Reagents and conditons*: i, $(COCl)_2$, DMF, CH_2Cl_2 (82%): ii, NaN_3, CH_2Cl_2 (92%); iii, C_6H_6, BnOH, Δ (85%); iv, 10% Pd–C, EtOH (55%); v, $LiAlH_4$, THF; vi, Ac_2O, pyr (61% over two steps).

dichloromethane, with sodium azide. The desired acyl azide **33** was isolated in 92% yield. Conversion into the carbamate **34**, hydrogenolysis to the amine **35**, lithium aluminium hydride reduction and acetylation gave the target monocarba-disaccharide **9** in 29% overall yield. Once again, the spectral data were consistent with the structure, and analysis of coupling data showed equatorial orientations of the C-1, -3, -4, and -5 substituents. Although the 2-H resonance was partly obscured by other signals, it could be observed as an apparent triplet at δ 5.09 using resolution-enhancement techniques, with coupling constants $J_{2,3}$ and $J_{1,2}$ of 9.5 Hz, confirming the axial orientation of 2-H. Collectively, analysis of the coupling-constant data indicates that the carbocyclic ring of compound **9** adopts a $^1C_4$-like conformation as depicted in Fig. 2.

In conclusion, we have demonstrated that the asymmetric Diels–Alder reaction of dienyl glucoside **1** can provide a method for accessing 1,3-glycosidically linked aminomono-carba-disaccharides. Further work is underway to establish methods for the introduction of other heteroatom functionality at C-4 in these systems and also for modifying the synthetic procedures to provide 1,1- and 1,4-glycosidically linked mono-carba-disaccharides.

Experimental

Mps were measured on a Gallenkamp capillary melting-point apparatus and are uncorrected. Specific optical rotations $[\alpha]_D$, given in 10^{-1} deg cm^2 g^{-1}, were measured at ≈22 °C using either a JASCO DIP-370 or DIP-1000 polarimeter with a cell of path length 1.0 dm. Varian Gemini 200 and VXR300 spectrometers were used to obtain ^{1}H (200 and 300 MHz) and ^{13}C (50 and 75 MHz) NMR spectra. Chemical shifts are reported as parts per million (ppm) using the δ-scale. Coupling constants (J) and separations are reported to the nearest 0.5 Hz. IR spectra were recorded on a Perkin-Elmer 1600 series FTIR spectrophotometer. HPLC separations were carried out with an Activon ODS column (25 × 1 cm) employing a JASCO PU-980 pump and JASCO UV-975 UV/vis detector. FAB mass spectra were recorded on a Kratos MSORF mass spectrometer; *m*-nitrobenzyl alcohol was used as the matrix and xenon as the ionising gas.

Elemental analyses were carried out by Dr R. G. Cunninghame and associates at the Campbell Microanalytical Laboratory, University of Otago, Dunedin, New Zealand. Thin-layer chromatography (TLC) was performed on Merck silica gel DC Alurolle Kieselgel 60F$_{254}$ plates and plates were visualised under a UV lamp and/or with a spray consisting of 5% w/v dodecamolybdophosphoric acid in ethanol with subsequent heating. Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). All chromatography solvents were reagent grade. THF was distilled from sodium/potassium–benzophenone ketyl under nitrogen, and dichloromethane was distilled from phosphorus pentaoxide. All other solvents and reagents were purified using the methods described by Perrin *et al.*[16]

Diels–Alder cycloaddition of diene 1 and maleic anhydride

A solution of freshly sublimed maleic anhydride (5.5 g, 56 mmol) and diene **1** (27.0 g, 55 mmol) in dry benzene (150 cm^3) was stirred for 24 h under an atmosphere of nitrogen. Evaporation of the mixture left a residue that comprised mainly a 75 : 25 mixture of the cycloadducts **10** and **11** by ^{1}H NMR spectroscopy. Addition of diethyl ether to the residue and filtration of the crystalline material gave (1*R*,2*R*,3*S*)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-5-(trimethylsiloxy)cyclohex-4-ene-1,2-dicarboxylic anhydride **10** as white crystals (19.0 g, 59%); mp 214–215 °C (lit.,[3] 212–213 °C). Removal of the solvent from the filtrate and slow crystallisation of the residue from dichloromethane–diethyl ether gave *(1S,2S,3R)-5-oxo-(2′,3′,4′,6′-tetra-O-acetyl-β-*D*-glucopyranosyloxy)cyclohexane-1,2-dicarboxylic anhydride* **12** (4.2 g, 15%) as a slightly impure solid. Recrystallisation from dichloromethane–diethyl ether yielded compound **12** as analytically pure colourless crystals (1.8 g, 6%); mp 176–179 °C (Found: C, 51.6; H, 5.3. $C_{22}H_{26}O_{14}$ requires C, 51.4; H, 5.1%) $[\alpha]_D$ +30 (*c* 0.3 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 1784 (anhydride C=O), 1750 (ester C=O) and 1722 (ketone C=O); δ_H (300 MHz; $CDCl_3$) 1.99, 2.01 and 2.11 (6, 3 and 3 H, each s, 4 × OAc), 2.36 (1 H, dd, *J* 18 and 2, 4-H), 2.78 (1 H, dd, *J* 18 and 4, 4-H), 2.79 (1 H, dd, *J* 18 and 10, 6-H), 2.88 (1 H, dd, *J* 18 and 8, 6-H), 3.37 (1 H, dd, *J* 10.5 and 3, 2-H), 3.58 (1 H, dt, *J* 8 and 10, 1-H), 3.67 (1 H, dt, *J* 9.5 and 3.5, 5′-H), 4.18 (2 H, d, separation 3.5, 6′-H$_2$), 4.55 (1 H, d, *J* 8, 1′-H), 4.82 (1 H, q, *J* 3.5, 3-H), 4.89 (1 H, dd, *J* 9 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H) and 5.16 (1 H, t, *J* 9, 3′-H); δ_C (75 MHz; d$_6$-DMSO) 20.2, 20.4, 20.5, 20.7, 35.6, 36.2, 44.7, 61.9, 68.3, 70.5, 70.9, 72.0, 72.3, 96.0, 169.0, 169.4, 169.7, 170.2, 170.7, 174.2 and 209.0 (5-CO); *m*/*z* (FAB) 515 (MH$^+$, 13%), 331 ($C_{14}H_{19}O_9^+$, 56) and 154 (100).

Sodium cyanoborohydride reduction of ketone 13

Sodium cyanoborohydride (6.70 g, 107 mmol) was added to a solution of ketone **13**[3] (11.2 g, 21.7 mmol) in glacial acetic acid (120 cm^3). After stirring of the mixture for 15 h, the solvent was removed *in vacuo* and the residue was partitioned between dichloromethane and hydrochloric acid (1 mol dm^{-3}). The aqueous layer was extracted with dichloromethane (3 × 40 cm^3) and the combined organic extracts were washed with aq. sodium hydrogen carbonate (2 × 100 cm^3). The combined basic aqueous layers were acidified with conc. hydrochloric acid and then extracted with dichloromethane (2 × 100 cm^3). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a white foam, shown to be an 83 : 17 mixture of the lactonic acids **14** and **15** on the basis of 200 MHz ^{1}H NMR analysis. Crystallisation of the residue from dichloromethane–diethyl ether gave *(1R,2R,3S,5S)-7-oxo-3-(2′,3′,4′,6′-tetra-O-acetyl-β-*D*-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carboxylic acid* **14** (8.10 g, 72%) as colourless crystals; mp 193–195 °C (Found: C, 51.5; H, 5.5. $C_{22}H_{28}O_{14}$ requires C, 51.2; H, 5.5%) $[\alpha]_D$ −13 (*c* 0.03 in CH_2Cl_2) $[\alpha]_D$ −34 (*c* 0.2 in Me_2CO); ν_{max} (KBr)/cm^{-1} 3000br (O–H), 1769 (lactone C=O) and 1743 (acid and ester C=O); δ_H (300 MHz; $CDCl_3$) 1.77 (1 H, d, *J* 11.5, 8-H$^{\beta}$), 1.95 (1 H, dd, *J* 15.5 and 4.5, 4-H$^{\beta}$), 1.99, 2.02, 2.07 and 2.10 (each 3 H, s, 4 × OAc), 2.55–2.67 (2 H, m, 4- and 8-H$^{\alpha}$), 3.00 (1 H, dd, *J* 4.5 and 2, 2-H), 3.06 (1 H, br d, *J* 5, 1-H), 3.68 (1 H, br dt, *J* 10 and 4, 5′-H), 4.18–4.21 (2 H, m, 6′-H$_2$), 4.56 (1 H, br t, *J* 4.5, 3-H), 4.70 (1 H, d, *J* 8, 1′-H), 4.85 (1 H, br t, *J* 5, 5-H), 4.93 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.06 (1 H, t, *J* 9, 4′-H) and 5.15 (1 H, t, *J* 9, 3′-H); δ_C (75 MHz; d$_6$-DMSO) 20.3, 20.4, 20.5, 34.7, 36.1, 36.9, 48.9, 61.6, 68.1, 70.3, 70.6, 72.2, 75.1, 75.7, 102.0, 168.8, 169.3, 169.6, 170.0, 170.4 and 175.5; *m*/*z* (FAB) 517 (MH$^+$, 2%), 331 ($C_{14}H_{19}O_9^+$, 7) and 154 (100).

Removal of the solvent from the filtrate gave a foam which was found to be the slightly impure lactonic acid **15** (1.67 g). Slow crystallisation from dichloromethane–diethyl ether–hexanes gave *(1R,2R,4S,7S)-6-oxo-7-(2′,3′,4′,6′-tetra-O-acetyl-β-*D*-glucopyranosyloxy)-5-oxabicyclo[2.2.2]octane-2-carboxylic acid*† **15** (0.730 g, 7%) as clear crystals; mp 91–93 °C (Found: C, 51.2; H, 5.8. $C_{22}H_{28}O_{14}$ requires C, 51.2; H, 5.5%) $[\alpha]_D$ −65 (*c* 0.5 in Me_2CO); ν_{max} (KBr)/cm^{-1} 3300 (O–H) and 1755 (acid, lactone and ester C=O); δ_H (300 MHz; $CDCl_3$) 1.89–2.12 (2 H, m, 3- and 8-H) overlapping with 2.00, 2.03, 2.08 and 2.10 (each 3 H, s, 4 × OAc), 2.17 (1 H, dd, *J* 14 and 9, 8-H), 2.32 (1 H, ddt, *J* 13.5, 6.5 and 3.5, 3-H), 2.83 (1 H, ddd, *J* 10.5, 7 and 1.5, 2-H), 3.00–3.45 (1 H, br s, COOH), 3.35 (1 H, br dd,

† Non-systematic numbering for the bicyclic ring.

J 3 and 1.5, 1-H), 3.75 (1 H, ddd, *J* 9.5, 4 and 2.5, 5′-H), 4.17 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.27 (1 H, dd, *J* 12.5 and 4, 6′-H), 4.39 (1 H, dt, *J* 9 and 3, 7-H), 4.76 (1 H, d, *J* 8, 1′-H), 4.76–4.81 (1 H, m, 4-H), 4.95 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.09 (1 H, t, *J* 9.5, 4′-H) and 5.23 (1 H, t, *J* 9.5, 3′-H); *m/z* (FAB) 539 (MNa^+, 7%), 517 (MH^+, 23), 331 ($C_{14}H_{19}O_9^+$, 45), 169 (90) and 136 (100).

(1*R*,2*R*,3*S*,5*S*)-7-Oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbonyl azide 16

Oxalyl dichloride (1.20 cm^3, 13.8 mmol) was added to a solution of lactonic acid **14** (4.50 g, 8.71 mmol) and dry DMF (6 drops) in dry dichloromethane (360 cm^3) at room temperature. Stirring was continued until the evolution of bubbles ceased (30 min). After removal of solvent under reduced pressure (<30 °C), the residue was dissolved in dry THF (100 cm^3) and sodium azide (4.5 g, 69 mmol) was added. The resulting mixture was stirred at 0 °C for 1 h, poured into water (200 cm^3) and extracted with dichloromethane (2 × 100 cm^3). The combined organic extracts were washed with water (100 cm^3), dried ($MgSO_4$) and the solvent removed. Crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **16** (4.24 g, 90%) as white crystals; mp 218–230 °C (decomp.) (Found: C, 48.8; H, 4.9; N, 7.4. $C_{22}H_{27}N_3O_{13}$ requires C, 48.8; H, 5.0; N, 7.8%) $[\alpha]_D$ −25 (*c* 1.1 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 2137 (N_3), 1775 (lactone C=O) and 1726 (ester and acyl azide C=O); δ_H (300 MHz; $CDCl_3$) 1.71 (1 H, d, *J* 11.5, 8-H^β), 1.89 (1 H, dd, *J* 16 and 5, 4-H^β), 1.98, 2.01, 2.06 and 2.10 (each 3 H, s, 4 × OAc), 2.50–2.70 (2 H, m, 4- and 8-H^α), 2.89 (1 H, dd, *J* 4.5 and 2, 2-H), 3.04–3.10 (1 H, m, 1-H), 3.68 (1 H, dt, *J* 9 and 3.5, 5′-H), 4.19 (2 H, d, separation 3.5, 6′-H_2), 4.47 (1 H, br t, *J* 4, 3-H), 4.71 (1 H, d, *J* 8, 1′-H), 4.80 (1 H, br t, *J* 4.5, 5-H), 4.94 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.05 (1 H, t, *J* 9.5, 4′-H) and 5.17 (1 H, t, *J* 9, 3′-H); *m/z* (FAB) 542 (MH^+, 33%) and 331 ($C_{14}H_{19}O_9^+$, 100).

(1*R*,2*R*,3*S*,5*S*)-2-Isocyanato-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octan-7-one 17

A suspension of acyl azide **16** (0.200 g, 0.369 mmol) in dry benzene (30 cm^3) was heated under reflux for 2 h. Removal of the solvent *in vacuo* and crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **17** as colourless crystals (0.185 g, 98%); mp 230–232 °C (Found: C, 51.4; H, 5.4; N, 2.8. $C_{22}H_{27}NO_{13}$ requires C, 51.5; H, 5.3; N, 2.7%) $[\alpha]_D$ −45 (*c* 0.9 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 2287 (NCO), 1768 (lactone C=O) and 1750 (ester C=O); δ_H (300 MHz; $CDCl_3$) 1.75 (1 H, d, *J* 12, 8-H^β), 1.88 (1 H, dd, *J* 15.5 and 5, 4-H^β), 1.99, 2.01, 2.08 and 2.11 (each 3 H, s, 4 × OAc), 2.49–2.59 (2 H, m, 4- and 8-H^α), 2.68–2.75 (1 H, m, 1-H), 3.67 and 3.71 [2 H, overlapping dt (*J* 10 and 3.5) and dd (*J* 4 and 2.5), 5′- and 2-H, respectively], 4.18 and 4.22 [3 H, overlapping d (separation 3.5) and t (*J* 4.5), 6′-H_2 and 3-H, respectively], 4.75 and 4.79 [2 H, overlapping d (*J* 8) and t (*J* 5), 1′- and 5-H, respectively], 5.02–5.12 (2 H, m, 2′- and 4′-H) and 5.19 (1 H, t, *J* 9.5, 3′-H); δ_C (75 MHz; $CDCl_3$) 20.6, 20.7 (2×), 20.8, 35.0, 37.2, 43.7, 56.6, 61.8, 68.6, 70.8, 71.9, 72.8, 72.9, 75.5, 101.1, 125.3, 169.5, 169.7, 170.4, 170.7 and 174.6; *m/z* (FAB) 514 (MH^+, 25%), 331 ($C_{14}H_{19}O_9^+$, 94) and 169 (100).

(1*R*,2*R*,3*S*,5*S*)-2-Amino-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octan-7-one 19

Triethylamine (0.120 cm^3, 0.861 mmol) was added to a stirred solution of isocyanate **17** (0.500 g, 0.974 mmol) in a mixture of THF (25 cm^3) and water (25 cm^3). After 10 min at room temperature, the solution was acidified with hydrochloric acid (1 mol dm^{-3}), poured into dichloromethane (100 cm^3) and extracted with hydrochloric acid (1 mol dm^{-3}; 3 × 60 cm^3). The combined aqueous extracts were basified using solid sodium hydrogen carbonate and extracted with dichloromethane (2 × 100 cm^3). The organic extracts were washed with water, dried ($MgSO_4$) and evaporated to leave a residue (0.240 g), which was crystallised from dichloromethane–diethyl ether to give the *title compound* **19** (0.168 g, 35%) as fine colourless needles; mp 191–194 °C (Found: C, 51.5; H, 6.0; N, 2.7. $C_{21}H_{29}NO_{12}$ requires C, 51.7; H, 6.0; N, 2.9%) $[\alpha]_D$ −38 (*c* 0.5 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3378 (N–H), 1751 (lactone C=O) and 1733 (ester C=O); δ_H (300 MHz; $CDCl_3$) 1.65–1.75 (3 H, br m, NH_2 and 8-H^β), 1.89 (1 H, dd, *J* 15 and 5.5, 4-H^β), 1.99, 2.01, 2.09 and 2.12 (each 3 H, s, 4 × OAc), 2.38–2.43 (1 H, m, 1-H), 2.44–2.56 (2 H, m, 4- and 8-H^α), 3.14–3.20 (1 H, m, 2-H), 3.64 (1 H, dt, *J* 9.5 and 3.5, 5′-H), 4.18 and 4.21 [3 H, overlapping d (separation 4) and t (*J* 4.5), 6′-H_2 and 3-H, respectively], 4.77 (1H, br t, *J* 4.5, 5-H), 4.82 (1 H, d, *J* 8, 1′-H), 5.03 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.08 (1 H, t, *J* 9.5, 4′-H) and 5.16 (1 H, t, *J* 9, 3′-H); δ_C (50 MHz; $CDCl_3$) 20.6, 20.7, 35.8, 37.2, 46.2, 55.5, 61.9, 68.5, 71.3, 71.8, 73.0, 75.9, 76.0, 101.7, 169.0, 169.3, 170.4, 170.6 and 176.4; *m/z* (FAB) 488 (MH^+, 83%), 331 ($C_{14}H_{19}O_9^+$, 27), 307 (42), 289 (30) and 136 (100).

4-Acetamido-1,6-di-*O*-acetyl-2,4-dideoxy-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-5a-carba-β-L-*lyxo*-hexopyranose 20

Lithium aluminium hydride (0.400 g, 10.5 mmol) was added carefully to a solution of amine **19** (0.529 g, 1.09 mmol) in dry THF (50 cm^3) and the resulting mixture was heated under reflux for 24 h. The reaction was quenched by successive additions of 'wet' diethyl ether (10 cm^3), water (1 cm^3) and aq. sodium hydroxide (15% w/v; 0.7 cm^3). Evaporation of the mixture gave a residue, which was dissolved in a mixture of acetic anhydride (10 cm^3) and pyridine (10 cm^3) and the solution was stirred for 48 h. Water was added and, after a further 3 h of stirring, the mixture was poured into hydrochloric acid (1 mol dm^{-3}; 200 cm^3) then extracted with dichloromethane. The organic layer was washed successively with hydrochloric acid (1 mol dm^{-3}) and water, dried ($MgSO_4$) and the solvent was removed. The residue was purified by silica gel column chromatography [EtOAc–hexanes (9 : 1) as eluent] giving the *title compound* **20** (0.547 g, 81%) as a colourless foam; R_f 0.6 (EtOAc) (Found: C, 52.2; H, 6.4; N, 2.2; MH^+, 618.2399. $C_{27}H_{39}NO_{15}$ requires C, 52.5; H, 6.4; N, 2.3%; MH^+, 618.2398) $[\alpha]_D$ −23 (*c* 0.2 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3387br (N–H), 2946, 1738 (ester C=O) and 1672 (amide C=O); δ_H (300 MHz; $CDCl_3$) 1.12 (1 H, br q, *J* 13, 5a-H^{ax}), 1.53 (1 H, q, *J* 12, 2-H^{ax}), 1.80–1.95 (2 H, m, 5-H and 5a-H^{eq}), 1.97, 1.98, 2.01, 2.03, 2.04, 2.05 and 2.08 (each 3 H, s, 6 × OAc and NAc), 2.22–2.33 (1 H, m, 2-H^{eq}), 3.70 (1 H, ddd, *J* 10, 5 and 2.5, 5′-H), 3.74–3.87 (2 H, m, 3- and 6-H), 4.06–4.16 (2 H, m, 6′- and 6-H), 4.26 (1 H, dd, *J* 12 and 5, 6′-H), 4.55 (1 H, br dt, *J* 10 and 4, 4-H), 4.62 (1 H, d, *J* 8, 1′-H), 4.76 (1 H, br tt, *J* 12 and 4, 1-H), 4.91 (1 H, dd, *J* 10 and 8, 2′-H), 5.02 (1 H, t, *J* 10, 4′-H), 5.17 (1 H, t, *J* 10, 3′-H) and 5.40 (1 H, br d, *J* 10, NH); δ_C (75 MHz; $CDCl_3$) 20.6, 20.7, 20.9 and 21.1 (6 × $OCOCH_3$), 23.2 ($NCOCH_3$), 28.6 (5a-CH_2), 34.0 (2-CH_2), 35.8 (5-CH), 46.0 (4-CH), 62.0 (6′-CH_2), 64.5 (6-CH_2), 68.4 (4′-CH), 68.6 (1-CH), 71.0 (2′-CH), 71.7 (5′-CH), 72.6 (3′-CH), 75.0 (3-CH), 99.8 (1′-CH) and 169.5, 169.6, 170.1, 170.5, 170.7 and 171.0 (7 × CO); *m/z* (FAB) 618 (MH^+, 25%), 558 ($MH^+ - CH_3CO_2H$, 6), 331 ($C_{14}H_{19}O_9^+$, 90) and 307 (100).

4-Acetamido-2,4-dideoxy-3-*O*-(β-D-glucopyranosyl)-5a-carba-β-L-*lyxo*-hexopyranose 7

IRA-400 (OH^-) Resin (1 g) was added to a solution of compound **20** (0.212 g, 0.343 mmol) in absolute methanol (43 cm^3) and the mixture was stirred at ambient temperature until the presence of starting material could not be detected by TLC (12 h). The mixture was filtered, the resin was washed with water (30 cm^3), and the combined filtrate and washings were

evaporated *in vacuo*. Purification of the glassy residue by semi-preparative reversed-phase HPLC [water–MeOH (7 : 3) as eluent; $\lambda = 220$ nm] gave the *title compound* **7** (0.092 g, 73%) as a glass (Found: C, 46.6; H, 7.6; N, 3.5. $C_{15}H_{27}NO_9 \cdot H_2O$ requires C, 47.1; H, 7.4; N, 3.7%) $[\alpha]_D$ −24 (*c* 0.1 in water); δ_H (300 MHz; D_2O) 1.10 (1 H, br dt, *J* 11 and 14, 5a-H^{ax}), 1.56 (1 H, q, *J* 12, 2-H^{ax}), 1.75–1.89 (2 H, m, 5-H and 5a-H^{eq}), 2.07 (3 H, s, NAc), 2.16–2.27 (1 H, m, 2-H^{eq}), 3.19 (1 H, dd, *J* 9 and 8, 2′-H), 3.31–3.52 (5 H, m, 3′-, 4′- and 5′-H and 6-H_2), 3.70 (1 H, dd, *J* 12 and 6, 6′-H), 3.79 (1 H, br tt, *J* 11 and 4, 1-H), 3.91 (1 H, dd, *J* 12 and 2, 6′-H), 4.06 (1 H, dt, *J* 13 and 4, 3-H) and 4.53 and 4.56 [2 H, overlapping t (*J* 4) and d (*J* 8), 4- and 1′-H, respectively]; δ_C (75 MHz; D_2O) 23.3 (NCO*C*H_3), 31.9 (5a-CH_2), 37.4 (2-CH_2), 39.1 (5-CH), 47.4 (4-CH), 62.0 (6′-CH_2), 63.5 (6-CH_2), 68.1 (1-CH), 71.0, 74.3 (2′-CH), 76.7, 76.8, 77.3, 101.8 (1′-CH) and 176.7 (CO); *m*/*z* (FAB) 366 (MH^+, 2%), 307 (12), 289 (10), 204 (10) and 154 (100).

Preparation of pseudo-disaccharide 7 from isocyanate 17

Triethylamine (1.00 cm^3, 7.17 mmol) was added to a solution of isocyanate **17** (0.25 g, 0.501 mmol) in a 1 : 1 mixture of THF–water (25 cm^3) and the mixture was stirred for 15 min. After removal of the solvent under reduced pressure, the residue was dissolved in dry THF (50 cm^3), and lithium aluminium hydride (0.227 g, 5.98 mmol) was carefully added; the resulting mixture was heated under reflux for 24 h. The reaction mixture was quenched by successive additions of 'wet' diethyl ether (10 cm^3), water (1 cm^3) and aq. sodium hydroxide (15% w/v; 0.7 cm^3). Evaporation of the mixture gave a colourless residue which was dissolved in a mixture of acetic anhydride (10 cm^3) and pyridine (10 cm^3) and this mixture was stirred for 48 h. Water (100 cm^3) was added and, after a further 3 h of stirring, the mixture was poured into hydrochloric acid (1 mol dm^{-3}; 200 cm^3) then extracted with dichloromethane (2 × 100 cm^3). The combined organic layers were washed successively with hydrochloric acid (1 mol dm^{-3}; 200 cm^3) and water (200 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. IRA-400 (OH^-) Resin (1 g) was added to a stirred solution of the crude residue in absolute methanol (50 cm^3). When the presence of compound **20** could not be detected by TLC (12 h), the mixture was filtered, the resin was washed with water (30 cm^3) and the combined filtrate and washings were evaporated *in vacuo*. Purification of the glassy residue by semi-preparative reversed-phase HPLC [water–MeOH (7 : 3) as eluent; $\lambda = 220$ nm] gave the title compound **7** (0.103 g, 56% based on isocyanate **17**).

Benzyl (1*R*,2*R*,3*S*,5*S*)-7-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbamate 18

A mixture of dry benzyl alcohol (0.380 g, 3.67 mmol) and isocyanate **17** (0.310 g, 0.604 mmol) in dry benzene (30 cm^3) was heated under reflux for 20 h. Evaporation of the mixture *in vacuo* and crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **18** as colourless crystals (0.351 g, 94%); mp 221–223 °C (Found: C, 55.7; H, 5.6; N, 2.2. $C_{29}H_{35}NO_{14}$ requires C, 56.0; H, 5.7; N, 2.25%) $[\alpha]_D$ −18 (*c* 0.5 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3414 (N–H), 2930, 1753 (lactone C=O), 1746 (ester C=O) and 1736 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 1.82 (1 H, d, *J* 11.5, 8-H$^{\beta}$), 1.91 (1 H, dd, *J* 15 and 5, 4-H$^{\beta}$), 1.98, 1.99, 2.02 and 2.08 (each 3 H, s, 4 × OAc), 2.46–2.63 (3 H, m, 1-H and 4- and 8-H$^{\alpha}$), 3.52 (1 H, dt, *J* 9 and 3.5, 5′-H), 4.07–4.20 (4 H, m, 2- and 3-H and 6′-H_2), 4.47 (1 H, d, *J* 8, 1′-H), 4.78 (1 H, br t, *J* 5, 5-H), 4.94–5.19 (5 H, m, 2′-, 3′- and 4′-H and OCH_2Ph), 5.68 (1 H, br d, *J* 9.5, NH) and 7.28–7.41 (5 H, m, C_6H_5); δ_C (50 MHz; $CDCl_3$) 20.4, 20.6 (2×), 20.8, 35.3, 36.9, 42.1, 53.1, 61.7, 67.3, 68.2, 71.5, 72.0, 72.9, 75.6, 75.8, 102.1, 128.3, 128.7, 136.1, 155.6, 168.8, 169.2, 170.4, 170.6 and 176.0; *m*/*z* (FAB) 622 (MH^+, 45%), 604 (8), 562 ($MH^+ - CH_3CO_2H$, 4), 331 ($C_{14}H_{19}O_9^+$, 86) and 169 (100).

Sodium cyanoborohydride reduction of ketone 12

Using the method for the preparation of lactones **14** and **15**, sodium cyanoborohydride (4.74 g, 75.5 mmol) was added to a solution of ketone **12** (7.75 g, 15.1 mmol) in glacial acetic acid (100 cm^3) and the mixture was stirred under a drying tube ($CaCl_2$) overnight. Work-up gave a foam which comprised a 75 : 25 mixture of the acids **21** and **22**.‡ Crystallisation of the mixture from dichloromethane–diethyl ether gave *(1S,2S,3R,5R)-7-oxo-3-(2′,3′,4′,6′-tetra-O-acetyl-β-*D*-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carboxylic acid* **21** as colourless crystals (4.50 g, 58%); mp 192–194 °C (Found: C, 51.0; H, 5.2. $C_{22}H_{28}O_{14}$ requires C, 51.2; H, 5.5%); $[\alpha]_D$ −25 (*c* 1.0 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3431 (O–H), 1755 (lactone C=O) and 1740 (ester and acid C=O); δ_H (300 MHz; $CDCl_3$) 1.78 (1 H, dd, *J* 16 and 4, 4-H$^{\beta}$), 1.81 (1 H, d, *J* 12, 8-H$^{\beta}$), 2.01, 2.03, 2.10 and 2.12 (each 3 H, s, 4 × OAc), 2.20–2.75 (1 H, br s, COOH), 2.45 (1 H, br d, *J* 15, 4-H$^{\alpha}$), 2.57 (1 H, ddt, *J* 12, 2 and 6, 8-H$^{\alpha}$), 3.00 (1 H, dd, *J* 4.5 and 1.5, 2-H), 3.04 (1 H, br d, *J* 5.5, 1-H), 3.67 (1 H, ddd, *J* 10, 4 and 2.5, 5′-H), 4.11 (1 H, dd, *J* 12.5 and 4, 6′-H), 4.35 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.68–4.72 (1 H, m, 3-H), 4.70 (1 H, d, *J* 7.5, 1′-H), 4.79 (1 H, br t, *J* 5, 5-H), 4.87 (1 H, dd, *J* 9 and 7.5, 2′-H) and 5.09–5.21 (2 H, m, 4′- and 3′-H); δ_C (75 MHz; $CDCl_3$) 20.7 (2×), 20.8, 20.9, 30.5, 36.5, 38.0, 49.8, 61.8, 68.6, 71.1, 71.6, 71.9, 72.8, 75.1, 96.5, 160.9, 169.4, 169.6, 170.5, 171.4 and 175.2; *m*/*z* (FAB) 1055 (M_2Na^+, 1%), 1033 (M_2H^+, 2), 539 (MNa^+, 13), 517 (MH^+, 23), 331 ($C_{14}H_{19}O_9^+$, 72) and 154 (100).

The mother liquors were concentrated under reduced pressure to give *(1S,2S,4R,7R)-6-oxo-7-(2′,3′,4′,6′-tetra-O-acetyl-β-*D*-glucopyranosyloxy)-5-oxabicyclo[2.2.2]octane-2-carboxylic acid*† **22** as a slightly impure colourless foam (0.930 g, 12%); ν_{max} (KBr)/cm^{-1} 3429 (O–H), 1762 (lactone and ester C=O) and 1712 (acid C=O); δ_H (300 MHz; $CDCl_3$) *inter alia* 1.82–1.98 (2 H, m, 3- and 8-H), 2.00, 2.03 (2×) and 2.11 (each 3 H, s, 4 × OAc), 2.05–2.17 (1 H, m, 8-H), 2.35 (1 H, br ddt, *J* 14.5, 6.5 and 3.5, 3-H), 2.87 (1 H, br ddd, *J* 10.5, 6.5 and 1.5, 2-H), 3.36 (1 H, br dd, *J* 3 and 1.5, 1-H), 3.72 (1 H, dt, *J* 9.5 and 3.5, 5′-H), 4.19 (1 H, dd, *J* 12 and 2.5, 6′-H), 4.23 (1 H, dd, *J* 12.5 and 4.5, 6′-H), 4.30 (1H, dt, *J* 9 and 3, 7-H), 4.65 (1 H, d, *J* 8, 1′-H), 4.75–4.80 (1 H, m, 5-H), 4.95 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.08 (1 H, t, *J* 9.5, 4′-H) and 5.20 (1 H, t, *J* 9.5, 3′-H); δ_C (75 MHz; $CDCl_3$) 20.7, 20.8, 28.4, 33.5, 37.3, 44.4, 62.1, 68.4, 71.1, 72.0, 72.7, 73.1, 99.5, 169.2, 169.4, 170.5, 171.1 and 174.9.

(1*S*,2*S*,3*R*,5*R*)-7-Oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbonyl azide 23

Using the procedure described for the preparation of acyl azide **16**, lactonic acid **21** (0.500 g, 0.97 mmol) gave a colourless solid, which was crystallised from dichloromethane–diethyl ether to give the title compound **23** (0.520 g, 99%) as colourless crystals; mp 205–215 °C (Found: C, 48.0; H, 5.1; N, 7.5. $C_{22}H_{27}N_3O_{13}$ requires C, 48.8; H, 5.0; N, 7.8%) $[\alpha]_D$ +15 (*c* 0.5 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 2143 (N_3), 1778 (lactone C=O), 1762 (ester C=O) and 1716 (acyl azide C=O); δ_H (300 MHz; $CDCl_3$) 1.70–1.81 (2 H, m, 4- and 8-H$^{\beta}$), 2.00, 2.02, 2.08 and 2.11 (each 3 H, s, 4 × OAc), 2.46 (1 H, br d, *J* 15, 4-H$^{\alpha}$), 2.57 (1 H, ddt, *J* 12, 2 and 6, 8-H$^{\alpha}$), 2.89 (1 H, dd, *J* 4.5 and 2, 2-H), 3.05 (1H, br d, *J* 5, 1-H), 3.67 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.15 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.22 (1 H, dd, *J* 12.5 and 4.5, 6′-H), 4.66 (1 H, br t, *J* 5, 3-H), 4.69 (1 H, d, *J* 8, 1′-H), 4.78 (1 H, br t, *J* 5, 5-H), 4.86 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.09 (1 H, t, *J* 9.5, 4′-H) and 5.21 (1 H, t, *J* 9.5, 3′-H); δ_C (75 MHz; $CDCl_3$) 20.7 (3×), 20.8, 30.5, 36.0, 37.8, 51.5, 61.9, 68.4, 71.0, 71.3, 72.0, 72.7, 74.6, 96.6, 169.2, 169.3, 170.4, 170.7, 174.1 and 175.8; *m*/*z* (FAB) 564 (MNa^+, 15%), 542 (MH^+, 3), 536 (33), 331 ($C_{14}H_{19}O_9^+$, 45) and (100).

‡ The ratio was determined on the methyl esters obtained from the acids **21** and **22** by the action of ethereal diazomethane.

(FAB) 564 (MNa^+, 15%), 542 (MH^+, 3), 536 (33), 331 ($C_{14}H_{19}O_9^+$, 45) and (100).

Benzyl (1*S*,2*S*,3*R*,5*R*)-7-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbamate 24

A mixture of acyl azide **23** (400 mg, 0.74 mmol) and dry benzyl alcohol (0.80 cm^3, 7.7 mmol) in dry benzene (15 cm^3) was heated to reflux under a drying tube ($CaCl_2$) for 24 h. The solution was concentrated under reduced pressure and the residue was dried *in vacuo* to a gel. Crystallisation from dichloromethane–diethyl ether–hexanes gave the *title compound* **24** (0.410 g, 89%) as colourless crystals; mp 197–199 °C (Found: C, 56.1; H, 5.7; N, 2.2. $C_{29}H_{35}NO_{14}$ requires C, 56.0; H, 5.7; N, 2.3%) $[\alpha]_D$ −34 (*c* 1.0 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3434 (N-H), 1770 (lactone C=O), 1755 (ester C=O) and 1716 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 1.76 (1 H, dd, *J* 15.5 and 5, 4-H^{β}), 1.88 (1 H, d, *J* 12, 8-H^{β}), 1.99, 2.00, 2.01 and 2.11 (each 3 H, s, 4 × OAc), 2.39 (1 H, br d, *J* 15.5, 4-H^{α}), 2.53 (1 H, ddt, *J* 11.5, 2 and 6, 8-H^{α}), 2.72 (1 H, br d, *J* 5.5, 1-H), 3.64 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 4.07 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.08–4.13 (1 H, m, 2-H), 4.19 (1 H, dd, *J* 12.5 and 4.5, 6′-H), 4.29 (1 H, br t, *J* 4.5, 3-H), 4.61 (1 H, d, *J* 8, 1′-H), 4.76 (1 H, br t, *J* 4.5, 5-H), 4.96 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.07 (1 H, t, *J* 9.5, 4′-H), 5.09 and 5.12 (each 1 H, d, *J* 11.5, OC*H*$_2$Ph), 5.22 (1 H, t, *J* 9.5, 3′-H), 5.95 (1 H, d, *J* 9.5, NH) and 7.28–7.42 (5 H, m, C_6H_5); δ_C (75 MHz; $CDCl_3$) 20.6 (3×), 20.8, 30.2, 37.2, 41.8, 52.9, 61.7, 67.0, 68.3, 70.8, 72.1, 72.4, 72.8, 75.1, 97.4, 128.1 (3×), 128.5 (2×), 136.3, 155.9, 169.3, 169.4, 170.3, 170.6 and 175.5; *m*/*z* (FAB) 644 (MNa^+, 1%), 622 (MH^+, 5), 578 (1), 331 ($C_{14}H_{19}O_9^+$, 13), 169 (53) and 154 (100).

(1*S*,2*S*,3*R*,5*R*)-2-Amino-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octan-7-one 25

A mixture of the benzyl carbamate **24** (400 mg, 0.64 mmol) and 10% palladium–carbon (50 mg) in ethanol (50 cm^3) was stirred under a hydrogen atmosphere overnight. The mixture was filtered through Celite® and the filtrate was concentrated under reduced pressure. The residue was dried *in vacuo* to a solid, which was crystallised from dichloromethane–diethyl ether to give the *title compound* **25** (0.180 g, 57%) as colourless crystals; mp 225–227 °C (Found: C, 51.5; H, 5.8; N, 2.9. $C_{21}H_{29}NO_{12}$ requires C, 51.7; H, 6.0; N, 2.9%) $[\alpha]_D$ −59 (*c* 0.5 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3380 (N-H), 1764 (lactone C=O) and 1752 (ester C=O); δ_H (300 MHz; $CDCl_3$) 1.66–1.82 (2 H, m, 4- and 8-H^{β}), 2.01, 2.02, 2.08 and 2.12 (each 3 H, s, 4 × OAc), 2.36–2.56 (3 H, m, 1-H and 4- and 8-H^{α}), 3.22 (1 H, br d, *J* 4, 2-H), 3.67 (1 H, ddd, *J* 10, 4 and 2.5, 5′-H), 4.16 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.21 (1 H, dd, *J* 12.5 and 4.5, 6′-H), 4.28 (1 H, br t, *J* 4.5, 3-H), 4.67 (1 H, d, *J* 8, 1′-H), 4.74 (1 H, br t, *J* 4.5, 5-H), 4.99 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.08 (1 H, t, *J* 9.5, 4′-H) and 5.23 (1 H, t, *J* 9.5, 3′-H); δ_C(75 MHz; $CDCl_3$) 20.7 (2×), 20.8 (2×), 30.9, 37.6, 45.2, 54.7, 61.8, 68.5, 70.8, 72.0, 72.7, 73.6, 75.4, 96.9, 169.3, 169.5, 170.4, 170.7 and 176.1; *m*/*z* (FAB) 510 (MNa^+, 4%), 488 (MH^+, 50), 331 ($C_{14}H_{19}O_9^+$, 10) and 169 (100).

4-Acetamido-1,6-di-*O*-acetyl-2,4-dideoxy-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-5a-carba-β-D-*lyxo*-hexopyranose 8

Treatment of compound **25** (80 mg, 0.16 mmol) with lithium aluminium hydride (100 mg, 2.6 mmol) in dry THF (10 cm^3) and subsequent acetylation as described for the preparation of compound **20** gave, after purification by flash chromatography [EtOAc–hexanes (4 : 1) as eluent], the *title compound* **8** (0.060 g, 63%) as a colourless foam (Found: C, 52.4; H, 6.5; N, 2.3. $C_{27}H_{39}NO_{15}$ requires C, 52.5; H, 6.4; N, 2.3%) $[\alpha]_D$ +2.7 (*c* 1.0 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3431 (N-H), 2977, 1756 (ester C=O) and 1679 (amide C=O); δ_H (300 MHz; $CDCl_3$) 1.33–1.47 (1 H, m, 5a-H^{ax}), 1.57 (1 H, br dt, *J* 13.5 and 10, 2-H^{ax}), 1.76–1.91 (1 H, m, 5a-H^{eq}), 1.92–2.15 (2 H, m, 2-H^{eq} and 5-H), 1.98, 2.00, 2.03, 2.04, 2.05 and 2.08 (6, 3, 3, 3, 3 and 3 H, each s, 6 × OAc and NAc), 3.67 (1 H, ddd, *J* 9.5, 4 and 2.5, 5′-H), 3.81 (1 H, dt, *J* 10 and 4.5, 3-H), 3.93 (1 H, dd, *J* 11 and 8, 6-H), 4.14 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.19 (1 H, dd, *J* 11 and 6, 6-H), 4.26 (1 H, dd, *J* 12.5 and 4, 6′-H), 4.43 (1 H, dt, *J* 8.5 and 4, 4-H), 4.56 (1 H, d, *J* 8, 1′-H), 4.78 (1 H, tt, *J* 10 and 5, 1-H), 4.94 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.06 (1 H, t, *J* 9.5, 4′-H), 5.16 (1 H, t, *J* 9.5, 3′-H) and 5.60 (1 H, br d, *J* 8.5, NH); δ_C(75 MHz; $CDCl_3$) 20.6, 20.7, 20.8, 21.0, 21.2, 23.4, 28.8, 33.1, 36.2, 48.4, 61.5, 64.9, 67.9, 68.2, 71.5, 72.1, 72.7, 76.0, 99.9, 169.3, 169.4, 170.3, 170.4, 170.7 and 171.0; *m*/*z* (FAB) 1235 (M_2H^+, 3%), 640 (MNa^+, 4), 618 (MH^+, 39), 331 ($C_{14}H_{19}O_9^+$, 79) and 169 (100).

(1*R*,2*R*,3*R*,4*S*)-4-Hydroxy-5-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)cyclohexane-1,2-dicarboxylic anhydride 26

Cycloadduct **10** (3.512 g, 5.99 mmol) was added to an excess of a freshly prepared solution of DMDO in dry acetone (90 cm^3) and the resulting yellow solution was stirred at ambient temperature for 1 h. The solution was filtered and the filtrate was concentrated *in vacuo*. The residual solid was crystallised from acetone–diethyl ether to give the *title compound* **26** as colourless crystals (2.704 g, 85%); mp 168–170 °C (Found: C, 49.9; H, 4.85. $C_{22}H_{26}O_{15}$ requires C, 49.8; H, 4.9%) $[\alpha]_D$ −91 (*c* 0.2 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3477br (O-H), 1866 and 1780 (anhydride C=O) and 1747 (ester and ketone C=O); δ_H (300 MHz; $CDCl_3$) 1.99, 2.03, 2.09 and 2.12 (each 3 H, s, 4 × OAc), 2.85–2.97 (1 H, m, 6-H), 3.02–3.14 (1 H, m, 6-H), 3.43–3.56 (2 H, m, 1- and 2-H), 3.72 (1 H, ddd, *J* 10, 5 and 2.5, 5′-H), 4.15 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.22 and 4.26 [2 H, overlapping d (*J* 2.5) and dd (*J* 12.5 and 2.5), 4- and 6′-H, respectively], 4.53 (1 H, t, *J* 3, 3-H), 4.64 (1 H, d, *J* 8, 1′-H), 4.95 (1 H, dd, *J* 10 and 8, 2′-H), 5.02 (1 H, t, *J* 10, 4′-H) and 5.19 (1 H, t, *J* 9.5, 3′-H); δ_C (50 MHz; d_6-DMSO) 20.2, 20.4, 20.5, 33.6 (6-CH_2), 36.0, 41.5, 61.6 (6′-CH_2), 68.1, 70.3 (2×), 70.6, 71.5, 79.3, 100.5, 168.8, 169.2, 169.5, 170.0, 171.5, 173.3 and 204.7 (5-CO); *m*/*z* (FAB) 531 (MH^+, 1%), 471 ($MH^+ - CH_3CO_2H$, 1), 331 ($C_{14}H_{19}O_9^+$, 19), 205 (7), 169 (29) and 154 (100).

(1*R*,2*R*,3*R*,4*R*,5*S*)-4,5-Dihydroxy-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)cyclohexane-1,2-dicarboxylic anhydride 30

A solution of acyloin **26** (1.022 g, 1.93 mmol) in glacial acetic acid (30 cm^3) was treated with sodium cyanoborohydride (0.613 g, 9.75 mmol) and stirred overnight (15 h) at room temperature. The solvent was removed *in vacuo* and the residue was partitioned between dichloromethane (50 cm^3) and hydrochloric acid (≈1 mol dm^{-3}; 100 cm^3). The aqueous layer was extracted with dichloromethane (2 × 40 cm^3) and the combined organic layers were washed with water (200 cm^3) and dried ($MgSO_4$). Removal of the solvent gave a residue, which was crystallised from dichloromethane–diethyl ether to yield the *title compound* **30** (0.578 g, 56%) as colourless crystals; mp 187–190 °C (Found: C, 49.5; H, 5.3. $C_{22}H_{28}O_{15}$ requires C, 49.6; H, 5.3%) $[\alpha]_D$ +16 (*c* 0.2 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3522 and 3490br (O-H), 1852 and 1780 (anhydride C=O) and 1749 and 1721 (ester C=O); δ_H (300 MHz; $CDCl_3$) 1.92–2.04 (1 H, m, 6-H) overlapping with 1.99, 2.04, 2.11 and 2.14 (each 3 H, s, 4 × OAc), 2.18 (1 H, dt, *J* 14 and 4.5, 6-H), 2.69 (1 H, br d, *J* 2.5, 4-OH), 2.81 (1 H, br d, *J* 2.5, 5-OH), 3.29 (1 H, dt, *J* 3.5 and 9, 1-H), 3.45 (1 H, dd, *J* 9.5 and 4.5, 2-H), 3.64 (1 H, ddd, *J* 10, 4 and 2.5, 5′-H), 4.02–4.15 (3 H, m, 4-, 5- and 6′-H), 4.24 (1 H, t, *J* 4, 3-H), 4.50 and 4.52 [2 H, overlapping dd (*J* 12.5 and 2) and d (*J* 8), 6′- and 1′-H, respectively], 4.89 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.03 (1 H, t, *J* 9.5, 4′-H) and 5.14 (1 H, t, *J* 9.5, 3′-H); *m*/*z* (FAB) 555 (MNa^+, 2%), 331 ($C_{14}H_{19}O_9^+$, 13), 176 (8) and 136 (100).

(1*R*,2*R*,3*R*,4*S*)-4-Acetoxy-5-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)cyclohexane-1,2-dicarboxylic anhydride 27

Acyloin **26** (1.060 g, 2.00 mmol) was added to a stirred solution of acetic anhydride (5 cm^3) and a catalytic amount of perchloric acid (70% v/v; 2 drops) cooled in an ice-bath. After 10 min, the mixture was poured into water (60 cm^3) and extracted with dichloromethane (2 × 50 cm^3). The organic extracts were dried ($MgSO_4$), and concentrated *in vacuo* (<40 °C). Crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **27** (0.958 g, 84%) as colourless crystals; mp 172–175 °C (Found: C, 50.6; H, 4.7. $C_{24}H_{28}O_{16}$ requires C, 50.4; H, 4.9%) $[\alpha]_D$ −106 (*c* 0.3 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 1864 and 1782 (anhydride C=O), 1752 (ester C=O) and 1734 (ketone C=O); δ_H (300 MHz; $CDCl_3$) 1.99, 2.02, 2.08, 2.10 and 2.13 (each 3 H, s, 5 × OAc), 2.95 (1 H, dd, *J* 15.5 and 8.5, 6-H), 3.06 (1 H, dd, *J* 15.5 and 10, 6-H), 3.48 (1 H, dd, *J* 10.5 and 3.5, 2-H), 3.58 (1 H, dt, *J* 8.5 and 10, 1-H), 3.76 (1 H, ddd, *J* 10, 5 and 2.5, 5′-H), 4.13 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.23 (1 H, dd, *J* 12.5 and 5.5, 6′-H), 4.51 (1 H, dd, *J* 3.5 and 2.5, 3-H), 4.65 (1 H, d, *J* 8, 1′-H), 4.95 (1 H, dd, *J* 10 and 8, 2′-H), 5.01 (1 H, t, *J* 10, 4′-H), 5.19 (1 H, t, *J* 9.5, 3′-H) and 5.34 (1 H, d, *J* 2.5, 4-H); *m*/*z* (FAB) 573 (MH^+, 2%), 513 ($MH^+ - CH_3CO_2H$, 3), 331 ($C_{14}H_{19}O_9^+$, 62), 169 (94) and 136 (100).

Sodium cyanoborohydride reduction of ketone 27

A solution of ketone **27** (2.57 g, 4.48 mmol) in glacial acetic acid (40 cm^3) was treated with sodium cyanoborohydride (1.55 g, 24.7 mmol) and stirred overnight. Work-up, as employed for the preparation of lactone **14**, gave a 75 : 25 mixture of lactonic acids **28** and **29** (1.97 g). Slow crystallisation of the residue from dichloromethane–diethyl ether gave *(1R,2R,3R,4R,5S)-4-acetoxy-7-oxo-3-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carboxylic acid* **28** as colourless crystals (1.33 g, 52%); mp 111–120 °C (Found: C, 50.2; H, 5.3. $C_{24}H_{30}O_{16}$ requires C, 50.2; H, 5.3%) $[\alpha]_D$ −29 (*c* 0.3 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3600–2700br (O-H), 1788 (lactone C=O) and 1743 (ester and acid C=O); δ_H (300 MHz; $CDCl_3$) 1.99, 2.01, 2.05, 2.09 and 2.11 (each 3 H, s, 5 × OAc), 2.16 (1 H, d, *J* 12.5, 8-H^{β}), 2.44 (1 H, dt, *J* 12 and 6, 8-H^{α}), 3.06 (1 H, br d, *J* 5.5, 1-H), 3.12 (1 H, dd, *J* 4.5 and 1.5, 2-H), 3.72 (1 H, dt, *J* 9.5 and 3.5, 5′-H), 4.23 (2 H, d, *J* 3.5, 6′-H_2), 4.33 (1 H, br d, *J* 4.5, 3-H), 4.72 (1 H, d, *J* 8, 1′-H), 4.76 (1 H, t, *J* 4.5, 5-H), 4.94 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.08 (1 H, t, *J* 9.5, 4′-H), 5.16 (1 H, t, *J* 9.5 Hz, 3′-H) and 5.46 (1 H, br d, *J* 4.5, 4-H); δ_C (50 MHz; $CDCl_3$) 20.5, 20.6, 20.7 (2×), 20.9, 32.6 (8-CH_2), 35.7, 47.2, 61.8 (6′-CH_2), 68.5, 68.9, 70.9, 71.9, 72.8, 74.7, 76.9, 102.0, 168.7, 169.4, 169.6, 170.8, 170.9, 171.3 and 175.1; *m*/*z* (FAB) 597 (MNa^+, 3%), 575 (MH^+, 3), 515 ($MH^+ - CH_3CO_2H$, 1), 331 ($C_{14}H_{19}O_9^+$, 30), 169 (63) and 136 (100).

Slow crystallisation of the mother liquor from dichloromethane–diethyl ether–hexanes gave *(1R,2R,4S,7R,8S)-8-acetoxy-6-oxo-7-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-5-oxabicyclo[2.2.2]octane-2-carboxylic acid*† **29** as colourless crystals (0.237 g, 9%); mp 203–204 °C (Found: C, 49.9; H, 5.5. $C_{24}H_{30}O_{16}$ requires C, 50.2; H, 5.3%) $[\alpha]_D$ −59 (*c* 0.3 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3378br (O-H) and 1750 (lactone, ester and acid C=O); δ_H (300 MHz; $CDCl_3$) 2.00, 2.03, 2.06, 2.11 and 2.13 (each 3 H, s, 5 × OAc), 2.00–2.35 (2 H, m, 3-H_2), 2.96 (1 H, ddd, *J* 10.5, 7 and 1.5, 2-H), 3.30–3.34 (1 H, m, 1-H), 3.74 (1 H, dt, *J* 10 and 3.5, 5′-H), 4.13 (1 H, br t, *J* 2.5, 7-H), 4.20 (1 H, dd, *J* 12.5 and 2.5, 6′-H), 4.26 (1 H, dd, *J* 12.5 and 3.5, 6′-H), 4.74 (1 H, d, *J* 8, 1′-H), 4.77–4.83 (1 H, m, 4-H), 4.97 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.05–5.13 (2 H, m, 8- and 4′-H) and 5.22 (1 H, t, *J* 9.5, 3′-H); δ_C (75 MHz; $CDCl_3$) 20.6, 20.7, 20.8, 23.5, 36.8, 42.1, 61.6, 68.2, 70.7, 72.0, 72.7, 77.4, 97.9, 169.0, 169.3, 169.5, 169.7, 170.5, 170.9 and 174.8; *m*/*z* (FAB) 597 (MNa^+, 4%), 575 (MH^+, 6), 515 ($MH^+ - CH_3CO_2H$, 1), 331 ($C_{14}H_{19}O_9^+$, 49), 169 (78) and 136 (100).

(1*R*,2*R*,3*R*,4*R*,5*S*)-4-Acetoxy-7-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbonyl chloride 32

To a solution of lactonic acid **28** (1.119 g, 1.95 mmol) in dry dichloromethane (50 cm^3) were added oxalyl dichloride (0.50 cm^3, 5.73 mmol) and a catalytic amount of dry DMF (2 drops). Stirring was continued until the evolution of bubbles ceased (30 min). The mixture was poured into water (100 cm^3), extracted with dichloromethane (2 × 30 cm^3) and the combined extracts were washed with water (200 cm^3), dried ($MgSO_4$) and the solvent was removed *in vacuo* (<30 °C). Crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **32** as colourless crystals (0.950 g, 82%); mp 160–167 °C (decomp.) (Found: C, 48.4; H, 4.8; Cl, 5.9. $C_{24}H_{29}ClO_{15}$ requires C, 48.6; H, 4.9; Cl, 6.0%); ν_{max} (KBr)/cm^{-1} 1818 (acyl chloride C=O), 1790 (lactone C=O) and 1758br (ester C=O); δ_H (300 MHz; $CDCl_3$) 1.98, 2.01, 2.05, 2.09 and 2.14 (each 3 H, s, 5 × OAc), 1.98–2.14 (1 H, m, 8-H^{β}), 2.40–2.50 (1 H, m, 8-H^{α}), 3.05 (1 H, br d, *J* 5, 1-H), 3.44 (1 H, dd, *J* 4.5 and 2, 2-H), 3.74 (1 H, ddd, *J* 9.5, 4 and 2.5, 5′-H), 4.21 (1 H, dd, *J* 12.5 and 4, 6′-H), 4.28 (1 H, dd, *J* 12.5 and 3, 6′-H), 4.46 (1 H, br d, *J* 4, 3-H), 4.71 and 4.75 [2 H, overlapping d (*J* 8) and t (*J* 4.5), 1′- and 5-H, respectively], 4.99 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.08 (1 H, t, *J* 9.5, 4′-H), 5.17 (1 H, t, *J* 9.5, 3′-H) and 5.66 (1 H, br d, *J* 4.5, 4-H); *m*/*z* (FAB) 595 and 593 (each MH^+, 0.5 and 2%), 331 ($C_{14}H_{19}O_9^+$, 32), 169 (67) and 154 (100).

(1*R*,4*S*,5*S*)-4-Acetoxy-7-oxo-6-oxabicyclo[3.2.1]oct-2-ene-2-carbonyl azide 31

Sodium azide (0.338 g, 5.20 mmol) was added to a stirred solution of acid chloride **32** (0.383 g, 0.646 mmol) in THF (30 cm^3) and the resulting reaction was monitored by TLC until complete (≈4 h). The reaction mixture was then poured into water (100 cm^3) and extracted with dichloromethane (2 × 50 cm^3), and the combined extracts were washed with water (200 cm^3), dried ($MgSO_4$) and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography [gradient elution; EtOAc–hexanes (1 : 1 ⟶ 7 : 3)] to give two fractions.

The first fraction was the *title compound* **31** (0.115 g, 71%) as a colourless solid; mp 90–91 °C (from CH_2Cl_2–Et_2O) (Found: C, 47.8; H, 3.5; N, 17.0. $C_{10}H_9N_3O_5$ requires C, 47.8; H, 3.6; N, 16.7%) $[\alpha]_D$ +271 (*c* 0.2 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 2142 (N_3), 1782 (lactone C=O), 1732 (ester C=O) and 1680 (unsaturated acyl azide C=O); δ_H(300 MHz; $CDCl_3$) 2.04 (1 H, d, *J* 12, 8-H^{β}), 2.13 (3 H, s, OAc), 2.49 (1 H, dt, *J* 12 and 5, 8-H^{α}), 3.76 (1 H, d, *J* 4.5, 1-H), 4.74–4.80 (1 H, m, 5-H), 5.40 (1 H, t, *J* 3, 4-H) and 6.87 (1 H, ddd, *J* 3.5, 1.5 and 1, 3-H); δ_C (75 MHz; $CDCl_3$) 20.8, 30.7, 36.6, 65.7, 75.2, 135.2, 135.8, 169.2, 169.6 and 174.0; *m*/*z* (FAB) 252 (MH^+, 17%), 167 (10) and 136 (100).

The second fraction was a mixture of the α- and β-anomer of tetra-*O*-acetyl-D-glucopyranose (0.219 g, 97%) as a clear syrup.

(1*R*,2*R*,3*R*,4*R*,5*S*)-4-Acetoxy-7-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbonyl azide 33

Sodium azide (0.544 g, 8.37 mmol) was added to a solution of acid chloride **32** (0.528 g, 0.891 mmol) in dichloromethane (50 cm^3) and the resulting mixture was stirred until starting material could not be detected by TLC (≈2 h). Water (100 cm^3) was added and the mixture was extracted with dichloromethane (2 × 50 cm^3). The combined extracts were washed with water (200 cm^3), dried ($MgSO_4$) and concentrated. Crystallisation of the residue from dichloromethane–diethyl ether gave the title compound **33** (0.493 g, 92%) as colourless crystals; mp 160–209 °C (decomp.) $[\alpha]_D$ −41 (*c* 0.3 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 2154 (N_3), 1789 (lactone C=O) and 1755 (ester and azide C=O); δ_H (300 MHz; $CDCl_3$) 1.99, 2.01, 2.05 and 2.09 (each 3 H, s,

4 × OAc), 2.11 and 2.13 [4 H, overlapping s and d (*J* 12.5), OAc and 8-H$^{\beta}$, respectively], 2.38–2.50 (1 H, m, 8-H$^{\alpha}$), 3.01–3.08 (2 H, m, 1- and 2-H), 3.72 (1 H, ddd, *J* 10, 4 and 3, 5′-H), 4.18–4.29 (3 H, m, 6′-H$_2$ and 3-H), 4.69 (1 H, d, *J* 8, 1′-H), 4.74 (1 H, t, *J* 5, 5-H), 4.96 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.08 (1 H, t, *J* 9.5, 4′-H), 5.17 (1 H, t, *J* 9.5, 3′-H) and 5.48 (1 H, br d, *J* 4.5, 4-H); *m*/*z* (FAB) 600 (MH$^+$, 7%), 594 (2), 331 ($C_{14}H_{19}O_9^+$, 52), 169 (64) and 139 (100).

Benzyl (1*R*,2*R*,3*R*,4*R*,5*S*)-4-acetoxy-7-oxo-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octane-2-carbamate 34

A mixture of dry benzyl alcohol (0.19 cm^3, 1.84 mmol) and acyl azide **33** (0.087 g, 0.145 mmol) in dry benzene (30 cm^3) was heated under reflux for 48 h. Evaporation of the mixture *in vacuo* and purification of the residue by silica gel column chromatography [gradient elution; EtOAc–hexanes (2 : 3⟶4 : 1)] gave the title compound **34** (0.084 g, 85%) as a clear oil (Found: MH$^+$, 680.2178. $C_{31}H_{38}NO_{16}$ requires MH$^+$, 680.2191); $[\alpha]_D$ −30 (*c* 0.3 in CH_2Cl_2); ν_{max} (Nujol)/cm^{-1} 3402 (N-H), 1785 (lactone C=O), 1754 (ester C=O) and 1723 and 1707 (carbamate C=O); δ_H (300 MHz; $CDCl_3$) 1.88, 1.97, 2.01, 2.08 and 2.10 (each 3 H, s, 5 × OAc), 2.27 (1 H, d, *J* 12.5, 8-H$^{\beta}$), 2.42 (1 H, br dt, *J* 12 and 6, 8-H$^{\alpha}$), 2.62 (1 H, dd, *J* 5.5 and 2.5, 1-H), 3.65 (1 H, dt, *J* 9.5 and 3.5, 5′-H), 3.95 (1 H, br d, *J* 4.5, 3-H), 4.20 and 4.24 [3 H, overlapping d (separation 3.5) and ddd (*J* 10, 5 and 2.5), 6′-H$_2$ and 2-H, respectively], 4.55 (1 H, d, *J* 8, 1′-H), 4.73 (1 H, t, *J* 5, 5-H), 4.97 (1 H, br t, *J* 8.5, 2′-H), 5.03–5.19 (4 H, m, OC*H*$_2$Ph, 3′- and 4′-H), 5.50 (1 H, br d, *J* 4.5, 4-H), 5.58 (1 H, br d, *J* 10, NH) and 7.32–7.38 (5 H, m, C_6H_5); δ_C (75 MHz; $CDCl_3$) 20.4, 20.7, 20.8, 20.9, 31.8, 41.4, 51.0, 61.7, 67.5, 68.2, 69.2, 71.7, 72.2, 72.9, 74.9, 78.9, 102.7, 128.5, 128.7, 135.9, 155.6, 168.9, 169.2, 169.3, 170.4, 170.8 and 175.2; *m*/*z* (FAB) 702 (MNa$^+$, 1%), 680 (MH$^+$, 4), 331 ($C_{14}H_{19}O_9^+$, 13), 169 (27) and 91 (100).

(1*R*,2*R*,3*R*,4*R*,5*S*)-4-Acetoxy-2-amino-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)-6-oxabicyclo[3.2.1]octan-7-one 35

A mixture of the benzyl carbamate **34** (0.075 g, 0.110 mmol) and 10% palladium–carbon (0.033 g, 0.45 mass equiv.) in ethanol (25 cm^3) was stirred under an atmosphere of hydrogen for 21 h. The mixture was filtered through a Celite® pad, which was then washed with dichloromethane (50 cm^3). The combined filtrate and washings were concentrated *in vacuo*. The residue was dissolved in dichloromethane (20 cm^3) and the solution was extracted with hydrochloric acid (≈1 mol dm^{-3}; 3 × 30 cm^3). The combined aqueous layers were basified using solid sodium hydrogen carbonate and extracted with dichloromethane (2 × 80 cm^3). The organic extracts were washed with water (200 cm^3), dried ($MgSO_4$) and the solvent was removed. Crystallisation of the residue from dichloromethane–diethyl ether gave the *title compound* **35** (0.033 g, 55%) as colourless crystals; mp 195–205 °C (Found: C, 50.6; H, 5.5; N, 2.5. $C_{23}H_{31}NO_{14}$ requires C, 50.6; H, 5.7; N, 2.6%) $[\alpha]_D$ −42 (*c* 0.2 in CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3419 (N-H), 1775 (lactone C=O) and 1746 (ester C=O); δ_H (300 MHz; $CDCl_3$) 1.99, 2.01, 2.07, 2.08 and 2.09 (each 3 H, s, 5 × OAc), 2.14 (1 H, d, *J* 11.5, 8-H$^{\beta}$), 2.28–2.43 (2 H, m, 8-H$^{\alpha}$ and 1-H), 3.28 (1 H, dd, *J* 5 and 2, 2-H), 3.69 (1 H, ddd, *J* 9.5, 4.5 and 3, 5′-H), 4.00 (1 H, br d, *J* 5, 3-H), 4.19 and 4.24 [2 H, overlapping dd (*J* 12 and 3) and dd (*J* 12 and 4.5), 6′-H$_2$], 4.72 and 4.76 [2 H, overlapping br t (*J* 5.5) and d (*J* 8), 5- and 1′-H, respectively], 5.03 (1 H, dd, *J* 9.5 and 8, 2′-H), 5.09 (1 H, t, *J* 9.5, 4′-H), 5.17 (1 H, t, *J* 9.5, 3′-H) and 5.40 (1 H, dt, *J* 4.5 and 1.5, 4-H); δ_C (75 MHz; $CDCl_3$) 20.6, 20.7, 20.8, 31.9, 45.2, 52.9, 61.8, 68.4, 69.9, 71.4, 72.0, 72.9, 75.0, 79.1, 102.2, 168.8, 169.0, 169.3, 170.3, 170.7 and 175.7; *m*/*z* (FAB) 1091 (M_2H^+, 2%), 568 (MNa$^+$, 5), 546 (MH$^+$, 26), 331 ($C_{14}H_{19}O_9^+$, 7) and 154 (100).

4-Acetamido-1,2,6-tri-*O*-acetyl-4-deoxy-3-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-5a-carba-β-L-galactopyranose 9

Lithium aluminium hydride (0.152 g, 4.01 mmol) was carefully added to a solution of amine **35** (0.078 g, 0.143 mmol) in dry THF (30 cm^3) and the resulting mixture was heated under reflux for 36 h. The work-up procedure and subsequent acetylation protocol was that used for the preparation of compound **16**. Purification of the residue obtained by silica gel column chromatography [EtOAc–hexanes (9 : 1) as eluent] gave the title compound **9** as a colourless syrup (0.059 g, 61%); R_f 0.6 (EtOAc) (Found: MH$^+$, 676.2455. $C_{29}H_{42}NO_{17}$ requires MH$^+$, 676.2453) $[\alpha]_D$ −20 (*c* 0.3 in CH_2Cl_2); ν_{max} (film)/cm^{-1} 3450 (N-H), 1744 (ester C=O) and 1688 and 1671 (amide C=O); δ_H (300 MHz; $CDCl_3$) 1.36 (1 H, br q, *J* 12.5, 5a-H^{ax}), 1.98, 2.01, 2.03, 2.06 and 2.08 (3, 6, 6, 6 and 3 H, each s, 7 × OAc and NAc) overlapping with 2.01–2.08 (2 H, m, 5-H and 5a-H^{eq}), 3.72 (1 H, ddd, *J* 10, 4.5 and 2.5, 5′-H), 3.78–3.87 (2 H, m, 3- and 6-H), 4.06 (1 H, dd, *J* 12.5 and 2, 6′-H), 4.16 (1 H, dd, *J* 11.5 and 7, 6-H), 4.35 (1 H, dd, *J* 12.5 and 4.5, 6′-H), 4.61 and 4.60–4.67 [2 H, overlapping d (*J* 7.5) and m, 1′- and 4-H, respectively], 4.79–4.91 (2 H, m, 1- and 2′-H), 5.06, 5.09 and 5.16 [3 H, overlapping t (*J* 10), t (*J* 9.5) and t (*J* 9), 4′-, 2- and 3′-H, respectively] and 5.60 (1 H, br d, *J* 9.5, NH); δ_C (75 MHz; $CDCl_3$) 20.6, 20.7, 20.8, 21.0, 23.4, 27.5, 35.5, 46.8, 61.8, 64.2, 68.1, 70.7, 71.0, 71.6, 71.8, 73.0, 98.9, 169.5 (2×), 170.1 (2×), 170.3, 170.5 (2×) and 170.8; *m*/*z* (FAB) 698 (MNa$^+$, 1%), 676 (MH$^+$, 10), 616 (MH$^+$ − CH_3CO_2H, 6), 331 ($C_{14}H_{19}O_9^+$, 50), 169 (95) and 136 (100).

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