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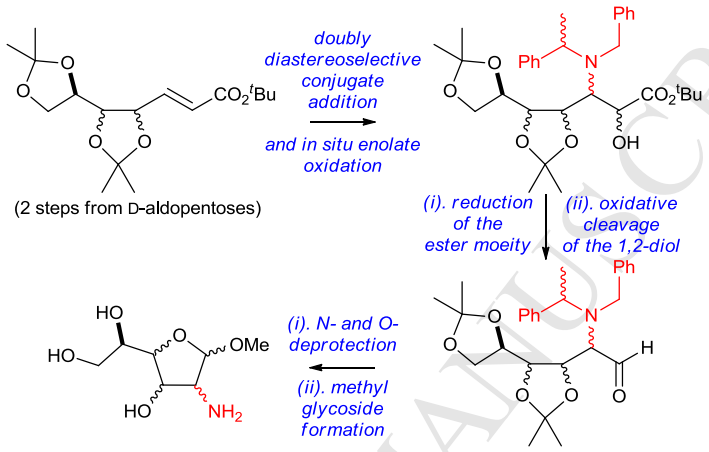

Asymmetric syntheses of the methyl glycosides of 2-deoxy-2-aminohexoses: D-allosamine, D-mannosamine, D-idosamine and D-talosamine

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Abstract

A range of the methyl glycosides of 2-deoxy-2-aminohexoses, comprising D-allosamine, D-mannosamine, D-idosamine and D-talosamine, were prepared from the corresponding D-aldopentoses via a seven step synthetic sequence. The doubly diastereoselective conjugate additions of the requisite antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide and in situ enolate oxidation with the requisite antipode of camphorsulfonyloxaziridine (CSO) was used as the key, stereodefining step. Sequential reduction of the resultant α-hydroxy-β-amino esters and oxidative cleavage of the C(1)–C(2) diol unit furnished the corresponding α-amino aldehydes. Subsequent *N*- and *O*-deprotection gave the target compounds (as mixtures of anomers) in good yield and high diastereoisomeric purity.

Key words: aminosugars, 2-deoxy-2-aminohexoses, lithium amide, conjugate addition, asymmetric synthesis

Dedicated to the memory of Professor Sandy McKillop.

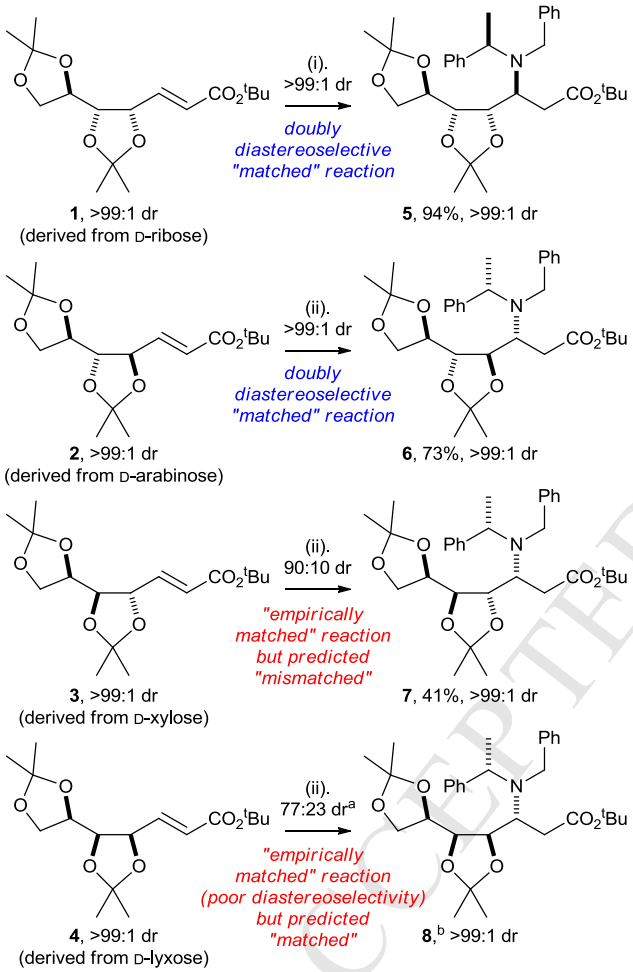
1. Introduction

Aminosugars are defined as "*monosaccharides having one alcoholic hydroxyl group replaced by an amino group*"; however, this category excludes glycosylamines [where such replacement occurs at the C(1)-position] and iminosugars [in which the endocyclic oxygen atom has been replaced by a nitrogen atom].[1] Aminosugars are ubiquitous in nature, occurring in plants, mammals, invertebrates and microorganisms,[2] and a great variety of aminosugars have been isolated from natural sources.[3] The class of aminosugars has been known for over one hundred and ninety years;[4] however, the intense fascination with these compounds

within the scientific community is relatively recent, and was initiated by the 1946 discovery of 2-deoxy-2-(*N*-methylamino)-L-glucosamine as a component in the antibiotic streptomycin.[5] Aminosugars play many important physiological roles, and a large assortment of biosynthetic materials contain aminosugar components. For example, nucleoside and aminoglycoside antibiotics,[6] chitin (exoskeletal material of *Crustacea*),[7] bacterial glycolipids,[8] serum mucoproteins (blood group antigen determinants),[9] anticoagulants,[10] and biopolymers responsible for cell recognition, differentiation and protection[11] all possess aminosugar residues. Aminosugars undergo biochemical reactions not only intracellularly, but also at the cell surface and within the extracellular matrix.[12] Due to this wide and varied biological activity, aminosugars have been targeted and extensively tested as causative agents and potential therapeutics for various diseases and medical conditions. Aminosugars have thus been linked to the pathogenesis of leukaemia,[13] liver abscesses,[14] and bacterial sepsis.[15] On the other hand, these compounds are used in the treatment of viral infections,[16] mycoses,[17] and colon, stomach, and liver cancers.[18] The well recognised biological importance of aminosugars has stimulated significant efforts towards the synthesis of this class of compounds.[19,20] Traditionally, aminosugars have been synthesised through multi-step transformations of other relatively inexpensive and readily available carbohydrates.[21] However, recent interest has increasingly focused on non-carbohydrate precursors as well.[22]

As part of our ongoing research programme concerning the asymmetric synthesis of enantiopure pyrrolidines and piperidines,[23] including iminosugars,[24] we have previously established the doubly diastereoselective[25] "matched" and "mismatched" pairings of chiral reagent and chiral substrate upon conjugate addition[26] of either antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide **9** to α,β-unsaturated esters **1**–**4** (which were all derived from D-aldopentoses), and employed these reactions as the key stereodefining step in the asymmetric syntheses of two novel dihydroxyhomoprolines.[27] The levels of diastereoselectivity obtained were variable and two of these polyoxygenated substrates were found not to conform to the usual pattern of "matching" and "mismatching" observed upon conjugate addition of either antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide **9** to chiral α,β-unsaturated esters,[28] although in each case diastereoisomerically pure (>99:1 dr) samples of the resultant β-amino esters were isolated after purification. The lithium amide conjugate addition reactions to α,β-unsaturated esters **1** and **2** conformed to the predicted outcomes in that the doubly diastereoselective "matched" reactions had proceeded with the same sense, and with an enhanced level, of diastereocontrol as those suggested by the substrate control experiments (upon conjugate addition of

an achiral lithium amide *viz*. lithium *N*-isopropyl-*N*-benzylamide), resulting in the preferential formation of the corresponding 3,4-*anti*-β-amino ester products **5** and **6**, respectively. In contrast to this, in the case of the D-lyxose derived α,β-unsaturated ester **4**, an erosion in diastereoselectivity was observed for the conjugate addition reactions of both antipodes of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide **9** compared with the analogous reaction with lithium *N*-isopropyl-*N*-benzylamide. Furthermore, in the case of **3**, the "empirically matched" conjugate addition reaction of (*S*)-**9** had proceeded to give the 3,4-*syn*-β-amino ester **7** preferentially, whilst the substrate control experiment had indicated preferential attack on the opposing face of the α,β-unsaturated ester **3**, giving a 3,4-*anti*-β-amino ester as the major product (Scheme 1).



Scheme 1. *Reagents and conditions*: (i) lithium (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*R*)-**9**, THF, –78 °C, 2 h; (ii) lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9**, THF, –78 °C, 2 h. [[a] 8% conversion to the corresponding β,γ-unsaturated ester was also observed; [b] an 86:14 mixture of **8** (>99:1 dr) and the corresponding β,γ-unsaturated ester was isolated].

It was envisaged that our diastereoselective aminohydroxylation procedure[26,29,30] could be combined with this doubly diastereoselective conjugate addition methodology in the synthesis of a range of 2-deoxy-2-aminohexoses: oxidation of the intermediate lithium (*Z*)-β-amino enolates,[31] formed upon conjugate addition of either lithium amide reagent (*R*)-**9** or (*S*)-**9** to α,β-unsaturated esters **1**–**4**, with the requisite antipode of

camphorsulfonyloxaziridine (CSO) **10** would give the corresponding α-hydroxy-β-amino esters **11**, and subsequent reduction followed by oxidative cleavage of the resultant 1,2-diols **12** would produce the corresponding α-amino aldehydes **13**, which constitute protected forms of the target 2-deoxy-2-aminohexoses (Fig. 1). Upon application of this procedure in the aminohydroxylation of achiral α,β-unsaturated esters,[26] we have observed that the combinations of lithium amide (*R*)-**9** and (–)-CSO **10**, and (*S*)-**9** and (+)-CSO **10**, offer marginally better levels of diastereoselectivity, although any combination of **9** and **10** yields the corresponding 2,3-*anti*-configured α-hydroxy-β-amino ester with reasonably high diastereoselectivity.

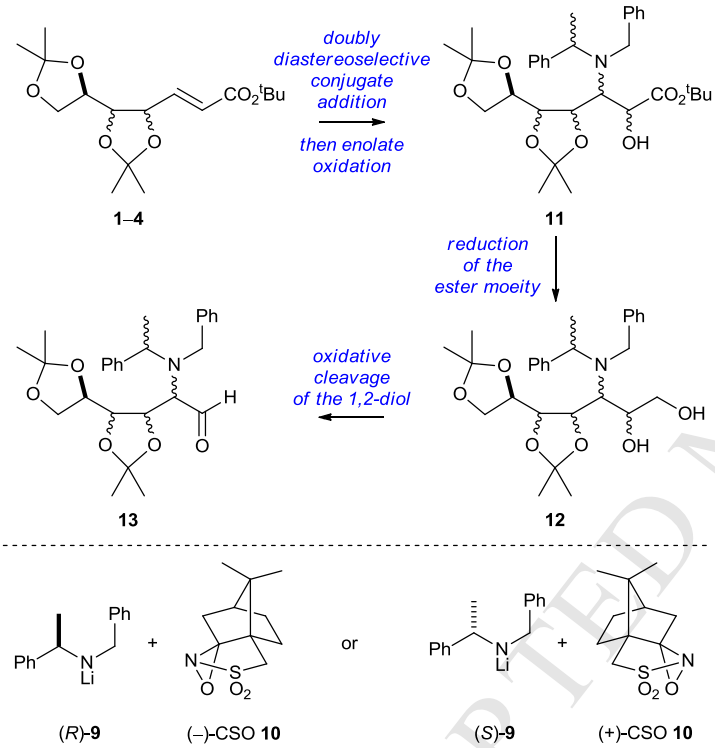


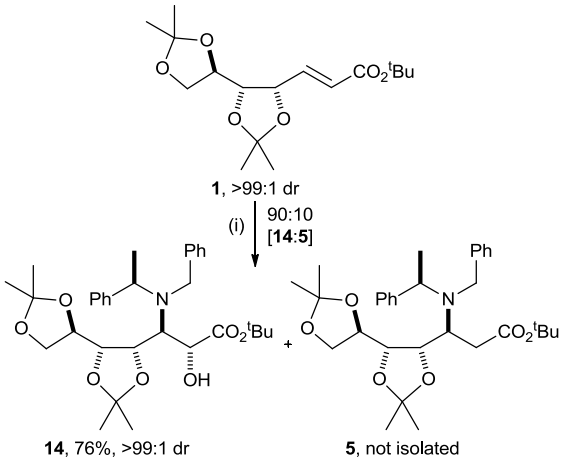
Figure 1. Proposed synthesis of protected 2-deoxy-2-aminohexoses **13**.

2. Results and discussion

2.1. Asymmetric synthesis of D-allosamine

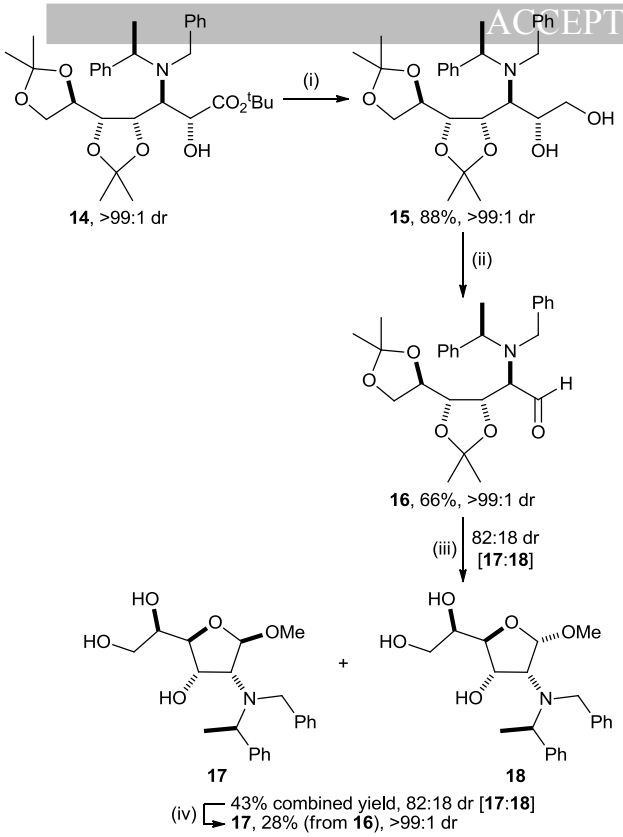
The conjugate addition of lithium (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*R*)-**9** to the D-ribose derived α,β-unsaturated ester **1** followed by in situ oxidation of the resultant lithium (*Z*)-β-amino enolate[31] with (–)-CSO **10** gave α-hydroxy-β-amino ester **14** (>99:1 dr) and the known β-amino ester **5**[27] (>99:1 dr) in a 90:10 ratio. After chromatographic purification of the crude reaction mixture **14** was isolated in 76% yield and >99:1 dr (Scheme 2). In the corresponding reaction with (+)-CSO, an 85:15 mixture of **14** and **5** was produced, from which **14** was isolated in 53% yield and >99:1 dr. The stereochemical outcomes of these reactions were initially assigned by analogy to the established outcomes observed upon aminohydroxylation

of achiral α,β-unsaturated esters[26] using this protocol, and was later confirmed unambiguously by single crystal X-ray diffraction analysis of a derivative of **14**.



Scheme 2. *Reagents and conditions*: (i) lithium (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*R*)-**9**, THF, –78 °C, 2 h, then (–)-CSO **10**, –78 °C to rt, 12 h.

Reduction of the ester moiety within **14** upon treatment with $LiAlH_4$ gave diol **15** which was isolated in 88% yield and >99:1 dr (Scheme 3). The relative configuration within **15** was assigned unambiguously by single crystal X-ray diffraction analysis,[32] and the absolute (2*R*,3*S*,4*S*,5*S*,6*R*,α*R*)-configuration within **15** was assigned relative to the known configurations of the D-ribose derived dioxolane units and the α-methylbenzyl fragment (Fig. 2); this analysis also secured the assigned configuration within α-hydroxy-β-amino ester **14**. Treatment of **15** with $NaIO_4$ effected cleavage of the 1,2-diol unit within **15** to give aldehyde **16** in 66% yield and >99:1 dr, then deprotection of the dioxolane units with HCl in MeOH was followed by in situ cyclisation to give an 82:18 mixture of 2-aminofuranose anomers **17** and **18**, respectively, which was isolated in 43% combined yield. Further chromatographic purification provided an analytically pure (>99:1 dr) sample of **17** in 28% yield from **16** (Scheme 3).[33] The regio- and stereochemistries within both **17** and **18** were assigned by ^{1}H NMR NOE and ^{1}H–^{13}C NMR HMBC spectroscopic analyses.



Scheme 3. *Reagents and conditions*: (i) $LiAlH_4$, THF, 0 °C to rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 24 h; (iii) HCl in MeOH, 50 °C, 24 h; (iv) further purification of an aliquot.

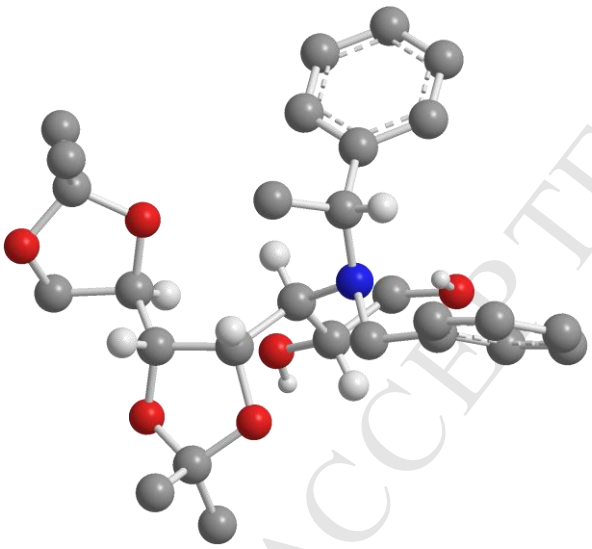
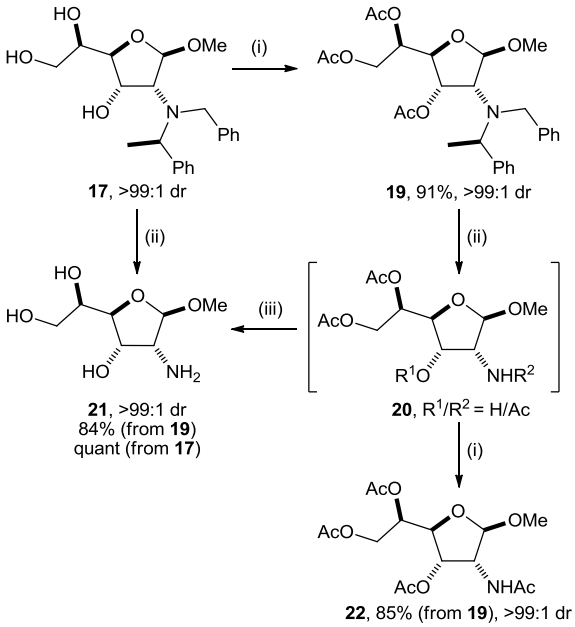


Figure 2. X-ray crystal structure of (2*R*,3*S*,4*S*,5*S*,6*R*,α*R*)-**15** (selected H atoms are omitted for clarity).

Further protecting group manipulation of the sample of **17** (>99:1 dr) produced a range of derivatives **19**–**22**. First, acetylation of the C(3)-, C(5)- and C(6)-hydroxyl groups within **17** gave **19** in 91% yield and >99:1 dr. Hydrogenolytic *N*-debenzylation of **19** produced a mixture compounds **20** [in which the C(3)-*O*-acetyl group had partially migrated onto the C(2)-amino substituent];[34] the composition of this mixture was confirmed upon treatment with Ac_2O which gave only **22** in 85% yield (from **19**) and >99:1 dr, and also upon hydrolysis of the mixture with KOH which gave only **21** in 84% yield (from **19**) and >99:1 dr. Methyl

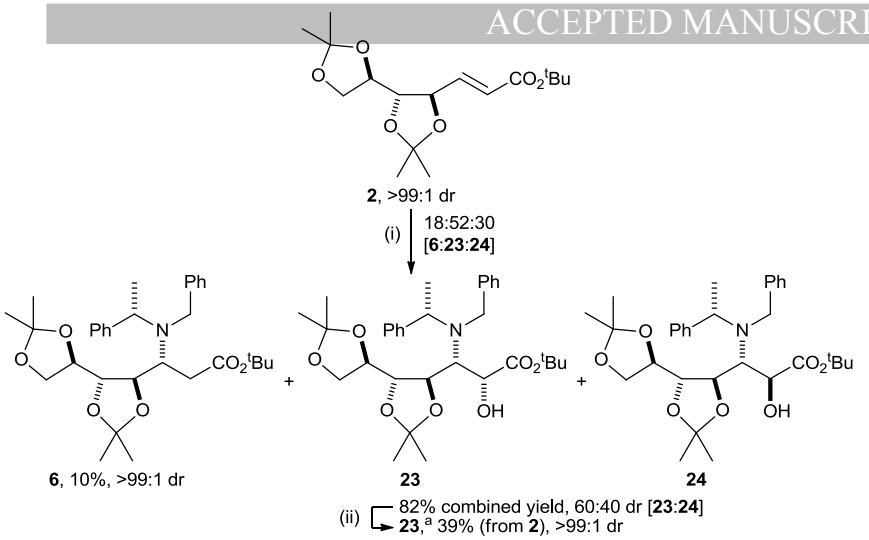
glycoside **21** was also produced directly from **17** upon hydrogenolysis in the presence of Pearlman's catalyst [$Pd(OH)_2$/C], and was isolated in quantitative yield and >99:1 dr after purification (Scheme 4). In each case, ^{1}H NMR NOE and ^{1}H–^{13}C NMR HMBC spectroscopic analyses of **19**, **21** and **22** confirmed the assigned regio- and stereochemistries: the ^{1}H NMR $^3J_{1,2}$ coupling constants for all the α-anomers in this series were in the range of 1.5–2.5 Hz, while all corresponding β-anomers possessed $^3J_{1,2}$ values of 4.7 Hz. Thus, it would appear that ^{1}H NMR $^3J_{1,2}$ coupling constants are diagnostic of the relative configuration between the C(1) and C(2) stereocentres within this series.



Scheme 4. *Reagents and conditions*: (i) Ac_2O, DMAP, pyridine, rt, 12 h; (ii) $Pd(OH)_2$/C, H_2 (1 atm), MeOH, rt, 18 h; (iii) KOH (1.0 M aq), MeOH/H_2O (1:1), rt, 4 h.

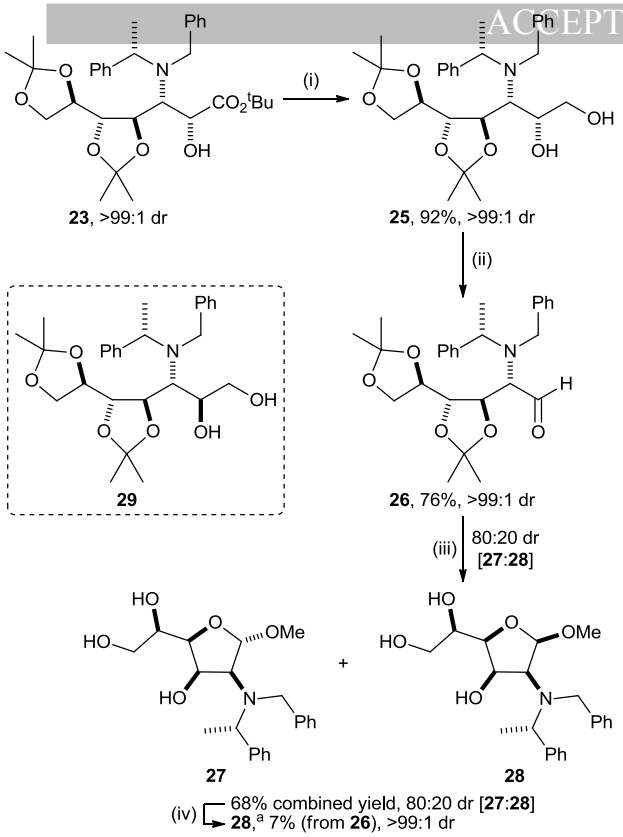
2.2. Asymmetric synthesis of D-mannosamine

For the D-arabinose derived α,β-unsaturated ester **2**, conjugate addition of lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9** followed by in situ oxidation of the resultant lithium (*Z*)-β-amino enolate[31] with (+)-CSO **10** gave an 18:52:30 mixture of the known β-amino ester **6**[27] (>99:1 dr), and α-hydroxy-β-amino esters **23** and **24**, respectively. After chromatographic purification, **6** was isolated in 10% yield and >99:1 dr, and a 60:40 mixture of **23** and **24** was isolated in 82% combined yield; further purification of an aliquot of this mixture allowed the isolation of an analytically pure sample of **23** in 39% yield (from **2**) and >99:1 dr (Scheme 5).[35]



Scheme 5. *Reagents and conditions*: (i) lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9**, THF, –78 °C, 2 h, then (+)-CSO **10**, –78 °C to rt, 12 h; (ii) further purification of an aliquot. [[a] a 20:80 mixture of **23** and **24**, respectively, was also isolated in 25% combined yield].

Reduction of **23** with $LiAlH_4$ gave diol **25** which was isolated in 92% yield and >99:1 dr (Scheme 6). The relative configuration within **25** was established by single crystal X-ray diffraction analysis of its C(2)-epimer **29**[32] (which was obtained in >99:1 dr upon reduction of the 60:40 mixture of **23** and **24**, respectively, with $LiAlH_4$ followed by recrystallisation to give **29**); the absolute (2*R*,3*R*,4*R*,5*S*,6*R*,α*S*)- and (2*S*,3*R*,4*R*,5*S*,6*R*,α*S*)-configurations within **25** and **29**, respectively, were in each case assigned relative to the known configurations of the D-arabinose derived dioxolane units and the α-methylbenzyl fragment (Fig. 3). This analysis therefore also secured the configurations within both **23** and **24**.[36] Oxidative cleavage of the C(1)–C(2) bond within **25** gave aldehyde **26** in 76% yield and >99:1 dr, and subsequent acid-mediated deprotection of the dioxolane units gave an 80:20 mixture of 2-aminofuranose anomers **27** and **28**, respectively, which was isolated in 68% combined yield. Further chromatographic purification of an aliquot provided an analytically pure (>99:1 dr) sample of the minor diastereoisomer **28** in 7% yield (from **26**), and ^{1}H NMR NOE and ^{1}H–^{13}C NMR HMBC spectroscopic analyses of this sample allowed both the regioselectivity of cyclisation and the configurations at C(1) within both **27** and **28** to be established.



Scheme 6. *Reagents and conditions*: (i) $LiAlH_4$, THF, 0 °C to rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 24 h; (iii) HCl in MeOH, 50 °C, 24 h; (iv) further purification of an aliquot. [[a] a 65:35 mixture of **27** and **28**, respectively, was also isolated in 16% combined yield].

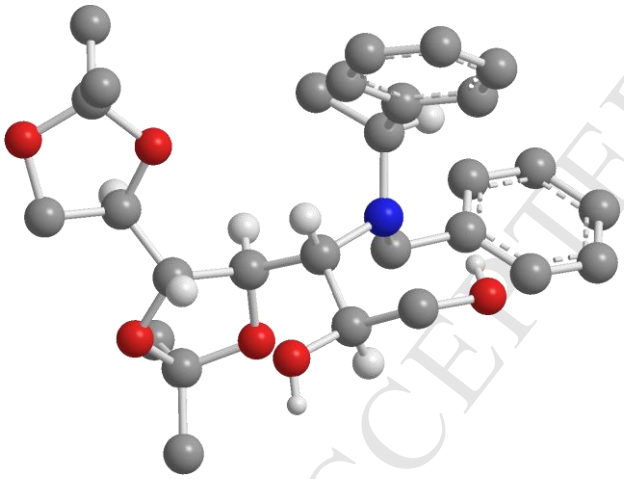
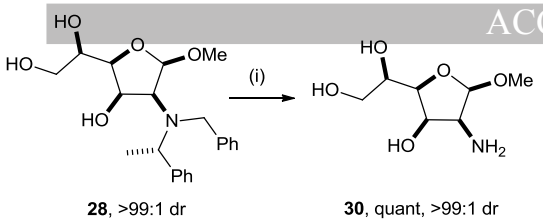


Figure 3. X-ray crystal structure of (2*S*,3*R*,4*R*,5*S*,6*R*,α*S*)-**29** (selected H atoms are omitted for clarity).

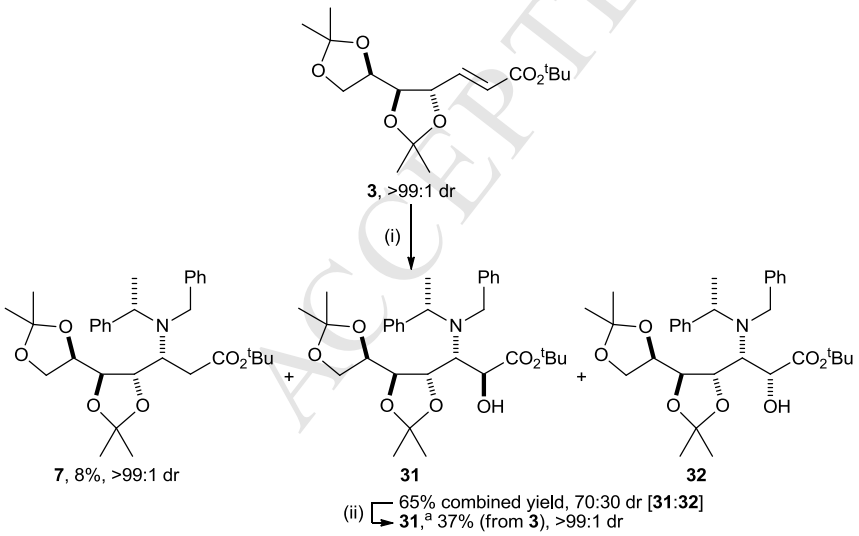
Removal of the *N*-benzyl and *N*-α-methylbenzyl protecting groups within **28** was achieved by hydrogenolysis in the presence of Pearlman's catalyst [$Pd(OH)_2$/C] which gave methyl glycoside **30** in quantitative yield and >99:1 dr, after chromatographic purification (Scheme 7). Again both ^{1}H NMR NOE and ^{1}H–^{13}C NMR HMBC spectroscopic analyses allowed the regioselectivity of cyclisation and the configuration at C(1) within **30** to be confirmed.



Scheme 7. *Reagents and conditions*: (i) $Pd(OH)_2/C$, H_2 (1 atm), MeOH, rt, 18 h.

2.3. Asymmetric synthesis of D-idosamine

For the D-xylose derived α,β-unsaturated ester **3**, we have shown that conjugate addition of lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9** followed by treatment of the resultant lithium (*Z*)-β-amino enolate with satd aq NH_4Cl gives the corresponding 3,4-*syn*-diastereoisomer **7** in 90:10 dr.[27] Application of the aminohydroxylation protocol to this substrate, treating the intermediate lithium (*Z*)-β-amino enolate with (+)-CSO **10** gave a mixture of the known β-amino ester **7**,[27] and α-hydroxy-β-amino esters **31** and **32**.[34,37] After purification of the crude reaction mixture, **7** was isolated in 8% yield and >99:1 dr, and a 70:30 mixture of **31** and **32**, respectively, was isolated in 65% combined yield; further purification of an aliquot of this mixture allowed the isolation of an analytically pure sample of **31** in 37% yield (from **3**) and >99:1 dr (Scheme 8). In this case, single crystal X-ray diffraction analysis of **31** allowed its relative configuration to be determined unambiguously,[32] with the absolute (2*S*,3*R*,4*S*,5*R*,6*R*,α*S*)-configuration within **31** being assigned relative to the known configurations of the D-xylose derived dioxolane units and the α-methylbenzyl fragment (Fig. 4); this analysis also allowed the configuration within **32** to be determined.[38]



Scheme 8. *Reagents and conditions*: (i) lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9**, THF, –78 °C, 2 h, then (+)-CSO **10**, –78 °C to rt, 12 h; (ii) further purification of an aliquot. [[a] a 15:85 mixture of **31** and **32**, respectively, was also isolated in 12% combined yield].

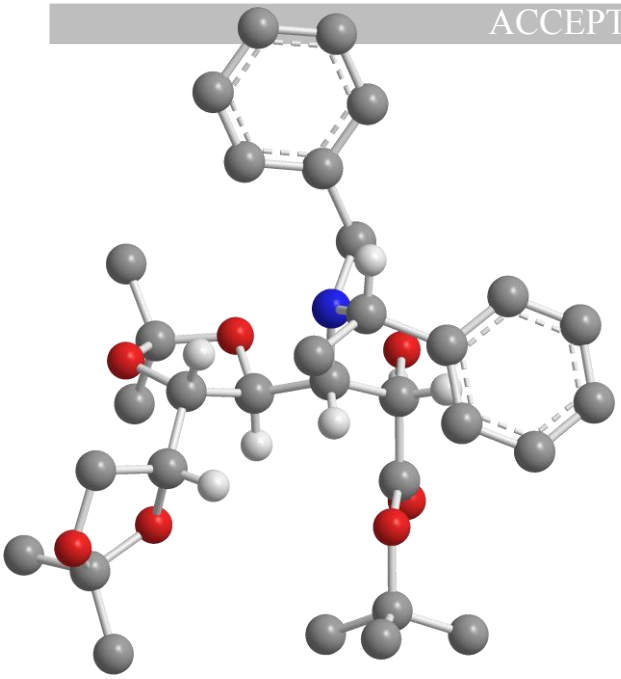
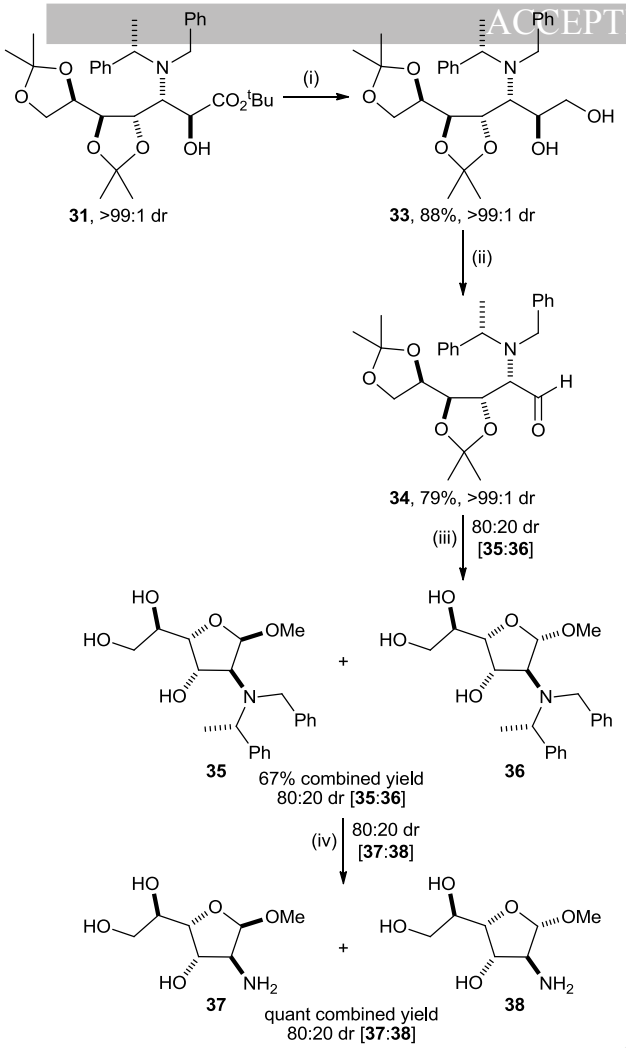


Figure 4. X-ray crystal structure of (2*S*,3*R*,4*S*,5*R*,6*R*,α*S*)-**31** (selected H atoms are omitted for clarity).

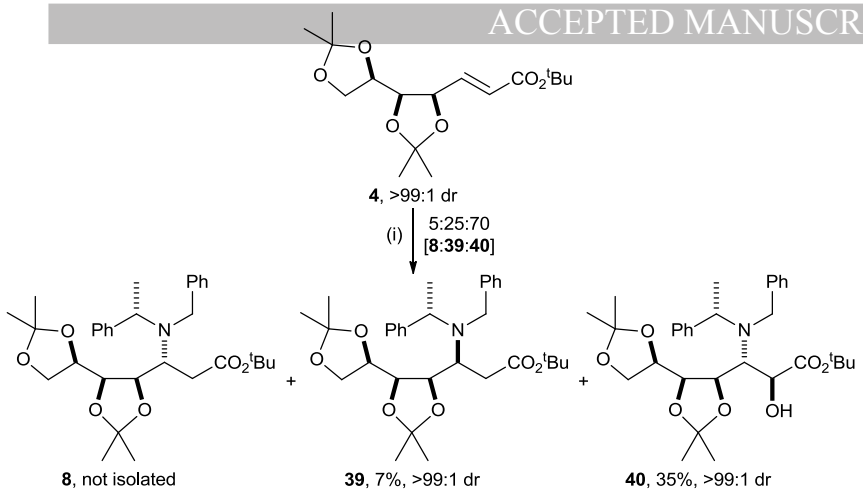
Reduction of the ester moiety within **31**, upon treatment with $LiAlH_4$, gave diol **33** in 88% yield and >99:1 dr, and subsequent oxidative cleavage of the 1,2-diol unit within **33** gave aldehyde **34** in 79% yield and >99:1 dr.[38] Treatment of **34** with HCl in MeOH gave an inseparable 80:20 mixture of 2-aminofuranose anomers **35** and **36**, respectively. Hydrogenolytic *N*-deprotection of this mixture gave an 80:20 mixture of **37** and **38**, respectively, in quantitative yield (Scheme 9). The regioselectivity of cyclisation and the configurations at C(1) within **35**–**38** were established in each case by ^{1}H NMR NOE and ^{1}H–^{13}C NMR HMBC spectroscopic analyses.



Scheme 9. *Reagents and conditions*: (i) $LiAlH_4$, THF, 0 °C to rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 24 h; (iii) HCl in MeOH, 50 °C, 24 h; (iv) $Pd(OH)_2/C$, H_2 (1 atm), MeOH, rt, 18 h.

2.4. Asymmetric synthesis of D-talosamine

For the D-lyxose derived α,β-unsaturated ester **4**, we have shown that conjugate addition of lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9** followed by treatment of the resultant lithium (*Z*)-β-amino enolate with satd aq NH_4Cl gives the corresponding 3,4-*anti*-diastereoisomer in 77:23 dr.[27] Application of the aminohydroxylation protocol to this substrate, treating the intermediate lithium (*Z*)-β-amino enolate with (+)-CSO **10**, gave a 5:25:70 mixture of the known β-amino esters **8** and **39**,[27] and α-hydroxy-β-amino ester **40**, respectively. After purification of the crude reaction mixture, **39** and **40** were isolated in 7 and 35% yield, respectively, and in >99:1 dr in each case (Scheme 10).[39] The relative configuration within **40** was established unambiguously via single crystal X-ray diffraction analysis,[32] and the absolute (2*S*,3*R*,4*R*,5*R*,6*R*,α*S*)-configuration within **40** was assigned by reference to the known configurations of the D-lyxose derived dioxolane units and the α-methylbenzyl fragment (Fig. 5).



Scheme 10. *Reagents and conditions*: (i) lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**9**, THF, –78 °C, 2 h, then (+)-CSO **10**, –78 °C to rt, 12 h.

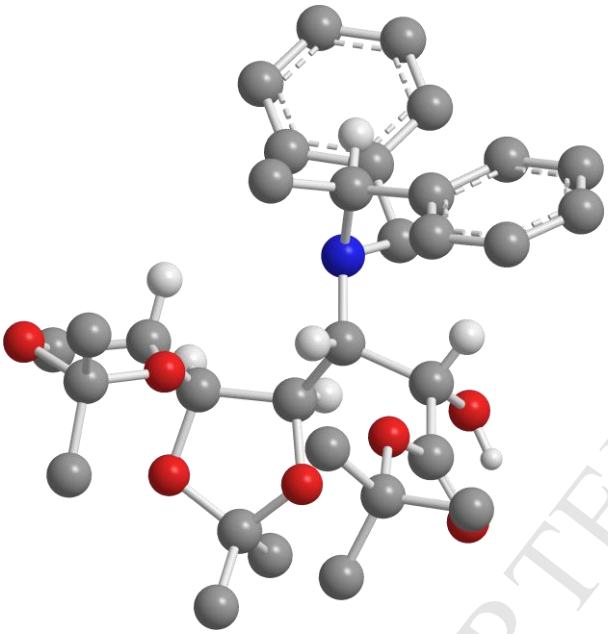
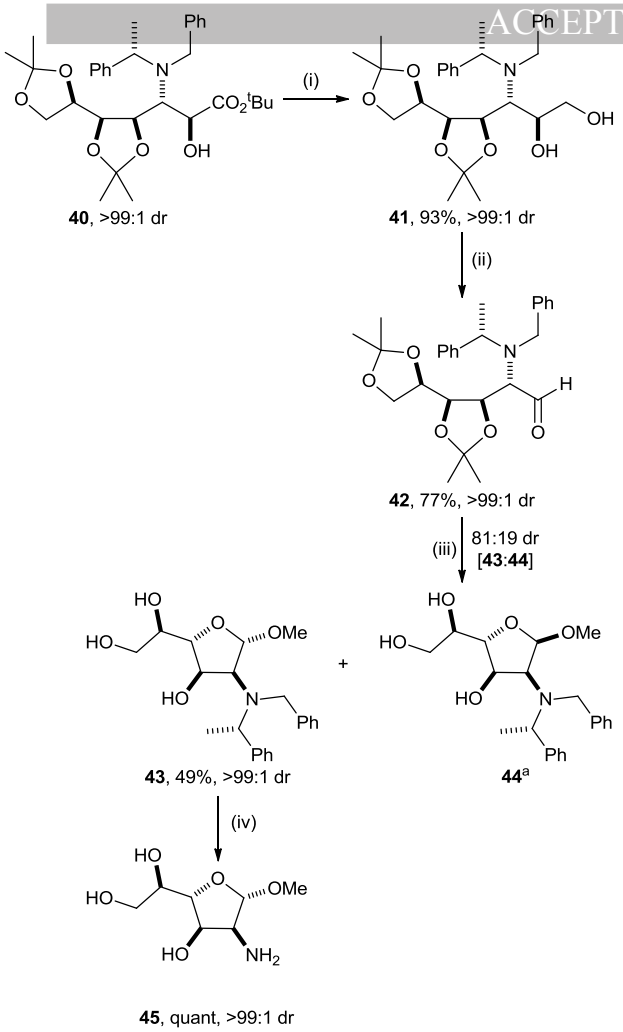


Figure 5. X-ray crystal structure of (2*S*,3*R*,4*R*,5*R*,6*R*,α*S*)-**40** (selected H atoms are omitted for clarity).

Reduction of **40** with $LiAlH_4$ gave **41** in 93% yield and >99:1 dr. Oxidative cleavage of the 1,2-diol unit within **41** gave aldehyde **42** in 77% isolated yield and >99:1 dr, and treatment of **42** with HCl in MeOH produced an 81:19 mixture of 2-aminofuranose anomers **43** and **44**, respectively. After chromatographic purification, the major diastereoisomer **43** was isolated in 49% yield and >99:1 dr. Subsequent hydrogenolytic deprotection of **43** gave **45** in quantitative yield and >99:1 dr (Scheme 11).



Scheme 11. *Reagents and conditions*: (i) $LiAlH_4$, THF, 0 °C to rt, 16 h; (ii) $NaIO_4$, MeOH, rt, 24 h; (iii) HCl in MeOH, 50 °C, 24 h; (iv) $Pd(OH)_2/C$, H_2 (1 atm), MeOH, rt, 18 h. [[a] a 33:67 mixture of **43** and **44** was isolated in 11% combined yield].

3. Conclusion

In conclusion, a range of D-aldopentoses were elaborated to the methyl glycosides of the corresponding 2-deoxy-2-aminohexoses via a seven step synthetic sequence employing the doubly diastereoselective conjugate additions of the requisite antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide and in situ enolate oxidation with the requisite antipode of camphorsulfonyloxaziridine (CSO) as the key, stereodefining step. In each case, the empirically "matched" pairings of enantiopure lithium amide reagent **9** and enantiopure oxidant **10** [i.e., (*S*)-**9** and (+)-**10**, and (*R*)-**9** and (–)-**10**] proved optimal upon aminohydroxylation of the enantiopure α,β-unsaturated esters, although in one case the preferential formation of the corresponding 2,3-*syn*-α-hydroxy-β-amino ester was noted. Sequential reduction of the resultant α-hydroxy-β-amino esters and oxidative cleavage of the C(1)–C(2) diol unit furnished the corresponding α-amino aldehydes. Subsequent *N*- and *O*-deprotection gave the target compounds which were isolated as mixtures of anomers. The conversion of the D-aldopentose derived α-hydroxy-β-amino

esters, produced using this methodology, into the corresponding 3-deoxy-3-aminoheptoses and 4-deoxy-4-aminohexoses is currently underway in our laboratory and will be reported in due course.

4. Experimental

4.1. General Experimental

Reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. BuLi was purchased as a solution in hexanes and titrated against diphenylacetic acid before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[40] Water was purified by an Elix® UV-10 system. All other reagents were used as supplied (analytical or HPLC grade) without prior purification. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq. $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Elemental analyses were recorded by the microanalysis service of the London Metropolitan University, U.K. Melting points were recorded on a Gallenkamp Hot Stage apparatus. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer using an ATR module. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. Spectra were recorded at rt. The field was locked by external referencing to the relevant deuteron resonance. $^1H–^1H$ COSY, $^1H–^{13}C$ HSQC, and $^1H–^{13}C$ HMBC NMR spectroscopic analyses were used to establish atom connectivity. When the diastereotopic methyl groups of acetonide functionalities could not be unambiguously assigned, the descriptor *Me*CMe was employed. In the ^1H and ^{13}C NMR spectra, these descriptors are intended to convey neither that the resonances are attributable to methyl groups that reside on the same, nor on different carbon atoms. Low-resolution mass spectra were recorded on a VG MassLab 20–250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

4.2. *tert*-Butyl (2*R*,3*S*,4*S*,5*S*,6*R*,α*R*)-2,4,5,6,7-pentahydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptanoate 14

BuLi (2.5 M in hexanes, 1.20 mL, 3.00 mmol) was added dropwise to a stirred solution of (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (643 mg, 3.04 mmol, >99:1 er) in THF (3 mL) at −78 °C, the resultant solution was stirred at −78 °C for 30 min. A solution of **1**[27] (500 mg, 1.52 mmol, >99:1 dr) in THF (2 mL) at −78 °C was then added dropwise and the reaction mixture was stirred at −78 °C for 2 h. (–)-CSO **10** (700 mg, 3.05 mmol) was then added and the resultant mixture was allowed to warm to rt over 12 h. The reaction mixture was then diluted with Et_2O (10 mL) and filtered. The filtrate was washed sequentially with 10% aq citric acid (10 mL), satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried and concentrated *in vacuo* to give a 90:10 mixture of **14** and **5**, respectively. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 89:11 increased to 83:17) gave **14** as a pale yellow oil (640 mg, 76%, >99:1 dr); $[\alpha]_D^{20}$ +9.7 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3502 (O–H), 2982, 2935 (C–H), 1731 (C=O); δ_H (400 MHz, $CDCl_3$) 1.14 (3H, s, *Me*CMe), 1.29 (3H, s, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.42 (3H, d, *J* 7.1, C(α)*Me*), 1.45 (3H, s, *Me*CMe), 1.51 (9H, s, C*Me*$_3$), 3.12 (1H, d, *J* 6.7, O*H*), 3.44 (1H, dd, *J* 7.9, 6.1, C(7)H_A), 3.62 (1H, app d, *J* 10.1, C(3)*H*), 3.73 (1H, d, *J* 15.9, NCH_AH$_B$Ph), 3.79 (1H, dd, *J* 7.9, 6.6, C(7)H_B), 4.14–4.23 (3H, m, C(5)*H*, C(6)*H*, C(α)*H*), 4.32–4.40 (3H, m, C(2)*H*, C(4)*H*, NCH$_A$$H_B$Ph), 7.19–7.46 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.3 (C(α)*Me*), 24.7, 25.9, 26.3, 26.7 (2 × C*Me*$_2$), 28.2 (C*Me*$_3$), 50.3 (N*C*H$_2$Ph), 59.7 (*C*(5)), 61.1 (*C*(α)), 65.6 (*C*(7)), 65.6, 70.6 (*C*(2), *C*(4)), 74.0, 74.5 (*C*(3), *C*(6)), 82.3 (*C*Me$_3$), 107.3, 109.0 (2 × *C*Me$_2$), 126.5, 127.4, 127.8, 128.2, 128.2, 128.8 (*o*,*m*,*p*-*Ph*), 142.3, 142.9 (*i*-*Ph*), 173.0 (*C*(1)); *m/z* (ESI^+) 578 ($[M+Na]^+$, 70%), 556 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{32}H_{45}NNaO_7^+$ ($[M+Na]^+$) requires 578.3088; found 578.3081.

4.3. (2*R*,3*S*,4*S*,5*S*,6*R*,α*R*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptan-1,2,4,5,6,7-hexaol 15

$LiAlH_4$ (1.0 M in THF, 1.40 mL, 1.40 mmol) was added dropwise to a stirred solution of **14** (350 mg, 0.631 mmol, >99:1 dr) in THF (5 mL) at 0 °C and the resultant mixture was allowed to warm to rt over 16 h. The reaction mixture was quenched by cautiously adding ice, then filtered through a short plug of Celite® (eluent Et_2O, 10 mL). The filtrate was then partitioned between H_2O (5 mL) and Et_2O (5 mL) and the organic layer was dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 50:50) gave **15** as a colourless viscous oil (270 mg, 88%, >99:1 dr). Further purification of an

aliquot via recrystallisation (CH_2Cl_2/*n*-heptane) gave an analytically pure sample of **15** as a white solid (>99:1 dr); $C_{28}H_{39}NO_6$ requires C, 69.25; H, 8.1; N 2.9%; found C, 69.2; H, 7.9; N, 3.0%; mp 65–69 °C; $[\alpha]_D^{20}$ –42.3 (*c* 0.3 in $CHCl_3$); ν_{max} (ATR) 3445 (O–H), 2985, 2945 (C–H), 1739 (C=O); δ_H (500 MHz, $CDCl_3$) 1.39–1.44 (9H, m, C(α)*Me*, 2 × *Me*CMe), 1.49 (3H, s, *Me*CMe), 1.58 (3H, s, *Me*CMe), 1.85 (1H, br s, C(1)O*H*), 2.80 (1H, s, C(2)O*H*), 3.09 (1H, app s, C(1)H_A), 3.38 (1H, app s, C(1)H_B), 3.62 (1H, app d, *J* 8.8, C(3)*H*), 3.83 (1H, d, *J* 14.2, NC$H_A$$H_B$Ph), 3.85–3.90 (2H, m, C(2)*H*, C(α)*H*), 3.93 (1H, dd, *J* 8.7, 5.9, C(7)H_A), 4.10 (1H, d, *J* 14.2, NCH$_A$$H_B$Ph), 4.14 (1H, dd, *J* 8.7, 6.2, C(7)H_B), 4.24 (1H, dd, *J* 9.3, 7.7, C(5)*H*), 4.56–4.61 (1H, m, C(6)*H*), 4.76 (1H, app d, *J* 7.7, C(4)*H*), 7.16–7.40 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 11.2 (C(α)*Me*), 23.3, 25.4, 26.5, 27.1 (2 × C*Me*$_2$), 52.1 (N*C*H$_2$Ph), 54.7 (*C*(3)), 56.6 (*C*(α)), 64.9 (*C*(1)), 68.3 (*C*(7)), 70.3 (*C*(2)), 73.7 (*C*(6)), 77.8 (*C*(4)), 79.0 (*C*(5)), 108.4, 109.8 (2 × *C*Me$_2$), 127.1, 127.2, 127.9, 128.4, 128.5, 129.1 (*o,m,p-Ph*), 140.4, 142.9 (*i-Ph*); *m/z* (ESI$^+$) 993 ([2M+Na]$^+$, 100%), 508 ([M+Na]$^+$, 15%), 486 ([M+H]$^+$, 80%); HRMS (ESI$^+$) $C_{28}H_{40}NO_6^+$ ([M+H]$^+$) requires 486.2850; found 486.2834.

4.4. (2*R*,3*S*,4*S*,5*R*,α*R*)-2-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-3,4,5,6,-di-*O*-isopropylidene-3,4,5,6-tetrahydroxyhexanal 16

$NaIO_4$ (220 mg, 1.03 mmol) was added to a stirred solution of **15** (170 mg, 0.351 mmol, >99:1 dr) in MeOH (10 mL) at rt, and the resultant mixture was left to stir at rt for 24 h. The resultant suspension was filtered through a short plug of Celite® (eluent MeOH, 15 mL), and the filtrate was concentrated *in vacuo*. The residue was diluted with Et_2O (20 mL) and filtered through a short plug of Celite® (eluent Et_2O, 20 mL), then the filtrate was concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 83:17) gave **16** as a yellow oil (105 mg, 66%, >99:1 dr); $[\alpha]_D^{20}$–80.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2986, 2936 (C–H), 1731 (C=O); δ_H (500 MHz, $CDCl_3$) 1.18 (3H, s, *Me*CMe), 1.24 (3H, s, *Me*CMe), 1.33 (6H, s, 2 × *Me*CMe), 1.38 (3H, d, *J* 6.9, C(α)*Me*), 3.87 (1H, dd, *J* 8.5, 5.4, C(6)H_A), 4.06–4.20 (5H, m, C(2)*H*, C(4)*H*, C(5)*H*, C(6)H_B, C(α)*H*), 4.21 (1H, d, *J* 15.1, NC$H_A$$H_B$Ph), 4.26 (1H, d, *J* 15.1, NCH$_A$$H_B$Ph), 4.65 (1H, app d, *J* 6.6, C(3)*H*), 7.20–7.55 (10H, m, *Ph*), 9.60 (1H, s, C(1)*H*); δ_C (125 MHz, $CDCl_3$) 16.9 (C(α)*Me*), 24.3, 25.1, 26.5, 26.7 (2 × C*Me*$_2$), 52.1 (N*C*H$_2$Ph), 58.4, 64.0, 73.9, 78.5 (*C*(2), *C*(4), *C*(5), *C*(α)), 68.3 (*C*(6)), 79.2 (*C*(3)), 109.1, 109.7 (2 × *C*Me$_2$), 126.8, 127.0, 127.7, 128.2, 128.2, 128.3 (*o,m,p-Ph*), 141.4, 143.7 (*i-Ph*), 202.5 (*C*(1)); *m/z* (ESI$^+$) 476 ([M+Na]$^+$, 100%), 454 ([M+H]$^+$, 85%); HRMS (ESI$^+$) $C_{27}H_{35}NNaO_5^+$ ([M+Na]$^+$) requires 476.2407; found 476.2400.

4.5. Methyl (1*R*,2*R*,3*S*,4*S*,5*R*,α*R*)-2-deoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-β-D-allofuranose 17

A solution of HCl in MeOH (1.25 M, 35 mL) was added to **16** (840 mg, 1.85 mmol), and the resultant mixture was heated at 50 °C for 24 h. The reaction mixture was then allowed to cool to rt, concentrated *in vacuo*, and the residue was partitioned between 2.0 M aq NaOH (30 mL) and CH_2Cl_2 (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give an 82:18 mixture of **17** and **18**, respectively. Purification via flash column chromatography (eluent CH_2Cl_2/MeOH, 96:4) gave an 82:18 mixture of **17** and **18**, respectively, as a pale yellow oil (305 mg, 43%). Further purification of an aliquot (75 mg) via flash column chromatography (eluent CH_2Cl_2/MeOH, 98:2) gave **17** as a pale yellow oil (50 mg, 28%, >99:1 dr); $[\alpha]_D^{20}$ +19.2 (*c* 0.3 in $CHCl_3$); ν_{max} (ATR) 3323 (O–H), 2970 (C–H); δ_H (400 MHz, MeOH-d_4) 1.45 (3H, d, *J* 7.1, C(α)*Me*), 3.03 (3H, s, O*Me*), 3.48–3.57 (2H, m, C(3)*H*, C(6)H_A), 3.70–3.74 (2H, m, C(2)*H*, C(6)H_B), 3.77–3.82 (3H, m, C(4)*H*, NCH_2Ph), 4.09 (1H, q, *J* 7.1, C(α)*H*), 4.28 (1H, d, *J* 2.5, C(1)*H*), 4.46 (1H, app q, *J* 3.3, C(5)*H*), 7.21–7.40 (10H, m, *Ph*); δ_C (100 MHz, MeOH-d_4) 15.6 (C(α)*Me*), 51.5 (N*C*H$_2$Ph), 54.6 (O*Me*), 57.4 (*C*(α)), 63.8 (*C*(6)), 65.9 (*C*(2)), 72.1 (*C*(5)), 73.7 (*C*(3)), 86.9 (*C*(4)), 106.0 (*C*(1)), 127.0, 127.4, 128.2, 128.2, 128.5, 128.5 (*o*,*m*,*p*-*Ph*), 140.4, 141.5 (*i*-*Ph*); *m/z* (ESI$^+$) 797 ([2M+Na]$^+$, 100%), 410 ([M+Na]$^+$, 85%), 388 ([M+H]$^+$, 85%); HRMS (ESI$^+$) $C_{22}H_{30}NO_5^+$ ([M+H]$^+$) requires 388.2118; found 388.2111. Data for **18**: δ_H (500 MHz, MeOH-d_4) 1.49 (3H, d, *J* 7.3, C(α)*Me*), 2.81 (3H, s, O*Me*), 3.58–3.60 (1H, m, C(3)*H*), 3.70–3.82 (5H, m, C(2)*H*, C(6)H_2, NCH_2Ph), 4.01 (1H, app d, *J* 4.1, C(4)*H*), 4.12–4.14 (1H, m, C(α)*H*), 4.34 (1H, app d, *J* 5.4, C(5)*H*), 4.45–4.47 (1H, m, C(1)*H*), 7.13–7.40 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) [selected peaks] 11.9 (C(α)*Me*), 53.3 (N*C*H$_2$Ph), 54.7 (O*Me*), 58.1 (*C*(α)), 64.4 (*C*(6)), 67.4 (*C*(2)), 72.5 (*C*(5)), 73.6 (*C*(3)), 88.3 (*C*(4)), 105.7 (*C*(1)), 128.7, 129.0, 129.0, 129.1, 129.3, 129.8 (*o*,*m*,*p*-*Ph*).

4.6. Methyl (1*R*,2*R*,3*S*,4*S*,5*R*,α*R*)-*O*,*O*,*O*-triacetyl-2-deoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-β-D-allofuranose 19

Ac_2O (0.12 mL, 1.3 mmol) and DMAP (5 mg) were added sequentially to a stirred solution of **17** (50 mg, 0.13 mmol, >99:1 dr) in pyridine (4 mL) at rt, and the resultant mixture was stirred at rt for 12 h. H_2O (10 mL) was then added and the reaction mixture was diluted with EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 5 mL) and the combined organic extracts were washed sequentially with satd aq $CuSO_4$ (10 mL), H_2O (10 mL) and brine (10 mL), then dried and concentrated *in vacuo*. Purification via

flash column chromatography (eluent 30–40 °C petrol/Et_2O, 50:50) gave **19** as a colourless oil (60 mg, 91%, >99:1 dr); $[\alpha]_D^{20}$ +16.4 (*c* 1.0 in MeOH); ν_{max} (ATR) 3023, 2967, 2837 (C–H), 1745 (C=O); δ_H (500 MHz, $CDCl_3$) 1.43 (3H, d, *J* 7.0, C(α)*Me*), 2.08 (3H, s, CO*Me*), 2.09 (3H, s, CO*Me*), 2.19 (3H, s, CO*Me*), 3.06 (3H, s, O*Me*), 3.82 (1H, d, *J* 15.3, NC$H_A$$H_B$Ph), 3.88 (1H, d, *J* 15.3, NC$H_A$$H_B$Ph), 3.94 (1H, q, *J* 7.0, C(α)*H*), 4.02 (1H, dd, *J* 7.5, 1.5, C(2)*H*), 4.10–4.14 (1H, m, C(6)H_A), 4.16 (1H, d, *J* 1.5, C(1)*H*), 4.17–4.22 (1H, m, C(4)*H*), 4.47 (1H, dd, *J* 9.7, 2.7, C(6)H_B), 5.10–5.13 (1H, m, C(5)*H*), 5.36 (1H, dd, *J* 7.5, 4.3, C(3)*H*), 7.26–7.47 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 17.7 (C(α)*Me*), 20.8, 20.9, 21.1 (3 × CO*Me*), 51.9 (NCH_2Ph), 55.4 (O*Me*), 57.1 (*C*(α)), 62.8 (*C*(6)), 63.0 (*C*(2)), 72.1 (*C*(5)), 74.9 (*C*(3)), 81.5 (*C*(4)), 106.7 (*C*(1)), 126.9, 127.3, 127.8, 128.1, 128.2, 128.4 (*o*,*m*,*p*-*Ph*), 140.3, 140.7 (*i*-*Ph*), 169.9, 170.1, 170.6 (3 × *C*OMe); *m/z* (ESI^+) 536 ($[M+Na]^+$, 60%); HRMS (ESI^+) $C_{28}H_{35}NNaO_8^+$ ($[M+Na]^+$) requires 536.2255; found 536.2249.

4.7. Methyl (1*R*,2*R*,3*S*,4*S*,5*R*)-2-deoxy-2-amino-β-D-allofuranose 21

Method A: $Pd(OH)_2$/C (43 mg, 50% w/w) was added to a stirred solution of **17** (85 mg, 0.22 mmol, >99:1 dr) in MeOH (5 mL) at rt. The resultant solution was degassed and saturated with H_2 before being stirred at rt under H_2 (1 atm) for 18 h. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH, 10 mL) and the filtrate was concentrated *in vacuo* to give **21** as a colourless oil (43 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ –54.4 (*c* 2.8 in MeOH); ν_{max} (ATR) 3355, 3300 (O–H, N–H), 2930 (C–H); δ_H (500 MHz, D_2O) 3.35 (3H, s, O*Me*), 3.56 (1H, dd, *J* 11.7, 6.0, C(6)H_A), 3.62–3.71 (3H, m, C(2)*H*, C(5)*H*, C(6)H_B), 3.91 (1H, dd, *J* 7.6, 4.4, C(4)*H*), 4.61 (1H, dd, *J* 6.0, 4.4, C(3)*H*), 5.08 (1H, d, *J* 2.5, C(1)*H*); δ_C (125 MHz, D_2O) 55.8 (O*Me*), 57.1 (*C*(2)), 62.6 (*C*(6)), 69.8 (*C*(3)), 72.2 (*C*(5)), 83.8 (*C*(4)), 105.4 (*C*(1)); *m/z* (ESI^+) 216 ($[M+Na]^+$, 55%), 194 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_7H_{15}NNaO_5^+$ ($[M+Na]^+$) requires 216.0842; found 216.0846.

Method B – Step 1: $Pd(OH)_2$/C (43 mg, 50% w/w) was added to a stirred solution of **19** (85 mg, 0.17 mmol, >99:1 dr) in MeOH (5 mL) at rt. The resultant solution was degassed and saturated with H_2 before being stirred at rt under H_2 (1 atm) for 18 h. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH, 10 mL) and the filtrate was concentrated *in vacuo* to give a mixture of compounds **20** as a colourless oil (52 mg).

Method B – Step 2: KOH (1.0 M aq, 1.0 mL) was added to a stirred solution of the mixture **20** (52 mg) in MeOH/H_2O (1:1, 4 mL) at rt, and the resultant mixture was stirred at rt for 4 h. The reaction mixture was

filtered through a short plug of Celite® (eluent MeOH, 5 mL), then dried and concentrated *in vacuo* to give **21** as a colourless oil (27 mg, 84% from **19**, >99:1 dr); $[\alpha]_D^{20}$ – 54.5 (*c* 1.0 in MeOH).

4.8. Methyl (1*R*,2*R*,3*S*,4*S*,5*R*)-*N*,*O*,*O*,*O*-tetraacetyl-2-deoxy-2-amino-β-D-allofuranose 22

Step 1: $Pd(OH)_2/C$ (20 mg, 50% w/w) was added to a stirred solution of **19** (40 mg, 78 μmol, >99:1 dr) in MeOH (5 mL) at rt. The resultant solution was degassed and saturated with H_2 before being stirred at rt under H_2 (1 atm) for 18 h. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH, 10 mL) and the filtrate was concentrated *in vacuo* to give a mixture of compounds **20** as a colourless oil (25 mg).

Step 2: Ac_2O (0.07 mL, 0.74 mmol) and DMAP (3 mg, 12% w/w) were added sequentially to a stirred solution of the mixture **20** (25 mg) in pyridine (2 mL) at rt, and the resultant mixture was stirred at rt for 12 h. H_2O (10 mL) was then added and the reaction mixture was diluted with EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 5 mL) and the combined organic extracts were washed sequentially with satd aq $CuSO_4$ (10 mL), H_2O (10 mL) and brine (10 mL), then dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent CH_2Cl_2/MeOH, 90:10) gave **22** as a colourless oil (24 mg, 85% from **19**, >99:1 dr); $[\alpha]_D^{20}$–18.8 (*c* 2.0 in $CHCl_3$); ν_{max} (ATR) 3282 (O–H, N–H), 2937 (C–H), 1747, 1662 (C=O); δ_H (500 MHz, C_6D_6) 1.81 (3H, s, CO*Me*), 1.82 (6H, s, 2 × CO*Me*), 1.94 (3H, s, CO*Me*), 3.24 (3H, s, O*Me*), 4.33 (1H, dd, *J* 12.2, 6.2, C(6)H_A), 4.41 (1H, dd, *J* 6.3, 4.9, C(4)*H*), 4.72 (1H, dd, *J* 12.2, 3.4, C(6)H_B), 4.91 (1H, d, *J* 2.2, C(1)*H*), 5.01–5.04 (1H, m, C(2)*H*), 5.60–5.63 (1H, m, C(5)*H*), 5.86 (1H, dd, *J* 5.7, 4.9, C(3)*H*), 6.19 (1H, d, *J* 7.9, N*H*); δ_C (125 MHz, C_6D_6) 20.2, 20.3, 20.6, 22.6 (4 × CO*Me*), 55.4 (O*Me*), 56.2 (*C*(2)), 63.0 (*C*(6)), 72.0 (*C*(5)), 73.2 (*C*(3)), 80.7 (*C*(4)), 108.4 (*C*(1)), 169.0, 169.6, 169.7, 170.1 (4 × *C*OMe); *m/z* (ESI^+) 384 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{15}H_{23}NNaO_9^+$ ($[M+Na]^+$) requires 384.1265; found 384.1252.

4.9. *tert*-Butyl (2*R*,3*R*,4*R*,5*S*,6*R*,α*S*)-2,4,5,6,7-pentahydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptanoate 23

BuLi (1.9 M in hexanes, 19.2 mL, 36.5 mmol) was added dropwise to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (7.70 g, 36.4 mmol, >99:1 er) in THF (40 mL) at –78 °C, and the resultant mixture was stirred at –78 °C for 30 min. A solution of **2**[27] (6.00 g, 18.3 mmol, >99:1 dr) in THF (20 mL) at –78 °C was then added dropwise and the resultant mixture was stirred at –78 °C for 2 h. (+)-CSO **10** (8.39 g, 36.6

mmol) was then added and the reaction mixture was allowed to warm to rt over 12 h. The reaction mixture was then diluted with Et_2O (120 mL) and filtered. The filtrate was washed sequentially with 10% aq citric acid (120 mL), satd aq $NaHCO_3$ (120 mL) and brine (120 mL), then dried and concentrated *in vacuo* to give an 18:52:30 mixture of **6**, **23** and **24**, respectively. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O/Et_3N, 83:16:1) gave **6** as a white solid (1.01g, 10%, >99:1 dr);[27] mp 56–60 °C; {lit.[27] mp 53–58 °C}; $[\alpha]_D^{25}$ +22.9 (*c* 1.0 in $CHCl_3$); {lit.[27] $[\alpha]_D^{25}$ +23.5 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.32 (3H, s, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.38 (6H, s, 2 × *Me*CMe), 1.41 (9H, s, C*Me*$_3$), 1.46 (3H, d, *J* 6.8, C(α)*Me*), 2.31 (1H, dd, *J* 15.4, 5.7, C(2)H_A), 2.36 (1H, dd, *J* 15.4, 6.9, C(2)H_B), 3.70 (1H, app t, *J* 7.5, C(5)*H*), 3.73–3.80 (3H, m, C(3)*H*, NCH_2Ph), 3.91 (1H, dd, *J* 8.0, 5.5, C(7)H_A), 4.04–4.17 (3H, m, C(6)*H*, C(7)H_B, C(α)*H*), 4.27 (1H, dd, *J* 7.6, 2.5, C(4)*H*), 7.19–7.40 (10H, m, *Ph*). Further elution gave a 60:40 mixture of **23** and **24**, respectively, as a pale yellow oil (8.31 g, 82%). Purification of an aliquot (540 mg) via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 91:9) gave **23** as a pale yellow oil (258 mg, 39% from **2**, >99:1 dr); $[\alpha]_D^{20}$ +25.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR); 3485 (O–H), 2984, 2936 (C–H), 1738 (C=O); δ_H (400 MHz, $CDCl_3$) 1.36 (9H, s, C*Me*$_3$), 1.39 (3H, s, *Me*CMe), 1.43 (3H, s, *Me*CMe), 1.46 (6H, s, 2 × *Me*CMe), 1.52 (3H, d, *J* 7.0, C(α)*Me*), 3.55 (1H, dd, *J* 6.1, 1.2, C(3)*H*), 3.72 (1H, app t, *J* 8.2, C(5)*H*), 3.81 (1H, d, *J* 14.0, NCH_AH$_B$Ph), 3.84 (1H, dd, *J* 8.5, 6.3, C(7)H_A), 4.05–4.10 (1H, m, C(6)*H*), 4.12–4.20 (3H, m, C(7)H_B, NCH$_A$$H_B$Ph, C(α)*H*), 4.29 (1H, dd, *J* 6.1, 3.6, C(2)*H*), 4.49 (1H, dd, *J* 7.8, 1.2, C(4)*H*), 7.20–7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 13.7 (C(α)*Me*), 25.6, 26.6, 27.0, 27.1 (2 × C*Me*$_2$), 27.9 (C*Me*$_3$), 51.6 (NCH_2Ph), 57.0 (*C*(α)), 58.4 (*C*(3)), 67.8 (*C*(2)), 68.3 (*C*(7)), 77.8 (*C*(6)), 78.7 (*C*(5)), 80.5 (*C*(4)), 81.4 (*C*Me$_3$), 109.8, 110.0 (2 × *C*Me$_2$), 127.1, 127.2, 128.1, 128.2, 128.4, 129.1 (*o,m,p-Ph*), 140.1, 142.9 (*i-Ph*), 172.8 (*C*(1)); *m/z* (ESI$^+$) 578 ([M+Na]$^+$, 40%), 556 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{32}H_{46}NO_7^+$ ([M+H]$^+$) requires 556.3269; found 556.3266. Further elution gave an 20:80 mixture of **23** and **24**, respectively, as a pale yellow oil (167 mg, 25%). Data for **24**: δ_H (400 MHz, $CDCl_3$) 1.33 (3H, s, *Me*CMe), 1.38 (6H, s, 2 × *Me*CMe), 1.47 (3H, s, *Me*CMe), 1.49 (3H, d, *J* 7.1, C(α)*Me*), 1.51 (9H, s, C*Me*$_3$), 3.13 (1H, d, *J* 6.1, O*H*), 3.67–3.70 (1H, m, C(2)*H*), 3.78 (1H, d, *J* 16.0, NCH_AH$_B$Ph), 3.83–3.85 (1H, m, C(3)*H*), 3.86–3.93 (2H, m, C(7)H_2), 4.05 (1H, q, *J* 7.1 C(α)*H*), 4.06–4.10 (1H, m, C(4)*H*), 4.21 (1H, d, *J* 16.0, NCH$_A$$H_B$Ph), 4.38–4.45 (2H, m, C(5)*H*, C(6)*H*), 7.21–7.45 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.0 (C(α)*Me*), 25.5, 26.4, 27.2, 27.9 (2 × C*Me*$_2$), 28.1 (C*Me*$_3$), 52.0 (NCH_2Ph), 57.5 (*C*(α)), 60.7 (*C*(3)), 64.9 (*C*(7)), 71.0 (*C*(2)), 76.6, 76.6, 79.4 (*C*(4)), (*C*(5)), (*C*(6)), 82.4 (*C*Me$_3$), 109.2, 109.5 (2 × *C*Me$_2$), 126.8, 127.3, 128.1, 128.2, 128.4, 128.5 (*o,m,p-Ph*), 140.4, 140.9 (*i-Ph*), 172.9 (*C*(1)).

4.10. (2*R*,3*R*,4*R*,5*S*,6*R*,α*S*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptan-1,2,4,5,6,7-hexaol 25

$LiAlH_4$ (1.0 M in THF, 0.60 mL, 0.60 mmol) was added dropwise to a stirred solution of **23** (150 mg, 0.270 mmol, >99:1 dr) in THF (2 mL) at 0 °C and the resultant mixture was allowed to warm to rt over 16 h. The reaction mixture was quenched by cautiously adding ice, then filtered through a short plug of Celite® (eluent Et_2O, 10 mL). The filtrate was then partitioned between H_2O (5 mL) and Et_2O (5 mL) and the organic layer was dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 50:50) gave **25** as a yellow oil (120 mg, 92%, >99:1 dr); $[\alpha]_D^{20}$ +29.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3446 (O–H), 2986, 2934 (C–H); δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, *Me*CMe), 1.42 (3H, s, *Me*CMe), 1.43 (3H, s, *Me*CMe), 1.50 (3H, s, *Me*CMe), 1.54 (3H, d, *J* 6.8, C(α)*Me*), 3.25–3.31 (1H, m, C(1)H_A), 3.26 (1H, app d, *J* 6.3, C(3)*H*), 3.44 (1H, app d, *J* 8.6, C(1)H_B), 3.73 (1H, app t, *J* 8.6 C(5)*H*), 3.78 (1H, d, *J* 13.6, NC$H_A$$H_B$Ph), 3.92 (1H, app dd, *J* 9.9, 4.3, C(2)*H*), 3.99 (1H, dd, *J* 8.6, 5.8, C(7)H_A), 4.09–4.14 (2H, m, C(6)*H*, C(α)*H*), 4.23 (1H, dd, *J* 8.6, 6.2, C(7)H_B), 4.30 (1H, d, *J* 13.6, NC$H_A$$H_B$Ph) 4.52 (1H, app d, *J* 8.3, C(4)*H*), 7.21–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 11.2 (C(α)*Me*), 25.9, 26.6, 26.6, 27.1 (2 × CMe_2), 52.1 (NCH_2Ph), 54.6 (*C*(3)), 55.9 (*C*(α)), 63.2 (*C*(1)), 68.4 (*C*(7)), 68.6 (*C*(2)), 78.0 (*C*(6)), 79.3 (*C*(5)), 81.6 (*C*(4)), 109.2, 110.2 (2 × *C*Me_2), 127.2, 127.3, 128.1, 128.3, 128.4, 129.3 (*o,m,p-Ph*), 140.3, 143.4 (*i-Ph*); *m/z* (ESI$^+$) 993 ($[2M+Na]^+$, 90%), 508 ($[M+Na]^+$, 10%), 486 ($[M+H]^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_6^+$ ($[M+H]^+$) requires 486.2850; found 486.2846.

4.11. (2*S*,3*R*,4*S*,5*R*,α*S*)-2-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-3,4,5,6,-di-*O*-isopropylidene-3,4,5,6-tetrahydroxyhexanal 26

$NaIO_4$ (265 mg, 1.24 mmol) was added to a stirred solution of **25** (120 mg, 0.247 mmol, >99:1 dr) in MeOH (5 mL) at rt, and the resultant mixture was left to stir at rt for 24 h. The resultant suspension was filtered through a short plug of Celite® (eluent MeOH, 5 mL), and the filtrate was concentrated *in vacuo*. The residue was diluted with Et_2O (5 mL) and filtered through a short plug of Celite® (eluent Et_2O, 5 mL), then the filtrate was concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 83:17) gave **26** as a pale yellow oil (85 mg, 76%, >99:1 dr); $[\alpha]_D^{24}$ +48.8 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2986 (C–H), 1728 (C=O); δ_H (400 MHz, $CDCl_3$) 1.18 (3H, s, *Me*CMe), 1.33 (3H, s, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.38 (3H, s, *Me*CMe), 1.50 (3H, d, *J* 6.8, C(α)*Me*), 3.77 (1H, app s, C(2)*H*), 3.95–3.98 (1H,

m, C(6)H_A), 4.04–4.07 (2H, m, C(4)*H*, C(5)*H*), 4.14–4.19 (2H, m, C(6)H_B, C(α)*H*), 4.23 (1H, d, *J* 14.6, NC$H_A$$H_B$Ph), 4.29 (1H, d, *J* 14.6, NC$H_A$$H_B$Ph), 4.38–4.40 (1H, m, C(3)*H*), 7.23–7.56 (10H, m, *Ph*), 9.67 (1H, d, *J* 1.3, C(1)*H*); δ_C (100 MHz, $CDCl_3$) 15.9 (C(α)*Me*), 25.6, 26.4, 26.8, 27.1 (2 × C*Me*$_2$), 52.3 (N*C*H$_2$Ph), 57.2 (*C*(α)), 64.6 (*C*(2)), 68.0 (*C*(6)), 77.5, 78.2 (*C*(4), *C*(5)), 82.1 (*C*(3)), 109.9, 110.0 (2 × *C*Me$_2$), 127.0, 127.1, 127.8, 128.2, 128.3, 128.6 (*o,m,p-Ph*), 140.6, 143.2 (*i-Ph*), 203.1 (*C*(1)); *m/z* (ESI$^+$) 476 ([M+Na]$^+$, 100%), 454 ([M+H]$^+$, 50%); HRMS (ESI$^+$) $C_{27}H_{35}NNaO_5^+$ ([M+Na]$^+$) requires 476.2407; found 476.2406.

4.12. Methyl (1*R*,2*S*,3*R*,4*S*,5*R*,α*S*)-2-deoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-α-D-mannofuranose 28

A solution of HCl in MeOH (1.25 M, 85 mL) was added to **26** (2.10 g, 4.64 mmol, >99:1 dr), and the resultant mixture was heated at 50 °C for 24 h. The reaction mixture was then allowed to cool to rt, concentrated *in vacuo*, and the residue was partitioned between 2.0 M aq NaOH (60 mL) and CH_2Cl_2 (60 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 60 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give an 80:20 mixture of **27** and **28**, respectively. Purification via flash column chromatography (eluent CH_2Cl_2/MeOH, 95:5) gave an 80:20 mixture of **27** and **28**, respectively, as a pale yellow oil (1.22 g, 68%). Further purification of an aliquot (300 mg) via flash column chromatography (eluent CH_2Cl_2/MeOH, 99:1) gave **28** as a pale yellow oil (33 mg, 7%, >99:1 dr); $[\alpha]_D^{20}$ –57.2 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3463 (O–H), 2932 (C–H); δ_H (500 MHz, MeOH-d_4) 1.49 (3H, d, *J* 6.9, C(α)*Me*), 2.73 (3H, s, O*Me*), 3.11 (1H, app t, *J* 4.1, C(2)*H*), 3.52 (1H, d, *J* 14.5, NC$H_A$$H_B$Ph), 3.63 (1H, dd, *J* 11.7, 5.7, C(6)H_A), 3.80 (1H, dd, *J* 11.7, 2.7, C(6)H_B), 3.86–3.93 (2H, m, C(4)*H*, C(5)*H*), 4.03 (1H, d, *J* 14.5, NC$H_A$$H_B$Ph), 4.39 (1H, d, *J* 3.8, C(1)*H*), 4.46 (1H, app t, *J* 4.0, C(3)*H*), 4.52 (1H, q, *J* 6.9, C(α)*H*), 7.12–7.55 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) 11.5 (C(α)*Me*), 54.5 (N*C*H$_2$Ph), 54.7 (O*Me*), 58.0 (*C*(α)), 65.0 (*C*(6)), 68.9 (*C*(2)), 72.1 (*C*(5)), 72.5 (*C*(3)), 82.8 (*C*(4)), 105.6 (*C*(1)), 127.5, 127.9, 128.7, 128.9, 129.5, 129.8 (*o,m,p-Ph*), 142.8, 144.8 (*i-Ph*); *m/z* (ESI$^+$) 797 ([2M+Na]$^+$, 100%), 410 ([M+Na]$^+$, 80%), 388 ([M+H]$^+$, 90%); HRMS (ESI$^+$) $C_{22}H_{30}NO_5^+$ ([M+H]$^+$) requires 388.2118; found 388.2115. Further elution gave a 65:35 mixture of **27** and **28**, respectively, as a pale yellow oil (70 mg, 16%). Data for **27**: δ_H (500 MHz, MeOH-d_4) 1.48 (3H, d, *J* 6.9, C(α)*Me*), 3.02 (3H, s, O*Me*), 3.46 (1H, app t, *J* 4.6, C(2)*H*), 3.57 (1H, dd, *J* 11.5, 6.2, C(6)H_A), 3.74 (1H, d, *J* 15.3, NC$H_A$$H_B$Ph), 3.76 (1H, dd, *J* 11.5, 3.2, C(6)H_B), 3.86–3.94 (2H, m, C(4)*H*, C(5)*H*) overlapping 3.94 (1H, d, *J* 15.3, NC$H_A$$H_B$Ph), 4.27 (1H, q, *J* 6.9, C(α)*H*), 4.42 (1H,

dd, *J* 4.7, 2.5, C(3)*H*), 4.62 (1H, d, *J* 4.4, C(1)*H*), 7.11–7.55 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) 13.1 (C(α)*Me*), 52.7 (N*C*H$_2$Ph), 55.7 (O*Me*), 58.9 (*C*(α)), 65.1 (*C*(6)), 70.9 (*C*(5)), 71.4 (*C*(2)), 73.3 (*C*(3)), 81.0 (*C*(4)), 106.8 (*C*(1)), 127.6, 128.0, 128.7, 129.0, 129.2, 129.6 (*o,m,p-Ph*), 142.7, 144.2 (*i-Ph*).

4.13. (2*S*,3*R*,4*R*,5*S*,6*R*,α*S*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptan-1,2,4,5,6,7-hexaol 29

$LiAlH_4$ (1.0 M in THF, 31.7 mL, 31.7 mmol) was added dropwise to a stirred solution of a 60:40 mixture of **23** and **24**, respectively, (8.00 g, 14.4 mmol) in THF (50 mL) at 0 °C and the resultant mixture was allowed to warm to rt over 16 h. The reaction mixture was quenched by cautiously adding ice, then filtered through a short plug of Celite® (eluent Et_2O, 100 mL). The filtrate was then partitioned between H_2O (50 mL) and Et_2O (50 mL) and the organic layer was dried and concentrated *in vacuo* to give a 60:40 mixture of **25** and **29**, respectively (6.93 g). Purification of an aliquot *via* flash column chromatography (eluent 30–40 °C petrol/Et_2O, 50:50) and recrystallisation ($CHCl_3$/*n*-heptane) gave an analytically pure sample of **29** as a white solid; mp 92–93 °C; $[\alpha]_D^{20}$ +24.8 (*c* 0.8 in $CHCl_3$); ν_{max} (ATR) 3460 (O–H), 2984, 2933 (C–H); δ_H (500 MHz, MeOH-d_4) 1.43 (3H, s, *Me*CMe), 1.44 (3H, s, *Me*CMe), 1.45 (3H, s, *Me*CMe), 1.46 (3H, s, *Me*CMe), 1.51 (3H, d, *J* 6.9, C(α)*Me*), 2.79 (1H, dd, *J* 11.3, 8.4, C(1)H_A), 3.22 (1H, dd, *J* 8.8, 1.0, C(3)*H*), 3.51 (1H, dd, *J* 11.3, 3.5, C(1)H_B), 3.88 (1H, d, *J* 14.2, NCH_AH$_B$Ph), 3.91–3.94 (1H, m, C(7)H_A), 3.98–4.04 (2H, m, C(2)*H*, C(α)*H*), 4.10–4.18 (3H, m, NCH$_A$$H_B$Ph, C(6)*H*, C(7)$H_B$), 4.38 (1H, app t, *J* 8.2, C(5)*H*), 4.46 (1H, dd, *J* 8.2, 1.0, C(4)*H*), 7.22–7.38 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) 13.6 (C(α)*Me*), 26.1, 27.2, 27.4, 27.5 (2 × C*Me*$_2$), 53.1 (N*C*H$_2$Ph), 57.8, 57.9 (*C*(3), (*C*(α)), 67.1 (*C*(1)), 68.9 (*C*(7)), 71.8 (*C*(2)), 79.5 (*C*(6)), 80.7 (*C*(5)), 82.7 (*C*(4)), 110.3, 111.1 (2 × *C*Me$_2$), 128.1, 128.3, 129.0, 129.3, 129.6, 130.3 (*o,m,p-Ph*), 142.1, 145.0 (*i-Ph*); *m/z* (ESI$^+$) 486 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_6^+$ ([M+H]$^+$) requires 486.2850; found 486.2847.

4.14. Methyl (1*R*,2*S*,3*R*,4*S*,5*R*)-2-deoxy-2-amino-β-D-mannofuranose 30

$Pd(OH)_2$/C (7 mg, 50% w/w) was added to a stirred solution of **28** (14 mg, 36 μmol, >99:1 dr) in MeOH (1 mL) at rt. The resultant solution was degassed and saturated with H_2 before being stirred at rt under H_2 (1 atm) for 18 h. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **30** as a colourless oil (7 mg, quant, >99:1 dr);[41] $[\alpha]_D^{20}$ –41.3 (*c* 0.4 in $CHCl_3$); ν_{max} (ATR) 3372 (O–H, N–H), 2923 (C–H); δ_H (500 MHz, MeOH-d_4) 3.29 (1H, app t, *J* 5.0,

C(2)*H*), 3.37 (3H, s, O*Me*), 3.67 (1H, dd, *J* 11.4, 5.7, C(6)H_A), 3.83 (1H, dd, *J* 11.4, 2.8, C(6)H_B), 3.89 (1H, ddd, *J* 8.8, 5.7, 2.8, C(5)*H*), 3.94 (1H, dd, *J* 8.8, 4.1, C(4)*H*), 4.15 (1H, dd, *J* 5.0, 4.1, C(3)*H*), 4.76 (1H, d, *J* 4.7, C(1)*H*); δ_C (125 MHz, MeOH-d_4) 55.8 (O*Me*), 58.2 (*C*(2)), 65.0 (*C*(6)), 72.1 (*C*(5)), 72.5 (*C*(3)), 82.6 (*C*(4)), 105.2 (*C*(1)); *m/z* (ESI$^+$) 216 ([M+Na]$^+$, 40%), 194 ([M+H]$^+$, 50%); HRMS (ESI$^+$) $C_7H_{15}NNaO_5^+$ ([M+Na]$^+$) requires 216.0842; found 216.0843.

4.15. *tert*-Butyl (2*S*,3*R*,4*S*,5*R*,6*R*,α*S*)-2,4,5,6,7-pentahydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptanoate 31

BuLi (1.7 M in hexanes, 53.8 mL, 91.5 mmol) was added dropwise to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (19.6 g, 92.8 mmol, >99:1 er) in THF (100 mL) at –78 °C, and the resultant solution was stirred at –78 °C for 30 min. A solution of **3**[27] (15.2 g, 46.3 mmol, >99:1 dr) in THF (50 mL) at –78 °C was then added dropwise and the reaction mixture was stirred at –78 °C for 2 h. (+)-CSO **10** (21.2 g, 92.4 mmol) was then added and the resultant mixture was allowed to warm to rt over 12 h. The reaction mixture was then diluted with Et_2O (250 mL) and filtered. The filtrate was washed sequentially with 10% aq citric acid (200 mL), satd aq $NaHCO_3$ (200 mL) and brine (200 mL), then dried and concentrated *in vacuo* to give a mixture of **7**, **31** and **32**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 83:17) gave **7** as a pale yellow oil (2.02 g, 8%, >99:1 dr);[27] $[\alpha]_D^{25}$ +5.0 (*c* 1.0 in $CHCl_3$); {lit.[27] $[\alpha]_D^{25}$ +4.7 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, s, *Me*CMe), 1.29 (3H, d, *J* 7.2, C(α)*Me*), 1.32 (3H, s, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.43 (3H, s, *Me*CMe), 1.44 (9H, s, C*Me*$_3$), 1.91 (1H, dd, *J* 15.2, 2.4, C(2)H_A), 2.49 (1H, dd, *J* 15.2, 10.8, C(2)H_B), 3.36 (1H, dt, *J* 10.8, 2.4, C(3)*H*), 3.52 (1H, d, *J* 15.4, NCH_AH$_B$Ph), 3.72–3.86 (3H, m, C(α)*H*, C(6)*H*, C(7)H_A), 3.99 (1H, dd, *J* 7.5, 6.1, C(7)H_B), 4.03 (1H, dd, *J* 8.2, 2.4, C(4)*H*), 4.37–4.42 (2H, m, C(5)*H*, NCH$_A$$H_B$Ph), 7.24–7.39 (8H, m, *Ph*), 7.50–7.52 (2H, m, *Ph*). Further elution gave a 70:30 mixture of **31** and **32**, respectively, as a yellow oil (16.8 g, 65%). Purification of an aliquot (2.13 g) via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 91:9) gave **31** as a white solid (1.20 g, 37%, >99:1 dr); mp 65–70 °C; $[\alpha]_D^{20}$ +17.0 (*c* 0.5 in $CHCl_3$); ν_{max} (ATR) 3524 (O–H), 2984, 2934 (C–H), 1731 (C=O); δ_H (400 MHz, $CDCl_3$) 1.25 (3H, d, *J* 7.0, C(α)*Me*), 1.29 (6H, s, 2 × *Me*CMe), 1.33 (3H, s, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.50 (9H, s, C*Me*$_3$), 3.24 (1H, d, *J* 8.6, O*H*), 3.31 (1H, app s, C(3)*H*), 3.41 (1H, app t, *J* 6.8, C(6)*H*), 3.80–3.91 (3H, m, C(7)H_2, NCH_AH$_B$Ph), 4.03 (1H, q, *J* 7.0, C(α)*H*), 4.09 (1H, dd, *J* 8.5, 1.9, C(4)*H*), 4.16 (1H, dd, *J* 8.6, 1.3, C(2)*H*), 4.28 (1H, dd, *J* 8.5, 1.7, C(5)*H*), 4.88 (1H, d, *J* 15.4, NCH$_A$$H_B$Ph), 7.22–7.52 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.2 (C(α)*Me*), 26.0, 26.0, 26.1, 27.0

(2 × C*Me*$_2$), 28.0 (C*Me*$_3$), 54.3 (NCH_2Ph), 56.3 (*C*(3)), 59.8 (*C*(α)), 66.0 (*C*(7)), 72.3 (*C*(2)), 73.5 (*C*(6)), 75.9 (*C*(5)), 77.9 (*C*(4)), 82.6 (*C*Me$_3$), 109.3, 109.5 (2 × *C*Me$_2$), 126.3, 127.4, 127.9, 128.2, 128.2, 128.4 (*o,m,p-Ph*), 142.8, 142.8 (*i-Ph*), 173.3 (*C*(1)); *m/z* (ESI$^+$) 578 ([M+Na]$^+$, 40%), 556 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{32}H_{45}NNaO_7^+$ ([M+Na]$^+$) requires 578.3088; found 578.3086. Further elution gave a 15:85 mixture of **31** and **32**, respectively, as a yellow oil (392 mg, 12%). Data for **32**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 1.38 (3H, s, *Me*CMe), 1.40 (3H, s, *Me*CMe), 1.41 (3H, s, *Me*CMe), 1.44 (3H, s, *Me*CMe), 1.49 (9H, s, C*Me*$_3$), 3.09 (1H, d, *J* 4.1, O*H*), 3.82–3.88 (1H, m, C(7)H_A), 4.01–4.04 (1H, m, C(7)H_B), 4.27 (1H, dd, *J* 4.1, 2.7, C(2)*H*), 7.21–7.51 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) [selected peaks] 21.1 (C(α)*Me*), 25.7, 26.2, 27.0, 27.4 (2 × C*Me*$_2$), 28.0 (C*Me*$_3$), 65.9 (*C*(7)), 70.2 (*C*(2)), 82.9 (*C*Me$_3$), 108.7, 109.4 (2 × *C*Me$_2$), 126.3, 127.4, 127.9, 128.2, 128.2, 128.3 (*o,m,p-Ph*), 142.8 (*i-Ph*), 174.0 (*C*(1)).

4.16. (2*S*,3*R*,4*S*,5*R*,6*R*,α*S*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptan-1,2,4,5,6,7-hexaol 33

$LiAlH_4$ (1.0 M in THF, 0.50 mL, 0.50 mmol) was added dropwise to a stirred solution of **31** (130 mg, 234 μmol, >99:1 dr) in THF (2 mL) at 0 °C and the resultant mixture was allowed to warm to rt over 16 h. The reaction mixture was quenched by cautiously adding ice, then filtered through a short plug of Celite® (eluent Et_2O, 10 mL). The filtrate was then partitioned between H_2O (5 mL) and Et_2O (5 mL) and the organic layer was dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 50:50) gave **33** as a pale yellow oil (100 mg, 88%, >99:1 dr); $[\alpha]_D^{25}$–21.4 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3451 (O–H), 2986, 2932 (C–H); δ_H (400 MHz, $CDCl_3$) 1.32–1.34 (6H, m, C(α)*Me*, *Me*CMe), 1.36 (3H, s, *Me*CMe), 1.37 (3H, s, *Me*CMe), 1.41 (3H, s, *Me*CMe), 2.92 (1H, app d, *J* 4.0, C(3)*H*), 3.42 (2H, app d, *J* 5.6, C(1)H_2), 3.58 (1H, app t, *J* 7.2, C(6)*H*), 3.70 (1H, dd, *J* 9.6, 5.1, C(2)*H*), 3.77 (1H, app t, *J* 7.8, C(7)H_A), 3.88 (1H, d, *J* 14.7, NC$H_A$$H_B$Ph), 3.88–3.92 (1H, m, C(7)H_B), 4.12 (1H, q, *J* 6.7, C(α)*H*), 4.35–4.37 (2H, m, C(4)*H*, C(5)*H*), 4.54 (1H, d, *J* 14.7, NC$H_A$$H_B$Ph), 7.25–7.47 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.7 (C(α)*Me*), 25.7, 26.1, 26.3, 27.1 (2 × C*Me*$_2$), 53.6 (NCH_2Ph), 55.9 (*C*(3)), 58.9 (*C*(α)), 65.2 (*C*(1)), 66.0 (*C*(7)), 71.7 (*C*(2)), 73.9 (*C*(6)), 76.2, 77.9 (*C*(4), *C*(5)), 109.1, 109.4 (2 × *C*Me$_2$), 126.7, 127.4, 127.9, 128.3, 128.4, 128.5 (*o,m,p-Ph*), 141.7, 143.4 (*i-Ph*); *m/z* (ESI$^+$) 993 ([2M+Na]$^+$, 90%), 508 ([M+Na]$^+$, 30%), 486 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{28}H_{40}NO_6^+$ ([M+H]$^+$) requires 486.2850; found 486.2850.

4.17. (2*S*,3*S*,4*R*,5*R*,α*S*)-2-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-3,4,5,6,-di-*O*-isopropylidene-3,4,5,6-tetrahydroxyhexanal 34

$NaIO_4$ (220 mg, 1.03 mmol) was added to a stirred solution of **33** (100 mg, 0.206 mmol) in MeOH (5 mL) at rt, and the resultant mixture was left to stir at rt for 24 h. The resultant suspension was filtered through a short plug of Celite® (eluent MeOH, 5 mL), and the filtrate was concentrated *in vacuo*. The residue was dissolved in Et_2O (5 mL) and filtered through a short plug of Celite® (eluent Et_2O, 5 mL), then the filtrate was concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 83:17) gave **34** as a yellow oil (74 mg, 79%, >99:1 dr); $[\alpha]_D^{25}$ –60.6 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 2986, 2935 (C–H), 1723 (C=O); δ_H (400 MHz, $CDCl_3$) 1.26 (3H, s, *Me*CMe), 1.37–1.40 (9H, m, C(α)*Me*, 2 × *Me*CMe), 1.43 (3H, s, *Me*CMe), 3.52 (1H, d, *J* 4.0, C(2)*H*), 3.85–3.94 (2H, m, C(5)*H*, C(6)H_A), 3.99 (1H, dd, *J* 6.8, 5.8, C(6)H_B), 4.16 (1H, q, *J* 7.0, C(α)*H*), 4.23 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 4.27 (1H, dd, *J* 8.2, 2.7, C(4)*H*), 4.43 (1H, d, *J* 14.8, NCH$_A$$H_B$Ph), 4.62 (1H, dd, *J* 8.2, 4.0, C(3)*H*), 7.25–7.48 (10H, m, *Ph*), 9.34 (1H, s, C(1)*H*); δ_C (100 MHz, $CDCl_3$) 19.9 (C(α)*Me*), 25.7, 26.1, 26.4, 27.1 (2 × CMe_2), 54.1 (N*C*H_2Ph), 59.2 (*C*(α)), 65.3 (*C*(2)), 66.0 (*C*(6)), 74.1 (*C*(5)), 76.2 (*C*(3)), 76.4 (*C*(4)), 109.4, 109.5 (2 × *C*Me_2), 126.9, 127.7, 127.8, 128.0, 128.4, 128.6 (*o*,*m*,*p*-*Ph*), 141.0, 142.5 (*i*-*Ph*), 202.8 (*C*(1)); *m/z* (ESI^+) 486 ($[M+MeOH+H]^+$, 100%), 476 ($[M+Na]^+$, 30%), 454 ($[M+H]^+$, 5%); HRMS (ESI^+) $C_{28}H_{40}NO_6^+$ ($[M+MeOH+H]^+$) requires 486.2850; found 486.2850.

4.18. Methyl (1*R*,2*S*,3*S*,4*R*,5*R*,α*S*)-2-deoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-β-D-idofuranose 35 and methyl (1*S*,2*S*,3*S*,4*R*,5*R*,α*S*)-2-deoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-α-D-idofuranose 36

A solution of HCl in MeOH (1.25 M, 25 mL) was added to **34** (800 mg, 1.77 mmol, >99:1 dr), and the resultant mixture was heated at 50 °C for 24 h. The reaction mixture was then allowed to cool to rt, concentrated *in vacuo*, and the residue was partitioned between 2.0 M aq NaOH (30 mL) and CH_2Cl_2 (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give an 80:20 mixture of **35** and **36**, respectively. Purification via flash column chromatography (eluent CH_2Cl_2/MeOH, 90:10) gave an 80:20 mixture of **35** and **36**, respectively, as a pale yellow oil (460 mg, 67%). Data for mixture: ν_{max} (ATR) 3400 (O–H), 2950 (C–H); *m/z* (ESI^+) 410 ($[M+Na]^+$, 40%), 388 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{22}H_{30}NO_5^+$ ($[M+H]^+$) requires 388.2118; found 388.2108. Data for **35**: δ_H (500 MHz, MeOH-d_4) 1.45 (3H, d, *J* 6.9, C(α)*Me*), 3.24 (3H, s, O*Me*), 3.30 (1H, dd, *J* 6.6, 5.0, C(2)*H*), 3.60–3.64 (2H, m, C(6)H_2), 3.88–3.92 (1H, m, C(5)*H*), 3.99 (1H, d, *J* 14.5,

NC*H*$_A$H$_B$Ph), 3.99 (1H, q, *J* 6.9, C(α)*H*), 4.02 (1H, dd, *J* 6.9, 3.8, C(4)*H*), 4.09 (1H, d, *J* 14.5, NCH$_A$*H*$_B$Ph), 4.36 (1H, d, *J* 5.0, C(1)*H*), 4.53 (1H, app t, *J* 6.8, C(3)*H*), 7.20–7.51 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) 16.1 (C(α)*Me*), 53.7 (N*C*H$_2$Ph), 55.3 (O*Me*), 57.9 (*C*(α)), 64.1 (*C*(6)), 69.7 (*C*(2)), 72.2 (*C*(5)), 72.4 (*C*(3)), 78.5 (*C*(4)), 105.1 (*C*(1)), 127.6, 127.7, 129.0, 129.0, 129.2, 129.6 (*o,m,p-Ph*), 143.6, 145.7 (*i-Ph*). Data for **36**: δ_H (500 MHz, MeOH-d_4) 1.43 (3H, d, *J* 6.6, C(α)*Me*), 3.06 (1H, app d, *J* 3.5, C(2)*H*), 3.24 (3H, s, O*Me*), 3.35–3.38 (2H, m, C(6)*H*$_2$), 3.75 (1H, d, *J* 14.8, NC*H*$_A$H$_B$Ph), 3.88–3.92 (2H, m, NCH$_A$*H*$_B$Ph, C(α)*H*), 4.24–4.26 (1H, m, C(5)*H*), 4.28 (1H, app t, *J* 4.3, C(3)*H*), 4.45 (1H, app d, *J* 4.7, C(4)*H*), 4.75 (1H, app s, C(1)*H*), 7.20–7.51 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) 16.5 (C(α)*Me*), 51.9 (N*C*H$_2$Ph), 55.3 (O*Me*), 57.9 (*C*(α)), 63.3 (*C*(6)), 69.9 (*C*(2)), 73.5 (*C*(5)), 75.4 (*C*(3)), 79.5 (*C*(4)), 105.4 (*C*(1)), 127.8, 128.1, 129.1, 129.1, 129.2, 129.3 (*o,m,p-Ph*), 142.5, 143.7 (*i-Ph*).

4.19. Methyl (1*R*,2*S*,3*S*,4*R*,5*R*)-2-deoxy-2-amino-β-D-idofuranose 37 and methyl (1*S*,2*S*,3*S*,4*R*,5*R*)-2-deoxy-2-amino-α-D-idofuranose 38

Pd(OH)$_2$/C (25 mg, 50% w/w) was added to a stirred solution of an 80:20 mixture of **35** and **36** (50 mg, 0.013 mmol) in MeOH (5 mL) at rt. The resultant solution was degassed and saturated with H_2 before being stirred at rt under H_2 (1 atm) for 18 h. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH, 40 mL) and the filtrate was concentrated *in vacuo* to give an 80:20 mixture of **37** and **38**, respectively, as a colourless oil (25 mg, quant). Data for mixture: ν_{max} (ATR) 3370, 3315 (O–H, N–H), 2935 (C–H); *m/z* (ESI$^+$) 216 ([M+Na]$^+$, 100%), 194 ([M+H]$^+$, 50%); HRMS (ESI$^+$) $C_7H_{15}NNaO_5^+$ ([M+Na]$^+$) requires 216.0842; found 216.0838. Data for **37**: δ_H (500 MHz, MeOH-d_4) 3.35–3.36 (1H, m, C(2)*H*), 3.43 (3H, s, O*Me*), 3.61–3.72 (2H, m, C(6)*H*$_2$), 3.92 (1H, app dd, *J* 10.9, 5.4, C(5)*H*), 4.03 (1H, dd, *J* 5.3, 2.4, C(3)*H*), 4.24 (1H, dd, *J* 10.9, 5.3, C(4)*H*), 4.74 (1H, d, *J* 1.3, C(1)*H*); δ_C (125 MHz, MeOH-d_4) 55.9 (O*Me*), 64.5 (*C*(6)), 65.3 (*C*(2)), 71.3 (*C*(5)), 78.6 (*C*(3)), 83.0 (*C*(4)), 111.2 (*C*(1)). Data for **38**: δ_H (500 MHz, MeOH-d_4) 2.82 (1H, app t, *J* 3.4, C(2)*H*), 3.44 (3H, s, O*Me*), 3.61–3.72 (2H, m, C(3)*H*, C(4)*H*), 3.74–3.83 (2H, m, C(6)*H*$_2$), 4.05–4.08 (1H, m, C(5)*H*), 4.63 (1H, d, *J* 2.8, C(1)*H*); δ_C (125 MHz, MeOH-d_4) 54.5 (*C*(2)), 55.8 (O*Me*), 62.6 (*C*(6)), 70.1 (*C*(5)), 70.3, 72.7 (*C*(3), *C*(4)), 104.1 (*C*(1)).

4.20. *tert*-Butyl (2*S*,3*R*,4*R*,5*R*,6*R*,α*S*)-2,4,5,6,7-pentahydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptanoate 40

BuLi (1.8 M in hexanes, 20.3 mL, 36.5 mmol) was added dropwise to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (7.7 mL, 36.4 mmol, >99:1 er) in THF (40 mL) at –78 °C, and the resultant mixture was stirred at –78 °C for 30 min. A solution of **4**[27] (6.00 g, 18.3 mmol, >99:1 dr) in THF (20 mL) at –78 °C was then added dropwise and the resultant mixture was stirred at –78 °C for 2 h. (+)-CSO **10** (8.39 g, 36.6 mmol) was then added and the reaction mixture was allowed to warm to rt over 12 h. The reaction mixture was then diluted with Et_2O (50 mL) and filtered. The filtrate was washed sequentially with 10% aq citric acid (40 mL), satd aq $NaHCO_3$ (40 mL) and brine (40 mL), then dried and concentrated *in vacuo* to give a 5:25:70 mixture of **8**, **39** and **40**, respectively. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 91:9 increased to 30–40 °C petrol/Et_2O, 75:25) gave **40** as a white solid (3.55 g, 35%, >99:1 dr); mp 107–112 °C; $[\alpha]_D^{25}$ +23.5 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3517 (O–H), 2982, 2935 (C–H), 1730 (C=O); δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, *Me*CMe), 1.41 (6H, s, 2 × *Me*CMe), 1.45 (3H, s, *Me*CMe), 1.55 (3H, d, *J* 7.3, C(α)*Me*), 1.57 (9H, s, C*Me*$_3$), 3.03 (1H, d, *J* 7.1, O*H*), 3.81 (1H, d, *J* 16.2, NC*H*$_A$H$_B$Ph), 3.90–3.94 (2H, m, C(2)*H*, C(7)*H*$_A$), 3.99 (1H, app d, *J* 6.6, C(3)*H*), 4.03–4.09 (2H, m, C(α)*H*, C(7)*H*$_B$), 4.28 (1H, app d, *J* 10.1, C(5)*H*), 4.41 (1H, d, *J* 16.2, NCH$_A$*H*$_B$Ph), 4.47–4.54 (2H, m, C(4)*H*, C(6)*H*), 7.22–7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.9 (C(α)*Me*), 25.0, 26.4, 26.6, 26.7 (2 × C*Me*$_2$), 28.0 (C*Me*$_3$), 50.5 (N*C*H$_2$Ph), 59.1, 59.5 (*C*(α), *C*(5)), 66.4 (*C*(7)), 71.1 (*C*(2)), 73.4, 73.9, 74.7 (*C*(3), *C*(4), *C*(6)), 81.9 (*C*Me$_3$), 107.8, 109.7 (2 × *C*Me$_2$), 126.6, 127.5, 127.7, 128.1, 128.4, 128.8 (*o*,*m*,*p*-*Ph*), 141.4, 141.6 (*i*-*Ph*), 173.2 (*C*(1)); *m/z* (ESI$^+$) 578 ([M+Na]$^+$, 75%), 556 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{32}H_{45}NNaO_7^+$ ([M+Na]$^+$) requires 578.3088; found 578.3096. Further elution gave **39** as a pale yellow oil (691 mg, 7%, >99:1 dr);[27] $[\alpha]_D^{25}$ –26.5 (*c* 1.0 in $CHCl_3$); {lit.[27] $[\alpha]_D^{25}$ –27.1 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.19 (3H, s, *Me*CMe), 1.23 (3H, d, *J* 7.0, C(α)*Me*), 1.36 (3H, s, *Me*CMe), 1.41 (3H, s, *Me*CMe), 1.50 (9H, s, C*Me*$_3$), 1.57 (3H, s, *Me*CMe), 1.86 (1H, dd, *J* 14.8, 2.3, C(2)*H*$_A$), 2.38 (1H, dd, *J* 14.8, 9.8, C(2)*H*$_B$), 3.50–3.53 (1H, m, C(7)*H*$_A$), 3.62–3.65 (1H, m, C(7)*H*$_B$), 3.69 (1H, app dd, *J* 9.8, 2.3, C(3)*H*), 3.85–3.89 (1H, m, C(5)*H*), 3.87 (1H, d, *J* 15.7, NC*H*$_A$H$_B$Ph), 3.96–4.01 (1H, m, C(6)*H*), 4.07 (1H, d, *J* 15.7, NCH$_A$*H*$_B$Ph), 4.19 (1H, dd, *J* 10.1, 5.8, C(4)*H*), 4.39 (1H, q, *J* 7.0, C(α)*H*), 7.20–7.43 (10H, m, *Ph*).

4.21. (2*S*,3*R*,4*R*,5*R*,6*R*,α*S*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-4,5,6,7-di-*O*-isopropylideneheptan-1,2,4,5,6,7-hexaol 41

$LiAlH_4$ (1.0 M in THF, 6.4 mL, 6.40 mmol) was added dropwise to a stirred solution of **40** (1.60 g, 2.88 mmol, >99:1 dr) in THF (20 mL) at 0 °C and the resultant mixture was allowed to warm to rt over 16 h. The reaction mixture was quenched by cautiously adding ice, then filtered through a short plug of Celite® (eluent Et_2O, 30 mL). The filtrate was then partitioned between H_2O (10 mL) and Et_2O (10 mL) and the organic layer was dried and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 67:33 increased to 30–40 °C petrol/Et_2O, 50:50) gave **41** as a colourless oil (1.30 g, 93%, >99:1 dr); $[\alpha]_D^{25}$ –11.3 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3476 (O–H), 2971, 2939 (C–H), 1739 (C=O); δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, *Me*CMe), 1.29 (3H, d, *J* 7.1, C(α)*Me*), 1.31 (3H, s, *Me*CMe), 1.38 (3H, s, *Me*CMe), 1.50 (3H, s, *Me*CMe), 2.48 (1H, dd, *J* 8.1, 5.3, C(1)O*H*), 3.07 (1H, d, *J* 8.8, C(2)O*H*), 3.20 (1H, dd, *J* 6.5, 3.5, C(3)*H*), 3.46–3.53 (1H, m, C(1)H_A), 3.57–3.63 (2H, m, C(1)H_B, C(6)*H*), 3.70–3.79 (2H, m, C(7)H_2), 3.96 (1H, d, *J* 16.0, NC$H_A$$H_B$Ph), 4.00–4.06 (2H, m, C(2)*H*, C(α)*H*), 4.17 (1H, dd, *J* 6.5, 3.3, C(5)*H*), 4.38 (1H, d, *J* 16.0, NC$H_A$$H_B$Ph), 4.47 (1H, app t, *J* 6.5, C(4)*H*), 7.24–7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.7 (C(α)*Me*), 24.8, 25.6, 26.3, 26.4 (2 × C*Me*$_2$), 51.1 (N*C*H_2Ph), 57.9 (*C*(3)), 59.9 (*C*(α)), 65.7, 65.9 (*C*(1), *C*(7)), 71.3 (*C*(2)), 74.0 (*C*(6)), 76.5, 76.9 (*C*(4), *C*(5)), 108.5, 109.6 (2 × *C*Me_2), 126.7, 127.5, 127.7, 128.1, 128.4, 128.5 (*o*,*m*,*p*-*Ph*), 142.3, 144.4 (*i*-*Ph*); *m*/*z* (ESI^+) 508 ($[M+Na]^+$, 100%), 486 ($[M+H]^+$, 95%); HRMS (ESI^+) $C_{28}H_{39}NNaO_6^+$ ($[M+Na]^+$) requires 508.2670; found 508.2666.

4.22. (2*S*,3*R*,4*R*,5*R*,α*S*)-2-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-3,4,5,6,-di-*O*-isopropylidene-3,4,5,6-tetrahydroxyhexanal 42

$NaIO_4$ (154 mg, 0.720 mmol) was added to a stirred solution of **41** (70 mg, 0.144 mmol, >99:1 dr) in MeOH (3 mL) at rt, and the resultant mixture was left to stir at rt for 24 h. The resultant suspension was filtered through a short plug of Celite® (eluent MeOH, 10 mL), and the filtrate was concentrated *in vacuo*. The residue was diluted with Et_2O (10 mL) and filtered through a short plug of Celite® (eluent Et_2O, 10 mL), and the filtrate was concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O, 83:17) gave **42** as a colourless oil (50 mg, 77%, >99:1 dr); $[\alpha]_D^{25}$ +18.9 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3028, 2985, 2935 (C–H), 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 1.24 (6H, s, 2 × *Me*CMe), 1.33 (3H, d, *J* 6.8, C(α)*Me*), 1.39 (3H, s, *Me*CMe), 1.42 (3H, s, *Me*CMe), 3.57–3.62 (2H, m, C(2)*H*, C(6)H_A), 3.68 (1H, dd, *J* 8.1, 6.6, C(6)H_B), 3.99–4.08 (2H, m, C(4)*H*, C(5)*H*), 4.17 (1H, d, *J* 15.9, NC$H_A$$H_B$Ph), 4.23 (1H, q, *J*

6.8, C(α)*H*), 4.30 (1H, d, *J* 15.9, NCH$_A$*H*$_B$Ph), 4.50 (1H, dd, *J* 7.2, 3.9, C(3)*H*), 7.23–7.45 (10H, m, *Ph*), 9.65 (1H, d, *J* 1.0, C(1)*H*); δ_C (100 MHz, $CDCl_3$) 20.6 (C(α)*Me*), 24.4, 25.6, 26.2, 26.3 (2 × C*Me*$_2$), 52.2 (NCH_2Ph), 60.9 (*C*(α)), 65.9 (*C*(6)), 66.4 (*C*(2)), 74.0 (*C*(5)), 77.2 (*C*(4)), 78.0 (*C*(3)), 109.1, 109.9 (2 × *C*Me$_2$), 126.7, 127.5, 127.6, 127.7, 128.3, 128.7 (*o,m,p-Ph*), 142.2, 144.5 (*i-Ph*), 203.4 (*C*(1)); *m/z* (ESI$^+$) 476 ([M+Na]$^+$, 100%), 454 ([M+H]$^+$, 95%); HRMS (ESI$^+$) $C_{27}H_{35}NNaO_5^+$ ([M+Na]$^+$) requires 476.2407; found 476.2406.

4.23. Methyl (1*S*,2*S*,3*R*,4*R*,5*R*,α*S*)-2-deoxy-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-α-D-talofuranose 43

A solution of HCl in MeOH (1.25 M, 30 mL) was added to **42** (730 mg, 1.61 mmol, >99:1 dr), and the resultant mixture was heated at 50 °C for 24 h. The reaction mixture was then allowed to cool to rt, concentrated *in vacuo*, and the residue was partitioned between 2.0 M aq NaOH (30 mL) and CH_2Cl_2 (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give an 81:19 mixture of **43** and **44**, respectively. Purification via flash column chromatography (eluent CH_2Cl_2/MeOH, 98:2) gave **43** as a pale yellow oil (304 mg, 49%, >99:1 dr); $[\alpha]_D^{25}$ –68.0 (*c* 1.0 in $CHCl_3$); ν_{max} (ATR) 3397 (O–H), 3062, 3028, 2932 (C–H); δ_H (400 MHz, MeOH-d_4) 1.43 (3H, d, *J* 7.1, C(α)*Me*), 3.09 (3H, s, O*Me*), 3.52–3.60 (2H, m, C(5)*H*, C(6)*H*$_A$), 3.65 (1H, dd, *J* 10.0, 4.2, C(6)*H*$_B$), 3.73 (1H, dd, *J* 7.1, 2.1, C(2)*H*), 3.74 (1H, d, *J* 14.9, NC*H*$_A$H$_B$Ph), 3.85 (1H, d, *J* 14.9, NCH$_A$*H*$_B$Ph), 3.90 (1H, app t, *J* 4.7, C(4)*H*), 4.03 (1H, q, *J* 7.1, C(α)*H*), 4.28 (1H, d, *J* 2.1, C(1)*H*), 4.33 (1H, dd, *J* 7.1, 4.7, C(3)*H*), 7.23–7.40 (10H, m, *Ph*); δ_C (100 MHz, MeOH-d_4) 16.5 (C(α)*Me*), 51.5 (NCH_2Ph), 54.8 (O*Me*), 57.4 (*C*(α)), 63.3 (*C*(6)), 65.2 (*C*(2)), 71.1 (*C*(3)), 73.8 (*C*(5)), 87.5 (*C*(4)), 106.0 (*C*(1)), 127.1, 127.5, 128.3, 128.3, 128.4, 128.5 (*o,m,p-Ph*), 140.4, 141.3 (*i-Ph*); *m/z* (ESI$^+$) 797 ([2M+Na]$^+$, 80%), 410 ([M+Na]$^+$, 95%), 388 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{30}NO_5^+$ ([M+H]$^+$) requires 388.2118; found 388.2116. Further elution gave a 33:67 mixture of **43** and **44**, respectively, as a pale yellow oil (70 mg, 11%). Data for **44**: δ_H (500 MHz, MeOH-d_4) 1.49 (3H, d, *J* 6.8, C(α)*Me*), 2.83 (3H, s, O*Me*), 3.14–3.16 (1H, m, C(2)*H*), 3.53–3.66 (3H, m, C(6)*H*$_2$, NC*H*$_A$H$_B$Ph), 3.71–3.75 (1H, m, C(5)*H*), 4.10 (1H, app t, *J* 2.1, C(4)*H*), 4.11 (1H, d, *J* 14.5, NCH$_A$*H*$_B$Ph), 4.25 (1H, dd, *J* 5.7, 1.0, C(3)*H*), 4.39 (1H, q, *J* 6.8, C(α)*H*), 4.51 (1H, d, *J* 3.8, C(1)*H*), 7.13–7.51 (10H, m, *Ph*); δ_C (125 MHz, MeOH-d_4) [selected peaks] 12.1 (C(α)*Me*), 54.7 (O*Me*), 54.8 (NCH_2Ph), 58.1 (*C*(α)), 64.1 (*C*(6)), 67.3 (*C*(2)), 73.5 (*C*(5)), 74.3 (*C*(3)), 87.5 (*C*(4)), 106.1 (*C*(1)).

4.24. Methyl (1*S*,2*S*,3*R*,4*R*,5*R*)-2-deoxy-2-amino-α-D-talofuranose 45

$Pd(OH)_2/C$ (23 mg, 50% w/w) was added to a stirred solution of **43** (46 mg, 0.12 mmol, >99:1 dr) in MeOH (2.5 mL) at rt. The resultant solution was degassed and saturated with H_2 before being stirred at rt under H_2 (1 atm) for 18 h. The reaction mixture was then filtered through a short plug of Celite® (eluent MeOH, 20 mL) and the filtrate was concentrated *in vacuo* to give **45** as a colourless oil (23 mg, quant, >99:1 dr); $[\alpha]_D^{20}$ +42.0 (*c* 1.0 in MeOH); ν_{max} (ATR) 3349, 3305 (O–H, N–H), 2926 (C–H); δ_H (400 MHz, MeOH-d_4) 3.18 (1H, dd, *J* 5.6, 2.0, C(2)*H*), 3.40 (3H, s, O*Me*), 3.56–3.68 (3H, m, C(5)*H*, C(6)H_2), 3.90 (1H, dd, *J* 9.8, 4.5, C(4)*H*), 4.26 (1H, app t, *J* 5.8, C(3)*H*), 4.71 (1H, d, *J* 2.0, C(1)*H*); δ_C (100 MHz, MeOH-d_4) 54.9 (O*Me*), 58.8 (*C*(2)), 63.5 (*C*(6)), 71.5 (*C*(3)), 73.1 (*C*(5)), 83.8 (*C*(4)), 109.7 (*C*(1)); *m/z* (ESI^+) 216 ($[M+Na]^+$, 100%), 194 ($[M+H]^+$, 60%); HRMS (ESI^+) $C_7H_{15}NNaO_5^+$ ($[M+Na]^+$) requires 216.0842; found 216.0844.

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[32] Crystallographic data (excluding structure factors) for compounds **15**, **29**, **31** and **40** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 983111–983114, respectively.

[33] Heating **17** (>99:1 dr) in methanolic HCl for 72 h produced a 22:78 mixture of **17** and **18**, respectively; this ratio was maintained even after resubjection for periods of over 7 days.

[34] Accurate determinations of the crude product distributions were not possible in these cases due to the complex and broad nature of the peaks in the ^{1}H NMR spectra of the crude reaction mixtures.

[35] In the corresponding reaction with (–)-CSO **10**, a 60:30:10 mixture of **6**, **23** and **24**, respectively, was produced, from which **6** was isolated in 50% yield and >99:1 dr, and a 70:30 mixture of **23** and **24** was isolated in 30% combined yield.

[36] Sequential reduction and oxidative cleavage of a 60:40 mixture of α-hydroxy-β-amino esters **23** and **24**, respectively, gave exclusively α-amino aldehyde **26** which was isolated in 75% yield and >99:1 dr, confirming that **23** and **24** (and **25** and **29**) are indeed related as C(2)-epimers. The overall yield of α-amino aldehyde **26** from α,β-unsaturated ester **2** in this case (i.e., 62% over three steps) is a significant improvement when compared to the analogous sequence via diastereoisomerically pure α-hydroxy-β-amino ester **23** (i.e., 27% over three steps); this therefore negated the requirement for the separation of **23** and **24**.

[37] The corresponding reaction with (–)-CSO **10** gave a mixture of **8**, **38** and **39**.[34] After purification of the crude reaction mixture by flash column chromatography, **8** was isolated in 45% yield and >99:1 dr, in addition to a 70:30 mixture of **38** and **39**, respectively, which was isolated in 32% combined yield.

[38] Sequential reduction and oxidative cleavage of a 70:30 mixture of α-hydroxy-β-amino esters **31** and **32**, respectively, gave exclusively α-amino aldehyde **34** which was isolated in 81% yield and >99:1 dr, confirming that **31** and **32** are indeed related as C(2)-epimers. The overall yield of α-amino aldehyde **34** from α,β-unsaturated ester **3** in this case (i.e., 53% over three steps) is a significant improvement when

compared to the analogous sequence via diastereoisomerically pure α-hydroxy-β-amino ester **31** (i.e., 26% over three steps); this therefore negated the requirement for the separation of **31** and **32**.

[39] The corresponding reaction with (–)-CSO **10** gave a 15:20:65 mixture of **8**, **38** and **39**, which were isolated in 9, 10 and 25% yield, respectively, and in >99:1 dr in each case.

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