Synthesis of novel analogues of the calicheamicin γ_1^I and esperamicin A_{1B} oligosaccharides

Stéphane Moutel [a] **and Jacques Prandi** *[b]

[a] *Institut de Chimie Organique et Analytique, Université d'Orléans, BP 6759, F-45067 Orléans Cedex 2, France. Fax: (33) 2-38-41-72-81; E-mail: stephane.moutel@univ-orleans.fr*
[b] *Institut de Pharmacologie et de Biochimie Structurale-CNRS, 205 route de Narbonne, F-31077 Toulouse Cedex, France*

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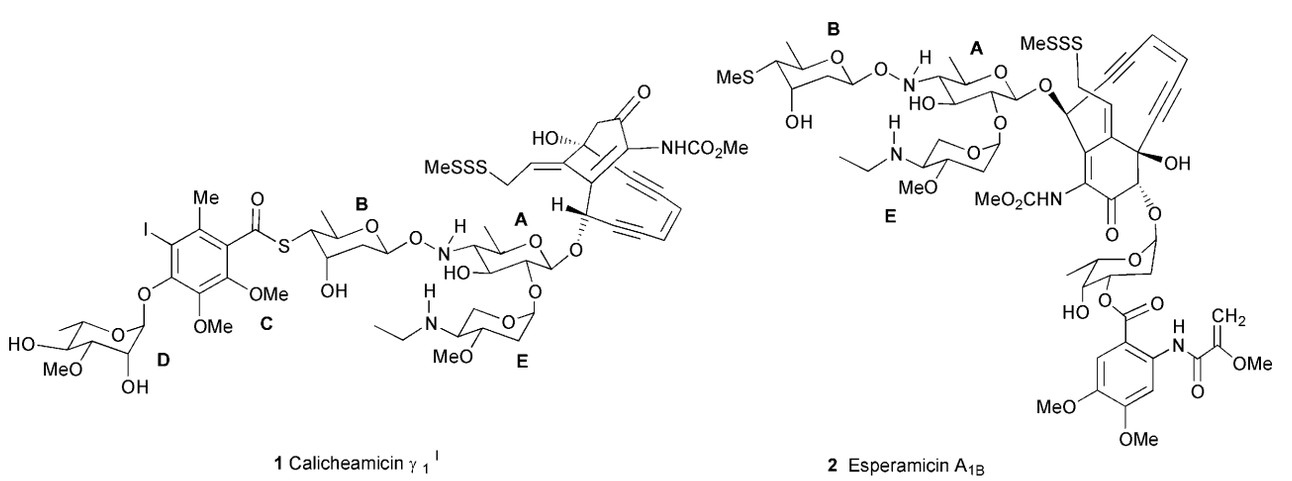
The chemical synthesis of three analogues of the calicheamicin γ_1^I **1** and esperamicin A_{1B} **2** oligosaccharides is described in which the carbohydrate ring E is replaced by a basic side chain E′. Our synthetic strategy begins with ABE′ fragment construction which possesses an unusual β N–O glycosidic bond. Glycosylation of the nitrone **20** and the appropriate activated sugar B **13** or **22** gives the disaccharides **23** and **24** respectively. Esperamicin A_{1B} oligosaccharide analogue **5** is obtained after two deprotection steps of the fragment **24**. After removal of the protecting groups of unit **23**, the fully deprotected disulfide **33** is reduced and immediately coupled with the deprotected aromatic unit C **30** (or CD **31**) to provide the calicheamicin γ_1^I oligosaccharide analogues **3** and **4**. We also report the synthesis of hemiacetal **7** in which the thioester function between the CD and B rings is replaced by an ester linkage. This arylsaccharide is a key intermediate required for the synthesis of a novel calicheamicin γ_1^I analogue **6**.

Introduction

Calicheamicin γ_1^I **1**[1] and esperamicin A_{1B} **2**,[1c,2] isolated respectively by fermentation of different strains of *Micromonospora echinospora spp. Calichensis* and *Actinomadura verrucosospora*, are some of the most potent antitumor antibiotics ever discovered (Fig. 1). These compounds, which are remarkable DNA-damaging agents, can initiate double-strand DNA scission[3] for calicheamicin γ_1^I and single-strand DNA scission[4] for esperamicin A_{1B}. The chemical structure of calicheamicins and esperamicins can be divided into two parts: the enediyne bicyclic core which is responsible for DNA cleavage following a Bergman cycloaromatisation[5] mecanism and the carbohydrate domain which plays a key role in the drug–DNA interaction.[6] For example, the oligosaccharide domain of calicheamicin γ_1^I is largely responsible for the selectivity and specificity of DNA cleavage, particularly towards TCCT, TCTC,[6a,7] TTTT[3b] sequences and has been shown to bind into the minor groove of the DNA.[6a,7] As a result of their potent biological activities, novel molecular architecture and unusual mechanism of action, there has been considerable interest shown by synthetic chemists in realising the total synthesis of these molecules and in gaining further understanding of the mechanism of action of this new class of natural products.[8]

The nature of the calicheamicin and esperamicin DNA-association is not fully understood and we wished to examine which structural features of the carbohydrate domain of calicheamicin γ_1^I **1** and esperamicin A_{1B} **2** are responsible for selective DNA recognition. Previous works have determined the roles of sugar rings D and E,[4a,7a,9] the aromatic ring-C[6b,10] and the unusual β N–O glycosidic bond[11] on the DNA–drug association phenomenon. In conclusion of these studies, the β N–O glycosidic bond, the iodide atom of ring-C, and the secondary amine of carbohydrate ring E were found important for DNA association. In this paper, we report the total synthesis of



1 Calicheamicin γ_1^I **2** Esperamicin A_{1B}

Fig. 1

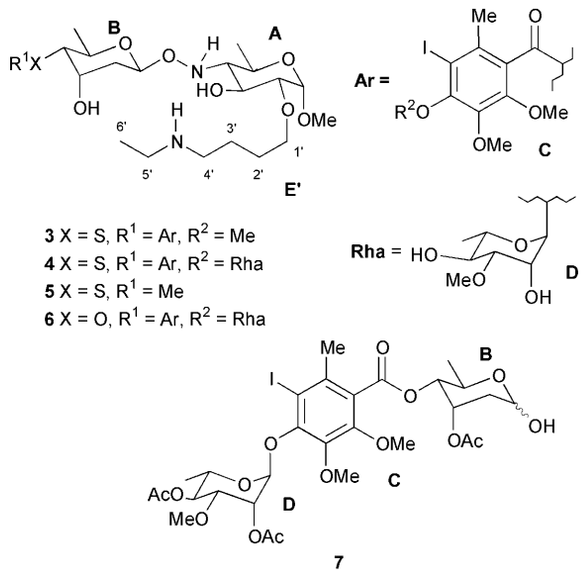


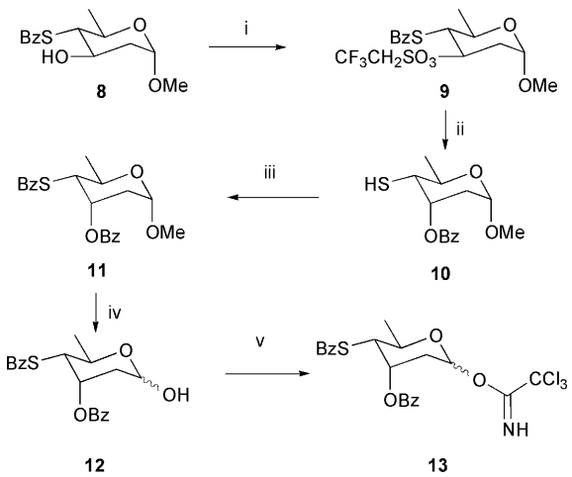
Fig. 2

oligosaccharides **3** and **4**[12] which are analogues of the calicheamicin γ_1^I oligosaccharide. To further understand the role played by the sugar ring E on the DNA–drug association, we chose to replace it by a basic chain E′ with or without the rhamnopyranosyl unit D. The oligosaccharide **5**, which is an analogue of esperamicin A_{1B} oligosaccharide is also described (Fig. 2). Our general strategy centres on the glycosylation of the AE′ moiety as a nitrone with thiosugar ring B using the approach described in our laboratory.[13] The final and crucial step is based on the coupling of the fully deprotected disaccharide ABE′ with aromatic unit CD (or C) using the selective formation of a thioester.[14]

In spite of recent efforts to obtain information on the nature of the association of calicheamicin with DNA,[11b,11c,15] no examples have been reported of the role played by the sulfur atom of the thioester linkage in the selective drug-DNA recognition. Hence we are also interested in the synthesis of analogue **6** (Fig. 2) which possesses an ester linkage in place of the thioester group found in the calicheamicins. We report the synthesis of the hemiacetal **7**,[16] a key precursor required for the synthesis of the novel calicheamicin γ_1^I oligosaccharide analogue **6** (Fig. 2). A retrosynthetic analysis of the analogue **6** suggests that its oligosaccharide portion can be constructed from the glycosylation of a nitrone AE with the hemiacetal **7**. Further disconnections led us to conclude that the hemiacetal **7** can be made from coupling of the arylrhamnopyranosyl subunit CD with an appropriate sugar B.

Results and discussion

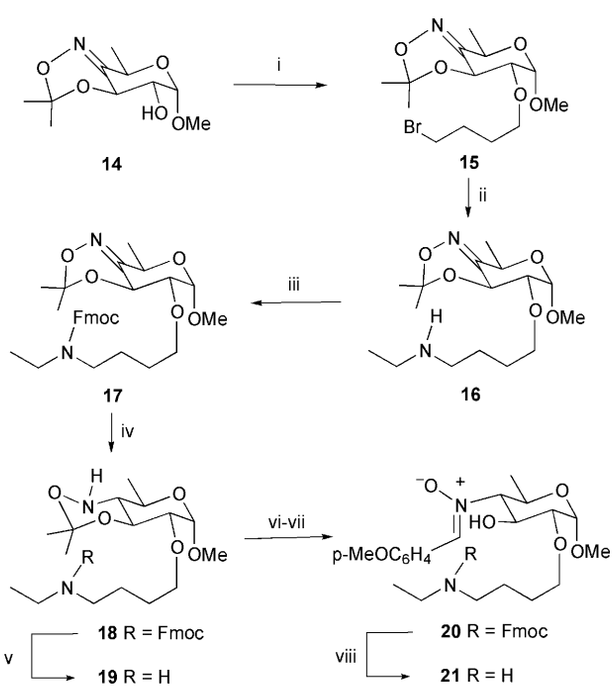
Our investigation began with the synthesis of sugar unit **13** (Scheme 1). This compound was prepared in 5 steps from the known compound **8**[17] using an intramolecular nucleophilic substitution as the key step. Alcohol **8** was converted into the 2,2,2-trifluoroethanesulfonate[18] **9** using commercially available 2,2,2-trifluoroethanesulfonyl chloride in the presence of pyridine. Subsequent heating of **9** at reflux in a mixture 1,2-dichloroethane–pyridine–water gave thiol **10**[17] in 68% yield over the 2 steps. Alcohol **8** was also successfully converted into the corresponding tosyl ester (toluene-*p*-sulfonyl chloride, pyridine, 60 °C, 18 h) in 76% yield but subsequent heating (24 h) in an identical fashion to that described earlier failed to effect conversion to thiol **10**. In this case, no reaction could be induced and the tosyl compound was recovered unchanged. Next, benzoylation of thiol **10** gave sugar **11** in 88% yield, which was subjected to acidic hydrolysis to provide the corresponding hemiacetal **12** as a 1 : 3 mixture of α and β anomers as



Scheme 1 *Reagents, conditions and yields*: (i) $CF_3CH_2SO_2Cl$, pyridine, CH_2Cl_2, rt, 2 h; (ii) $ClCH_2CH_2Cl$, pyridine, water, reflux, 1 h, 68% from **8**; (iii) BzCl, pyridine, rt, 5 h, 88%; (iv) water–AcOH 2 : 1, reflux, 2 h, 85% ; (v) Cl_3CCN, DBU, CH_2Cl_2, rt, 1 h, 100%.

judged by ^{1}H NMR spectroscopy. Final activation of hemiacetal **12** using trichloroacetonitrile[19] in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) furnished trichloroacetimidate **13**.

The preparation of the nitrone **20** began with alkylation of the known alcohol **14**[13] with 1,4-dibromobutane in the presence of sodium hydride to give **15** in 61% yield (Scheme 2).

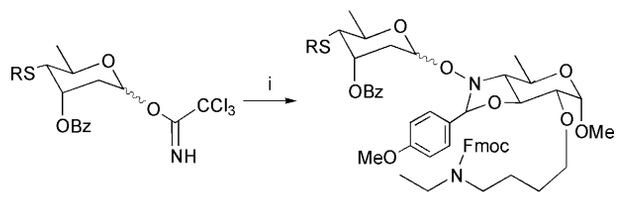


Scheme 2 *Reagents, conditions and yields*: (i) 1,4-dibromobutane, NaH, DMF, 0 °C, 3 h, 61%; (ii) $EtNH_2$, rt, 10 h; (iii) FmocCl, K_2CO_3, THF–water 2.5 : 1, 0 °C, 45 min, 76% from **15**; (iv) $NaBH_3CN$, BF_3 : Et_2O, CH_2Cl_2, −30 °C, 4 h, 86%; (v) morpholine, rt, 2 h, 53%; (vi) 0.3 M HCl in MeOH–water 3 : 1, rt, 90 min; (vii) *p*-$MeOC_6H_4CHO$, toluene, reflux, 1 h, 82% from **18**; (viii) morpholine, rt, 2 h, 60%.

Displacement of the bromide **15** with a large excess of ethylamine followed by protection of the secondary amine **16** with a fluoren-9-ylmethoxycarbonyl protecting group gave the amine **17** in 76% yield over the 2 steps. Selective reduction of the oxime bond of **17** with sodium cyanoborohydride in the presence of boron trifluoride–diethyl ether furnished the hydroxylamine **18** in 86% yield.[13,8i] The presence of the Fmoc group complicated NMR assignment at room temperature due to the presence of rotamers;[20] this group was thus removed to yield

the free amine **19**. In the ^{1}H NMR spectrum of this compound, the appearance of a multiplet at δ 2.85, assigned to H-4, with two large vicinal coupling constants ($J_{3,4} = J_{5,4} = 10.0$ Hz) and a small vicinal coupling constant ($J_{NH,4} = 4.0$ Hz) confirmed the desired D-*gluco* configuration. Acidic hydrolysis of ketal **18** followed by condensation of the resulting hydroxylamine with *p*-methoxybenzaldehyde in toluene gave nitrone **20** in 82% yield from **18**. The Fmoc-protected amine **20** was treated with morpholine to yield the more readily characterisable free amine **21**.

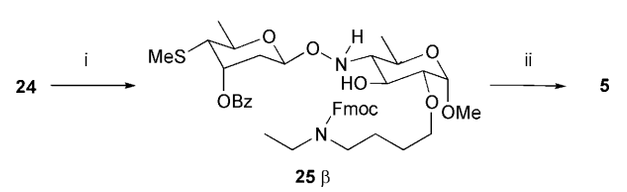
Next, glycosylation of nitrone **20** with trichloroacetimidates **13** and **22**[8i] promoted by silver trifluoromethanesulfonate[21] gave disaccharides **23** (92% yield) and **24** (76% yield) respectively, both as inseparable mixtures of α and β anomers (Scheme 3). The stereochemistry of the major component for



Scheme 3 *Reagents, conditions and yields*: (i) **20**, AgOTf, CH_2Cl_2, 4Å molecular sieves, −20 °C, 2 h, 92% (for **13** ⟶ **23**); 76% (for **22** ⟶ **24**).

each disaccharide **23** and **24** was readily determined as having the β-configuration as judged by the ^{1}H NMR vicinal coupling constants ($J_{1B,2Bax} = 10.5$ Hz, $J_{1B,2Beq} = 2.0$ Hz for **23** and **24**). In fact, each disaccharide consisted of four diastereoisomers because of the creation of another chiral centre at the *N*,*O*-acetal carbon atom. To account for the unusual selectivity of these glycosylation reactions involving a 2-deoxyglycoside,[22] a 1,3-participation of the benzoyl group at the C-3 position of sugar B has been invoked.[8h,23] A related observation has been reported in a synthesis of digitoxin.[24]

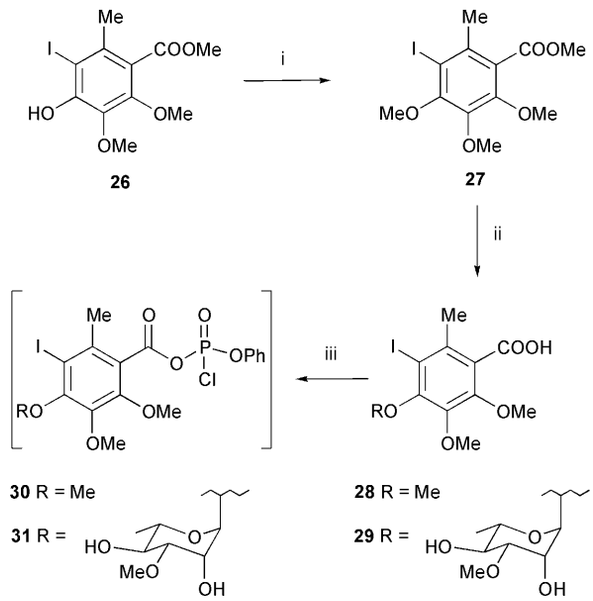
Deprotection of the *N*,*O*-acetal within disaccharide **24** was achieved using a catalytic amount of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[25] (DDQ) in aqueous acetonitrile (Scheme 4).



Scheme 4 *Reagents, conditions and yields*: (i) DDQ, CH_3CN–water 9 : 1, 0 °C, 3 h, 65%; (ii) K_2CO_3, MeOH, rt, 2 h, 91%.

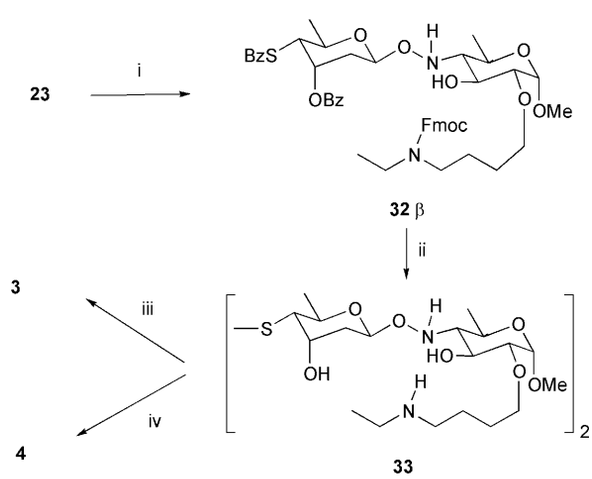
At this stage, column chromatography allowed separation of the β-anomer **25** (48%) from the unwanted α-anomer (17%).[26] Treatment of the resulting β-compound **25** with potassium carbonate in anhydrous methanol effected simultaneous deprotection of the Fmoc and benzoyl groups to give **5**, the analogue of esperamicin A_{1B} oligosaccharide in 91% yield.

Our efforts towards the synthesis of calicheamicin γ_1^I oligosaccharide analogues **3** and **4** carried on with the preparation of ring C (and CD). Methylation of known phenol **26**[27] (94% yield) followed by subsequent saponification of ester **27** provided the corresponding carboxylic acid **28** in 95% yield (Scheme 5). Final activation of this carboxylic acid into mixed anhydride **30** was accomplished using phenyl dichlorophosphate[28] in the presence of pyridine. Using a similar procedure, known 4-rhamnosyl-substituted benzoic acid **29**[8h] was transformed into mixed anhydride **31**. In this case it is notable that the formation of the mixed anhydride was successfully accomplished in the presence of two free sugar hydroxy groups as described by Kahne and co-workers[8h] in the synthesis of the calicheamicin γ_1^I oligosaccharide.



Scheme 5 *Reagents, conditions and yields*: (i) Me_2SO_4, K_2CO_3, acetone, rt, 24 h, 94%; (ii) 2.5 M NaOH, reflux, 6 h, 95%; (iii) $PhOP(O)Cl_2$, pyridine, 1,2-dimethoxyethane (DME), rt, 1 h.

The crucial step in our approach to the synthesis of calicheamicin γ_1^I oligosaccharide analogues **3** and **4** was the selective coupling of mixed anhydrides **30** and **31** and the fully deprotected disulfide **33**. First, treatment of disaccharide **23** using the method described above for the preparation of **25**β gave the desired β-anomer **32** (75%) and the unwanted α-anomer (13%)[26] separable after column chromatography (Scheme 6). Surprisingly, treatment of the resulting β-anomer

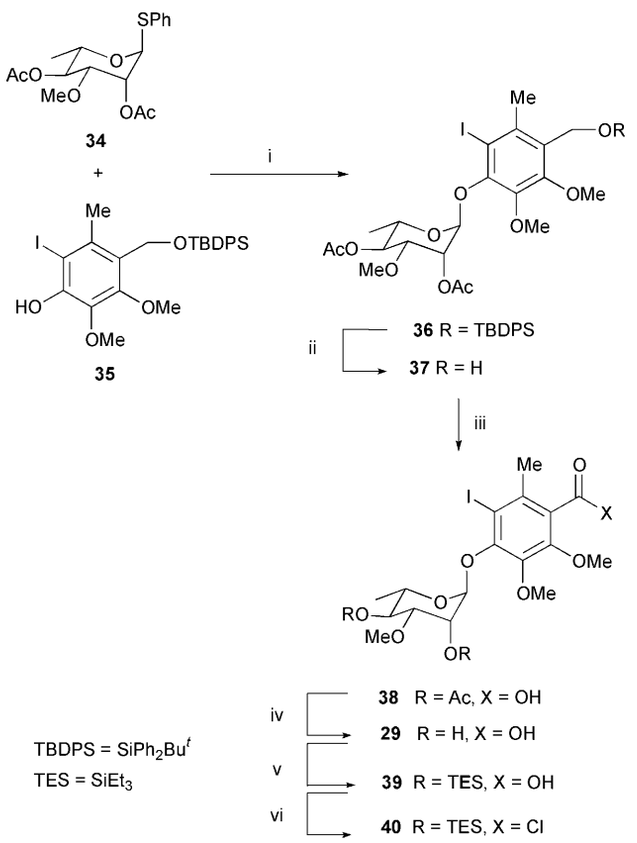


Scheme 6 *Reagents, conditions and yields*: (i) DDQ, CH_3CN–water 9 : 1, 0 °C, 1 h, 88%; (ii) K_2CO_3, MeOH, rt, 2 h, 72%; (iii) Bu^n_3P, DME 0 °C, 1 h; then **30**, rt, 24 h, 53%; (iv) Bu^n_3P, DME, 0 °C, 1 h; then **31**, rt, 24 h, 72%.

32 under basic conditions as described earlier provided only the disulfide **33** in 72% yield instead of the expected thiol. The chemical structure of disulfide **33** was elucidated using mass spectroscopy in conjunction with ^{1}H NMR analysis. Significantly, no doublet ($J_{4,SH} \approx 10$–15 Hz) at $\delta \approx 1.60$ due to the presence of a thiol proton was observed in the ^{1}H NMR spectrum. Disulfide **33** was reduced with a large excess of tri-*n*-butylphosphine in 1,2-dimethoxyethane (DME) and then added to a solution of mixed anhydride **30** to furnish the calicheamicin γ_1^I oligosaccharide analogue **3** in 53% yield. The same protocol

using mixed anhydride **31** provided the calicheamicin γ_1^I oligosaccharide analogue **4** in 72% yield. Both oligosaccharides **3** and **4** were thoroughly characterised, including 1D- and 2D-NMR analysis. Thioester-bond formation was confirmed by the chemical shifts (H-4 of unit B at δ 3.68 for both compounds **3** and **4**). In both cases, we have observed the formation of only the desired thioester without competing formation of amide or ester linkages.

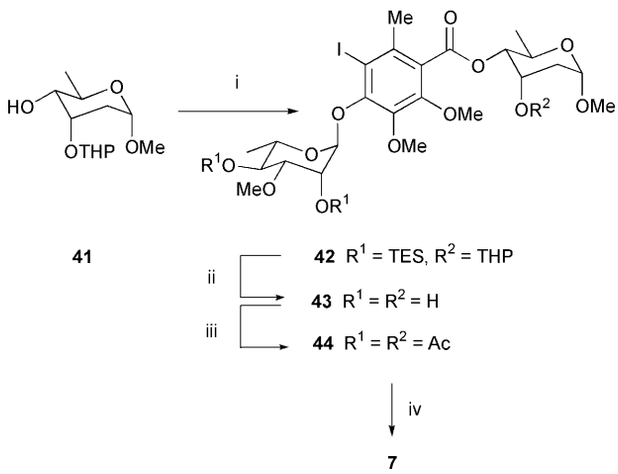
Our approach to the synthesis of hemiacetal **7**,[16] which is an intermediate for the synthesis of the novel calicheamicin γ_1^I analogue **6**, employed thiorhamnoside **34**[8f] and the phenol **35**[8h] as starting materials. In this part, we wished to develop a new approach to the synthesis of 4-rhamnosyloxy-substituted benzoic acid **29**.[8h] Glycosylation of thioglycoside **34** with phenol **35** in presence of *N*-iodosuccinimide[29] (NIS) and a catalytic amount of trimethylsilyl trifluoromethanesulfonate as promoter produced the expected aryl α-L-rhamnoside **36** in 68% yield (Scheme 7). The stereochemistry of the newly formed



Scheme 7 *Reagents, conditions and yields*: (i) NIS, $TMSOTf$, CH_2Cl_2, 4 Å molecular sieves, 0 °C, 2 h, 68%; (ii) TBAF, THF, rt, 4 h, 75%; (iii) $RuCl_3$, $NaIO_4$, CCl_4–CH_3CN–water 1 : 1 : 3, rt, 1 h, 60%; (iv) H_2O_2, LiOH, THF–water 3 : 1, rt, 2 h, 79%; (v) Et_3SiOTf, pyridine, DMAP, CH_2Cl_2, rt, 1 h, 80%; (vi) $(COCl)_2$, CH_2Cl_2, rt, 1 h.

α-glycosidic bond was confirmed by a small vicinal coupling constant ($J_{1,2}$ = 2.0 Hz) for the anomeric hydrogen to the neighbouring H-2 hydrogen. No aryl β-L-rhamnoside was observed in this case. Treatment of this aryl α-L-rhamnoside with tetra-*n*-butylammonium fluoride (TBAF) and subsequent Sharpless oxidation[30] of the resulting primary alcohol **37** gave acid **38**. Smooth removal of acetate groups was performed in the presence of lithium hydroxide and hydrogen peroxide[31] to yield known aryl rhamnoside **29**.[8h] Silylation of both hydroxy groups [triethylsilyl trifluoromethanesulfonate, pyridine, 4-(dimethylamino)pyridine (DMAP)] and treatment of the resulting carboxylic acid **39**[8f,32] with oxalyl dichloride furnished acid chloride **40**.[8f]

The completion of the synthesis of hemiacetal **7** involved the introduction of a participating group at the 3-position[8h,23] of B-ring which should give preferential β-glycoside formation during coupling with an appropriate AE nitrone. This group should be removable without deprotection of the ester linkage between the CD and B rings. We chose to protect hydroxy groups of sugar rings B and D with the acetate protecting group. The acetate group should be removed selectively using the guanidine–guanidinium nitrate reagent.[33] First, known alcohol **41**[24b] was converted into its corresponding sodium salt (NaH, THF, rt, 1 h) then coupled with acid chloride **40** to give ester **42**[16] in 67% yield (Scheme 8). Removal of both triethylsilyl



Scheme 8 *Reagents, conditions and yields*: (i) NaH, THF, 1 h; then **40**, 0 °C, 30 min, 67%; (ii) 1% HCl in dry MeOH, rt, 15 min, 75%; (iii) Ac_2O, pyridine, rt, 3 h, 83%; (iv) water–AcOH 2 : 1, reflux, 2 h, 73%.

and tetrahydropyran-*2*-yl groups was achieved using acidic conditions (1% HCl in dry methanol) and subsequent acetylation of the resulting triol **43** yielded oligosaccharide **44** in 62% over the two steps. Final acidic hydrolysis of methyl α-glycoside **44** afforded the desired hemiacetal **7** in 73% yield and as a 1 : 4 mixture of α and β anomers. In future work, we plan to couple **7** with a nitrone along lines similar to those described herein, to complete the synthesis of novel calicheamicin γ_1^I analogue **6**.

We have undertaken some preliminary studies to evaluate the DNA binding properties of oligosaccharides **3** and **4**. The circular dichroism spectrum of oligosaccharide **4** was recorded in the presence of oligonucleotide 5′-d(CCCGGTCCTAAG) using conditions described by Ellestad.[34] Although we observed some small effects which indicated that oligosaccharide **4** was binding the double-strand DNA, problems with the solubility of these analogues precluded a more detailed study.

In summary, we have described the synthesis of complex calicheamicin γ_1^I and esperamicin A_{1B} oligosaccharides **3**–**5**, in good yield and good stereoselectivity, which are potential DNA ligands. Studies to evaluate the DNA-binding properties of these oligosaccharides are ongoing. We have also reported the synthesis of hemiacetal **7**, which is a precursor to the synthesis of calicheamicin γ_1^I analogue **6**. Continuing studies directed towards the total synthesis of analogue **6** are in progress.

Experimental

General

Reactions requiring anhydrous conditions were performed using oven-dried glassware and conducted under a positive pressure of argon. Anhydrous solvents were prepared with standard protocols and were freshly distilled. All reactions were monitored by TLC on 0.2 mm Merck silica gel plates ($60F_{254}$) using UV light, ethanol–sulfuric acid (10 : 1) solution or 2% phosphomolybdic acid solution as spot-visualisation agent. Flash column chromatography was performed on Merck silica gel 60 (0.036–0.063 mm). Optical rotations were determined at

20–25 °C using a Perkin-Elmer polarimeter (model 41), and specific optical rotation-values $[\alpha]_D$ are given in 10^{-1} deg cm^2 g^{-1}. NMR spectra were recorded on a Bruker AVANCE DPX 250 spectrometer with $SiMe_4$ as internal reference. *J*-Values are given in Hz. IR spectra were recorded on a Perkin-Elmer TF PARAGON 1000 PC spectrophotometer. Mass spectra were recorded under CI^+ conditions using ammonia on a Ribermag R10-10 spectrometer at the Centre de Mesures Physiques, Orléans University or under ion-spray conditions on a Perkin-Elmer SCIEX API 300 spectrometer at the Institut de Chimie Organique et Analytique, Orléans University. Accurate masses were recorded under Fast Atom Bombardment (FAB) accurate mass method using a NOBA matrix on Micromass Autospec high-resolution instrument or under positive-ion electrospray on a Finnigan MAT 900 XLT high-resolution mass spectrometer. Elemental analyses were carried out at the Service Central de Microanalyses du CNRS at Vernaison, France.

Methyl 4-*S*-benzoyl-2,6-dideoxy-4-thio-3-*O*-(2,2,2-trifluoroethylsulfonyl)-α-D-*arabino*-hexopyranoside 9

To a stirred solution of alcohol **8**[17] (50 mg, 0.18 mmol) and pyridine (43 μL, 0.53 mmol) in dry CH_2Cl_2 (1 mL) at 0 °C was added 2,2,2-trifluoroethanesulfonyl chloride (26 μL, 0.23 mmol). The solution was stirred at room temperature for 2 h and then diluted with water. The organic layer was extracted, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The yellow solid **9** (65 mg) was used immediately in the next step.

Methyl 3-*O*-benzoyl-2,6-dideoxy-4-thio-α-D-*ribo*-hexopyranoside 10[17]

A solution of **9** (65 mg, 0.15 mmol) in 1,2-dichloroethane (3.5 mL), pyridine (25 μL, 0.30 mmol) and water (300 μL) was heated at reflux for 1 h. The solvent was removed under reduced pressure, finally by coevaporation with toluene. Column chromatography (heptane–ethyl acetate 4:1) provided thiol **10** (34 mg, 68% from compound **8**) as a colorless oil; ν_{max} (thin film)/cm^{-1} 2576 (SH), 1717 (C=O); δ_H (250 MHz; $CDCl_3$) 1.42 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.64 (1H, d, $J_{4,SH}$ 10.0, SH), 2.06 (1H, ddd, $J_{2eq,2ax}$ 15.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 4.0, H-2ax), 2.33 (1H, ddd, $J_{2eq,1}$ 1.0, $J_{2eq,3}$ 3.0, $J_{2eq,2ax}$ 15.0, H-2eq), 2.84 (1H, td, $J_{5,4} = J_{4,SH} = 10.0$, $J_{4,3}$ 3.0, H-4), 3.35 (3H, s, OCH_3), 4.19 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.0, H-5), 4.77 (1H, d, $J_{1,2}$ 4.0, H-1), 5.34 (1H, m, $J_{3,4} = J_{3,2ax} = J_{3,2eq} = 3.0$, H-3), 7.40–7.60 (3H, m, ArH), 8.10 (2H, m, ArH).

Methyl 3-*O*,4-*S*-dibenzoyl-2,6-dideoxy-4-thio-α-D-*ribo*-hexopyranoside 11

Benzoyl chloride (490 μL, 4.23 mmol) was added dropwise to a stirred solution of thiol **10** (597 mg, 2.11 mmol) in dry pyridine (3 mL) at 0 °C. The mixture was stirred for 5 h at room temperature and diluted with CH_2Cl_2. The organic layer was washed successively with water, saturated aq. $NaHCO_3$, then brine, and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* to give a yellow oil. Column chromatography (toluene–acetone 50:1) provided compound **11** (715 mg, 88%) as a colorless oil; $[\alpha]_D$ +308 (*c* 1.43, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 1720 (O–C=O), 1670 (S–C=O); δ_H (250 MHz; $CDCl_3$) 1.40 (3H, d, $J_{5,6}$ 6.5, H_3-6), 2.23 (1H, ddd, $J_{2eq,2ax}$ 15.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 4.0, H-2ax), 2.38 (1H, ddd, $J_{2eq,1}$ 1.0, $J_{2eq,3}$ 3.0, $J_{2eq,2ax}$ 15.0, H-2eq), 3.35 (3H, s, OCH_3), 4.11 (1H, dd, $J_{5,4}$ 10.5, $J_{4,3}$ 3.0, H-4), 4.48 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.5, H-5), 4.97 (1H, d, $J_{1,2}$ 4.0, H-1), 5.45 (1H, m, $J_{3,4} = J_{3,2ax} = J_{3,2eq} = 3.0$, H-3), 7.40–7.66 (6H, m, ArH), 7.97 (2H, m, ArH), 8.20 (2H, m, ArH); δ_C (62.9 MHz; $CDCl_3$) 190.0 (SC=O), 165.7 (OC=O), 136.5 (CH arom), 133.6 (C arom), 132.9 (CH arom), 130.5 (CH arom), 130.1 (CH arom), 129.8 (CH arom), 129.0 (CH arom), 128.6 (CH arom), 128.3 (CH arom), 128.2 (CH arom), 127.4 (CH arom), 125.2 (CH arom), 97.4 (C-1), 69.9 (C-3), 63.5 (C-5), 55.2 (OCH_3), 47.8 (C-4), 34.0 (C-2), 18.8 (C-6); *m*/*z* 404 $(M + NH_4)^+$ (Found: C, 64.89; H 5.40. $C_{21}H_{22}O_5S$ requires C, 65.27; H, 5.74%).

3-*O*,4-*S*-Dibenzoyl-2,6-dideoxy-4-thio-α- and -β-D-*ribo*-hexopyranose 12

A solution of compound **11** (140 mg, 0.36 mmol) in a mixture of water (4 mL) and AcOH (2 mL) was heated at reflux for 2 h. The solution was evaporated, then final traces of solvent were coevaporated (3×) with toluene. Column chromatography (heptane–ethyl acetate 2:1) provided hemiacetal **12** (115 mg, 85%) as a colorless, oily, 1:3 mixture of the α- and β-isomers. For β-isomer: δ_H (250 MHz; $CDCl_3$) 1.41 (3H, d, $J_{5,6}$ 6.0, H_3-6), 1.97 (1H, ddd, $J_{2eq,2ax}$ 14.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 9.5, H-2ax), 2.44 (1H, ddd, $J_{2eq,1}$ 2.0, $J_{2eq,3}$ 3.0, $J_{2eq,2ax}$ 14.0, H-2eq), 4.00 (1H, dd, $J_{5,4}$ 10.8, $J_{4,3}$ 3.0, H-4), 4.24 (1H, dq, $J_{5,6}$ 6.0, $J_{5,4}$ 10.8, H-5), 5.23 (1H, dd, $J_{1,2ax}$ 9.5, $J_{1,2eq}$ 2.0, H-1), 5.61 (1H, m, $J_{3,4} = J_{3,2ax} = J_{3,2eq} = 3.0$, H-3), 7.40–7.66 (6H, m, ArH), 7.97 (2H, m, ArH), 8.20 (2H, m, ArH). For α-isomer: δ_H (250 MHz; $CDCl_3$) 1.38 (3H, d, $J_{5,6}$ 6.0, H_3-6), 2.25 (1H, ddd, $J_{2eq,2ax}$ 15.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 4.0, H-2ax), 2.36 (1H, ddd, $J_{2eq,1}$ 1.2, $J_{2eq,3}$ 3.0, $J_{2eq,2ax}$ 15.0, H-2eq), 4.07 (1H, dd, $J_{5,4}$ 10.5, $J_{4,3}$ 3.0, H-4), 4.63 (1H, dq, $J_{5,6}$ 6.0, $J_{5,4}$ 10.5, H-5), 5.40 (1H, d, $J_{1,2}$ 4.0, H-1), 5.57 (1H, m, $J_{3,4} = J_{3,2ax} = J_{3,2eq} = 3.0$, H-3), 7.40–7.66 (6H, m, ArH), 7.97 (2H, m, ArH), 8.20 (2H, m, ArH); *m*/*z* 390 $(M + NH_4)^+$, 355 (M − OH).

3-*O*,4-*S*-Dibenzoyl-2,6-dideoxy-4-thio-α- and -β-D-*ribo*-hexopyranosyl trichloroacetimidate 13

To a stirred solution of hemiacetal **12** (39 mg, 0.10 mmol) in dry CH_2Cl_2 (1.5 mL) at room temperature were added trichloroacetonitrile (105 μL, 1.05 mmol) and DBU (8 μL, 0.05 mmol). The mixture was stirred for 1 h and subsequent filtration on basic alumina HF_{254} (CH_2Cl_2) provided imidate **13** (49 mg, quantitative) as a yellow solid.

Methyl 2-*O*-(4′-bromobutyl)-4,6-dideoxy-4-hydroxyimino-3-*O*,-4-(*hydroxyimino O*)-isopropylidene-α-D-*xylo*-hexopyranoside 15

To a stirred solution of alcohol **14**[13] (511 mg, 2.21 mmol) in dry DMF (35 mL) at 0 °C were added 1,4-dibromobutane (528 μL, 4.42 mmol) and sodium hydride (60% dispersion in oil washed with heptane; 69 mg, 2.87 mmol). The mixture was stirred for 3 h at 0 °C and treated with *tert*-butyl alcohol. The solution was diluted with water and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. Column chromatography (heptane–ethyl acetate 4:1 containing 0.2% Et_3N) provided oxime **15** (494 mg, 61%) as a colorless oil; $[\alpha]_D$ +74 (*c* 1.09, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 1.40 (3H, d, $J_{5,6}$ 6.0, H_3-6), 1.42 and 1.50 (2 × 3H, 2s, CMe_2), 1.74 (2H, m, $J_{3',2'}$ 7.0, H_2-3′), 1.97 (2H, m, H_2-2′), 3.45 (2H, t, $J_{3',4'}$ 7.0, H_2-4′), 3.48 (3H, s, OCH_3), 3.51 (1H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 9.5, H-2), 3.67 (1H, dt, $J_{1',2'}$ 7.0, $J_{1',1'}$ 10.0, H-1′), 3.75 (1H, dt, H-1′), 4.44 (1H, q, $J_{5,6}$ 6.0, H-5), 4.52 (1H, d, $J_{2,3}$ 9.5, H-3), 4.82 (1H, d, $J_{1,2}$ 3.5, H-1); δ_C (62.9 MHz; $CDCl_3$) 154.3 (C-4), 99.2 (CMe_2), 98.0 (C-1), 79.9 (C-2), 71.0 (C-1′), 66.0 (C-3), 63.7 (C-5), 55.8 (OCH_3), 33.5 (C-4′), 29.3, 28.4 (C-3′, -2′), 26.8 (CMe_2), 20.7 (CMe_2), 14.5 (C-6); *m*/*z* 366 and 368 (MH^+) (Found: C, 46.06; H, 6.71; N, 3.75. $C_{14}H_{24}BrNO_5$ requires C, 45.91; H, 6.60; N, 3.82%).

Methyl 4,6-dideoxy-2-*O*-[4′-(ethylamino)-butyl]-4-hydroxyimino-3-*O*,4-(*hydroxyimino O*)-isopropylidene-α-D-*xylo*-hexopyranoside 16

A solution of oxime **15** (480 mg, 1.31 mmol) in DMF (3 mL) was added dropwise to a stirred solution of ethylamine (11 mL) at 0 °C. The mixture was stirred for 10 h at room temperature then evaporated to dryness. Column chromatography (CH_2Cl_2–MeOH 8:1 containing 2% of 32% aq. ammonia) provided a pale yellow oil. This oil was dissolved in CH_2Cl_2 (5 mL) and the

solution was saturated with gaseous ammonia at room temperature for 15 min. The resulting solution was filtered from a white solid on Celite and the solvent removed to afford compound **16** (433 mg) as a colorless oil; δ_H (250 MHz; $CDCl_3$) 1.10 (3H, t, $J_{5',6'}$ 7.0, H_3-6′), 1.32 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.34 and 1.42 (2 × 3H, 2s, CMe_2), 1.58 (4H, m, H_2-2′, -3′), 2.64 (2H, m, H_2-4′), 2.66 (2H, m, H_2-5′), 3.41 (3H, s, OCH_3), 3.45 (1H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 9.5, H-2), 3.56 (1H, m, H-1′), 3.70 (1H, m, H-1′), 4.36 (1H, m, $J_{5,6}$ 6.5, H-5), 4.44 (1H, d, $J_{2,3}$ 9.5, H-3), 4.76 (1H, d, $J_{1,2}$ 3.5, H-1), 6.00 (1H, br s, NH); δ_C (62.9 MHz; $CDCl_3$) 154.2 (C-4), 99.1 (*C*Me_2), 97.9 (C-1), 79.8 (C-2), 71.8 (C-1′), 66.0 (C-3), 63.5 (C-5), 55.6 (OCH_3), 48.9 (C-4′), 43.7 (C-5′), 27.5 (C-3′), 26.7 (C*Me*$_2$), 26.5 (C-2′), 20.6 (C*Me*$_2$), 14.6, 14.4 (C-6, -6′); *m*/*z* 331 $(MH)^+$.

Methyl 4,6-dideoxy-2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]butyl}-4-hydroxyimino-3-*O*,4-(*hydroxyimino O*)-isopropylidene-α-D-*xylo*-hexopyranoside 17

To a stirred solution of amine **16** (433 mg, 1.31 mmol) in THF–water (2.5 : 1; 3.7 mL) at 0 °C were added K_2CO_3 (363 mg, 2.62 mmol) and fluoren-9-ylmethyl chloroformate (510 mg, 1.97 mmol) over a period of 30 min. The mixture was stirred for 45 min at 0 °C and diluted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. Column chromatography (heptane–ethyl acetate 4 : 1 containing 0.2% Et_3N) provided tertiary amine **17** (550 mg, 76% from compound **15**) as a colorless oil; $[\alpha]_D$ +42 (*c* 1.04, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 1700 (C=O); δ_H (250 MHz; $CDCl_3$) 0.90–1.10 (3H, m, H_3-6′), 1.39 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.40 and 1.50 (2 × 3H, 2s, CMe_2), 1.40–1.60 (4H, m, H_2-2′, -3′), 3.00 (1H, br s, H-4′), 3.25 (3H, m, H_2-5′, H-4′), 3.48 (3H, s, OCH_3), 3.58 (1H, br s, H-2), 3.60 (1H, br s, H-1′), 3.70 (1H, br s, H-1′), 4.22 (1H, m, H Fmoc), 4.50 (4H, m, H-3, -5, CH_2 Fmoc), 4.80 (1H, br s, H-1), 7.30–7.44 (4H, m, Fmoc), 7.60 (2H, d, Fmoc), 7.78 (2H, d, Fmoc); δ_C (62.9 MHz; $CDCl_3$) 154.3 (C-4), 144.1 (C arom), 141.3 (C arom), 127.5 (CH arom), 126.9 (CH arom), 124.7 (CH arom), 119.8 (CH arom), 99.1 (*C*Me_2), 98.0 (C-1), 79.8 (C-2), 71.6 (C-1′), 66.0 (C-3), 63.6 (C-5), 55.7 (OCH_3), 47.4 (CH Fmoc), 46.5 (C-4′), 42.2 (C-5′), 27.0, 26.8 (C-2′, -3′, C*Me*$_2$), 20.6 (C*Me*$_2$), 14.5 (C-6), 13.8 (C-6′); *m*/*z* 553 $(MH)^+$ (Found: C, 67.05; H, 7.43; N, 4.87. $C_{31}H_{40}N_2O_7$ requires C, 67.37; H, 7.29; N, 5.07%).

Methyl 4,6-dideoxy-2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]butyl}-4-hydroxyamino-3-*O*,4-(*hydroxyamino O*)-isopropylidene-α-D-glucopyranoside 18

A solution of compound **17** (564 mg, 1.02 mmol) and sodium cyanoborohydride (1 M in THF; 20.4 mL, 20.4 mmol) in dry CH_2Cl_2 (16 mL) at −30 °C was treated with BF_3–Et_2O (501 μL, 4.08 mmol) dropwise over a period of 3 h. After a further 1 h at −30 °C, the mixture was neutralised with a solution of ammonia–aq. ammonium chloride (1 : 1; 2 mL), allowed to warm to room temperature, and diluted with CH_2Cl_2. The organic phase was washed with brine, then dried over $MgSO_4$. The solvent was removed *in vacuo* and column chromatography (heptane–ethyl acetate 2 : 1) provided the hydroxylamine **18** (490 mg, 86%) as a colorless oil; $[\alpha]_D$ +25 (*c* 1.06, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3442 (NH), 1689 (C=O); δ_H (250 MHz; $CDCl_3$) 1.02 (3H, m, H_3-6′), 1.15 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.36 and 1.58 (2 × 3H, 2s, CMe_2), 1.36 (2H, m, H_2-3′), 1.56 (2H, m, H_2-2′), 2.84 (1H, dd, $J_{3,4} = J_{4,5}$ = 10.0, H-4), 3.01 (1H, m, H-4′), 3.21 (3H, m, H_2-5′, H-4′), 3.39 (3H, s, OCH_3), 3.40 (1H, br s, H-2), 3.57 (1H, br s, H-1′), 3.67 (1H, br s, H-1′), 3.67 (1H, dq, $J_{5,6}$ 6.5, $J_{4,5}$ 10.0, H-5), 4.16 (1H, dd, $J_{2,3} = J_{3,4}$ = 10.0, H-3), 4.22 (1H, m, H Fmoc), 4.46 (2H, m, CH_2 Fmoc), 4.74 (1H, br s, H-1), 7.27–7.43 (4H, m, Fmoc), 7.57 (2H, d, Fmoc), 7.76 (2H, d, Fmoc); δ_C (62.9 MHz; $CDCl_3$) 156.0 (N=CO), 144.2 (C arom), 141.3 (C arom), 127.5 (CH arom), 126.9 (CH arom), 124.8 (CH arom), 119.8 (CH arom), 101.4 (*C*Me_2), 98.9 (C-1), 77.6 (C-2), 71.1, 70.7 (C-4, -1′), 66.5 (CH_2 Fmoc), 64.4, 63.0 (C-5, -3), 55.2 (OCH_3), 47.5 (CH Fmoc), 46.8 (C-4′), 42.3 (C-5′), 27.2 (C*Me*$_2$, C-3′), 24.8 (C-2′), 19.9 (C*Me*$_2$), 17.1 (C-6), 13.7 (C-6′); *m*/*z* 555 $(MH)^+$ (Found: C, 67.12; H, 7.92; N, 4.77. $C_{31}H_{42}N_2O_7$ requires C, 67.13; H, 7.63; N, 5.05%).

Methyl 4,6-dideoxy-2-*O*-[4′-(ethylamino)-butyl]-4-hydroxyamino-3-*O*,4-(*hydroxyamino O*)-isopropylidene-α-D-glucopyranoside 19

The hydroxylamine **18** (22 mg, 40 μmol) was treated with morpholine (0.5 mL) at room temperature. After 2 h, the solvent was removed and the residue was subjected to column chromatography (CH_2Cl_2–MeOH 6 : 1 containing 2% Et_3N) to give a colorless oil. This oil was dissolved in CH_2Cl_2 (0.5 mL), and the solution was saturated with gaseous ammonia and stirred at room temperature for 15 min. The resulting solution was filtered from a white solid on Celite and the solvent was removed to afford amine **19** (7 mg, 53%) as a colorless oil; $[\alpha]_D$ +42 (*c* 0.65, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 1.11 (3H, t, $J_{5',6'}$ 7.0, H_3-6′), 1.16 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.37 and 1.60 (2 × 3H, 2s, CMe_2), 1.59 (4H, m, H_2-2′, -3′), 2.62 (2H, t, $J_{4',3'}$ 7.0, H_2-4′), 2.65 (2H, q, $J_{5',6'}$ 7.0, H_2-5′), 2.85 (1H, dt, $J_{3,4} = J_{4,5}$ = 10.0, $J_{4,NH}$ 4.0, H-4), 3.41 (3H, s, OCH_3), 3.43 (1H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 10.0, H-2), 3.57 (1H, dt, $J_{1',1'}$ 10.0, $J_{1',2'}$ 6.0, H-1′), 3.70 (1H, dt, $J_{1',1'}$ 10.0, $J_{1',2'}$ 6.0, H-1′), 3.71 (1H, dq, $J_{5,6}$ 6.5, $J_{4,5}$ 10.0, H-5), 4.18 (1H, dd, $J_{2,3} = J_{3,4}$ = 10.0, H-3), 4.76 (1H, d, $J_{1,2}$ 3.5, H-1), 5.15 (1H, s, $J_{NH,4}$ 4.0, NH); δ_C (62.9 MHz; $CDCl_3$) 101.4 (*C*Me_2), 98.9 (C-1), 77.6 (C-2), 71.4, 70.7 (C-1′, -4), 64.3, 63.0 (C-5, -3), 55.2 (OCH_3), 49.5 (C-4′), 44.0 (C-5′), 27.8, 27.7 (C*Me*$_2$, C-3′), 26.5 (C-2′), 19.9 (C*Me*$_2$), 17.1 (C-6), 15.2 (C-6′); *m*/*z* 333 $(MH)^+$.

Methyl 4,6-dideoxy-2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]butyl}-4-(4-methoxybenzylideneamino)-α-D-glucopyranoside 4-*N*-oxide 20

A solution 0.3 M HCl in MeOH–water (3 : 1; 4 mL) was added to the hydroxylamine **18** (56 mg, 100 μmol) at room temperature. The mixture was stirred for 90 min, then neutralised with solid $NaHCO_3$ and diluted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and the solvent removed *in vacuo* to give a white solid. This solid was taken up in dry toluene (3 mL) and treated with *p*-methoxybenzaldehyde (16 μL, 130 μmol). The mixture was refluxed for 1 h, then evaporated to dryness. Column chromatography (CH_2Cl_2–acetone 4 : 1) provided nitrone **20** (52 mg, 82% from compound **18**) as a colorless oil; $[\alpha]_D$ +14 (*c* 0.73, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3417 (OH), 1689 (C=O); δ_H (250 MHz; $CDCl_3$) 1.00 (3H, m, H_3-6′), 1.24 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.32–1.70 (4H, m, H_2-2′), 3.10–3.42 (6H, m, H_2-5′, -4′, H-2, -4), 3.42 (3H, s, OCH_3), 3.56 (1H, br s, H-1′), 3.74 (1H, br s, H-1′), 3.84 (3H, s, OCH_3), 4.21 (1H, m, H Fmoc), 4.46 (3H, m, H-5, CH_2 Fmoc), 4.66 (1H, td, $J_{3,2} = J_{3,4}$ = 9.5, $J_{3,OH}$ 3.5, H-3), 4.82 (1H, br s, H-1), 6.92 (2H, d, *J* 9.0, ArH), 7.27–7.43 (5H, m, ArH, CH=N), 7.56 (2H, d, ArH), 7.75 (2H, d, ArH), 8.24 (2H, d, *J* 9.0, ArH); δ_C (62.9 MHz; $CDCl_3$) 161.0 (C arom), 156.0 (NC=O), 144.1 (C arom), 141.3 (C arom), 135.7 (CH=N), 130.8 (CH arom), 127.5 (CH arom), 126.9 (CH arom), 124.8 (CH arom), 123.2 (C arom), 119.8 (CH arom), 113.8 (CH arom), 97.2 (C-1), 81.6, 80.7 (C-2, -4), 70.5 (C-1′), 67.0, 66.9 (C-3, CH_2 Fmoc), 63.9 (C-5), 55.3 (OCH_3), 55.1 (OCH_3), 47.3 (CH Fmoc), 46.5 (C-4′), 42.0 (C-5′), 27.0 (C-3′), 25.0 (C-2′), 17.4 (C-6), 13.8 (C-6′); *m*/*z* 633 $(MH)^+$ (Found: C, 68.33; H, 7.08; N, 4.49. $C_{36}H_{44}N_2O_8$ requires C, 68.33; H, 7.01; N, 4.43%).

Methyl 4,6-dideoxy-2-*O*-[4′-(ethylamino)butyl]-4-(4-methoxybenzylideneamino)-α-D-glucopyranoside 4-*N*-oxide 21

Deprotection of nitrone **20** (23 mg, 36 μmol) was carried out as described for the preparation of **19** (column chromatography,

CH_2Cl_2–MeOH 8:1 containing 2% Et_3N) and gave amine **21** (9 mg, 60%) as a white solid; $[\alpha]_D$ +35 (*c* 0.94, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3420 (NH); δ_H (250 MHz; $CDCl_3$) 1.03 (3H, t, $J_{5',6'}$ 7.5, H_3-6′), 1.24 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.62–1.75 (4H, m, H_2-2′, -3′), 2.58 (2H, q, $J_{5',6'}$ 7.5, H_2-5′), 2.59 (1H, dt, $J_{4',3'}$ 6.5, $J_{4',4'}$ 12.0, H-4′), 2.70 (1H, dt, $J_{4',3'}$ 6.5, $J_{4',4'}$ 12.0, H-4′), 3.31 (1H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 10.0, H-2), 3.40 (1H, dd, $J_{3,4} = J_{4,5}$ = 10.0, H-4), 3.43 (3H, s, OCH_3), 3.58 (1H, dt, $J_{1',1'}$ 10.0, $J_{1',2'}$ 6.0, H-1′), 3.80 (1H, dt, $J_{1',1'}$ 10.0, $J_{1',2'}$ 6.0, H-1′), 3.85 (3H, s, OCH_3), 4.45 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.0, H-5), 4.56 (1H, dd, $J_{3,2} = J_{3,4}$ = 10.0, H-3), 4.79 (1H, d, $J_{1,2}$ 3.5, H-1), 6.90 (2H, d, *J* 9.0, ArH), 7.35 (1H, s, CH=N), 8.25 (2H, d, *J* 9.0, ArH); δ_C (62.9 MHz; $CDCl_3$) 161.0 (C arom), 135.4 (CH=N), 130.7 (CH arom), 123.3 (C arom), 113.7 (CH arom), 97.6 (C-1), 82.0, 81.9 (C-2), 71.8 (C-1′), 66.5 (C-3), 63.8 (C-5), 55.3, 55.1 (2 × OCH_3), 48.8 (C-4′), 43.9 (C-5′), 27.3 (C-3′), 26.8 (C-2′), 17.4 (C-6), 14.7 (C-6′); *m*/*z* 411 $(MH)^+$.

Methyl 4,6-dideoxy-4-(*hydroxyamino O*)-(3-*O*,4-*S*-dibenzoyl-2,6-dideoxy-4-thio-β- and α-D-*ribo*-hexopyranosyl)2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]butyl}-4-hydroxyamino-3-*O*,4-(*hydroxyamino N*)-(4-methoxybenzylidene)-α-D-glucopyranoside 23

A solution of nitrone **20** (30 mg, 47 μmol) in dry CH_2Cl_2 (3 mL) was added to imidate **13** (49 mg, 95 μmol). The solution was cooled to −20 °C and powdered 4 Å molecular sieves were added. After 15 min, AgOTf (24 mg, 95 μmol) was added and the solution was stirred for 2 h in the dark. The mixture was filtered on Celite and the solvent removed *in vacuo*. Column chromatography (heptane–ethyl acetate 3:2) provided **23** (43 mg, 92%) as a colorless oil and as a mixture of α and β anomers. Major β-compound: δ_H (250 MHz; $CDCl_3$) 1.00 (3H, m, H_3-6′), 1.30–1.60 (4H, m, H_2-2′, -3′), 1.32 (3H, d, $J_{5,6}$ 6.0, H_3-6A), 1.54 (3H, d, $J_{5,6}$ 6.0, H_3-6B), 1.85 (1H, m, $J_{2eq,2ax}$ 18.0, $J_{2ax,3}$ 2.5, $J_{2ax,1}$ 10.5, H-2axB), 2.04 (1H, m, H-2eqB), 2.75 (1H, dd, $J_{3,4} = J_{4,5}$ = 9.5, H-4A), 3.20–3.30 (5H, m, H_2-4′, -5′ H-2A), 3.34 (3H, s, OCH_3), 3.41 (3H, s, OCH_3), 3.55–3.70 (2H, m, H_2-1′), 3.83 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 11.0, H-4B), 3.95 (1H, dq, $J_{5,6}$ 6.0, $J_{5,4}$ 9.5, H-5A), 4.21 (1H, m, H-5B), 4.33 (1H, dd, $J_{2,3} = J_{3,4}$ = 9.5, H-3A), 4.43 (3H, m, H Fmoc, CH_2 Fmoc), 4.62 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.5, H-1B), 4.83 (1H, br s, H-1A), 5.10 (1H, s, H aminoacetal), 5.45 (1H, m, H-3B), 6.55 (2H, d, $J_{o,m}$ 8.5, 2H benzylidene), 7.25–7.90 (m, ArH).

Methyl 4-(*hydroxyamino O*)-(3-*O*-benzoyl-2,6-dideoxy-4-*S*-methyl-4-thio-β- and α-D-*ribo*-hexopyranosyl)-4,6-dideoxy-2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]-butyl}-3-*O*,4-(*hydroxyamino N*)-(4-methoxybenzylidene)-α-D-glucopyranoside 24

A solution of nitrone **20** (55 mg, 87 μmol) in dry CH_2Cl_2 (5 mL) was added to imidate **22**[8i] (75 mg, 0.16 mmol). The solution was cooled to −20 °C and powdered 4 Å molecular sieves were added. After 15 min at −20 °C, the mixture was treated with AgOTf (45 mg, 174 μmol) and the solution was stirred for 2 h in the dark at room temperature. The mixture was filtered on Celite and the solvent removed *in vacuo*. Column chromatography (heptane–ethyl acetate 3:1) provided compound **24** (59 mg, 76%) as a white foam (mixture of α and β anomers). Major β-compound: δ_H (250 MHz; $CDCl_3$) 0.92 (3H, m, H_3-6′), 1.30–1.63 (4H, m, H_2-2′, -3′), 1.35 (3H, d, $J_{5,6}$ 6.0, H_3-6A), 1.49 (3H, d, $J_{5,6}$ 6.0, H_3-6B), 1.62 (1H, m, $J_{2eq,2ax}$ 18.0, $J_{2ax,3}$ 2.5, $J_{2ax,1}$ 10.5, H-2axB), 1.96 (1H, m, H-2eqB), 2.04 (3H, s, SCH_3), 2.35 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 9.5, H-4B), 2.70 (1H, dd, $J_{3,4} = J_{4,5}$ = 9.5, H-4A), 2.90–3.23 (5H, m, H_2-4′, -5′, H-2A), 3.30 (3H, s, OCH_3), 3.38 (3H, s, OCH_3), 3.40–3.70 (2H, m, H_2-1′), 3.92 (1H, dq, $J_{5,6}$ 6.0, $J_{5,4}$ 9.5, H-5A), 4.18 (1H, m, H-5B), 4.29 (1H, dd, $J_{2,3} = J_{3,4}$ = 9.5, H-3A), 4.40 (3H, m, H Fmoc, CH_2 Fmoc), 4.56 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.5, H-1B), 4.79 (1H, br s, H-1A), 5.06 (1H, s, H aminoacetal), 5.47 (1H, m, H-3B), 6.53 (d, 2H, $J_{o,m}$ 8.5, 2H benzylidene), 7.20–7.78 (m, ArH).

Methyl 4-(3-*O*-benzoyl-2,6-dideoxy-4-*S*-methyl-4-thio-β-D-*ribo*-hexopyranosyloxyamino)-4,6-dideoxy-2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]butyl}-α-D-glucopyranoside β-(and α)-25

A solution of DDQ (0.01 M in CH_3CN–water 9:1; 295 μL, 2.95 μmol) was added over a period of 3 h to the oxazolidine **24** (53 mg, 59 μmol) at 0 °C. The solution was neutralised by addition of saturated aq. $NaHCO_3$ and diluted with CH_2Cl_2. The organic layer was extracted, dried over $MgSO_4$, filtered and evaporated to dryness. Column chromatography (heptane–ethyl acetate 1:2) provided β-**25** (22 mg, 48%) as a colorless oil; $[\alpha]_D$ +35 (*c* 2.20, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3451 (OH, NH), 1720 [Ph(C=O)O], 1690 [O(C=O)N]; δ_H (250 MHz; $CDCl_3$) 0.99 (3H, m, H_3-6′), 1.32 (3H, d, $J_{5,6}$ 6.5, H_3-6A), 1.44 (3H, d, $J_{5,6}$ 6.5, H_3-6B), 1.60 (4H, br s, H_2-2′), 1.70 (1H, ddd, $J_{2eq,2ax}$ 14.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 10.0, H-2axB), 2.10 (3H, s, SCH_3), 2.12 (1H, ddd, $J_{2eq,2ax}$ 14.0, $J_{2eq,3}$ 3.0, J_{2eq1} 2.0, H-2eqB), 2.30 (1H, dd, $J_{3,4} = J_{4,5}$ 9.5, H-4A), 2.45 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 10.5, H-4B), 2.98 (1H, m, H-4′), 3.18 (3H, m, H-4′, H_2-5′), 3.23 (1H, dd, $J_{2,1}$ 3.5, $J_{2,3}$ 9.5, H-2A), 3.33 (3H, s, OCH_3), 3.40–3.66 (2H, m, H_2-1′), 3.87 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 9.5, H-5A), 4.02 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.5, H-5B), 4.16 (1H, dd, $J_{3,4} = J_{2,3}$ = 9.5, H-3A), 4.18 (1H, m, H Fmoc), 4.44 (2H, q, CH_2 Fmoc), 4.71 (1H, br s, H-1A), 4.97 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.0, H-1B), 5.59 (1H, m, H-3B), 6.65 (1H, br s, NH), 7.24–7.46 (6H, m, ArH), 7.55 (3H, m, ArH), 7.72 (2H, m, ArH), 8.00 (2H, dd, ArH); δ_C (62.9 MHz; $CDCl_3$) 165.5 (OC=O), 156.0 (NC=O), 144.1 (C arom), 141.3 (C arom), 133.2 (C arom), 129.9 (C arom), 129.6 (CH arom), 128.5 (CH arom), 127.5 (CH arom), 126.9 (CH arom), 124.8 (CH arom), 119.8 (CH arom), 100.0 (C-1B), 97.6 (C-1A), 81.0 (C-2A), 71.5 (C-1′), 70.4 (C-3B, -5B), 68.0 (C-4A), 66.4 (C-3A, CH_2 Fmoc), 63.9 (C-5A), 55.1 (OCH_3), 53.1 (C-4B), 47.4 (CH Fmoc), 46.7 (C-4′), 41.7 (C-5′), 34.7 (C-2B), 26.8 (C-3′), 24.6 (C-2′), 19.8 (C-6B), 17.9 (C-6A), 15.7 (SCH_3), 13.7 (C-6′); *m*/*z* 779 $(MH)^+$.

Further elution (heptane–ethyl acetate 1:2) gave α-**25** (8 mg, 17%) as a colorless oil; $[\alpha]_D$ +74 (*c* 0.78, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 0.97 (3H, m, H_3-6′), 1.13 (3H, d, $J_{5,6}$ 6.0, H_3-6A), 1.41 (3H, d, $J_{5,6}$ 6.0, H_3-6B), 1.60 (4H, br s, H_2-2′, -3′), 1.99 (1H, m, H-2axB), 2.12 (3H, s, SCH_3), 2.30 (2H, m, H-4A, H-2eqB), 2.54 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 10.5, H-4B), 2.97 (1H, br s, H-4′), 3.05–3.25 (7H, m, H-4′, H_2-5′, H-2A, OCH_3), 3.49 (1H, br s, H-1′), 3.66 (2H, m, H-5A, H-1′), 3.91 (1H, dd, $J_{3,4} = J_{2,3}$ = 10.0, H-3A), 4.19 (1H, dd, H Fmoc), 4.28 (1H, m, H-5B), 4.43 (2H, m, CH_2 Fmoc), 4.67 (1H, br s, H-1A), 5.06 (1H, dd, $J_{1,2ax}$ 4.5, $J_{1,2eq}$ ≈1–2, H-1B), 5.39 (1H, m, $J_{3,4} = J_{3,2ax}$ = 3.0, H-3B), 6.30 (1H, br s, NH), 7.26–7.56 (12H, m, Fmoc, ArH), 7.72 (2H, dd, Fmoc), 8.05 (2H, dd, OBz).

Methyl 4,6-dideoxy-4-(2,6-dideoxy-4-*S*-methyl-4-thio-β-D-*ribo*-hexopyranosyloxyamino)-2-*O*-[4′-(ethylamino)butyl]-α-D-glucopyranoside 5

To a stirred solution of β-**25** (17 mg, 22 μmol) in dry MeOH (0.8 mL) at room temperature was added solid potassium carbonate (9 mg, 65 μmol). The mixture was stirred for 2 h, then evaporated to dryness. Column chromatography (CH_2Cl_2–MeOH 1:1 containing 1% of 32% aq. ammonia) provided a colorless oil (12 mg). This oil was dissolved in CH_2Cl_2 (0.5 mL) and the solution was saturated with gaseous ammonia at room temperature for 15 min. The resulting solution was filtered from a white solid on Celite and the solvent removed to afford amine **5** (9 mg, 91%) as a colorless oil; $[\alpha]_D$ +34 (*c* 0.86, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3417 (NH, OH); δ_H (250 MHz; $CDCl_3$) 1.10 (3H, t, $J_{5',6'}$ 7.0, H_3-6′), 1.29 (3H, d, $J_{5,6}$ 6.5, H_3-6B), 1.35 (3H, d, $J_{5,6}$ 6.5, H_3-6A), 1.49 (1H, ddd, $J_{2eq,2ax}$ 13.5, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 10.0, H-2axB), 1.61 (4H, m, H_2-2′), 2.07 (3H, s, SCH_3), 2.08 (1H, ddd, $J_{2eq,2ax}$ 13.5, $J_{2eq,3}$ 3.0, J_{2eq1} 2.0, H-2eqB), 2.30 (1H, dt,

$J_{3,4} = J_{4,5} = 9.5$, $J_{NH,4}$ 1.5, H-4A), 2.44 (1H, dd, $J_{4,3}$ 2.5, $J_{4,5}$ 10.0, H-4B), 2.63 (2H, q, $J_{5',6'}$ 7.0, H_2-5′), 2.64 (2H, t, $J_{4',3'}$ 7.0, H_2-4′), 3.24 (1H, dd, $J_{2,1}$ 3.5, $J_{2,3}$ 9.5, H-2A), 3.36 (3H, s, OCH_3), 3.58 (1H, m, H-1′), 3.69 (1H, m, H-1′), 3.79 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.0, H-5B), 3.89 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 9.5, H-5A), 4.05 (1H, m, H-3B), 4.14 (1H, dd, $J_{3,4} = J_{2,3} = 9.5$, H-3A), 4.72 (1H, d, $J_{1,2}$ 3.5, H-1A), 4.94 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.0, H-1B), 6.54 (1H, d, $J_{NH,4}$ 1.5, NHO); δ_C (62.9 MHz; $CDCl_3$) 99.6 (C-1B), 97.7 (C-1A), 81.6 (C-2A), 71.0 (C-1′), 68.8 (C-5B), 68.0 (C-4A), 66.0 (C-3A), 64.4, 64.2 (C-3B, -5A), 55.8 (C-4B), 55.1 (OCH_3), 49.1 (C-4′), 43.9 (C-5′), 35.1 (C-2B), 27.7 (C-3′), 26.6 (C-2′), 20.0 (C-6B), 18.2 (C-6A), 14.6 (C-6′), 13.7 (SCH_3); *m/z* 453 $(MH)^+$ (Found: MH^+, 453.2624. $C_{20}H_{41}N_2O_7S$ requires *m/z* 453.2634).

Methyl 3-iodo-4,5,6-trimethoxy-2-methylbenzoate 27

Solid potassium carbonate (39 mg, 0.28 mmol) and dimethyl sulfate (15 μL, 0.15 mmol) were added to a stirred solution of the phenol **26**[27] (50 mg, 0.14 mmol) in acetone (1.3 mL). The suspension was vigorously stirred for 24 h at room temperature, then filtered on Celite and the solvent removed *in vacuo*. Column chromatography (heptane–ethyl acetate 4 : 1) provided title compound **27** (49 mg, 94%) as a colorless oil; δ_H (250 MHz; $CDCl_3$) 2.32 (3H, s, CH_3), 3.84 (6H, s, OCH_3, CO_2CH_3), 3.86 (3H, s, OCH_3), 3.88 (3H, s, OCH_3); δ_C (62.9 MHz; $CDCl_3$) 167.7 (C=O), 154.4 (C-4), 150.8 (C-6), 143.5 (C-5), 133.6 (C-2), 125.3 (C-1), 94.0 (C-3), 61.7 (OCH_3), 60.9 (OCH_3), 60.6 (OCH_3), 52.5 (CO_2CH_3) 25.4 ($ArCH_3$).

3-Iodo-4,5,6-trimethoxy-2-methylbenzoic acid 28

Compound **27** (49 mg, 0.13 mmol) in aq. 2.5 M NaOH (1 mL) and methanol (0.5 mL) was heated at reflux for 6 h. The mixture was then carefully poured into cold 5% aq. hydrochloric acid and extracted with Et_2O (3×). The organic phase was dried over $MgSO_4$, and concentrated. Column chromatography (CH_2Cl_2–methanol 10 : 1) provided acid **28** (45 mg, 95%) as a white solid; ν_{max} (KBr)/cm^{-1} 3422 (OH), 1580 (CO_2H); δ_H (250 MHz; $CDCl_3$) 2.23 (3H, s, CH_3), 3.76 (3H, s, OCH_3), 3.77 (6H, s, 2 × OCH_3); δ_C (62.9 MHz; $CDCl_3$) 153.7 (C-4), 149.9 (C-6), 143.4 (C-5), 133.3 (C-2), 125.8 (C-1), 94.8 (C-3), 62.1 (OCH_3), 60.9 (OCH_3), 60.6 (OCH_3), 25.5 ($ArCH_3$); *m/z* 353 (MH^+).

Methyl 4-(3-*O*,4-*S*-dibenzoyl-2,6-dideoxy-4-thio-β-D-*ribo*-hexopyranosyloxyamino)-4,6-dideoxy-2-*O*-{4′-[*N*-ethyl-*N*-(fluoren-9-ylmethoxycarbonyl)amino]butyl}-α-D-glucopyranoside β-(and α)-32

A solution of DDQ (0.01 M in CH_3CN–water 9 : 1; 344 μL, 3.44 μmol) was added over a period of 1 h to **23** (68 mg, 69 μmol) at 0 °C. The solution was then neutralised with saturated aq. $NaHCO_3$ and diluted with CH_2Cl_2. The organic layer was extracted, dried over $MgSO_4$, filtered and evaporated to dryness. Column chromatography (heptane–ethyl acetate 1 : 1) provided compound β-**32** (45 mg, 75%) as a white foam; $[a]_D$ +92 (*c* 1.12, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3474 (OH, NH), 1720 [Ph(C=O)O], 1694 [O(C=O)N], 1670 [Ph(C=O)S]; δ_H (250 MHz; $CDCl_3$) 1.02 (3H, m, H_3-6′), 1.26 (3H, d, $J_{5,6}$ 6.5, H_3-6A), 1.41 (3H, d, $J_{5,6}$ 6.5, H_3-6B), 1.60 (4H, br s, H_2-2′, -3′), 1.94 (1H, ddd, $J_{2eq,2ax}$ 14.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 10.0, H-2axB), 2.22 (1H, ddd, $J_{2eq,2ax}$ 14.0, $J_{2eq,3}$ 2.5, J_{2eq1} 2.0, H-2eqB), 2.35 (1H, dd, $J_{3,4} = J_{4,5} =$ 10.0, H-4A), 3.03 (2H, br s, H_2-5′), 3.20 (br 2H, s, H_2-4′), 3.26 (1H, dd, $J_{2,1}$ 3.5, $J_{2,3}$ 10.0, H-2A), 3.37 (3H, s, OCH_3), 3.42–3.70 (2H, br s, H_2-1′), 3.91 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.0, H-5A), 3.95 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 11.0, H-4B), 4.22 (3H, m, H-3A, -5B, H Fmoc), 4.47 (2H, br s, CH_2 Fmoc), 4.75 (1H, br s, H-1A), 5.05 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.0, H-1B), 5.58 (1H, m, $J_{3,4} = J_{3,2ax} =$ 3.0, $J_{3,2eq}$ 2.5, H-3B), 6.65 (1H, br s, NH), 7.27–7.62 (12H, m, Fmoc, ArH), 7.75 (2H, dd, Fmoc), 7.91 (2H, dd, SBz), 8.04 (2H, dd, OBz); δ_C (62.9 MHz; $CDCl_3$) 189.4 (SC=O), 165.1 (OC=O), 156.0 (NC=O), 144.1 (C arom), 141.3 (C arom), 136.4 (C arom), 133.6 (C arom), 133.3 (CH arom), 129.7 (CH arom), 129.6 (CH arom), 128.6 (CH arom), 128.5 (CH arom), 127.5 (CH arom), 127.4 (CH arom), 126.9 (CH arom), 125.8 (CH arom), 124.8 (CH arom), 119.8 (CH arom), 100.1 (C-1B), 97.6 (C-1A), 81.0 (C-2A), 71.9 (C-1′), 70.7, 70.0 (C-3B, C-5B), 68.1 (C-4A), 66.4 (C-3A, CH_2 Fmoc), 63.9 (C-5A), 55.1 (OCH_3), 47.8, 47.4 (C-4B, CH Fmoc), 46.7 (C-4′), 42.2 (C-5′), 34.7 (C-2B), 26.8 (C-3′), 24.7 (C-2′), 19.0 (C-6B), 18.0 (C-6A), 13.7 (C-6′); *m/z* 869 $(MH)^+$ (Found: C, 65.99; H, 6.32; N, 3.10. $C_{48}H_{56}N_2O_{11}S$ requires C, 66.34; H, 6.49; N, 3.22%).

Further elution (heptane–ethyl acetate 1 : 1) gave α-**32** (8 mg, 13%) as a white foam; δ_H (250 MHz; $CDCl_3$) 0.99 (3H, m, H_3-6′), 1.12 (3H, d, $J_{5,6}$ 6.0, H_3-6A), 1.30–1.60 (4H, m, H_2-2′, -3′), 1.33 (3H, d, $J_{5,6}$ 6.0, H_3-6B), 2.16 (1H, ddd, $J_{2eq,2ax}$ 15.0, $J_{2ax,3}$ 3.0, $J_{2ax,1}$ 4.0, H-2axB), 2.35 (2H, ddd, H-4A, -2eqB), 2.97 (1H, br s, H-4′), 3.08–3.25 (7H, m, H-4′, H_2-5′, H-2A, OCH_3), 3.48 (1H, br s, H-1′), 3.66 (2H, m, H-5A, -1′), 3.90 (1H, dd, $J_{3,4} = J_{2,3} = 10.0$, H-3A), 4.01 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 10.5, H-4B), 4.18 (1H, t, H Fmoc), 4.43 (3H, m, CH_2 Fmoc, H-5B), 4.67 (1H, br s, H-1A), 5.13 (1H, dd, $J_{1,2ax}$ 4.0, $J_{1,2eq} \approx$ 1–2, H-1B), 5.32 (1H, m, $J_{3,4} = J_{3,2ax} = 3.0$, H-3B), 6.65 (1H, br s, NH), 7.26–7.56 (12H, m, Fmoc, ArH), 7.71 (2H, dd, Fmoc), 7.90 (2H, dd, SBz), 8.06 (2H, dd, OBz).

Bis{methyl 4,6-dideoxy-2-*O*-[4′-(ethylamino)butyl]-4-(2,4,6-trideoxy-β-D-*ribo*-hexopyranosyloxyamino)-α-D-glucopyranosid-4-yl} disulfide 33

To a stirred solution of compound β-**32** (41 mg, 47 μmol) in dry MeOH (2 mL) at room temperature was added solid potassium carbonate (26 mg, 189 μmol). The mixture was stirred for 2 h and evaporated to dryness. Column chromatography (CH_2Cl_2–MeOH 1 : 1 containing 1% of 32% aq. ammonia) provided a colorless oil (20 mg). This oil was dissolved in CH_2Cl_2 (1 mL), and the solution was saturated with gaseous ammonia and stirred at room temperature for 15 min. The resulting solution was filtered from a white solid on Celite and the solvent was removed to afford disulfide **33** (15 mg, 72%) as a colorless oil; $[a]_D$ +52 (*c* 0.78, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3458 (NH), 3276 (OH); δ_H (250 MHz; $CDCl_3$) 1.07 (3H, t, $J_{5',6'}$ 7.5, H_3-6′), 1.29 (3H, d, $J_{5,6}$ 6.5, H_3-6B), 1.35 (3H, d, $J_{5,6}$ 6.5, H_3-6A), 1.59 (5H, m, H_2-2′, H-2axB), 2.02 (1H, ddd, $J_{2eq,2ax}$ 13.5, $J_{2eq,3}$ 3.5, $J_{2eq,1}$ 2.0, H-2eqB), 2.30 (1H, td, $J_{4,NH}$ 2.0, $J_{3,4} = J_{4,5} = 10.0$, H-4A), 2.60 (2H, m, H_2-4′), 2.60 (2H, q, $J_{5',6'}$ 7.5, H_2-5′), 2.66 (1H, dd, $J_{4,3}$ 2.5, $J_{4,5}$ 10.0, H-4B), 3.21 (1H, dd, $J_{2,1}$ 3.5, $J_{2,3}$ 10.0, H-2A), 3.36 (3H, s, OCH_3), 3.55 (1H, m, H-1′), 3.68 (1H, m, H-1′), 3.73 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.0, H-5B), 3.88 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.0, H-5A), 3.96 (1H, m, $J_{3,4} = J_{3,2a} = 2.5$, $J_{3,2e}$ 3.5, H-3B), 4.12 (1H, dd, $J_{3,4} = J_{2,3} = 10.0$, H-3A), 4.72 (1H, d, $J_{2,1}$ 3.5, H-1A), 4.95 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.0, H-1B), 6.52 (1H, d, $J_{4,NH}$ 2.0, NHO); δ_C (62.9 MHz; $CDCl_3$) 99.6 (C-1B), 97.7 (C-1A), 81.6 (C-2A), 71.0 (C-1′), 68.0 (C-4A, -5B), 66.0 (C-3A), 65.4 (C-3B), 64.1 (C-5A), 59.3 (C-4B), 55.1 (OCH_3), 49.2 (C-4′), 44.0 (C-5′), 36.1 (C-2B), 27.6 (C-3′), 26.7 (C-2′), 20.0 (C-6B), 18.2 (C-6A), 14.9 (C-6′); *m/z* 875 $(MH)^+$.

Methyl 4,6-dideoxy-4-[2,6-dideoxy-4*S*-(3-iodo-4,5,6-trimethoxy-2-methylbenzoyl)-4-thio-β-D-*ribo*-hexopyranosyloxyamino]-2-*O*-[4′-(ethylamino)butyl]-α-D-glucopyranoside 3

Preparation of mixed anhydride 30. Pyridine (10 μL, 119 μmol) and phenyl dichlorophosphate (9 μL, 60 μmol) were added to a stirred solution of acid **28** (14 mg, 40 μmol) in DME (195 μL) at 0 °C. The mixture was stirred for 1 h at room temperature.

Preparation of 3. Tri-*n*-butylphosphine (147 μL, 596 μmol) was added to a stirred solution of disulfide **33** (12 mg, 13 μmol) in DME (240 μL). The mixture was stirred for 1 h at room temperature and then added to a stirred solution of the above mixed anhydride **30** at 0 °C. The resulting mixture was stirred for 24 h at room temperature, filtered through a short

pad of Celite, and the solvent was removed *in vacuo*. Column chromatography (CH_2Cl_2–MeOH; 6:1 containing 1% of 32% aq. ammonia) gave a white solid (16 mg). This solid was dissolved in CH_2Cl_2 (1 mL), and the solution was saturated with ammonia and stirred at room temperature for 15 min. The resulting solution was filtered on Celite and the solvent was removed to afford amine **3** (11 mg, 53%) as a colorless oil; $[\alpha]_D$ +28 (*c* 0.63, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3432 (NH, OH), 1673 [(C=O)S]; δ_H (250 MHz; $CDCl_3$) 1.10 (3H, t, $J_{5',6'}$ 7.5, H_3-6′), 1.32 (3H, d, $J_{5,6}$ 6.5, H_3-6A), 1.37 (3H, d, $J_{5,6}$ 6.5, H_3-6B), 1.61 (4H, m, H_2-2′, -3′), 1.75 (1H, m, $J_{2eq,2ax}$ 13.5, $J_{2eq,3}$ 3.0, $J_{2eq,1}$ 10.0, H-2axB), 1.98 (1H, ddd, $J_{2eq,2ax}$ 13.5, $J_{2eq,3}$ 3.0, $J_{2eq,1}$ 2.0, H-2eqB), 2.31 (3H, s, CH_3), 2.34 (1H, td, $J_{3,4} = J_{4,5} = 9.5$, $J_{4,NH}$ 2.0, H-4A), 2.63 (2H, q, $J_{5',6'}$ 7.5, H_2-5′), 2.64 (2H, m, H_2-4′), 3.24 (1H, dd, $J_{2,1}$ 3.5, $J_{2,3}$ 9.5, H-2A), 3.38 (3H, s, OCH_3), 3.56 (1H, m, H-1′), 3.68 (1H, m, H-1′), 3.68 (1H, dd, $J_{4,3}$ 2.5, $J_{4,5}$ 10.5, H-4B), 3.84 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.89 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 10.5, H-5B), 4.00 (1H, dq, $J_{5,6}$ 6.5, $J_{5,4}$ 9.5 H-5A), 4.14 (1H, dd, $J_{3,4} = J_{2,3} = 9.5$, H-3A), 4.27 (1H, m, H-3B), 4.73 (1H, d, $J_{2,1}$ 3.5, H-1A), 5.02 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.0, H-1B), 6.60 (1H, d, $J_{4,NH}$ 2.0, NHO); δ_C (62.9 MHz; $CDCl_3$) 192.0 (C=O), 150.3 (C-6), 143.6 (C-5), 132.9 (C-2), 130.3 (C-1), 99.6 (C-1B), 97.7 (C-1A), 94.3 (C-3), 81.8 (C-2A), 71.1 (C-1′), 68.7 (C-5B), 68.0 (C-4A, -3B), 66.0 (C-3A), 64.2 (C-5A), 61.8 (Ar-OCH_3), 60.9 (Ar-O*C*H_3), 60.6 (Ar-O*C*H_3), 55.1 (OCH_3), 51.9 (C-4B), 49.2 (C-4′), 44.0 (C-5′), 36.6 (C-2B), 27.7 (C-3′), 26.7 (C-2′), 24.9 (Ar-*C*H_3), 19.2 (C-6B), 18.3 (C-6A), 14.7 (C-6′); *m*/*z* 773 (MH^+).

Methyl 4,6-dideoxy-4-{4-*S*-[4-(6-deoxy-3-*O*-methyl-α-L-mannopyranosyloxy)-3-iodo-5,6-dimethoxy-2-methylbenzoyl]-2,6-dideoxy-4-thio-β-D-*ribo*-hexopyranosyloxyamino}-2-*O*-[4′-(ethylamino)butyl]-α-D-glucopyranoside 4

Preparation of mixed anhydride 31. Pyridine (6 μL, 70 μmol) and phenyl dichlorophosphate (5 μL, 35 μmol) were added to a stirred solution of compound **29**[8h] (see below) (12 mg, 23 μmol) in DME (115 μL) at 0 °C. The mixture was stirred for 1 h at room temperature.

Preparation of 4. Tri-*n*-butylphosphine (63 μL, 272 μmol) was added to a stirred solution of disulfide **33** (5.3 mg, 6 μmol) in DME (110 μL). The mixture was stirred for 1 h at room temperature and then was added to a stirred solution of the mixed anhydride **31** at 0 °C. The mixture was stirred for 24 h at room temperature, filtered through a short pad of Celite and the solvent was removed *in vacuo*. Column chromatography (CH_2Cl_2–MeOH 8:1 containing 1% of 32% aq. ammonia) gave a white solid (12 mg). This solid was dissolved in CH_2Cl_2 (0.5 mL), then the solution was saturated with ammonia and stirred at room temperature for 15 min. The resulting solution was filtered on Celite and the solvent was removed to afford compound **4** (8 mg, 72%) as a white solid; $[\alpha]_D$ −5 (*c* 0.54, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3417 (NH, OH), 1660 [(C=O)S]; δ_H (250 MHz; $CDCl_3$) 1.26 (3H, t, $J_{5',6'}$ 7.5, H_3-6′), 1.27 (3H, d, $J_{5,6}$ 6.0, H_3-6D), 1.31 (3H, d, $J_{5,6}$ 6.0, H_3-6A), 1.36 (3H, d, $J_{5,6}$ 6.0, H_3-6B), 1.74 (1H, m, H-2axB), 1.87 (4H, m, H_2-2′, -3′), 2.00 (1H, ddd, H-2eqB), 2.32 (3H, s, CH_3), 2.41 (1H, dd, $J_{3,4} = J_{4,5} = 10.0$, H-4A), 2.74 (1H, m, H-4′), 2.89 (2H, q, $J_{5',6'}$ 7.5, H_2-5′), 2.89 (1H, m, H-4′), 3.37 (3H, s, OCH_3), 3.40 (1H, dd, $J_{2,1}$ 3.5, $J_{2,3}$ 10.0, H-2A), 3.54 (3H, s, OCH_3), 3.61 (1H, dd, $J_{3,4} = J_{4,5} = 9.5$, H-4D), 3.68 (1H, dd, $J_{4,3}$ 2.5, $J_{4,5}$ 10.0, H-4B), 3.61–3.72 (2H, m, H_2-1′), 3.80 (3H, s, OCH_3), 3.81 (1H, dd, $J_{2,3}$ 3.0, $J_{3,4}$ 9.5, H-3D), 3.82 (1H, m, H-5A), 3.85 (3H, s, OCH_3), 4.02 (1H, dq, $J_{5,6}$ 6.0, $J_{5,4}$ 10.0, H-5B), 4.05 (1H, dd, $J_{3,4} = J_{2,3} = 10.0$, H-3A), 4.16 (1H, dq, $J_{4,5}$ 9.5, $J_{5,6}$ 6.0, H-5D), 4.26 (1H, m, H-3B), 4.45 (1H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.0, H-2D), 4.75 (1H, d, $J_{2,1}$ 3.5, H-1A), 5.06 (1H, dd, $J_{1,2eq}$ 2.0, $J_{1,2ax}$ 10.0, H-1B), 5.69 (1H, d, $J_{1,2}$ 2.0, H-1D), 6.65 (1H, s, NHO); δ_C (62.9 MHz; $CDCl_3$) 192.2 (C=O), 151.3 (C-4), 150.6 (C-6), 142.9 (C-5), 133.4 (C-2), 130.4 (C-1), 102.5 (C-1D), 99.7 (C-1B), 97.2 (C-1A), 93.4 (C-3), 81.3 (C-2A), 80.8 (C-3D), 71.1 (C-1′), 70.3 (C-5D, -4D), 69.0 (C-5B), 68.1 (C-3B), 66.9 (C-2D), 66.4 (C-3A), 64.8 (C-5A), 61.6 (Ar-O*C*H_3), 60.8 (Ar-O*C*H_3), 57.1 (OCH_3), 54.9 (OCH_3), 51.9 (C-4B), 47.5 (C-4′), 42.9 (C-5′), 36.8 (C-2B), 29.7 (C-3′), 28.4 (C-2′), 25.3 (Ar-*C*H_3), 19.2 (C-6B), 18.3 (C-6A), 17.5 (C-6D), 11.1 (C-6′). *m*/*z* 919 (MH^+) (Found: MH^+, 919.2764. $C_{36}H_{60}IN_2O_{15}S$ requires *m*/*z*, 919.2759).

4-[(*tert*-Butyldiphenylsiloxy)methyl]-2-iodo-5,6-dimethoxy-3-methylphenyl 2,4-di-*O*-acetyl-6-deoxy-3-*O*-methyl-α-L-mannopyranoside 36

To a stirred solution of the phenol **35**[8h] (160 mg, 0.28 mmol), sulfide **34**[8f] (111 mg, 0.31 mmol) and powdered 4 Å molecular sieves in dry CH_2Cl_2 (6.5 mL) at 0 °C were successively added NIS (83 mg, 0.37 mmol) and a solution of TMSOTf (1 M in toluene, 29 μL, 29 μmol). The mixture was stirred for 2 h at 0 °C, neutralised with Et_3N, filtered on Celite and the solvent evaporated. Column chromatography (heptane–ethyl acetate 5:1) provided compound **36** (155 mg, 68%) as a colorless oil; $[\alpha]_D$ −14 (*c* 1.87, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 1.04 (9H, s, Bu^t), 1.21 (3H, d, $J_{5,6}$ 6.0, H_3-6), 2.13 (3H, s, OAc), 2.16 (3H, s, OAc), 2.51 (3H, s, CH_3), 3.44 (3H, s, OCH_3), 3.63 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 4.03 (1H, dd, $J_{2,3}$ 3.5, $J_{3,4}$ 10.0, H-3), 4.41 (1H, dq, $J_{4,5}$ 10.0, $J_{5,6}$ 6.0, H-5), 4.76 (2H, s, CH_2), 5.10 (1H, dd, $J_{3,4} = J_{4,5} = 10.0$, H-4), 5.56 (1H, d, $J_{1,2}$ 2.0, H-1), 5.79 (1H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.5, H-2), 7.34–7.44 (6H, m, ArH), 7.66–7.71 (4H, m, ArH); δ_C (62.9 MHz; $CDCl_3$) 170.2 (C=O), 170.1 (C=O), 153.0 (C-1), 149.5 (C-5), 142.7 (C-6), 138.0 (C arom), 135.7 (C arom), 133.5 (CH arom), 129.6 (CH arom), 129.0 (CH arom), 127.5 (CH arom), 100.8 (C-1D), 93.5 (C-2), 77.2 (C-3D), 72.2, 69.0, 67.9 (C-5D, -4D, -2D), 61.2 (Ar-O*C*H_3), 60.7 (Ar-O*C*H_3), 58.6 (Ar-*C*H_2OSi), 57.7 (OCH_3), 26.8 [(*C*H_3)$_3$CSi], 25.5 (Ar-*C*H_3), 21.0 (*C*H_3C=O), 19.3 [(CH$_3$)$_3$-*C*Si], 17.3 (C-6D); *m*/*z* 824 ($M + NH_4$)$^+$ (Found: C, 55.18; H, 5.94. $C_{37}H_{47}IO_{10}Si$ requires C, 55.09; H, 5.87%).

4-(Hydroxymethyl)-2-iodo-5,6-dimethoxy-3-methylphenyl 2,4-di-*O*-acetyl-6-deoxy-3-*O*-methyl-α-L-mannopyranoside 37

To a stirred solution of compound **36** (38 mg, 47 μmol) in dry THF (2.8 mL) at room temperature was added solid TBAF (49 mg, 188 μmol). The mixture was stirred for 4 h, then evaporated to dryness. Column chromatography (heptane–ethyl acetate 1:1) provided the alcohol **37** (20 mg, 75%) as a colorless oil; $[\alpha]_D$ −19 (*c* 1.36, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3441 (OH), 1748 (C=O); δ_H (250 MHz; $CDCl_3$) 1.19 (3H, d, $J_{5,6}$ 6.5, H_3-6), 2.13 (3H, s, OAc), 2.16 (3H, s, OAc), 2.56 (3H, s, CH_3), 3.44 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.04 (1H, dd, $J_{2,3}$ 3.5, $J_{3,4}$ 10.0, H-3), 4.37 (1H, dq, $J_{4,5}$ 10.0, $J_{5,6}$ 6.5, H-5), 4.76 (2H, s, CH_2), 5.10 (1H, dd, $J_{3,4} = J_{4,5} = 10.0$, H-4), 5.60 (1H, d, $J_{1,2}$ 2.0, H-1), 5.76 (1H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.5, H-2); δ_C (62.9 MHz; $CDCl_3$) 170.2 (C=O), 170.1 (C=O), 153.2 (C-1), 149.7 (C-5), 142.8 (C-6), 137.0 (C-3), 128.9 (C-4), 100.6 (C-1D), 93.8 (C-2), 76.4 (C-3D), 72.1, 69.0, 67.9 (C-5D, -4D, -2D), 61.5 (Ar-O*C*H_3), 60.8 (Ar-O*C*H_3), 58.2 (Ar-*C*H_2OSi), 57.7 (OCH_3), 25.2 (Ar-*C*H_3), 21.0 (*C*H_3C=O), 17.4 (C-6D); *m*/*z* 586 ($M + NH_4$)$^+$ (Found: C, 44.45; H, 5.17. $C_{21}H_{29}IO_{10}$ requires C, 44.38; H, 5.14%).

4-(2,4-Di-*O*-acetyl-6-deoxy-3-*O*-methyl-α-L-mannopyranosyloxy)-3-iodo-5,6-dimethoxy-2-methylbenzoic acid 38

To a stirred solution of alcohol **37** (125 mg, 220 μmol) in CCl_4–CH_3CN (1:1; 3 mL) at 0 °C were successively added water (4.5 mL), sodium periodate (188 mg, 879 μmol) and ruthenium trichloride hydrate (12 mg, 55 μmol). The mixture was vigorously stirred for 1 h at room temperature, diluted with water and extracted with CH_2Cl_2. The aqueous phase was acidified with acetic acid, extracted (5×) with CH_2Cl_2, and the extracts were dried over $MgSO_4$. Column chromatography (heptane–ethyl acetate 1:1 containing 1% acetic acid) provided acid **38** (76 mg,

60%) as a colorless oil; ν_{max} (thin film)/cm^{-1} 3423 (OH), 1738 (C=O), 1643 (CO_2H); δ_H (250 MHz; $CDCl_3$) 1.19 (3H, d, $J_{5,6}$ 6.5, H_3-6), 2.13 (3H, s, OAc), 2.17 (3H, s, OAc), 2.49 (3H, s, CH_3), 3.44 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.04 (1H, dd, $J_{2,3}$ 3.5, $J_{3,4}$ 10.0, H-3), 4.33 (1H, dq, $J_{4,5}$ 10.0, $J_{5,6}$ 6.5, H-5), 5.10 (dd, 1H, $J_{3,4} = J_{4,5} = 10.0$, H-4), 5.67 (1H, d, $J_{1,2}$ 2.0, H-1), 5.75 (1H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.5, H-2); δ_C (62.9 MHz; $CDCl_3$) 170.2 (C=O), 170.2 (C=O), 151.4, 151.1 (C-4, C-5), 142.7 (C-6), 134.6 (C-3), 125.9 (C-1), 100.6 (C-1D), 97.3 (C-2), 77.2 (C-3D), 72.1, 69.2, 67.8 (C-5D, -4D, -2D), 61.8 (Ar-OCH_3), 60.9 (Ar-OCH_3), 57.8 (OCH_3), 26.1 (Ar-CH_3), 21.0 (CH_3C=O), 17.4 (C-6D); *m*/*z* 600 $(M + NH_4)^+$.

4-(6-Deoxy-3-*O*-methyl-α-L-mannopyanosyloxy)-3-iodo-5,6-dimethoxy-2-methylbenzoic acid 29[8h]

Solid lithium hydroxide monohydrate (26 mg, 618 μmol) was added to a stirred mixture of acid **38** (90 mg, 154 μmol) and hydrogen peroxide (30% in water, 38 μL, 1.24 mmol) in a mixture THF–water (3 : 1; 5 mL) at 0 °C. The resulting mixture was stirred for 2 h at room temperature, acidified with 5% aq. hydrochloric acid, concentrated *in vacuo*, and coevaporated with toluene. Column chromatography (ethyl acetate–methanol 10 : 1 containing 1% acetic acid) provided diol **29** (61 mg, 79%) as a white solid; ν_{max} (thin film)/cm^{-1} 3406 (OH), 1631 (CO_2H); δ_H (250 MHz; $CDCl_3$) 1.30 (3H, d, $J_{5,6}$ 6.0, H_3-6), 2.50 (3H, s, CH_3), 3.58 (3H, s, OCH_3), 3.65 (1H, dd, $J_{3,4} = J_{4,5} = 9.5$, H-4), 3.86 (1H, dd, $J_{2,3}$ 3.5, $J_{3,4}$ 9.5, H-3), 3.86 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 4.19 (1H, dq, $J_{4,5}$ 9.5, $J_{5,6}$ 6.0, H-5), 4.48 (1H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.5, H-2), 5.78 (1H, d, $J_{1,2}$ 2.0, H-1).

4-(6-Deoxy-3-*O*-methyl-2,4-bis-*O*-triethylsilyl-α-L-mannopyranosyloxy)-3-iodo-5,6-dimethoxy-2-methylbenzoic acid 39[8f,32]

To a stirred solution of acid **29**[8h] (43 mg, 86 μmol) in dichloromethane (1.3 mL) at 0 °C were successively added pyridine (56 μL, 690 μmol), DMAP (42 mg, 345 μmol) and dropwise triethylsilyl trifluoromethanesulfonate (97 μL, 431 μmol). The solution was stirred for 1 h, at room temperature, then poured into saturated aq. $NaHCO_3$. The organic layer was separated, dried over $MgSO_4$, and the solvent removed *in vacuo*. Column chromatography (heptane–ethyl acetate 2 : 1 containing 1% acetic acid) provided acid **39** (50 mg, 80%) as a colorless oil; δ_H (250 MHz; $CDCl_3$) 0.60 [6H, q, *J* 8.0, Si(CH_2CH_3)$_3$], [0.62 [6H, q, *J* 8.0, Si(CH_2CH_3)$_3$], 0.94 [9H, t, *J* 8.0, Si(CH_2CH_3)$_3$], 0.95 [9H, t, *J* 8.0, Si(CH_2CH_3)$_3$], 1.21 (3H, d, $J_{5,6}$ 6.0, H_3-6), 2.47 (3H, s, CH_3), 3.40 (3H, s, OCH_3), 3.56 (1H, dd, $J_{2,3}$ 2.5, $J_{3,4}$ 9.0, H-3), 3.71 (1H, dd, $J_{3,4} = J_{4,5} = 9.0$, H-4), 3.79 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.08 (1H, dq, $J_{4,5}$ 9.0, $J_{5,6}$ 6.0, H-5), 4.41 (1H, dd, $J_{1,2} = J_{2,3} = 2.5$, H-2), 5.41 (1H, d, $J_{1,2}$ 2.0, H-1).

Methyl 2,6-dideoxy-4-*O*-[4-(6-deoxy-3-*O*-methyl-2,4-bis-*O*-triethylsilyl-α-L-mannopyranosyl-oxy)-3-iodo-5,6-dimethoxy-2-methylbenzoyl]-3-*O*-(tetrahydropyran-2-yl)-α-D-*ribo*-hexopyranoside 42

Methyl 2,6-dideoxy-3-*O*-(tetrahydropyran-2-yl)-α- and -β-D-*ribo*-hexopyranoside **41**[24b] (17 mg, 66 μmol) as a solution in THF (0.1 mL) was stirred in the presence of sodium hydride (60% dispersion in oil) (3 mg, 66 μmol) at 0 °C for 10 min and for a further 1 h at room temperature.

Oxalyl dichloride (101 μL) was added at room temperature to a stirred solution of acid **39** (16 mg, 22 μmol) in dichloromethane (0.5 mL). The resulting solution was stirred for 1 h then the solvent was removed *in vacuo*. Acid chloride **40**[8f] was taken up in THF (0.1 mL) and added to the above solution of the sodium salt of carbohydrate **41** at 0 °C. The mixture was stirred for 30 min at room temperature, then neutralised with saturated aq. $NaHCO_3$ and evaporated to dryness. Column chromatography (heptane–ethyl acetate 8 : 1) provided ester **42** (14 mg, 67%) as a colorless oil; $[a]_D$ +18 (*c* 1.00, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 0.66 [12H, 2 q, *J* 7.5, 2 × Si(CH_2CH_3)$_3$], 0.99 [18H, 2 t, *J* 7.5, 2 × Si(CH_2CH_3)$_3$], 1.24 (3H, d, $J_{5,6}$ 6.5, H_3-6D), 1.34 (3H, d, $J_{5,6}$ 6.5, H_3-6B), 1.50–1.80 (6H, m, OTHP), 1.92 (1H, dt, $J_{2ax,1} = J_{2ax,3} = 4.0$, $J_{2eq,2ax}$ 14.0, H-2Bax), 2.14 (1H, m, $J_{2eq,1}$ 4.0, $J_{2eq,3}$ 6.5, $J_{2eq,2ax}$ 14.0, H-2Beq), 2.44 (3H, s, CH_3), 3.33–3.50 (2H, m, OTHP), 3.35 (3H, s, OCH_3), 3.44 (3H, s, OCH_3), 3.60 (1H, dd, $J_{2,3}$ 2.0, $J_{3,4}$ 9.0, H-3D), 3.74 (1H, dd, $J_{3,4} = J_{4,5} = 9.0$, H-4D), 3.80 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.10 (1H, dq, $J_{4,5}$ 9.0, $J_{5,6}$ 6.5, H-5D), 4.33 (2H, m, H-3B, -5B), 4.45 (1H, dd, $J_{1,2} = J_{2,3} = 2.0$, H-2D), 4.70 (1H, t, $J_{1,2eq} = J_{1,2ax} = 4.0$, H-1B), 4.83 (1H, m, OTHP), 5.05 (1H, dd, $J_{4,3}$ 3,0, $J_{4,5}$ 7.5, H-4B), 5.41 (1H, d, $J_{1,2}$ 2.0, H-1D); δ_C (62.9 MHz; $CDCl_3$) 166.7 (C=O), 151.8, 151.3 (C-6, -4), 143.0 (C-5), 134.2 (C-2), 125.8 (C-1), 104.5 (C-1D), 97.3 (C-1B), 95.0 (C-THP), 93.5 (C-3), 81.3 (C-3D), 77.2 (C-4B), 75.1, 72.3, 68.6, 66.8 (C-5D, -4D, -2D, -3B), 64.6 (C-5B), 62.2 (C THP), 61.5 (Ar-OCH_3), 60.7 (Ar-OCH_3), 57.2 (OCH_3), 55.2 (OCH_3), 31.1, 30.4 (C-2B, C THP), 26.1 (Ar-CH_3), 25.5 (C THP), 19.3 (C THP), 18.0 (C-6D), 17.5 (C-6B), 6.9 (CH_3CH_2Si), 6.7 (CH_3CH_2Si), 5.1 (CH_3CH_2Si); 4.8 (CH_3CH_2Si).

Methyl 2,6-dideoxy-4-*O*-[4-(6-deoxy-3-*O*-methyl-α-L-mannopyranosyloxy)-3-iodo-5,6-dimethoxy-2-methylbenzoyl]-α-D-*ribo*-hexopyranoside 43

Cold 1% HCl solution in dry methanol (150 μL) was added to ester **42** (14 mg, 15 μmol). The solution was stirred for 15 min at room temperature, then neutralised with 5% aq. $NaHCO_3$ and evaporated to dryness. Column chromatography (dichloromethane–methanol 30 : 1) provided triol **43** (7 mg, 75%) as a colorless oil; $[a]_D$ +17 (*c* 0.70, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 1.30 (3H, d, $J_{5,6}$ 6.0, H_3-6), 1.34 (3H, d, $J_{5,6}$ 6.0, H_3-6), 2.04 (1H, dt, $J_{2ax,1} = J_{2ax,3} = 3.5$, $J_{2eq,2ax}$ 15.0, H-2Bax), 2.19 (1H, ddd, $J_{2eq,1}$ 1.0, $J_{2eq,2ax}$ 15.0, H-2Beq), 2.42 (3H, s, CH_3), 3.40 (3H, s, OCH_3), 3.56 (1H, d, $J_{3,OH}$ 8.5, OH-3B), 3.58 (3H, s, OCH_3), 3.64 (1H, dd, $J_{3,4} = J_{4,5} = 9.5$, H-4D), 3.84 (3H, s, OCH_3), 3.85 (1H, m, H-3D), 3.91 (3H, s, OCH_3), 4.13–4.32 (3H, m, H-5D, -3B, -5B), 4.40 (1H, m, H-2D), 4.80 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 10.0, H-4B), 4.83 (1H, dd, $J_{1,2ax}$ 3.5, $J_{1,2eq} \approx 1$–2, H-1B), 5.74 (1H, d, $J_{1,2}$ 1.5, H-1D); δ_C (62.9 MHz; $CDCl_3$) 166.4 (C=O), 151.2, 151.1 (C-6, -4), 142.8 (C-5), 134.0 (C-2), 125.1 (C-1), 102.4 (C-1D), 98.4 (C-1B), 93.1 (C-3), 80.8 (C-3D), 77.2 (C-4B), 71.1 (C-4D), 70.3 (C-5D), 66.9 (C-2D), 65.3 (C-5B), 61.5 (Ar-OCH_3), 61.0 (C-3B), 60.8 (Ar-OCH_3), 57.1 (OCH_3), 55.2 (OCH_3), 35.2 (C-2B), 25.7 (Ar-CH_3); 17.5 (C-6B, -6D).

Methyl 3-*O*-acetyl-2,6-dideoxy-4-*O*-[4-(2,4-di-*O*-acetyl-6-deoxy-3-*O*-methyl-α-L-mannopyranosyl-oxy)-3-iodo-5,6-dimethoxy-2-methylbenzoyl]-α-D-*ribo*-hexopyranoside 44

A solution of triol **43** (7 mg, 10.9 μmol) in a mixture of acetic anhydride (0.2 mL) and pyridine (0.3 mL) was stirred for 3 h at room temperature and then for 2 h at 50 °C. The solution was evaporated to dryness, then coevaporated with toluene. Column chromatography (heptane–ethyl acetate 2 : 1) provided triacetate **44** (7 mg, 83%) as a colorless oil; $[a]_D$ +27 (*c* 0.70, $CHCl_3$); δ_H (250 MHz; $CDCl_3$) 1.20 (3H, d, $J_{5,6}$ 6.0, H_3-6), 1.32 (3H, d, $J_{5,6}$ 6.0, H_3-6), 2.03 (1H, m, $J_{2ax,1}$ 4.5, $J_{2ax,3}$ 4.0, $J_{2eq,2ax}$ 15.0, H-2Bax), 2.05 (3H, s, OAc), 2.14 (3H, s, OAc), 2.17 (3H, s, OAc), 2.26 (1H, m, $J_{2eq,1}$ 1.5, $J_{2eq,3}$ 4.0, $J_{2eq,2ax}$ 15.0, H-2Beq), 2.36 (3H, s, CH_3), 3.36 (3H, s, OCH_3), 3.44 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 4.04 (1H, dd, $J_{4,3}$ 10.0, $J_{3,2}$ 3.0, H-3D), 4.33 (2H, m, H-5D, -5B), 4.73 (1H, m, $J_{1,2ax}$ 4.5, $J_{1,2eq}$ 1.5, H-1B), 4.94 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 9.0, H-4B), 5.11 (1H, dd, $J_{3,4} = J_{4,5} = 10.0$, H-4D), 5.34 (1H, m, $J_{3,2ax} = J_{3,2eq} = 4.0$, $J_{4,3}$ 3.0, H-3B), 5.64 (1H, d, $J_{1,2}$ 2.0, H-1D), 5.75 (1H, dd, $J_{1,2}$ 2.0, $J_{3,2}$ 3.0, H-2D); δ_C (62.9 MHz; $CDCl_3$) 170.5 (C=O), 170.2 (C=O), 170.1 (C=O), 163.9 (C=O), 151.2; 150.9 (C-6, -4), 143.0 (C-5), 134.0 (C-2), 125.2 (C-1), 104.5 (C-1D), 97.3 (C-1B), 95.5 (C-3), 77.2 (C-3D, -4B), 73.6; 72.1; 69.1; 67.8 (C-5D, -4D, -2D, -3B), 62.8 (C-5B), 61.4 (Ar-OCH_3), 60.9 (Ar-OCH_3), 57.8

(OCH_3), 55.3 (OCH_3), 33.1 (C-2B), 25.7 (Ar-CH_3), 21.2 (CH_3C=O); 17.4 (C-6B, -6D).

3-*O*-Acetyl-2,6-dideoxy-4-*O*-[4-(6-deoxy-2,4-di-*O*-acetyl-3-*O*-methyl-α-L-mannopyranosyloxy)3-iodo-5,6-dimethoxy-2-methylbenzoyl]-α and -β-D-*ribo*-hexopyranose 7

A stirred solution of triacetate **44** (7 mg, 9 μmol) in water–AcOH 2:1 (0.8 mL) was heated at reflux for 2 h. On cooling, the solvent was removed under reduced pressure, and final traces were removed by coevaporation (3×) with toluene. Column chromatography (heptane–ethyl acetate 1:2) provided hemiacetal **7** (5 mg, 73%) as a colorless, oily, 3–4:1 mixture of β and α anomers; major β-anomer: δ_H (250 MHz; $CDCl_3$) 1.20 (3H, d, $J_{5,6}$ 6.5, H_3-6), 1.37 (3H, d, $J_{5,6}$ 6.0, H_3-6), 1.86 (1H, ddd, $J_{2ax,1}$ 9.0, $J_{2ax,3}$ 2.5, $J_{2eq,2ax}$ 14.5, H-2Bax), 2.08 (3H, s, OAc), 2.14 (3H, s, OAc), 2.17 (3H, s, OAc), 2.27 (1H, ddd, $J_{2eq,1}$ 2.0, $J_{2eq,3}$ 4.0, $J_{2eq,2ax}$ 14.5, H-2Beq), 2.35 (3H, s, CH_3), 2.88 (1H, d, $J_{1,OH}$ 6.5, OH), 3.44 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.85 (3H, s, OCH_3), 4.04 (1H, dd, $J_{4,3}$ 10.0, $J_{3,2}$ 3.0, H-3D), 4.13 (1H, m, H-5), 4.33 (1H, m, H-5), 4.90 (1H, dd, $J_{4,3}$ 3.0, $J_{4,5}$ 9.5, H-4B), 5.10 (1H, dd, $J_{3,4} = J_{4,5}$ 10.0, H-4D), 5.16 (1H, m, H-1B), 5.58 (1H, m, H-3B), 5.63 (1H, d, $J_{1,2}$ 2.0, H-1D), 5.74 (1H, dd, $J_{1,2}$ 2.0, $J_{3,2}$ 3.0, H-2D).

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