Organic & Biomolecular Chemistry

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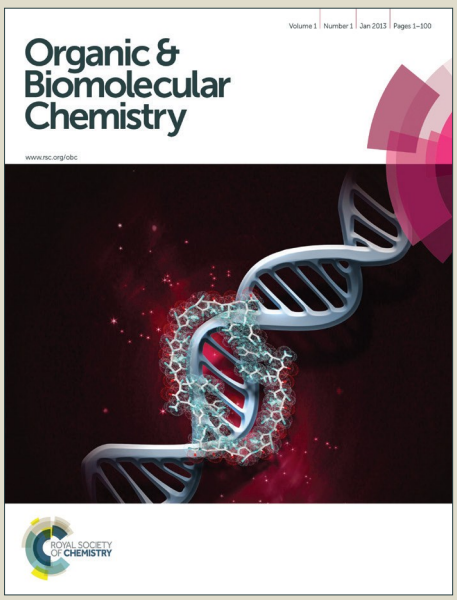

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ARTICLE

Synthesis and anti-mycobacterial activity of glycosyl sulfamides of arabinofuranose

Cite this: DOI: 10.1039/x0xx00000x

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Received 00th January 2015,
Accepted 00th January 2015

DOI: 10.1039/x0xx00000x

www.rsc.org/

A series of *arabino N*-glycosyl sulfamides, forced to adopt the furanose form by removal of the 5-hydroxyl group, were synthesised as putative isosteric mimics of decaprenolphosphoarabinose, the donor processed by arabinosyltransferases during mycobacterial cell wall assembly. Compounds showed moderate anti-mycobacterial activity, which was maximal for a C_{10} sulfamide side chain.

Introduction

Glycosyltransferases use activated sugar phosphate donor substrates for the construction of myriad oligosaccharide structures that have widespread importance throughout Biology. Selective inhibition[1] of these enzymes could have many potential therapeutic benefits, particularly in relation to halting the assembly of oligosaccharide structures that are essential for pathogen viability and/or infectivity.

Significant effort has therefore been expended in the search for inhibitors of glycosyltransferases, including investigations of the inhibitory properties of modified donor substrates.[2,3] However the instability of glycosyl phosphates, together with their unfavourable pharmacokinetic properties, makes them unattractive as potential drug candidates. Therefore the synthesis of isosteric mimics of glycosyl phosphates has attracted attention as a potentially more fruitful avenue for investigation.[4]

Decaprenolphosphoarabinose **1** (DPA, Scheme 1) is the donor substrate used by arabinosyl transferases[5] during the stepwise assembly of mycobacterial arabinomanan and arabinogalactan, both of which are key components of the mycobacterial cell wall. Metabolically stable analogues of DPA may therefore inhibit mycobacterial arabinosyltransferases, and in turn arabinan biosynthesis, and so compromise mycobacterial viability.[6,7]

As part of a program[8] into the synthesis of mimics of DPA as novel anti-mycobacterial agents, suitable isosteric replacement for the labile glycosyl phosphate was sought. Building on previous reports of the biological activity of configurationally stable S-glycosyl sulfonamides[9] and sulfenamides,[10,11] we attempted the synthesis of a variety of glycosyl sulfonamides, sulfamates and sulfamides of arabinofuranose;[12] it was envisaged that decoration with suitable hydrophobic chains would produce mimics of DPA that may display useful anti-mycobacterial activity. However it was discovered that upon de-protection these materials all unexpectedly underwent both mutarotation and furanose to pyranose interconversion. The pyranose materials were found to predominate at equilibrium in aqueous solution.[12] Subsequent assays[13] of these materials against mycobacterial strains revealed only low to modest anti-bacterial activity; a result that was perhaps unsurprising given the existence of the materials in predominantly the pyranose, rather that the desired furanose form.

However crystallographic studies[12] that had revealed the unexpected adoption of the pyranose form revealed the tetrahedral nature of the sulfamide group, and further intrigued our interest in the potential use of sulfamide as an isosteric mimic of phosphate. It was therefore thought worthwhile continuing in a search for biologically active mimics of DPA using the sulfamide group to replace phosphate. However in order to curtail the unexpected furanose to pyranose isomerisation, removal of the 5-hydroxyl group of arabinose was required. Herein we report the synthesis and anti-mycobacterial activity of a series of arabinofuranose glycosyl sulfamides that lack the hydroxyl group at position-5, and are therefore unable to adopt a pyranose form.

Results and Discussion

Synthesis of glycosyl sulfamides

Previously we reported[14] on the synthesis of a variety of arabinose derivatives that were modified at position-5 as putative chain terminators of mycobacterial arabinomannan and arabinogalactan biosynthesis. Since that chemistry was well established, advanced intermediates that had first been synthesised during that work were now employed in this study as precursors to the targeted glycosyl sulfamides. Therefore following our previous procedures, selective access to the 5-hydroxyl group of D-arabinose **2** was achieved by a sequence

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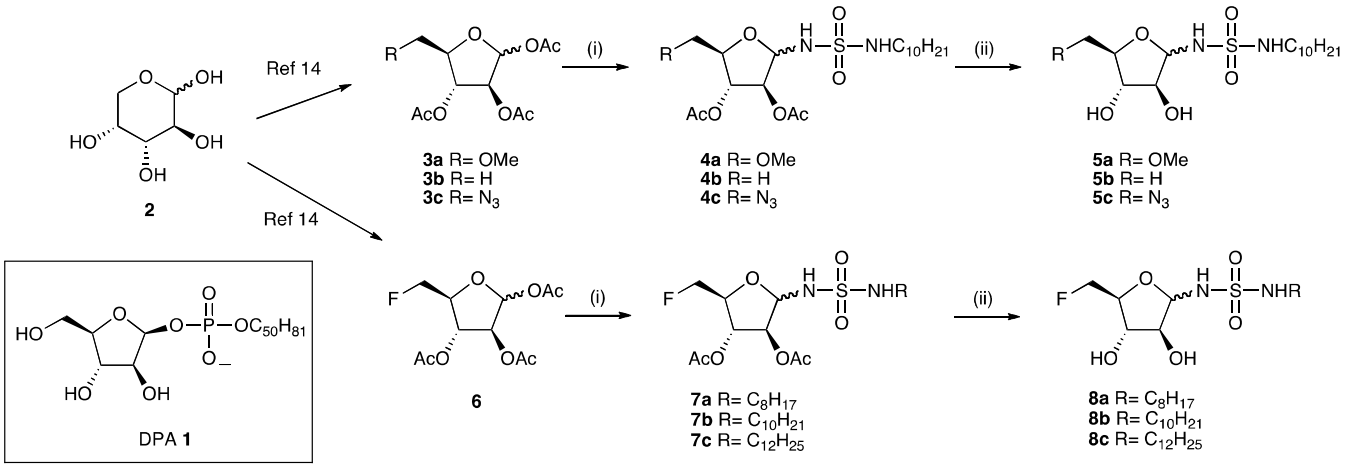

Scheme 1. Synthesis of arabinofuranosyl glycosyl sulfamides. *Reagents and conditions*: (i) $BF_3.OEt_2$, $RNHSO_2NH_2$, DCM, rt, 16 h; **4a**, 75 %; **4b**, 57 %; **4c**, 56 %; **7a**, 53 %; **7b**, 61%; **7c**, 52 %; (ii) Na/MeOH, rt, 16 h; **5a**, 82 %; **5b**, 81 %; **5c**, 62 %; **8a**, 75 %; **8b**, 72 %; **8c**, 78 %.

involving trityl protection of the primary hydroxyl group, acetylation and trityl group removal. Subsequent functionalization of position-5, allowed access to 5-methoxy ether **3a**, the 5-deoxy compound **3b**, and the 5-azide **3c** as previously reported.[14]

Studies performed on the pyranose glycosyl sulfamides had revealed that a C_{10} alkyl chain appeared to be optimal for biological activity of glycosyl sulfamides.[13] Therefore glycosyl acetates **3a-c** were treated with n-decyl sulfamide and $BF_3.OEt_2$ at room temperature in dry DCM which lead to formation of the corresponding glycosyl sulfamides **4a-c** in each case as an seperarable 1:1 mixture of anomers. De-protection by Zemplen de-acetylation then yielded the corresponding diols **5a-c**.

The 5-fluoride **6** was also accessed from D-arabinose **2** using the sequence previously described.[14] In this case three different glycosyl sulfamides of differing alkyl chain lengths were accessed in order to study any effect of chain length on biological activity. Thus fluoride **6** was treated with n-octyl, n-decyl and n-dodecylsulfamide and $BF_3.OEt_2$ in dry DCM at room temperature to give the corresponding glycosyl sulfamides **7a-c**, again as 1:1 mixtures of anomers. De-acetylation then yielded diols **8a-c** (Scheme 1).

Biological Activity

Glycosyl sulfamides were tested[15] for biological activity against *M. smegmatis* using an Alamar Blue microplate assay.[16] Additionally both isoniazid (INH, MIC 4 μg/mL) and n-decylsulfamide **9** were also assayed as controls (Table 1). The three n-decyl glycosylsulfamides **5a-c** displayed significant anti-mycobacterial, with all three giving MIC values of 31 μg/mL. On the other hand n-decylsulfamide ($NH_2SO_2NHC_{10}H_{21}$) **9** had a high MIC value (500 μg/mL), indicating that whilst the sulfamide alone did possess some very modest anti-mycobacterial activity, that this was enhanced by more than two orders of magnitude by conjugation to arabinofuranose derivative. Interestingly comparison of the activities of **5a-c** with the previously reported pyranose n-decyl glycosylsulfamide possessing an unmodified hydroxyl at position-5 (MIC 62 μg/mL)[13] revealed that compounds **5a-c**, which are fixed in the furanose form, were at least twice as potent.

Table 1 Anti-mycobacterial activity of glycosyl sulfamides.

Compound	MIC (μg/mL)[a]	MIC (μM)[a]
Isoniazid (**INH**)	4	29
Ethambutol (**EB**)	0.5	1.8
$NH_2SO_2NHC_{10}H_{21}$ **9**	500	2117
5a	31	81
5b	31	88
5c	31	79
8a	250	731
8b	31	84
8c	1000	2511

[a] MIC = minimum inhibitory concentration; the lowest concentration of the compound which inhibited the growth of *M. smegmatis* >90% in the Alamar Blue assay. Isoniazid (**INH,** MIC 4 μg/mL), ethambutol (**EB,** MIC 0.5 μg/mL), and decylsulfamide **9** were used as controls.

Previously systematic variation of the influence of alkyl chain length had revealed the C_{10} chain to be optimal for anti-mycobacterial activity in the cases of glycosyl sulfamides. Investigation of the 5-fluoro arabinofuranose **8a-c** derivatives again showed this to be the case; sulfamide **8a**, with a C_8 alkyl chain, had an MIC of 250 μg/mL, and was an order of magnitude less active than the C_{10} derivative **8b** (MIC 31 μg/mL). This result correlated with studies on a series of glycosyl sulfones,[8a] for which maximal activity was observed

for a sulfone with a side chain containing 12 carbon atoms, i.e. a material with a total chain length of 13 atoms from the anomeric centre, as is the case for **8b**. Interestingly anti-mycobacterial activity was very significantly reduced by increasing the alkyl chain by two further C atoms, as demonstrated by the low activity of the C_{12} derivative **8c** observed in this study (MIC 1000 μg/mL).

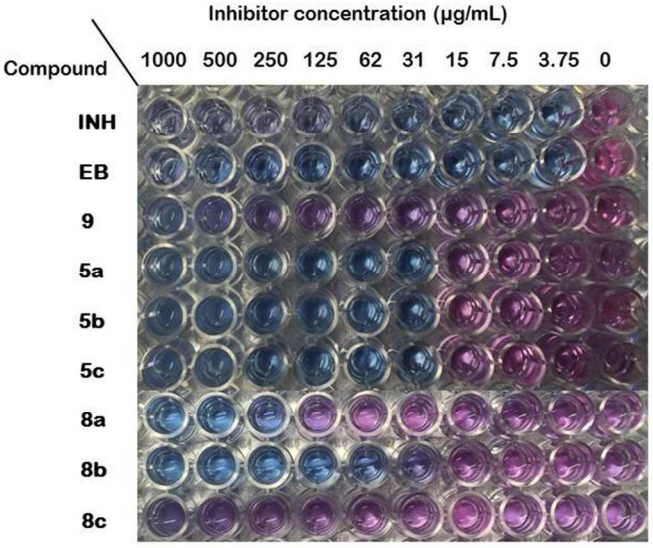

Fig. 1 Alamar Blue assay of compounds **5a-c** and **8a-c** plus controls.

In closing it must be borne in mind that although sulfamides **5a-c** and **8a-c** were designed as mimics of DPA, their mode of action, as putative inhibitors of mycobacterial arabinosyltransferases, is as yet un-demonstrated; confirmatory inhibition assays are be required. However the observations that the activity of n-decylsulfamide **9** was approximately 20-fold lower than the corresponding glycosylsulfamides **5a-c** and **8b**, and that the furanose sulfamides reported in this work are all more active than analogous pyranose materials, do point to the importance of the carbohydrate portion of these materials.[17] However the most active compounds reported in this study are still an order of magnitude less active than isoniazid, and further augmentation of biological activity is required before compounds such as these could be considered as promising lead candidates for the development of new anti-mycobacterial agents.

Conclusions

A series of glycosyl sulfamides of arabinofuranose were synthesised by modification of the 5-position to remove the hydroxyl group required for isomerisation to the thermodynamically preferred pyranose form. Compounds were tested for anti-mycobacetrial and showed moderate levels of activity (MIC 31 μg/mL) in Alamar Blue assays against *M. smegmatis*.

Experimental

General methods

All reactions were carried out in oven-dried, nitrogen-purged glassware under an atmosphere of nitrogen. Melting points were recorded on an Electrothermal melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Polarimeter 341 with a path length of 1 dm. Concentrations are given in g / 100 mL. Infrared spectra were recorded on a Perkin-Elmer Spectrum One. Proton and carbon nuclear magnetic resonance (δ_H, δ_C) spectra were recorded on Agilent Technologies 400 MR (400 MHz) or Varian VNMR500 (500 MHz) spectrometers. All chemical shifts are quoted on the δ-scale in ppm using residual solvent as an internal standard. High-resolution mass spectra were recorded with a Bruker maXis 3G UHR-TOF mass spectrometer. Thin Layer Chromatography (t.l.c.) was carried out on Merck silica gel $60F_{254}$ aluminium-backed plates. Visualisation of the plates was achieved using a UV lamp (λ_{max} = 254 or 365 nm), and/or 5% w/v ammonium molybdate in 2 M sulfuric acid. Flash column chromatography was carried out using Sorbsil C60 40/60 silica. Unless preparative details are provided, all reagents were commercially available or made following literature procedures. "Petrol" refers to the fraction of light petroleum ether boiling in the range of 40-60 °C.

General Procedure A: The glycosyl acetate (**2a-c** or **5**, 1 equiv.) and the sulfamide (1 equiv.) were stirred at room temperature in dry DCM (15 mL) under nitrogen. $BF_3.OEt_2$ (2 equiv.) was added dropwise, and the mixture was then stirred at room temperature for 16 h. The reaction was then quenched by the dropwise addition of excess triethylamine (~0.3 mL), and the resulting mixture was filtered through Celite®, eluting with ethyl acetate, and concentrated *in vacuo* to give a residue which was purified by flash chromatography.

General Procedure B: The di-acetate (**4a-c** or **6a-c**) was dissolved in dry methanol (~5 mL) and the mixture stirred at room temperature. Sodium metal (0.1 equiv.) was added, and the mixture was then stirred for 1 h. Dowex® 50WX8 (H^+) ion exchange resin was then added until the pH was neutral. The reaction mixture was then filtered and concentrated *in vacuo* to give a residue which was purified by flash chromatography.

***N*-(Decyl)-*N*'-(2,3-di-*O*-acetyl-5-*O*-methyl-α,β-D-arabinofuranosyl)sulfamide 4a.** General Procedure A, using glycosyl acetate **3a** (100 mg, 0.3 mmol) and n-decylsulfamide (81 mg, 0.3 mmol), and purification by flash chromatography (petrol: ethyl acetate, 2:1, R_f 0.2), afforded glycosylsulfamide **4a** (120 mg, 75 %, α:β, 1:1) as a colourless oil; υ_{max} (neat) 3256 (N-H), 1756 (s, C=O), 1362 (s, S=O), 1167 (s, S=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) α anomer: 0.87 (3H, t, *J* 6.7 Hz, C<u>H</u>$_3$), 1.21-1.36 (14H, m, 7 x C<u>H</u>$_2$), 1.50-1.58 (2H, m, NHCH$_2$C<u>H</u>$_2$), 2.10, 2.11 (6H, 2 x s, 2 x OAc), 2.99-3.08 (2H, m, C<u>H</u>$_2$NH), 3.40 (3H, s, OC<u>H</u>$_3$), 3.55-3.59 (2H, m, H-5, H-5'), 4.21 (1H, aq, *J* 4.3 Hz, H-4), 5.09-5.15 (2H, m, H-2, H-3), 5.31 (1H, d, $J_{NH,1}$

9.1 Hz, H-1), 5.37 (1H, d, $J_{NH,1}$ 9.0 Hz, NH); β anomer: 0.87 (3H, t, J 6.7 Hz, CH_3), 1.21-1.36 (14H, m, 7 x CH_2), 1.50-1.58 (2H, m, $NHCH_2CH_2$), 2.09, 2.12 (6H, 2 x s, 2 x OAc), 2.99-3.08 (2H, m, CH_2NH), 3.46 (3H, s, OCH_3), 3.55-3.59 (1H, m, H-5), 3.64 (1H, dd, $J_{5,5'}$ 10.6 Hz, $J_{4,5'}$ 3.1Hz, H-5'), 3.93-3.97 (1H, m, H-4), 5.20-5.27 (2H, m, H-2, H-3), 5.45 (1H, dd, $J_{NH,1}$ 10.8 Hz, $J_{1,2}$ 5.3 Hz, H-1), 5.78 (1H, d, $J_{NH,1}$ 10.6 Hz NH); δ_C (100.5 MHz, $CDCl_3$) 14.1 (q, CH_3), 20.7, 20.7, 20.7, 20.8 (4 x q, 2 x OAc-α, 2 x OAc-β), 22.6, 26.7, 29.2, 29.3, 29.5, 29.5, 29.5, 31.9 (8 x t, 8 x CH_2), 43.2, 43.5 (2 x t, $NHCH_2\alpha$, $NHCH_2\beta$), 59.4 (q, OCH_3), 72.1, 72.1 (t, C-5α, C-5β), 75.8 (d, C-2β), 75.8 (d, C-3β), 76.8 (d, C-3α), 79.9 (d, C-2α), 80.9 (d, C-4β), 82.1 (d, C-4α), 83.1 (d, C-1β), 88.1 (d, C-1α), 169.5, 169.7, 169.8, 170.3 (4 x s, 2 x OAc-α, 2 x OAc-β); HRMS (ESI) calculated for $C_{20}H_{39}N_2O_8S$: 467.2422. Found 467.2432 (MH^+).

***N*-(Decyl)-*N*'-(2,3-di-*O*-acetyl-5-deoxy-α,β-D-arabinofuranosyl)sulfamide 4b.** General Procedure A, using glycosyl acetate **3b** (190 mg, 0.7 mmol) and n-decylsulfamide (172 mg, 0.7 mmol), and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.6), afforded glycosylsulfamide **4b** (180 mg, 57 %, α:β, 1:1) as a pale yellow waxy solid; υ_{max} (neat) 3294 (N-H), 1743 (s, C=O), 1372 (s, S=O), 1162 (s, S=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) α anomer: 0.86 (3H, t, J 6.7 Hz, CH_3), 1.24-1.40 (17H, m, 7 x CH_2, CH_3), 1.50-1.57 (2H, m, $NHCH_2CH_2$), 2.11, 2.15 (6H, 2 x s, 2 x OAc), 2.99-3.08 (2H, m, CH_2NH), 4.16-4.24 (1H, m, H-4), 4.81-4.85 (1H, m, H-3), 5.08 (1H, s, H-2), 5.26 (1H, d, $J_{NH,1}$ 8.6 Hz, H-1), 5.59 (1H, d, $J_{NH,1}$ 9.0Hz, NH); β anomer: 0.86 (3H, t, J 6.7 Hz, CH_3), 1.24-1.40 (17H, m, 7 x CH_2, CH_3), 1.50-1.57 (2H, m, $NHCH_2CH_2$), 2.08, 2.10 (6H, 2 x s, 2 x OAc), 2.99-3.08 (2H, m, CH_2NH), 3.81-3.88 (1H, m, H-4), 4.71-4.74 (1H, m, H-3), 5.15-5.19 (1H, m, H-2), 5.33 (1H, dd, $J_{NH,1}$ 10.8 Hz, $J_{1,2}$ 4.1 Hz, H-1), 5.51 (1H, d, $J_{NH,1}$ 11.0 Hz NH); δ_C (100.5 MHz, $CDCl_3$) 14.1 (q, CH_3), 18.9, 19.2 (2 x q, C-5α, C-5β), 20.7, 20.7, 20.8, 20.8 (4 x q, 2 x OAc-α, 2 x OAc-β), 22.6, 26.7, 29.2, 29.3, 29.3, 29.4, 29.5, 31.8 (8 x t, 8 x CH_2), 43.4, 43.4 (2 x t, $NHCH_2\alpha$, $NHCH_2\beta$), 75.9 (d, C-2β), 77.8 (d, C-4β), 79.6 (d, C-4α), 80.3 (d, C-3β), 80.5 (d, C-2α), 80.6 (d, C-3α), 83.4 (d, C-1β), 88.0 (d, C-1α), 169.2, 169.7, 169.8, 169.8 (4 x s, 2 x OAc-α, 2 x OAc-β); HRMS (ESI) calculated for $C_{19}H_{37}N_2O_7S$: 437.2316. Found 437.2302 (MH^+).

***N*-(Decyl)-*N*'-(2,3-di-*O*-acetyl-5-azido-α,β-D-arabinofuranosyl)sulfamide 4c.** General Procedure A, using glycosyl acetate **3c** (90 mg, 0.3 mmol) and n-decylsulfamide (70 mg, 0.3 mmol), and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.6), afforded glycosyl sulfamide **4c** (80 mg, 56 %, α:β, 1:1) as a pale yellow waxy solid; υ_{max} (neat) 3273 (N-H), 2098 (N_3), 1743 (s, C=O), 1370 (s, S=O), 1165 (s, S=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) α anomer: 0.87 (3H, t, J 6.3 Hz, CH_3), 1.22-1.36 (14H, m, 7 x CH_2), 1.50-1.61 (2H, m, $NHCH_2CH_2$), 2.11, 2.19 (6H, 2 x s, 2 x OAc), 3.01-3.14 (2H, m, CH_2NH), 3.37-3.48 (1H, m, H-5), 3.53-3.63 (1H, m, H-5'), 4.21-4.26 (1H, m, H-4), 4.36-4.49 (1H, m, $NHCH_2$), 5.03-5.06 (1H, m, H-3), 5.16 (1H, d, J 1.6 Hz, H-2), 5.35 (1H, d, $J_{NH,1}$ 9.4 Hz, H-1), 5.49-5.56 (1H, m, NH); β anomer: 0.87 (3H, t, J 6.3 Hz, CH_3), 1.22-1.36 (14H, m, 7 x CH_2), 1.50-1.61 (2H, m, $NHCH_2CH_2$), 2.13, 2.13 (6H, 2 x s, 2 x OAc), 3.01-3.14 (2H, m, CH_2NH), 3.37-3.48 (1H, m, H-5), 3.53-3.63 (1H, m, H-5'), 3.91-3.95 (1H, m, H-4), 4.36-4.49 (1H, m, $NHCH_2$), 4.91-4.94 (1H, m, H-3), 5.18-5.21 (1H, m, H-2), 5.42 (1H, dd, $J_{NH,1}$ 10.6 Hz, $J_{1,2}$ 3.5 Hz, H-1), 5.49-5.56 (1H, m, NH); δ_C (100.5 MHz, $CDCl_3$) 14.1 (q, CH_3), 20.6, 20.7 (2 x q, 2 x OAc), 22.6, 26.7, 29.2, 29.3, 29.4, 29.5, 29.5, 31.9 (8 x t, 8 x CH_2), 43.5, 43.6 (2 x t, $NHCH_2\alpha$, $NHCH_2\beta$), 51.7, 51.7 (t, C-5α, C-5β), 75.6 (d, C-2β), 76.5, 77.1 (2 x d, C-3α, C-3β), 79.7 (d, C-2α), 81.3 (d, C-4β), 82.6 (d, C-4α), 83.8 (d, C-1β), 88.1 (d, C-1α), 169.7, 169.9 (2 x s, 2 x OAc); HRMS (ESI) calculated for $C_{19}H_{35}N_5NaO_7S$: 500.2149. Found 500.2157 (MNa^+).

***N*-(Decyl)-*N*'-(5-*O*-methyl-α,β-D-arabinofuranosyl)sulfamide 5a.** General Procedure B, using glycosyl sulfamide **4a** (60 mg, 0.1 mmol) and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.1), afforded diol **5a** (40 mg, 82 %, α:β, 1:1) as a white solid; m.p. 91-93 °C (MeOH/DCM); υ_{max} (neat) 3280 (N-H), 1347 (s, S=O), 1141 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3CN) α anomer: 0.91 (3H, t, J 6.7 Hz, CH_3), 1.25-1.39 (14H, m, 7 x CH_2), 1.49-1.56 (2H, m, $NHCH_2CH_2$), 2.93-3.01 (2H, m, CH_2NH), 3.37 (3H, s, OCH_3), 3.47-3.54 (2H, m, H-5, H-5'), 3.87-3.92 (2H, m, H-2), 3.93-3.98 (1H, m, H-3), 4.04 (1H, aq, J 4.2 Hz, H-4), 4.92 (1H, d, $J_{NH,1}$ 10.4 Hz, H-1), 5.00-5.08 (1H, m, $NHCH_2$), 5.98 (1H, d, $J_{NH,1}$ 10.2 Hz, NH); β anomer: 0.91 (3H, t, J 6.7 Hz, CH_3), 1.25-1.39 (14H, m, 7 x CH_2), 1.49-1.56 (2H, m, $NHCH_2CH_2$), 2.93-3.01 (2H, m, CH_2NH), 3.38 (3H, s, OCH_3), 3.47-3.54 (2H, m, H-5, H-5'), 3.80 (1H, aq, J 3.5 Hz, H-4), 3.82-3.86 (2H, m, H-2), 3.93-3.98 (1H, m, H-3), 5.00-5.08 (1H, m, $NHCH_2$), 5.12 (1H, dd, $J_{NH,1}$ 10.2 Hz, $J_{1,2}$ 3.9 Hz, H-1), 5.76 (1H, d, $J_{NH,1}$ 10.6 Hz, NH); δ_C (100.5 MHz, CD_3CN) 13.4 (q, CH_3), 22.4, 26.5, 29.0, 29.0, 29.0, 29.1, 29.3, 31.6 (8 x t, 8 x CH_2), 43.0, 43.0 (2 x t, $NHCH_2\alpha$, $NHCH_2\beta$), 58.5, 58.6 (2 x q, $OCH_3\alpha$, $OCH_3\beta$), 72.5, 72.8 (t, C-5α, C-5β), 76.1 (d, C-2β), 76.6 (d, C-3β, C-3α), 79.9 (d, C-2α), 82.8 (d, C-4β), 84.4 (d, C-4α), 85.3 (d, C-1β), 89.9 (d, C-1α); HRMS (ESI) calculated for $C_{16}H_{35}N_2O_6S$: 383.2210. Found 383.2214 (MH^+).

***N*-(Decyl)-*N*'-(5-deoxy-α,β-D-arabinofuranosyl)sulfamide 5b.** General Procedure B, using glycosyl sulfamide **4b** (80 mg, 0.2 mmol) and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.1), afforded diol **5b** (52 mg, 81 %, α:β, 2:1) as a white solid; m.p. 100-102 °C (MeOH/DCM); υ_{max} (neat) 3287 (N-H), 1318 (s, S=O), 1149 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3OD) α anomer: 0.89 (3H, t, J 7.0 Hz, CH_3), 1.24-1.38 (17H, m, 7 x CH_2, CH_3), 1.49-1.57 (2H, m, $NHCH_2CH_2$), 2.94-3.02 (2H, m, CH_2NH), 3.66-3.70 (1H, m, H-3), 3.87-3.95 (2H, m, H-2, H-4), 4.91 (1H, d, $J_{1,2}$ 4.3 Hz, H-1); β anomer: 0.89 (3H, t, J 7.0 Hz, CH_3), 1.24-1.38 (17H, m, 7 x CH_2, CH_3), 1.49-1.57 (2H, m, $NHCH_2CH_2$), 2.94-3.02 (2H, m, CH_2NH), 3.57 (1H, at, J 6.7 Hz, H-3), 3.66-3.70 (1H, m, H-4), 3.87-3.95 (1H, m, H-2), 5.11 (1H, d, $J_{1,2}$ 4.7 Hz, H-1); δ_C (100.5 MHz,

CD_3OD) 13.1 (q, CH_3), 17.6, 18.4 (2 x q, C-5α, C-5β), 22.3, 26.5, 29.0, 29.0, 29.1, 29.3, 31.7 (7 x t, 8 x CH_2), 42.6, 42.7 (2 x t, NHC$\underline{H}_2$α, NHC$\underline{H}_2$β), 76.5 (d, C-2β), 77.8 (d, C-4β), 78.5 (d, C-4α), 80.8 (d, C-3β), 81.0 (d, C-2α), 81.1 (d, C-3α), 84.4 (d, C-1β), 88.4 (d, C-1α); HRMS (ESI) calculated for $C_{15}H_{33}N_2O_5S$: 353.2105. Found 353.2112 (MH^+).

***N*-(Decyl)-*N*'-(5-azido-α,β-D-arabinofuranosyl)sulfamide 6d.** General Procedure B, using glycosyl sulfamide **4c** (80 mg, 0.2 mmol) and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.1), afforded diol **5c** (42 mg, 62 %, α:β, 1:1) as a white solid; m.p. 99-101 °C (MeOH/DCM); υ_{max} (neat) 3293 (N-H), 2103 (N_3), 1340 (s, S=O), 1141 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3CN) α anomer: 0.90 (3H, t, *J* 6.7 Hz, C$\underline{H}_3$), 1.25-1.39 (14H, m, 7 x C$\underline{H}_2$), 1.48-1.57 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.95-3.03 (2H, m, C$\underline{H}_2$NH), 3.34-3.50 (2H, m, H-5, H-5'), 3.83-3.90 (1H, m, H-3), 3.92-3.98 (1H, m, H-2), 4.01 (1H, aq, *J* 3.9 Hz, H-4), 4.93 (1H, dd, $J_{NH,1}$ 10.2 Hz, $J_{1,2}$ 3.9 Hz, H-1), 4.99-5.12 (1H, m, N$\underline{H}$CH$_2$), 6.07 (1H, d, $J_{NH,1}$ 10.2 Hz, N$\underline{H}$); β anomer: 0.90 (3H, t, *J* 6.7 Hz, C$\underline{H}_3$), 1.25-1.39 (14H, m, 7 x C$\underline{H}_2$), 1.48-1.57 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.95-3.03 (2H, m, C$\underline{H}_2$NH), 3.34-3.50 (2H, m, H-5, H-5'), 3.72-3.80 (1H, m, H-4), 3.83-3.90 (1H, m, H-3), 3.92-3.98 (1H, m, H-2), 5.17 (1H, dd, $J_{NH,1}$ 10.0 Hz, $J_{1,2}$ 4.1 Hz, H-1), 4.99-5.12 (1H, m, N$\underline{H}$CH$_2$), 5.83 (1H, d, $J_{NH,1}$ 10.2 Hz, N$\underline{H}$); δ_C (100.5 MHz, CD_3CN) 13.4 (q, CH_3), 22.4, 26.5, 29.0, 29.0, 29.1, 29.3, 31.7 (7 x t, 8 x CH_2), 43.0 (t, NHCH$_2$α, NHCH$_2$β), 52.2, 52.7 (t, C-5α, C-5β), 75.9 (d, C-2β), 76.3, 77.1 (2 x d, C-3α, C-3β), 79.9 (d, C-2α), 81.9 (d, C-4β), 82.1 (d, C-4α), 85.2 (d, C-1β), 89.1 (d, C-1α); HRMS (ESI) calculated for $C_{15}H_{31}N_5NaO_5S$: 416.1938. Found 416.1944 (MNa^+).

***N*-(Octyl)-*N*'-(2,3-di-*O*-acetyl-5-fluoro-α,β-D-arabinofuranosyl)sulfamide 7a.** General Procedure A, using glycosyl acetate **6** (60 mg, 0.2 mmol) and n-octylsulfamide (44 mg, 0.2 mmol), and purification by flash chromatography (petrol: ethyl acetate, 2:1, R_f 0.35), afforded glycosyl sulfamide **4c** (48 mg, 53 %, α:β, 1:1) as a pale yellow waxy solid; υ_{max} (neat) 3279 (N-H), 1735 (s, C=O), 1369 (s, S=O), 1152 (s, S=O) cm^{-1};δ_H (400 MHz, $CDCl_3$) α anomer: 0.87 (3H, t, *J* 6.7 Hz, C$\underline{H}_3$), 1.20-1.36 (10H, m, 5 x C$\underline{H}_2$), 1.51-1.58 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.14, 2.15 (6H, 2 x s, 2 x OAc), 3.01-3.13 (2H, m, C$\underline{H}_2$NH), 4.22-4.31 (1H, m, H-4), 4.51-4.56 (1H, m, H-5), 4.63-4.67 (1H, m, H-5'), 5.13 (1H, at, *J* 2.8 Hz, H-3), 5.16 (1H, at, *J* 2.3 Hz, H-2), 5.33 (1H, dd, $J_{NH,1}$ 9.6 Hz, $J_{1,2}$ 2.2 Hz, H-1), 5.37 (1H, d, $J_{NH,1}$ 11.0 Hz N$\underline{H}$); β anomer: 0.87 (3H, t, *J* 6.7 Hz, C$\underline{H}_3$), 1.20-1.36 (10H, m, 5 x C$\underline{H}_2$), 1.51-1.58 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.11, 2.13 (6H, 2 x s, 2 x OAc), 3.01-3.13 (2H, m, C$\underline{H}_2$NH), 3.90-4.01 (1H, m, H-4), 4.51-4.56 (1H, m, H-5), 4.63-4.67 (1H, m, H-5'), 5.05 (1H, dd, $J_{3,4}$ 3.5 Hz, $J_{2,3}$ 2.3 Hz, H-3), 5.22 (1H, dd, $J_{1,2}$ 4.1 Hz, $J_{2,3}$ 2.2 Hz, H-2), 5.48 (1H, dd, $J_{NH,1}$ 6.7 Hz $J_{1,2}$ 4.7 Hz, H-1), 5.45-5.46 (1H, m, N$\underline{H}$); δ_C (100.5 MHz, $CDCl_3$) 14.0 (q, CH_3), 20.6, 20.7, 20.7, 20.7 (4 x q, 2 x OAcα, 2 x OAcβ), 22.6, 26.7, 29.1, 29.4, 29.4, 31.7 (6 x t, 6 x CH_2), 43.4, 43.6 (2 x t, NHCH$_2$α, NHCH$_2$β), 75.2 (d, C-2β), 75.4 (d, $J_{c3\text{-}F}$ 6.1 Hz, C-3β), 75.9 (d, $J_{C3\text{-}F}$ 6.1 Hz, C-3α), 79.6 (d, C-2α), 81.5 (d, $J_{C4\text{-}F}$ 18.3 Hz, C-4β), 81.7 (d, $J_{C4\text{-}F}$ 19.8 Hz, C-4α), 82.1 (d, $J_{C5\text{-}F}$ 174.0 Hz, C-5β), 82.1 (d, $J_{C5\text{-}F}$ 174.0 Hz, C-5α), 83.7 (d, C-1β), 88.1 (d, C-1α), 169.3, 169.8, 169.9, 170.0 (4 x s, 2 x OAcα, 2 x OAcβ); δ_F (376.6 MHz, $CDCl_3$) -229.14 (td, $J_{F,H\ geminal}$ 40.1 Hz, $J_{F,H\ vicinal}$ 23.8 Hz, F-β), -229.34 (td, $J_{F,H\ geminal}$ 42.0 Hz, $J_{F,H\ vicinal}$ 23.8 Hz, F-α); HRMS (ESI) calculated for $C_{17}H_{32}FN_2O_7S$: 427.1909. Found 427.1900 (MH^+).

***N*-(Decyl)-*N*'-(2,3-di-*O*-acetyl-5-fluoro-α,β-D-arabinofuranosyl)sulfamide 7b.** General Procedure A, using glycosyl acetate **6** (75 mg, 0.3 mmol) and n-decylsulfamide (63 mg, 0.3 mmol), and purification by flash chromatography (petrol: ethyl acetate, 2:1, R_f 0.4), afforded glycosylsulfamide **7b** (74 mg, 61 %, α:β, 1:1) as a pale yellow waxy solid; υ_{max} (neat) 3279 (N-H), 1735 (s, C=O), 1369 (s, S=O), 1152 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3CN) α anomer: 0.78 (3H, t, *J* 6.3 Hz, C$\underline{H}_3$), 1.13-1.30 (14H, m, 7 x C$\underline{H}_2$), 1.41-1.52 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.00, 2.00 (6H, 2 x s, 2 x OAc), 2.87-2.96 (2H, m, C$\underline{H}_2$NH), 4.20-4.32 (1H, m, H-4), 4.40-4.49 (1H, m, H-5), 4.51-4.61 (1H, m, H-5'), 5.04 (1H, at, *J* 3.9 Hz, H-3), 5.14 (1H, dd, $J_{NH,1}$ 9.0 Hz, $J_{1,2}$ 3.1 Hz, H-1), 5.21-5.24 (1H, m, H-2), 5.69-5.82 (1H, m, CH$_2$N$\underline{H}$), 6.93 (1H, d, $J_{NH,1}$ 9.0 Hz, N$\underline{H}$); β anomer: 0.78 (3H, t, *J* 6.3 Hz, C$\underline{H}_3$), 1.13-1.30 (14H, m, 7 x C$\underline{H}_2$), 1.41-1.52 (2H, m, NHCH$_2$C$\underline{H}_2$), 1.95, 1.98 (6H, 2 x s, 2 x OAc), 2.87-2.96 (2H, m, C$\underline{H}_2$NH), 3.88-3.99 (1H, m, H-4), 4.40-4.49 (1H, m, H-5), 4.51-4.61 (1H, m, H-5'), 4.97 (1H, at, *J* 3.1 Hz, H-3), 5.16-5.19 (1H, m, H-2), 5.33 (1H, dd, $J_{NH,1}$ 10.8 Hz $J_{1,2}$ 4.5 Hz, H-1), 5.69-5.82 (1H, m, CH$_2$N$\underline{H}$), 6.72 (1H, d, $J_{NH,1}$ 11.0 Hz, N$\underline{H}$); δ_C (100.5 MHz, CD_3CN) 13.3 (q, CH_3), 19.7, 19.7, 19.7 (3 x q, 2 x OAcα, 2 x OAcβ), 22.3, 26.5, 28.3, 28.5, 28.6, 28.8, 29.0, 31.6 (8 x t, 8 x CH_2), 42.8, 42.8 (2 x t, NHCH$_2$α, NHCH$_2$β), 74.6 (d, C-2β), 75.0 (d, $J_{c3\text{-}F}$ 7.6 Hz, C-3β), 75.2 (d, $J_{C3\text{-}F}$ 6.9 Hz, C-3α), 79.2 (d, $J_{C4\text{-}F}$ 19.8 Hz, C-4β), 79.5 (d, C-2α), 80.1 (d, $J_{C4\text{-}F}$ 19.8 Hz, C-4α), 82.3 (d, $J_{C5\text{-}F}$ 171.7 Hz, C-5β), 82.3 (d, $J_{C5\text{-}F}$ 171.7 Hz, C-5α), 84.0 (d, C-1β), 87.6 (d, C-1α), 168.9, 169.1, 169.3, 169.6 (4 x s, 2 x OAcα, 2 x OAcβ); δ_F (376.6 MHz, $CDCl_3$) -229.18 (td, $J_{F,H\ geminal}$ 46.7 Hz, $J_{F,H\ vicinal}$ 23.8 Hz, F-β), -229.52 (td, $J_{F,H\ geminal}$ 47.7 Hz, $J_{F,H\ vicinal}$ 26.7 Hz, F-α); HRMS (ESI) calculated for $C_{19}H_{35}FN_2NaO_7S$: 477.2041. Found 477.2063 (MNa^+).

***N*-(Dodecyl)-*N*'-(2,3-di-*O*-acetyl-5-fluoro-α,β-D-arabinofuranosyl)sulfamide 7c.** General Procedure A, using glycosyl acetate **6** (70 mg, 0.3 mmol) and n-dodecylsulfamide (66 mg, 0.3 mmol), and purification by flash chromatography (petrol: ethyl acetate, 2:1, R_f 0.4), afforded glycosyl sulfamide **7c** (62 mg, 52 %, α:β, 1:1) as a pale yellow waxy solid; ; υ_{max} (neat) 3282 (N-H), 1755 (s, C=O), 1368 (s, S=O), 1151 (s, S=O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) α anomer: 0.87 (3H, t, *J* 6.8 Hz, C$\underline{H}_3$), 1.22-1.36 (18H, m, 9 x C$\underline{H}_2$), 1.51-1.60 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.14, 2.15 (6H, 2 x s, 2 x OAc), 3.03-3.15 (2H, m, C$\underline{H}_2$NH), 4.22-4.31 (1H, m, H-4), 4.48-4.56 (1H, m, H-5), 4.61-4.68 (1H, m, H-5'), 5.13 (1H, at, *J* 2.7 Hz, H-3), 5.14-5.17 (1H, m, H-2), 5.33 (1H, s, H-1); β anomer: 0.87 (3H, t, *J* 6.8 Hz, C$\underline{H}_3$), 1.22-1.36 (18H, m, 9 x C$\underline{H}_2$), 1.51-1.60 (2H, m, NHCH$_2$C$\underline{H}_2$), 2.12 (6H, 1 x s, 2 x OAc), 3.03-3.15 (2H, m,

C$\underline{H}_2$NH), 3.90-4.01 (1H, m, H-4), 4.48-4.56 (1H, m, H-5), 4.61-4.68 (1H, m, H-5'), 5.06 (1H, dd, $J_{2,3}$ 2.3 Hz, $J_{3,4}$ 3.5 Hz, H-3), 5.22 (1H, dd, $J_{1,2}$ 4.3 Hz, $J_{2,3}$ 2.0 Hz, H-2), 5.28 (1H, d, $J_{NH,1}$ 11.0 Hz, N$\underline{H}$), 5.48 (1H, dd, $J_{NH,1}$ 11.0 Hz, $J_{1,2}$ 4.7 Hz, H-1); δ_C (100.5 MHz, $CDCl_3$) 14.1 (q, CH_3), 20.7, 20.8, (2 x q, 2 x OAcα, 2 x OAcβ), 22.6, 26.6, 29.2, 29.3, 29.4, 29.5, 29.5, 29.6, 29.6, 31.9 (10 x t, 10 x CH_2), 43.5, 43.7 (2 x t, $NHCH_2\alpha$, $NHCH_2\beta$), 75.3 (d, C-2β), 75.4 (d, J_{c3-F} 6.9 Hz, C-3β), 76.0 (d, J_{C3-F} 6.1 Hz, C-3α), 79.5 (d, C-2α), 80.6 (d, J_{C4-F} 18.3 Hz, C-4β), 81.9 (d, J_{C4-F} 19.8 Hz, C-4α), 82.1 (d, J_{C5-F} 172.4 Hz, C-5β), 82.1 (d, J_{C5-F} 175.5 Hz, C-5α), 83.7 (d, C-1β), 88.2 (d, C-1α), 169.2, 169.7, 169.8, 169.9 (4 x s, 2 x OAcα, 2 x OAcβ); δ_F (376.6 MHz, $CDCl_3$) -229.15 (td, $J_{F,H\ geminal}$ 47.7 Hz, $J_{F,H\ vicinal}$ 23.8 Hz, F-β), -229.6 (td, $J_{F,H\ geminal}$ 48.6 Hz, $J_{F,H\ vicinal}$ 27.7 Hz, F-α); HRMS (ESI) calculated for $C_{21}H_{40}FN_2O_7S$: 483.2535. Found 483.2523 (MH^+).

***N*-(Octyl)-*N*'-(5-fluoro-α,β-D-arabinofuranosyl)sulfamide**

8a. General Procedure B, using glycosyl sulfamide **7a** (40 mg, 0.1 mmol) and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.1), afforded diol **8a** (24 mg, 75 %, α:β, 1:1) as a white solid; m.p. 123-125 °C (MeOH/DCM); υ_{max} (neat) 3290 (N-H), 1347 (s, S=O), 1142 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3CN) α anomer: 0.91 (3H, t, *J* 7.4 Hz, C$\underline{H}_3$), 1.25-1.38 (10H, m, 5 x C$\underline{H}_2$), 1.48-1.57 (2H, m, $NHCH_2C\underline{H}_2$), 2.93-3.02 (2H, m, C$\underline{H}_2$NH), 3.91 (1H, at, *J* 4.3 Hz, H-3), 3.96 (1H, at, *J* 4.3 Hz, H-2), 4.03-4.11 (1H, m, H-4), 4.38-4.48 (1H, m, H-5), 4.51-4.60 (1H, m, H-5'), 4.91 (1H, d, $J_{1,2}$ 3.9 Hz, H-1), 5.07 (1H, br s, N$\underline{H}$); β anomer: 0.91 (3H, t, *J* 7.4 Hz, C$\underline{H}_3$), 1.25-1.38 (10H, m, 5 x C$\underline{H}_2$), 1.48-1.57 (2H, m, $NHCH_2C\underline{H}_2$), 2.93-3.02 (2H, m, C$\underline{H}_2$NH), 3.81-3.89 (1H, m, H-4), 3.91 (1H, at, *J* 4.3 Hz, H-3), 4.00-4.02 (1H, m, H-2), 4.38-4.48 (1H, m, H-5), 4.51-4.60 (1H, m, H-5'), 5.19 (1H, d, $J_{1,2}$ 4.3 Hz, H-1), 5.07 (1H, br s, N$\underline{H}$); δ_C (100.5 MHz, CD_3CN) 13.4 (q, CH_3), 22.4, 26.5, 28.9, 28.9, 29.0, 31.6 (6 x t, 6 x CH_2), 43.0 (t, $NHCH_2\alpha$, $NHCH_2\beta$), 74.7, 75.5 (2 x d, J_{C3-F} 6.9 Hz, C-3β, C-3α), 75.7 (d, C-2β), 79.9 (d, C-2α), 81.5 (d, J_{C4-F} 19.8 Hz, C-4β), 81.6 (d, J_{C4-F} 19.1 Hz, C-4α), 83.0 (d, J_{C5-F} 200.7 Hz, C-5β), 83.3 (d, J_{C5-F} 137.3 Hz, C-5α), 85.0 (d, C-1β), 89.1 (d, C-1α); δ_F (376.6 MHz, $CDCl_3$) -226.26 (td, $J_{F,H\ geminal}$ 49.6 Hz, $J_{F,H\ vicinal}$ 19.1 Hz, F-β), -228.46 (td, $J_{F,H\ geminal}$ 48.6 Hz, $J_{F,H\ vicinal}$ 21.0 Hz, F-α); HRMS (ESI) calculated for $C_{13}H_{28}FN_2O_5S$: 343.1697. Found 343.1700 (MH^+).

***N*-(Decyl)-*N*'-(5-fluoro-α,β-D-arabinofuranosyl)sulfamide**

8b. General Procedure B, using glycosyl sulfamide **7b** (60 mg, 0.1 mmol) and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.1), afforded diol **8b** (35 mg, 72 %, α:β, 3:1) as a white solid; m.p. 98-100 °C (MeOH/DCM); υ_{max} (neat) 3293 (N-H), 1329 (s, S=O), 1143 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3OD) α anomer: 0.89 (3H, t, *J* 6.8 Hz, C$\underline{H}_3$), 1.24-1.40 (14H, m, 7 x C$\underline{H}_2$), 1.49-1.56 (2H, m, $NHCH_2C\underline{H}_2$), 2.94-3.04 (2H, m, C$\underline{H}_2$NH), 3.93 (1H, at, *J* 2.7 Hz, H-3), 3.97 (1H, at, *J* 3.5 Hz, H-2), 3.99-4.06 (1H, m, H-4), 4.37-4.47 (1H, m, H-5), 4.49-4.58 (1H, m, H-5'), 4.93 (1H, d, $J_{1,2}$ 4.7 Hz, H-1); β anomer: 0.89 (3H, t, *J* 6.8 Hz, C$\underline{H}_3$), 1.24-1.40 (14H, m, 7 x C$\underline{H}_2$), 1.49-1.56 (2H, m, $NHCH_2C\underline{H}_2$), 2.94-3.04 (2H, m, C$\underline{H}_2$NH), 3.82-3.89 (1H, m, H-4), 3.91 (1H, at, *J* 4.3 Hz, H-3), 3.98-4.00 (1H, m, H-2), 4.37-4.47 (1H, m, H-5), 4.49-4.58 (1H, m, H-5'), 5.24 (1H, d, $J_{1,2}$ 4.3 Hz, H-1); δ_C (100.5 MHz, CD_3OD) 13.0 (q, CH_3), 22.3, 26.5, 29.0, 29.0, 29.1, 29.3, 31.7 (7 x t, 8 x CH_2), 42.6 (t, $NHCH_2\alpha$, $NHCH_2\beta$), 74.3, 75.6 (2 x d, J_{C3-F} 6.9 Hz, C-3β, C-3α), 75.7 (d, C-2β), 80.1 (d, C-2α), 80.9 (d, J_{C4-F} 19.1 Hz, C-4β), 81.7 (d, J_{C4-F} 19.8 Hz, C-4α), 82.0 (d, J_{C5-F} 170.9 Hz, C-5β), 82.7 (d, J_{C5-F} 170.1 Hz, C-5α), 85.2 (d, C-1β), 88.6 (d, C-1α); δ_F (376.6 MHz, CD_3OD) -227.20 (td, $J_{F,H\ geminal}$ 47.7 Hz, $J_{F,H\ vicinal}$ 19.1 Hz, F-β), -230.70 (td, $J_{F,H\ geminal}$ 47.7 Hz, $J_{F,H\ vicinal}$ 23.8 Hz, F-α); HRMS (ESI) calculated for $C_{15}H_{32}FN_2O_5S$: 371.2010. Found 371.2022 (MH^+).

***N*-(dodecyl)-*N*'-(5-fluoro-α,β-D-arabinofuranosyl)sulfamide**

8c. General Procedure B, using glycosyl sulfamide **7c** (50 mg, 0.1 mmol) and purification by flash chromatography (petrol: ethyl acetate, 1:1, R_f 0.1), afforded diol **8c** (32 mg, 78 %, α:β, 1:1) as a white solid; m.p. 129-131 °C (MeOH/DCM); υ_{max} (neat) 3293 (N-H), 1326 (s, S=O), 1142 (s, S=O) cm^{-1}; δ_H (400 MHz, CD_3CN) α anomer: 0.90 (3H, t, *J* 6.8 Hz, C$\underline{H}_3$), 1.26-1.38 (18H, m, 9 x C$\underline{H}_2$), 1.48-1.57 (2H, m, $NHCH_2C\underline{H}_2$), 2.91-3.04 (2H, m, C$\underline{H}_2$NH), 3.91 (1H, at, *J* 4.7 Hz, H-3), 3.96 (1H, at, *J* 4.3 Hz, H-2), 4.03-4.11 (1H, m, H-4), 4.38-4.48 (1H, m, H-5), 4.50-4.60 (1H, m, H-5'), 4.91 (1H, d, $J_{1,2}$ 3.9 Hz, H-1), 5.06 (1H, br s, N$\underline{H}$); β anomer: 0.90 (3H, t, *J* 6.8 Hz, C$\underline{H}_3$), 1.26-1.38 (18H, m, 9 x C$\underline{H}_2$), 1.48-1.57 (2H, m, $NHCH_2C\underline{H}_2$), 2.91-3.04 (2H, m, C$\underline{H}_2$NH), 3.80-3.89 (1H, m, H-4), 3.91 (1H, at, *J* 4.3 Hz, H-3), 3.99-4.02 (1H, m, H-2), 4.38-4.48 (1H, m, H-5), 4.50-4.60 (1H, m, H-5'), 5.19 (1H, d, $J_{1,2}$ 4.3 Hz, H-1), 5.06 (1H, br s, N$\underline{H}$); δ_C (100.5 MHz, CD_3CN) 13.4 (q, CH_3), 22.4, 26.5, 28.4, 29.0, 29.1, 29.3, 29.3, 29.4, 29.4, 31.6 (10 x t, 10 x CH_2), 43.0 (t, $NHCH_2\alpha$, $NHCH_2\beta$), 74.7, 75.5 (2 x d, J_{C3-F} 6.9 Hz, C-3β, C-3α), 75.7 (d, C-2β), 80.0 (d, C-2α), 81.5 (d, J_{C4-F} 19.1 Hz, C-4β), 81.6 (d, J_{C4-F} 19.1 Hz, C-4α), 83.0 (d, J_{C5-F} 168.6 Hz, C-5β), 83.3 (d, J_{C5-F} 168.6 Hz, C-5α), 85.0 (d, C-1β), 89.1 (d, C-1α); δ_F (376.6 MHz, $CDCl_3$) -226.24 (td, $J_{F,H\ geminal}$ 49.6 Hz, $J_{F,H\ vicinal}$ 19.1 Hz, F-β), -228.44 (td, $J_{F,H\ geminal}$ 48.7 Hz, $J_{F,H\ vicinal}$ 22.9 Hz, F-α); HRMS (ESI) calculated for $C_{17}H_{36}FN_2O_5S$: 399.2323. Found 399.2331 (MH^+).

Alamar Blue Assay

The anti-mycobacterial activity of glycosyl sulfamides and controls were performed using *M. smegmatis*. Test compounds and isoniazid were prepared in DMSO at 40 mg/mL, and subsequent 2 fold serial dilutions were performed in 100 µl of LB/T media in 96 well microplates, producing compound concentrations across the plate of 1000, 500, 250, 125, 62, 31, 15, 7.5, and 3.75 µg/mL. Approximately 4.5 x 10^6 cfu/mL of *M. smegmatis* was added to each well to give a total volume of 200 µl. Control wells contained only bacteria with 2.5 % DMSO in LB/T media. The plates were incubated at 37 °C for 18 hours. After this time, 10 µl of Alamar Blue dye was added to all wells, and the plate was then incubated for another 5 hours. The wells were then observed for a colour change (blue

to pink), and the MIC value was determined by visual observation.

Acknowledgements

We gratefully acknowledge the University of Canterbury (Postgraduate Scholarship to KS) and the Biomolecular Interaction Centre for funding. We also thank Dr Moritz Lassé for technical assistance.

Notes and references

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Electronic Supplementary Information (ESI) available: associated spectra for all compounds. See DOI: 10.1039/c000000x/

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