Carbohydrate Research 344 (2009) 739–746

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Stereoselective synthesis of β-*arabino* glycosyl sulfones as potential inhibitors of mycobacterial cell wall biosynthesis

Benjamin Ayers [a], Hilary Long [b], Edith Sim [b], Iain A. Smellie [a], Brendan L. Wilkinson [a], Antony J. Fairbanks [c,*]

[a] Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, UK
[b] Department of Pharmacology, Oxford University, Mansfield Road, Oxford OX1 3QT, UK
[c] Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch 8140, New Zealand

ARTICLE INFO

Article history:
Received 28 October 2008
Received in revised form 16 January 2009
Accepted 3 February 2009
Available online 12 February 2009

Keywords:
Carbohydrates
Thioglycosides
Glycosyl sulfones
Arabinose
Mycobacteria
Tuberculosis

ABSTRACT

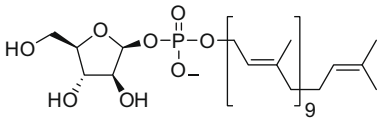
A series of β-*arabino* glycosyl sulfones with varying alkyl chain lengths were synthesised in a stereoselective fashion as putative mimics of decaprenolphosphoarabinose (DPA), and as potential inhibitors of mycobacterial cell wall biosynthesis. Biological testing against *Mycobacterium bovis BCG* revealed low to moderate anti-mycobacterial activity with marked dependence on alkyl chain length, which was maximal for a C-12 chain.

1. Introduction

Mycobacterium tuberculosis, the bacterium responsible for tuberculosis (TB), is probably the most prevalent of the pathogenic strains of mycobacteria. Tuberculosis has once again emerged as a major threat to human health; up to one third of the world's population is currently estimated to have latent infection,[1] whilst between two and three million people die annually from active infection. Although a number of drug treatments for TB are currently available strains of these mycobacteria have already developed antibiotic resistance.[2] Widespread recognition of the pressing need to develop new therapeutic agents active against TB has therefore led to the establishment of major global initiatives to fund drug discovery programs and to facilitate screening of compounds in the search for novel and useful anti-mycobacterial bioactivity.[3]

The cell walls of mycobacteria are complex, and pertinently to this study contain two polysaccharides, lipoarabinomannan (LAM) and arabinogalactan (AG), the structures of which are unique to mycobacteria and which are crucial to mycobacterial viability. Inhibition of the biosynthesis of these carbohydrate portions of the cell wall therefore represents an attractive therapeutic opportunity for the development of new drugs to combat TB, and correspondingly has been a field of intense interest over recent years.[4] Approaches adopted have included the attempted inhibition of various glycosyl transferases,[5] and of the Galp/Galf mutase enzyme responsible for a crucial pyranose/furanose isomerisation during assembly of the galactan cell wall component.[6] Particular attention has focussed on attempted inhibition of the biosynthesis of mycobacterial arabinan,[7] which is assembled stepwise by arabinosyl transferases that use decaprenolphophoarabinose **1** (DPA, Fig. 1) as the glycosyl donor. Metabolically stable analogues of DPA may inhibit these arabinosyl transferases, and thus inhibit arabinan biosynthesis, which would correspondingly be expected to have significantly deleterious effects on mycobacterial growth and survival.

In order to design mimics of DPA which may be expected to display useful in vivo activity replacement of the labile and highly polar glycosyl phosphate with a stable isostere could be considered an essential first step. Additionally, it would not be unreasonable



1

Figure 1. Decaprenolphophoarabinose **1** (DPA).

* Corresponding author. Tel.: +44 1865 275 647; fax: +44 1865 275 674.
E-mail address: antony.fairbanks@chem.ox.ac.uk (A.J. Fairbanks).

0008-6215/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2009.02.006

to expect that an alkyl chain, or other extended hydrophobic group of a certain minimum length, would be required to mimic the large decaprenyl moiety of DPA. Lowary, who has been one of the leading proponents in the field, has, amongst other approaches,[7c–e] reported the synthesis of a variety of β-*C*-glycosyl sulfones[8] and *C*-phosphonates of arabinofuranose as mimics of DPA, and therefore as putative anti-tubercular agents. In a somewhat related vein, von Itzstein more recently reported the synthesis and bioactivity of a variety of galactofuranosyl alkyl thioglycosides, glycosyl sulfones, sulfenamides and sulfonamides[9] which are presumed to act as inhibitors of the biosynthesis of galactofuranose components of the mycobacterial cell wall. Efforts from our laboratory have included a recent report on the synthesis and anti-mycobacterial activity of a series of glycosyl triazoles as putative mimics of DPA.[10]

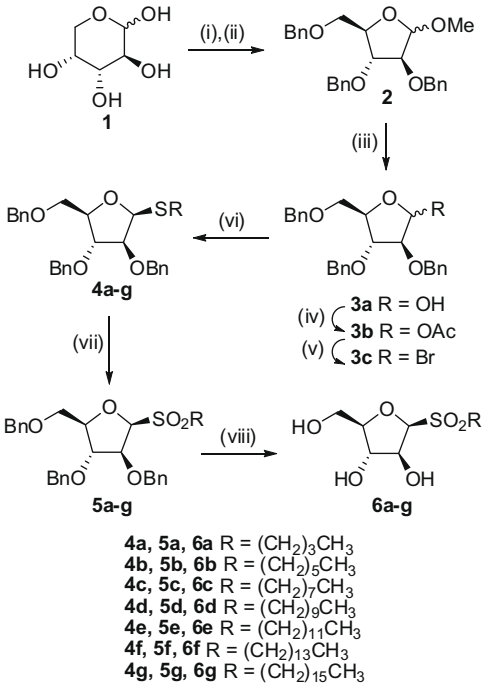
In light of the greater bond length of C–S as compared to C–O, and mindful of the ease with which thioglycosides may be synthesised by direct nucleophilic substitution at the anomeric centre, it was decided to access a variety of β-glycosyl sulfones of arabinofuranose, which were analogous to the *C*-glycosyl sulfones previously reported by Lowary,[6b] but which lacked the methylene unit between the anomeric centre and the sulfur atom. Moreover, systematic variation of alkyl chain length as a mimic of the extended polyprenyl side chain of DPA would facilitate further refinement of the somewhat unclear structure–activity relationships which have been observed in previous studies.

This paper reports the stereoselective synthesis of a series of β-arabinofuranose glycosyl sulfones as putative mimics of DPA, together with anti-bacterial activity observed in a variety of cell growth assays against both *Mycobacterium bovis BCG* and *E. coli*.

2. Results and discussion

2.1. Synthesis

Fischer glycosylation of arabinose **1** with 1 equiv of acetyl chloride in methanol provided methyl arabinofuranoside, which was then immediately benzylated to give the fully protected furanoside **2**[11] (α:β ratio, 1:2.3, Scheme 1). Acid-catalysed hydrolysis of the methyl glycoside by prolonged heating in 80% aqueous acetic acid provided hemiacetals **3a,**[12] which were then acetylated giving glycosyl acetates **3b**[13] (α:β ratio, 1.7:1). Conversion to the glycosyl bromide **3c** (α:β ratio, ~6:1) was most conveniently achieved by treatment with trimethylsilyl bromide (TMSBr) in dichloromethane (DCM, α:β ratio, 7:1), and bromide **3c**[14] was used directly for subsequent steps without extensive purification. Various methods were then investigated for the synthesis of the required β-thioglycosides. Attempts to access the dodecyl thioglycoside **4e** directly from hemiacetals **3a** by acid-catalysed reaction with dodecylthiol, using a procedure published by Wong[15] for the synthesis of the corresponding ethyl and phenyl β-thioglycosides, led to the formation of anomeric mixtures of products and unsurprisingly to a considerable quantity of open chain dithioacetal.[16] Efforts therefore focused on substitution reactions of the glycosyl bromide. Reaction of **3c** with dodecylthiol alone in DCM did give the desired thioglycoside **4e**, but as an inseparable anomeric mixture in which the undesired α-anomer unexpectedly predominated (α:β ratio, 4:1). It is reasonable to expect that direct S_N2 substitution of **3c** (α:β ratio, 7:1) would have led to the formation of an anomeric mixture (1:7, α:β) favouring the desired product. It was therefore considered that either the reaction had proceeded by a S_N1-type pathway to a significant extent, or that in situ epimerisation of **3c** competed with substitution, or that HBr produced during the reaction had caused undesired extensive epimerisation of the desired β-product. In order to both remove HBr and increase the nucleophilicity of the thiol by de-protonation, the hindered base 2,4,6-tri-*tert*-butylpyrimidine (TTBP) was added to the reaction mixture, and this had a significant and beneficial effect on the stereoselectivity; in this case the desired β-anomer was produced as the sole reaction product.



Scheme 1. Reagents and conditions: (i) AcCl, MeOH rt, 6 h, 80%, α:β, 4:1; (ii) NaH, BnBr, DMF, rt, 16 h, 87%; (iii) 80% aqueous AcOH, 115 °C, 48 h, 73%; (iv) Ac_2O, pyridine, rt, 16 h, 94%, α:β, 1.7:1; (v) TMSBr, CH_2Cl_2, −40 °C to rt, 0.5 h, α:β, 4:1; (vi) RSH, TTBP, CH_2Cl_2, rt, 16–17 h; **4a**, 94%, **4b**, 85%, **4c**, 83%, **4d**, 80%, **4e**, 63%, **4f**, 97%, **4g**, 80% (all over two steps); (vii) MCPBA, $NaHCO_3$, CH_2Cl_2, 16 h; **5a**, 83%, **5b**, 78%, **5c**, 84%, **5d**, 88%, **5e**, 87%, **5f**, 83%, **5g**, 86%; (viii) H_2, 10% Pd on C, MeOH or MeOH:EtOAc, 1:1, or EtOAc, rt, 24 h; **6a**, 72%, **6b**, 82%, **6c**, 80%, **6d**, 75%, **6e**, 94%, **6f**, 88%, **6g**, 81%.

With an appropriate procedure in place that would allow stereoselective access to the desired β-*arabino* thioglycosides from the corresponding thiols, consideration was given to the range of thioglycosides that should be synthesised. It was concluded that appropriate mapping of hydrophobic space could be economically achieved by only accessing alternate members of a homologous series of *n*-alkyl thioglycosides, in which the alkyl chain contained even numbers of carbon atoms. Glycosyl bromide **3c** was therefore reacted with the series of straight-chain alkyl thiols $CH_3(CH_2)_nSH$, (where n = an odd number from 3 to 15); in all cases reaction of the thiol with **3c** in the presence of TTBP in DCM produced the corresponding β-thioglycoside **4a**–**f** as a single anomer in 60–97% yields over two steps from acetate **3b**. Subsequent oxidation by treatment with *meta*chloroperbenzoic acid (MCPBA, 3 equiv) in DCM in the presence of $NaHCO_3$ in fact produced mainly the glycosyl sulfoxide. However, omission of the base and the use of a larger excess of MCPBA (5 equiv) led to exclusive formation of the desired sulfone, and this procedure produced the glycosyl sulfones **5a**–**f** in 78–86% yield, as the sole reaction products in each case. Finally, removal of the benzyl protecting groups was achieved by catalytic hydrogenation in the presence of 10% Pd on carbon, in a solvent mixture of MeOH and 10% acetic acid by volume, producing the de-protected glycosyl sulfones **6a**–**e**. For reasons of compound solubility the solvent polarity was decreased for the de-protection of the tetradecyl sulfone **6f** and the hexadecyl sulfone **6g** (solvents: 1:1 mixture of MeOH/EtOAc, and neat EtOAc, respectively, 10% AcOH v/v was added in both cases).

2.2. Biological testing

Anti-mycobacterial testing of de-protected sulfones **6a**–**g** was initially performed using a spot test on *M. bovis BCG*; *M. bovis*

BCG cultures were spotted onto 6-well plates containing solid media and the test compounds were then added at various concentrations.[17] These cultures were then grown in an incubator at 37 °C for 7–14 days and any effect of the test compound on cell growth was measured. In this manner, compounds **6a–g** were tested for biological activity, at concentrations of 0 (control), 2, 20, 200 and 2000 μg mL^{-1}. Whilst the *n*-butyl sulfone **6a** only displayed activity at the highest concentration (2 mg/mL), all the compounds completely inhibited mycobacterial growth at the 200 μg/mL level, though none displayed activity at or below the 20 μg/mL level. A second series of spot tests was performed on *E. coli.* (strain JM109) in which none of the compounds **6a–g** displayed any anti-bacterial effects at the highest concentrations (2 mg/mL), indicating a selective anti-mycobacterial mode of action. The minimum inhibitory concentrations (MICs) of the anti-mycobacterial activity of sulfones **6a–g** were then measured somewhat more accurately in a second series of tests on *M. bovis BCG* using the Alamar Blue microplate assay, in which the Alamar Blue dye changes from the oxidised indigo blue (and non-fluorescent) form to the reduced pink (and fluorescent) form in the presence of growing bacteria (Fig. 2)[18] The results are shown in Table 1 and Figure 2.

The dependence of anti-mycobacterial activity upon alkyl chain length is shown in Table 1 and Figure 2. For sulfones **6a–d** biological activity increases as side chain hydrophobicity is increased; a reasonable expectation since the natural DPA substrate contains an extended decaprenol side chain that is highly non-polar in nature.[19] The *n*-butyl sulfone **6a** is only active at extremely high concentrations (MIC ~2 mg/mL), whereas the less polar *n*-decyl sulfone **6d** is at least 20 times more active (MIC between 62 and 125 μg/mL). However, this increase in activity with alkyl chain length then reaches a maximum, which is observed for the C-12 sulfone **6e** (MIC 62 μg/mL). This result corroborates the earlier findings of Lowary during his work on *arabino C*-glycosyl sulfones[8b] with the caveat that their C-glycosides contain an extra methylene unit between the sulfur atom and the anomeric centre. Activity then subsequently decreases for sulfones **6f–g** which possess more extended alkyl chains (MICs between 250 and 125 μg/mL), indicating that there is not a simple correlation between increased hydrophobicity and biological activity.

A comparison of these results with those of other recent studies is worthwhile. Our recent studies on glycosyl triazoles[10] revealed that for the *n*-alkyl derivatives, the compound possessing a C-8 chain was more active than the one that contained a C-10 chain; the reverse of the situation is observed here. Moreover, in that study the most active glycosyl triazole, which was approximately twice as active as compound **6e**, in fact contained a more extended

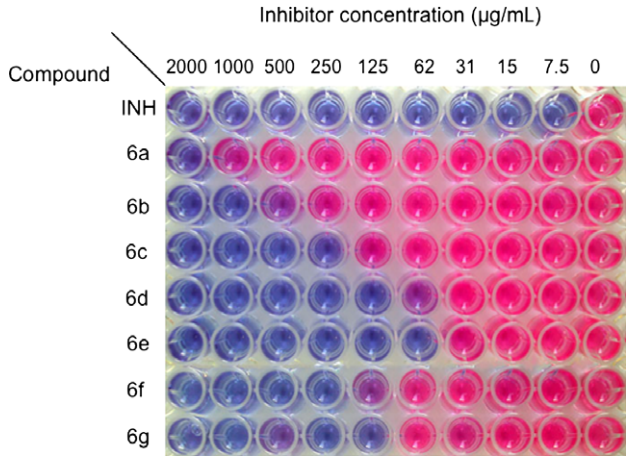


Figure 2. Alamar blue assay of *M. bovis BCG* with de-protected glycosyl sulfones **6a–g** and control with isoniazid (INH).

Table 1
Inhibitory effects of de-protected glycosyl sulfones **6a–g** against *M. bovis BCG*

Compound	R^2	MIC[a] (μg/mL)
INH	–	0.1
6a	$-(CH_2)_3CH_3$	2000
6b	$-(CH_2)_5CH_3$	500
6c	$-(CH_2)_7CH_3$	250
6d	$-(CH_2)_9CH_3$	125 > X > 62
6e	$-(CH_2)_{11}CH_3$	62
6f	$-(CH_2)_{13}CH_3$	250 > X > 125
6g	$-(CH_2)_{15}CH_3$	125

[a] MIC = minimum inhibitory concentration; the lowest concentration of the compound which inhibited the growth of *M. bovis BCG* >90% from the Alamar Blue assay. Isoniazid (INH) was used as a control (MIC 0.1 μg/mL).

C-15 chain that also incorporated an ether linkage. Direct comparison of these studies with the related work on galactofuranose mimics reported by von Itzstein[9] is perhaps less appropriate. However, it is notable that the most active compounds identified in those studies, which are more than an order of magnitude more potent than the most active compounds reported by us, contain branched side chains which comprised two *n*-octyl alkyl units. Finally, the fact that optimal bioactivity is reached for a C-12 chain and that the longer chains result in lower bioactivity is also worthy of comment. We concede[20] that this is possibly an effect of the physical properties of the longer chain sulfones, which may be prone to aggregation in the testing medium, rather than being due to an actual reduction in binding affinity. However, we currently lack any evidence to substantiate this hypothesis. It should also be reiterated that in our previous study[10] a triazole with a C-15 side chain was found to be the most active.

In terms of arriving at more definite conclusions a certain degree of caution must be exercised. Firstly, it should be borne in mind that the optimal anti-mycobacterial activity observed herein is rather modest; even the most potent compound **6e** is at least two orders of magnitude less active than isoniazid (INH). Moreover, the precise molecular target of these and analogous compounds is still unclear at this juncture. Although the compounds in this and the related study[10] have been designed as mimics of DPA, identification of their mode of action, for example, as inhibitors of mycobacterial arabinosyl transferases, would require further investigation. However, the low activity of these compounds means that such further studies are likely to be of only limited value in the context of future anti-tubercular drug development.

3. Experimental

3.1. General

Melting points were recorded on a Kofler hot block and are uncorrected. Proton and carbon nuclear magnetic resonance (δ_H, δ_C) spectra were recorded on Bruker AV 400 (400 MHz), or Bruker AMX 500 (500 MHz) spectrometers. All chemical shifts are quoted on the δ-scale in ppm using residual solvent as an internal standard. Low resolution mass spectra were recorded on a Micromass Platform 1 spectrometer using electrospray ionisation in either positive or negative polarity (ES^+ or ES^-), or using a VG Micromass spectrometer. High-resolution mass spectra were recorded on a Walters 2790-Micromass LCT electrospray ionisation mass spectrometer, using either electrospray ionisation (NH_3, Cl) techniques as stated. *M/z* values are reported in Daltons and are followed by their percentage abundance in parentheses. Optical rotations were measured on a Perkin–Elmer 241 polarimeter with a path length of 1 dm. Concentrations are given in g/100 mL. Microanalyses were performed by the Inorganic Chemistry Laboratory Elemental Analysis service, Oxford University, UK. Thin Layer Chromatography (TLC) was carried out on Merck Kieselgel $60F_{254}$ pre-coated

glass-backed plates. Visualisation of the plates was achieved using a u.v. lamp (λ_{max} = 254 or 365 nm), and/or ammonium molybdate (5% in 2 M sulfuric acid), or sulfuric acid (5% in ethanol). Flash column chromatography was carried out using Sorbsil C60 40/60 silica. Alcohol-free dichloromethane was dried on an alumina column. Anhydrous DMF, pyridine, methanol and toluene were purchased from Sigma Aldrich. 'Petrol' refers to the fraction of light petrol ether boiling in the range of 40–60 °C. TTBP was re-crystallised from methanol. Compounds **2**,[11] **3a**,[12] **3b**,[13] and **3c**,[14] were prepared using the route shown in Scheme 1, and exhibited spectroscopic data in agreement with those reported previously.

3.2. General procedure A: synthesis of thioglycosides

To a solution of the crude glycosyl bromide **3c** (1 equiv) and TTBP (2.5 equiv) in dry DCM (15 mL) under argon, the corresponding thiol (2 equiv) was added. After 18 h, TLC (toluene/ethyl acetate, 30:1) indicated formation of a single product. The reaction mixture was diluted in DCM (50 mL), washed with sodium bicarbonate (3 × 50 mL of a saturated solution) and brine (1 × 50 mL of a saturated solution). The organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (toluene, until TTBP fully eluted, then toluene/ethyl acetate, 30:1) to afford thioglycosides **4a**–**g**.

3.3. General procedure B: oxidation of thioglycosides

The thioglycosides **4a**–**g** (1 equiv) were dissolved in DCM (10 mL) under argon. *m*CPBA (5 equiv) was added, and after 16 h TLC (petrol/ethyl acetate, 5:1) indicated formation of a single product. The reaction was quenched with sodium thiosulfate (30 mL of a saturated solution) and was stirred vigorously for 30 min. The biphasic solution was diluted with DCM (20 mL) and the phases were separated. The aqueous phase was back-extracted with DCM (3 × 20 mL), the organic phases were combined, washed with sodium bicarbonate (3 × 50 mL of a saturated solution) and brine (1 × 50 mL of a saturated solution). The organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (petrol/ethyl acetate, 5:1) to afford glycosyl sulfones **5a**–**g**.

3.4. General procedure C: de-protection of sulfone

The protected glycosyl sulfone (1 equiv) was dissolved in either MeOH (**5a**–**e**), a 1:1 mixture of MeOH and EtOAc (**5f**), or EtOAc (**5g**), before AcOH (10%, v/v) was added. 10% Pd–C was then added (40% w/w of the starting material) and the reaction was stirred under an atmosphere of hydrogen for 16 h. After this time, TLC (ethyl acetate) indicated the formation of a single product. The reaction mixture was filtered through Celite® and was concentrated in vacuo. The residue was dissolved in ethyl acetate (50 mL), washed with sodium bicarbonate (3 × 50 mL of a saturated solution) and brine (1 × 50 mL of a saturated solution). The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (ethyl acetate) to afford the de-protected glycosyl sulfones **6a**–**g**.

3.5. Butyl 2,3,5-tri-*O*-benzyl-1-thio-β-D-arabinofuranoside (4a)

Procedure A: Method as described above afforded the butyl thioglycoside **4a** (600 mg, 94%) as a clear oil; $[\alpha]_D^{25}$ −48.7 (*c*, 1.0 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.41 Hz, CH_3), 1.38–1.46 (2H, m, CH_2), 1.60–1.67 (2H, m, CH_2), 2.68 (2H, td, *J* 7.5 Hz, *J* 2.5 Hz, CH_2), 3.66 (1H, dd, $J_{4,5}$ 6.5 Hz, $J_{5,5'}$ 9.8 Hz, H-5), 3.74 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5}$ 9.8 Hz, H-5′), 4.06 (1H, at, *J* 4.0 Hz, H-3), 4.16 (1H, td, $J_{3,4}$ 4.3 Hz, $J_{4,5}$ 6.5 Hz, $J_{4,5'}$ 6.5 Hz, H-4), 4.18 (1H, dd, $J_{1,2}$ 4.9 Hz, $J_{2,3}$ 3.8 Hz, H-2), 4.47–4.69 (6H, m, $PhCH_2$), 5.40 (1H, d, $J_{1,2}$ 4.9 Hz, H-1), 7.20–7.41 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 13.7 (q, CH_3), 21.4, 30.6, 32.0 (3 × t, CH_2), 71.4 (t, C-5), 71.9, 72.3, 73.3 (3 × t, $PhCH_2$), 82.0, 83.8, 84.3, 87.1 (4 × d, C-4, C-3, C-2, C-1), 125.3, 127.6, 127.7, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.7, 129.0, 129.8 (15 × d, Ar-H), 137.5, 137.8, 138.2 (3 × s, Ar-C); *m/z* (ESI)$^+$ 515.2 (M+Na$^+$, 16), 510.2 ($M + NH_4^+$, 100%). HRMS *m/z* calcd for $C_{30}H_{36}O_4S$ [M+Na]$^+$: 515.2232. Found: 515.2214.

3.6. Hexyl 2,3,5-tri-*O*-benzyl-1-thio-β-D-arabinofuranoside (4b)

Procedure A: Method as described above afforded the hexyl thioglycoside **4b** (480 mg, 85%) as a clear oil; $[\alpha]_D^{25}$ −43.3 (*c*, 1.1 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.0 Hz, CH_3), 1.25–1.35 (4H, m, CH_2), 1.39 (2H, quin., *J* 7.2 Hz, CH_2), 1.64 (2H, quin., *J* 7.5 Hz, CH_2), 2.67 (2H, td, *J* 7.5 Hz, *J* 2.7 Hz, CH_2), 3.66 (1H, dd, $J_{4,5}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5), 3.74 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5′), 4.06 (1H, at, *J* 4.0 Hz, H-3), 4.16 (1H, td, $J_{3,4}$ 4.3 Hz, $J_{4,5}$ 6.5 Hz, $J_{4,5'}$ 6.5 Hz, H-4), 4.18 (1H, dd, $J_{1,2}$ 4.9 Hz, $J_{2,3}$ 4.9 Hz, H-2), 4.48–4.68 (6H, m, $PhCH_2$), 5.40 (1H, d, $J_{1,2}$ 4.9 Hz, H-1), 7.24–7.39 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.0 (q, CH_3), 21.5, 28.7, 29.9, 30.9, 31.4 (5 × t, CH_2), 71.4 (t, C-5), 71.9, 72.3, 73.3 (3 × t, $PhCH_2$), 82.0, 83.8, 84.3, 87.1 (4 × d, C-4, C-3, C-2, C-1), 125.3, 127.6, 127.7, 127.8, 127.8, 127.9, 127.9, 128.0, 128.2, 128.2, 128.3, 128.3, 128.4, 128.4, 129.0 (15 × d, Ar-H), 137.5, 137.8, 138.2 (3 × s, Ar-C); *m/z* (ESI)$^+$ 543.3 (M+Na$^+$, 19), 538.3 ($M + NH_4^+$, 100%). HRMS *m/z* calcd for $C_{32}H_{40}O_4S$ [M+Na]$^+$: 543.2545. Found: 543.2535.

3.7. Octyl 2,3,5-tri-*O*-benzyl-1-thio-β-D-arabinofuranoside (4c)

Procedure A: Method as described above afforded the octyl thioglycoside **4c** (395 mg, 83%) as a clear oil; $[\alpha]_D^{25}$ −42.2 (*c*, 1.1 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8 Hz, CH_3), 1.23–1.34 (8H, m, CH_2), 1.35–1.44 (2H, m, CH_2), 1.64 (2H, quin., *J* 7.5 Hz, CH_2), 2.67 (2H, td, *J* 7.5 Hz, *J* 2.8 Hz, CH_2), 3.66 (1H, dd, $J_{4,5}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5), 3.74 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5′), 4.06 (1H, at, *J* 3.9 Hz, H-3), 4.16 (1H, td, $J_{3,4}$ 4.3 Hz, $J_{4,5}$ 6.5 Hz, $J_{4,5'}$ 6.5 Hz, H-4), 4.19 (1H, dd, $J_{1,2}$ 4.9 Hz, $J_{2,3}$ 3.8 Hz, H-2), 4.50–4.68 (6H, m, $PhCH_2$), 5.40 (1H, d, $J_{1,2}$ 4.9 Hz, H-1), 7.21–7.41 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 22.6, 29.0, 29.2, 29.7, 29.9, 30.9, 31.8 (7 × t, CH_2), 71.4 (t, C-5), 71.9, 72.3, 73.3 (3 × t, $PhCH_2$), 82.0, 83.8, 84.3, 87.1 (4 × d, C-4, C-3, C-2, C-1), 127.6, 127.6, 127.7, 127.7, 127.8, 127.8, 127.8, 127.9, 127.9, 128.2, 128.3, 128.4, 128.4, 128.4, 128.7 (15 × d, Ar-H), 137.5, 137.8, 138.2 (3 × s, Ar-C); *m/z* (ESI)$^+$ 571.3 (M+Na$^+$, 17), 566.3 ($M + NH_4^+$, 100%). HRMS *m/z* calcd for $C_{34}H_{44}O_4S$ [M+Na]$^+$: 571.2858. Found: 571.2836.

3.8. Decyl 2,3,5-tri-*O*-benzyl-1-thio-β-D-arabinofuranoside (4d)

Procedure A: Method as described above afforded the decyl thioglycoside **4d** (500 mg, 80%) as a clear oil; $[\alpha]_D^{25}$ −39.3 (*c*, 1.2 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8 Hz, CH_3), 1.23–1.35 (12H, m, CH_2), 1.35–1.42 (2H, m, CH_2), 1.64 (2H, quin., *J* 7.5 Hz, CH_2), 2.67 (2H, td, *J* 7.5 Hz, *J* 2.8 Hz, CH_2), 3.66 (1H, dd, $J_{4,5}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5), 3.74 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5′), 4.06 (1H, at, *J* 4.0 Hz, H-3), 4.16 (1H, td, $J_{3,4}$ 4.3 Hz, $J_{4,5}$ 6.5 Hz, $J_{4,5'}$ 6.5 Hz, H-4), 4.19 (1H, dd, $J_{1,2}$ 4.9 Hz, $J_{2,3}$ 3.8 Hz, H-2), 4.48–4.68 (6H, m, $PhCH_2$), 5.40 (1H, d, $J_{1,2}$ 4.9 Hz, H-1), 7.24–7.40 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 22.7, 29.0, 29.2, 29.3, 29.6, 29.6, 29.9, 30.3, 30.9 (9 × t, CH_2), 71.4 (t, C-5), 71.9, 72.3, 73.3 (3 × t, $PhCH_2$), 82.0, 83.8, 84.2, 87.1 (4 × d, C-4, C-3, C-2, C-1), 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.1, 128.2, 128.3, 128.4, 128.5, 128.7, 129.8, 130.9 (15 × d, Ar-H), 137.5, 137.8, 138.2 (3 × s, 3 × Ar-C); *m/z* (ESI)$^+$ 599.3 (M+Na$^+$,

18), 594.3 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{36}H_{48}O_4S$ [M+Na]$^+$: 599.3171. Found: 599.3157.

3.9. Dodecyl β-D-thio-2,3,5-tri-*O*-benzylarabinofuranoside (4e)

Procedure A: Method as described above afforded the dodecyl thioglycoside **4e** (190 mg, 63% over 2 steps; $[\alpha]^{23}$ −70 (c 1.0 $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J* 6.7 Hz, alkyl C*H*$_3$), 1.25–1.41 (16H, m, alkyl C*H*$_2$) 1.60–1.69 (2H, m, alkyl C*H*$_2$), 2.64–4.71 (2H, m, alkyl C*H*$_2$), 3.66 (1H, dd, $J_{4,5}$ 6.6 Hz, $J_{5,5'}$ 9.9 Hz, H-5), 3.75 (1H, dd, $J_{4,5'}$ 6.3 Hz, $J_{5,5'}$ 9.9 Hz, H-5′), 4.06 (1H, at, $J_{2,3}$ 4.0 Hz, $J_{3,4}$ 4.0 Hz, H-3), 4.15–4.20 (2H, m, H-2, H-4), 4.51–4.66 (6H, m, 3 × OC*H*$_2$C$_6$H$_5$), 5.41 (1H, d, $J_{1,2}$ 4.8 Hz H-1), 7.25–7.38 (15H, m, 3 × OCH$_2$C$_6$*H*$_5$); δ_C (100.6 MHz, $CDCl_3$) 14.1 (alkyl *C*H$_3$), 22.7, 29.0, 29.3, 29.4, 29.6, 29.6, 29.7, 29.7, 30.0, 30.9, 31.9 (11 × alkyl *C*H$_2$), 71.4 (C-5), 71.9, 72.3, 73.3 (OCH$_2$C$_6$H$_5$) 82.1 (C-4), 83.8, 84.3 (C-2, C-3), 87.1 (C-1), 127.6, 127.7, 127.8, 127.8, 127.9, 128.3, 128.4 (PhCH), 137.5, 137.8, 138.2 (Ar-*C*); *m/z* (ES$^+$) 627 (M+Na$^+$, 100%); HRMS (ES$^+$) Calcd Na-$C_{38}H_{52}O_4S$ 627.3479. Found: 627.3481).

3.10. Tetradecyl 2,3,5-tri-*O*-benzyl-1-thio-β-D-arabinofuranoside (4f)

Procedure A: Method as described above afforded the tetradecyl thioglycoside **4f** (802 mg, 97%) as a clear oil; $[\alpha]_D^{25}$ −38.2 (*c,* 1.1 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8 Hz, CH_3), 1.25–1.34 (20H, m, CH_2), 1.35–1.44 (2H, m, CH_2), 1.61–1.68 (2H, m, CH_2), 2.67 (2H, td, *J* 7.1 Hz, *J* 2.8 Hz, CH_2), 3.66 (1H, dd, $J_{4,5}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5), 3.74 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5′), 4.06 (1H, at, *J* 4.0 Hz, H-3), 4.16 (1H, td, $J_{3,4}$ 4.3 Hz, $J_{4,5}$ 6.5 Hz, $J_{4,5'}$ 6.5 Hz, H-4), 4.19 (1H, dd, $J_{1,2}$ 4.9 Hz, $J_{2,3}$ 3.8 Hz, H-2), 4.48–4.69 (6H, m, PhCH_2), 5.40 (1H, d, $J_{1,2}$ 4.9 Hz, H-1), 7.24–7.39 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 29.0, 29.3, 29.4, 29.6, 29.6, 29.7, 29.7, 29.9, 30.4, 30.9, 31.8, 31.9, 32.1 (13 × t, CH_2), 71.9 (t, C-5), 72.1, 72.3, 73.3 (3 × t, PhCH_2), 82.0, 83.8, 84.3, 87.1 (4 × d, C-4, C-3, C-2, C-1), 127.5, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.2, 128.2, 128.3, 128.4, 128.7, 128.8, 130.9 (15 × d, Ar-H), 137.8, 138.2, 138.4 (3 × s, Ar-C); *m/z* (ESI)$^+$ 655.4 (M+Na$^+$, 21), 650.4 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{40}H_{56}O_4S$ [M+Na]$^+$: 655.3797. Found: 655.3768.

3.11. Hexadecyl 2,3,5-tri-*O*-benzyl-1-thio-β-D-arabinofuranoside (4g)

Procedure A: Method as described above afforded the hexadecyl thioglycoside **4f** (692 mg, 80%) as a white waxy solid, mp 33 °C; $[\alpha]_D^{25}$ −37.0 (*c,* 1.0 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8 Hz, CH_3), 1.20–1.35 (24H, m, CH_2), 1.35–1.43 (2H, m, CH_2), 1.64 (2H, quin., *J* 7.5 Hz, CH_2), 2.67 (2H, td, *J* 7.1 Hz, *J* 2.8 Hz, CH_2), 3.66 (1H, dd, $J_{4,5}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5), 3.74 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 9.9 Hz, H-5′), 4.06 (1H, at, *J* 3.9 Hz, H-3), 4.16 (1H, td, $J_{3,4}$ 4.3 Hz, $J_{4,5}$ 6.5 Hz, $J_{4,5'}$ 6.5 Hz, H-4), 4.18 (1H, dd, $J_{1,2}$ 4.9 Hz, $J_{2,3}$ 3.8 Hz, H-2), 4.49–4.68 (6H, m, PhCH_2), 5.40 (1H, d, $J_{1,2}$ 4.9 Hz, H-1), 7.22–7.39 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.2 (q, CH_3), 28.4, 29.0, 29.1, 29.2, 29.3, 29.4, 29.6, 29.6, 29.7, 29.7, 29.9, 30.4, 30.7, 30.9, 31.3 (15 × t, CH_2), 71.4 (t, C-5), 71.9, 72.3, 73.3 (3 × t, PhCH_2), 82.0, 83.8, 84.3, 87.1 (4 × d, C-4. C-3, C-2, C-1), 127.6, 127.6, 127.7, 127.8, 127.8, 127.8, 127.9, 128.0, 128.1, 128.2, 128.2, 128.3, 128.4, 129.0, 129.8 (15 × d, Ar-H), 137.5, 137.8, 138.2 (3 × s, Ar-C); *m/z* (ESI)$^+$ 683.4 (M+Na$^+$, 18), 678.4 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{42}H_{60}O_4S$ [M+Na]$^+$: 683.4110. Found: 683.4084.

3.12. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl butyl sulfone (5a)

Procedure B: Method as described above afforded the butyl sulfone **5a** (425 mg, 83%) as a clear oil; $[\alpha]_D^{25}$ −4.2 (*c,* 1.1 in $CHCl_3$); ν_{max} (KBr disc) 1317 (s, S=O, asymm. stretch), 1100 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.4 Hz, CH_3), 1.38 (2H, app. sext., *J* 7.4 Hz, CH_2), 1.72–1.86 (2H, m, CH_2), 2.99 (1H, ddd, *J* 13.8 Hz, *J* 10.4 Hz, *J* 5.8 Hz, C*H*H′), 3.12 (1H, ddd, *J* 13.8 Hz, *J* 10.4 Hz, *J* 5.8 Hz, CH*H*′), 3.64 (1H, dd, $J_{4,5}$ 4.9 Hz, $J_{5,5'}$ 10.2 Hz, H-5), 3.75 (1H, dd, $J_{4,5'}$ 6.3 Hz, $J_{5,5'}$ 10.2 Hz, H-5′), 4.24–4.31 (2H, m, H-3, H-4), 4.48–4.60 (6H, m, H-2, 2 × PhCH_2, PhC*H*H′), 4.81 (1H, d, J_{AB} 11.5 Hz, PhCH*H*′), 4.98 (1H, d, $J_{1,2}$ 5.7 Hz, H-1), 7.19–7.39 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 13.5 (q, CH_3), 21.8, 22.9, 50.7 (3 × t, CH_2), 81.7, 83.2, 83.5, 91.8 (4 × d, C-4, C-2, C-3, C-1), 127.7, 127.7, 127.8, 127.8, 128.0, 128.0, 128.1, 128.2, 128.3, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6 (15 × d, Ar-H), 136.8, 137.3, 137.8 (3 × s, Ar-C); *m/z* (ESI)$^+$ 547.3 (M+Na$^+$, 14), 542.3 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{30}H_{36}O_6S$ [M+Na]$^+$: 547.2130. Found: 547.2117. (Found: C, 68.48; H, 7.11. $C_{30}H_{36}O_6S$ requires C, 68.58; H, 6.92%).

3.13. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl hexyl sulfone (5b)

Procedure B: Method as described above afforded the hexyl sulfone **5b** (332 mg, 78%) as a clear oil; $[\alpha]_D^{25}$ −7.4 (*c,* 1.1 in $CHCl_3$); ν_{max} (KBr disc) 1317 (s, S=O, asymm. stretch), 1102 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.0 Hz, CH_3), 1.20–1.39 (6H, m, CH_2), 1.72–1.89 (2H, m, CH_2), 2.98 (1H, ddd, *J* 13.7 Hz, *J* 10.6 Hz, *J* 5.6 Hz, C*H*H′), 3.12 (1H, ddd, *J* 13.7 Hz, *J* 10.6 Hz, *J* 5.6 Hz, CH*H*′), 3.64 (1H, dd, $J_{4,5}$ 5.0 Hz, $J_{5,5'}$ 10.3 Hz, H-5), 3.75 (1H, dd, $J_{4,5'}$ 6.3 Hz, $J_{5,5'}$ 10.3 Hz, H-5′), 4.24–4.31 (2H, m, H-3, H-4), 4.49–4.60 (6H, m, H-2, 2 × PhCH_2, PhC*H*H′), 4.81 (1H, d, J_{AB} 11.5 Hz, PhCH*H*′), 4.98 (1H, d, $J_{1,2}$ 5.5 Hz, H-1), 7.19–7.39 (15H, m, 15 × Ar-H); δ_C (125 MHz, $CDCl_3$) 13.9 (q, CH_2), 20.9, 22.3, 28.2, 31.2, 50.9 (5 × t, CH_2), 70.2 (t, C-5), 72.7, 73.6, 73.8 (3 × t, PhCH_2), 81.7, 83.1, 83.5, 91.1 (4 × d, C-4, C-2, C-3, C-1), 127.7, 127.7, 127.8, 128.0, 128.1, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6, 129.0 (11 × d, Ar-H), 136.8, 137.3, 137.8 (3 × s, 3 × Ar-C); *m/z* (ESI)$^+$ 575.3 (M+Na$^+$, 29), 570.3 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{32}H_{40}O_6S$ [M+Na]$^+$: 575.2443. Found: 575.2433.

3.14. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl octyl sulfone (5c)

Procedure B: Method as described above afforded the octyl sulfone **5c** (320 mg, 84%) as a clear oil; $[\alpha]_D^{25}$ −18.8 (*c,* 1.0 in $CHCl_3$); ν_{max} (KBr disc) 1317 (s, S=O, asymm. stretch), 1100 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 7.0 Hz, CH_3), 1.19–1.39 (10H, m, CH_2), 1.69–1.88 (2H, m, CH_2), 2.98 (1H, ddd, *J* 13.7 Hz, *J* 10.6 Hz, *J* 5.6 Hz, C*H*H′), 3.12 (1H, ddd, *J* 13.7 Hz, *J* 10.3 Hz, *J* 5.8 Hz, CH*H*′), 3.64 (1H, dd, $J_{4,5}$ 4.9 Hz, $J_{5,5'}$ 10.1 Hz, H-5), 3.75 (1H, dd, $J_{4,5'}$ 6.3 Hz, $J_{5,5'}$ 10.1 Hz, H-5′), 4.23–4.36 (2H, m, H-3, H-4), 4.49–4.61 (6H, m, H-2, 2 × PhCH_2, PhC*H*H′), 4.81 (1H, d, J_{AB} 11.5 Hz, PhCH*H*′), 4.98 (1H, d, $J_{1,2}$ 5.8 Hz, H-1), 7.15–7.42 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 20.9, 22.6, 28.6, 28.9, 29.0, 31.7, 51.0 (7 × t, CH_2), 70.2 (t, C-5), 72.3, 73.3, 73.6 (3 × t, PhCH_2), 81.8, 83.2, 83.5, 91.8 (4 × d, C-4, C-2, C-3, C-1), 127.7, 127.7, 127.8, 127.8, 128.0, 128.0, 128.1, 128.2, 128.3, 128.3, 128.4, 128.5, 128.5, 128.6, 128.6 (15 × d, Ar-H), 136.8, 137.3, 137.8 (3 × s, Ar-C); *m/z* (ESI)$^+$ 603.3 (M+Na$^+$, 23), 598.3 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{34}H_{44}O_6S$ [M+Na]$^+$: 603.2756. Found: 603.2738. (Found: C, 70.13; H, 7.56. $C_{34}H_{44}O_6S$ requires C, 70.31; H, 7.64%).

3.15. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl decyl sulfone (5d)

Procedure B: Method as described above afforded the decyl sulfone **5d** (250 mg, 88%) as a clear oil; $[\alpha]_D^{25}$ −35.0 (*c,* 1.0 in $CHCl_3$); ν_{max} (KBr disc) 1317 (s, S=O, asymm. stretch), 1099 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 6.9 Hz, CH_3),

1.20–1.37 (14H, m, CH_2), 1.73–1.88 (2H, m, CH_2), 2.98 (1H, ddd, *J* 13.7 Hz, *J* 10.6 Hz, *J* 5.6 Hz, C*H*H′), 3.11 (1H, ddd, *J* 13.7 Hz, *J* 10.6 Hz, *J* 5.7 Hz, CH*H*′), 3.64 (1H, dd, $J_{4,5}$ 4.9 Hz, $J_{5,5'}$ 10.2 Hz, H-5), 3.75 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 10.2 Hz, H-5′), 4.24–4.31 (2H, m, H-3, H-4), 4.47–4.59 (6H, m, H-2, 2 × $PhCH_2$, PhC*H*H′), 4.81 (1H, d, J_{AB} 11.5 Hz, PhCH*H*′), 4.98 (1H, d, $J_{1,2}$ 5.7 Hz, H-1), 7.19–7.38 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 20.9, 22.7, 28.6, 29.1, 29.2, 29.3, 29.4, 31.8, 51.0 (9 × t, CH_2), 70.2 (t, C-5), 72.3, 73.3, 73.6 (3 × t, $PhCH_2$), 81.8, 83.2, 83.5, 91.8 (4 × d, C-4, C-2, C-3, C-1), 127.7, 127.7, 127.8, 127.8, 128.0, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.5, 128.6, 129.0, 129.7 (15 × d, Ar-H), 136.8, 137.3, 137.8 (3 × s, Ar-C); *m/z* $(ESI)^+$ 631.3 (M+Na^+, 68), 626.3 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{36}H_{48}O_6S$ [M+Na]$^+$: 599.3171. Found: 599.3157. (Found: C, 70.64; H, 7.69. $C_{36}H_{48}O_6S$ requires C, 71.02; H, 7.95%).

3.16. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl dodecyl sulfone (5e)

Procedure B: Method as described above afforded the dodecyl sulfone **5e** (160 mg, 87%); $[\alpha]_D^{25}$ −49.2 (*c,* 0.85 in $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 6.6 Hz, alkyl C*H*$_3$), 1.24–1.39 (16H, m, alkyl C*H*$_2$) 1.73–1.88 (2H, m, alkyl C*H*$_2$), 2.95–3.17 (2H, m, alkyl C*H*$_2$), 3.65 (1H, dd, $J_{4,5}$ 6.3 Hz, $J_{5,5'}$ 10.4 Hz, H-5), 3.77 (1H, dd, $J_{4,5'}$ 5.1 Hz, $J_{5,5'}$ 10.4 Hz, H-5′), 4.27–4.32 (2H, m, H-3, H-4), 4.51–4.60 (6H, m, H-2, 2 × OC*H*$_2$C$_6$H$_5$, OC*H*HC$_6$H$_5$), 4.83 (1H, d, *J* 11.4 OCH*H*C$_6$H$_5$), 5.00 (1H, d, $J_{1,2}$ 5.6 Hz H-1), 7.23–7.38 (15H, m, 3 × OCH$_2$C$_6$*H*$_5$); δ_C (100.6 MHz, $CDCl_3$) 14.1 (alkyl *C*H$_3$), 21.0, 22.7, 28.6, 28.61, 29.1, 29.3, 29.5, 29.6, 31.9, 51.0 (11 × alkyl *C*H$_2$), 70.3 (C-5), 70.3, 72.3, 73.7 (O*C*H$_2$C$_6$H$_5$) 81.8, 83.2, 83.5 (C-2, C-3, C-4), 91.8 (C-1), 127.7, 127.8, 127.8, 128.2, 128.3, 128.4, 128.5, 128.5 (Ph*C*H), 136.9, 137.4, 137.8 (Ar-*C*); *m/z* (ES^+) 659 (M+Na^+, 100%); HRMS (ES^+) Calcd $NaC_{38}H_{52}O_6S$ 659.3377. Found: 659.3377).

3.17. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl tetradecyl sulfone (5f)

Procedure B: Method as described above afforded the tetradecyl sulfone **5f** (607 mg, 83%) as a clear oil; $[\alpha]_D^{25}$ −47.0 (*c,* 1.3 in $CHCl_3$); ν_{max} (KBr disc) 1322 (s, S=O, asymm. stretch), 1103 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8 Hz, CH_3), 1.18–1.44 (22H, m, CH_2), 1.71–1.89 (2H, m, CH_2), 2.98 (1H, ddd, *J* 13.7 Hz, *J* 10.5 Hz, *J* 5.6 Hz, C*H*H′), 3.12 (1H, ddd, *J* 13.7 Hz, *J* 10.5 Hz, *J* 5.6 Hz, CH*H*′), 3.64 (1H, dd, $J_{4,5}$ 5.0 Hz, $J_{5,5'}$ 10.2 Hz, H-5), 3.76 (1H, dd, $J_{4,5'}$ 6.5 Hz, $J_{5,5'}$ 10.2 Hz, H-5′), 4.20–4.33 (2H, m, H-3, H-4), 4.45–4.62 (6H, m, H-2, 2 × $PhCH_2$, PhC*H*H′), 4.82 (1H, d, J_{AB} 11.5 Hz, PhCH*H*′), 4.99 (1H, d, $J_{1,2}$ 5.7 Hz, H-1), 7.18–7.39 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 21.0, 28.2, 28.6, 29.1, 29.3, 29.3, 29.5, 29.6, 29.6, 29.7, 31.9, 51.0 (12 × t, CH_2), 70.3 (t, C-5), 72.3, 73.3, 73.6 (3 × t, $PhCH_2$), 81.8, 83.2, 83.5, 91.8 (4 × d, C-4, C-2, C-3, C-1), 127.7, 127.7, 127.8, 127.8, 128.0, 128.1, 128.2, 128.3, 128.3, 128.4, 128.5, 128.5, 128.5, 128.6, 128.6 (15 × d, Ar-H), 136.8, 137.3, 137.8 (3 × s, Ar-C); *m/z* $(ESI)^+$ 687.4 (M+Na^+, 14), 682.4 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{40}H_{56}O_6S$ [M+Na]$^+$: 687.3695. Found: 687.3685.

3.18. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl hexadecyl sulfone (5g)

Procedure B: Method as described above afforded the hexadecyl sulfone **5g** (543 mg, 86%) as a white, waxy solid, mp 47–48 °C; $[\alpha]_D^{25}$ −55.1 (*c,* 1.3 in $CHCl_3$); ν_{max} (KBr disc) 1322 (s, S=O, asymm. stretch), 1103 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8 Hz, CH_3), 1.20–1.45 (26H, m, CH_2), 1.71–1.89 (2H, m, CH_2), 2.98 (1H, ddd, *J* 13.7 Hz, *J* 10.6 Hz, *J* 5.6 Hz, C*H*H′), 3.12 (1H, ddd, *J* 13.7 Hz, *J* 10.4 Hz, *J* 5.6 Hz, CH*H*′), 3.64 (1H, dd, $J_{4,5}$ 4.9 Hz, $J_{5,5'}$ 10.2 Hz, H-5), 3.76 (1H, dd, $J_{4,5'}$ 6.3 Hz, $J_{5,5'}$ 10.2 Hz, H-5′), 4.24–4.32 (2H, m, H-3, H-4), 4.46–4.60 (6H, m, H-2, 2 × $PhCH_2$, PhC*H*H′), 4.82 (1H, d, J_{AB} 11.5 Hz, PhCH*H*′), 4.98 (1H, d, $J_{1,2}$ 5.5 Hz, H-1), 7.19–7.41 (15H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 14.1 (q, CH_3), 20.9, 22.7, 28.6, 29.1, 29.3, 29.4, 29.5, 29.6, 29.7, 29.7, 31.9, 51.0 (12 × t, CH_2), 70.3 (t, C-5), 72.3, 73.3, 73.6 (3 × t, $PhCH_2$), 81.8, 83.2, 83.5, 91.8 (4 × d, C-4, C-2, C-3, C-1), 127.7, 127.7, 127.7, 127.8, 128.0, 128.0, 128.1, 128.2, 128.2, 128.3, 128.4, 128.5, 128.5, 129.0, 129.7 (15 × d, Ar-H), 136.8, 137.4, 137.8 (3 × s, Ar-C); *m/z* $(ESI)^+$ 715.4 (M+Na^+, 22), 710.4 ((M + NH_4^+, 100%). HRMS *m/z* calcd for $C_{42}H_{60}O_6S$ [M+Na]$^+$: 715.4008. Found: 715.3980. (Found: C, 72.79; H, 8.76. $C_{42}H_{60}O_6S$ requires C, 72.79; H, 8.73%).

3.19. β-D-Arabinofuranosyl butyl sulfone (6a)

Procedure C: Method as described above afforded de-protected butyl sulfone **6a** (128 mg, 0.533 mmol) as a clear oil; $[\alpha]_D^{25}$ +221 (*c,* 1.0 in acetone); δ_H (500 MHz, acetone-d_6) 0.93 (3H, t, *J* 7.3 Hz, CH_3), 1.40–1.51 (2H, app. sext., *J* 7.4 Hz, CH_2), 1.77 (2H, quin., *J* 7.7 Hz, CH_2), 3.10 (1H, dt, *J* 8.0 Hz, *J* 13.7 Hz, C*H*H′), 3.26 (1H, dt, *J* 8.0 Hz, *J* 13.9 Hz, CH*H*′), 3.76–3.85 (2H, m, H-5, H-5′), 4.06 (1H, aq, *J* 3.6 Hz, H-4), 4.28 (1H, aq, *J* 3.6 Hz, H-3), 4.39–4.46 (2H, m, 5-OH, H-2), 4.73 (1H, d, $J_{3,3\text{-OH}}$ 4.1 Hz, 3-OH), 4.83 (1H, d, $J_{1,2}$ 4.7 Hz, H-1), 5.08 (1H, d, $J_{2,2\text{-OH}}$ 7.3 Hz, 2-OH); δ_C (125 MHz, acetone-d_6) 13.9 (q, CH_3), 22.5, 23.5, 51.5 (3 × t, CH_2), 63.0 (t, C-5), 77.6, 78.2, 88.8, 94.7 (4 × d, C-3, C-2, C-4, C-1); ν_{max} (KBr disc) 3450–3500 (br s, OH), 1304 (s, S=O, asymm. stretch), 1134 (s, S=O, symm. stretch) cm^{-1}; *m/z* $(ESI)^+$ 785.2 (3M+Na^+, 17), 780.3 ((3M + NH_4^+, 9), 531.2 (2M+Na^+, 96), 526.2 (2M + NH_4^+, 100), 277.1 (M+Na^+, 29), 272.1 (M + NH_4^+, 77%). HRMS *m/z* calcd for $C_9H_{18}O_6S$ [M+Na]$^+$: 277.0722. Found: 277.0716.

3.20. β-D-Arabinofuranosyl hexyl sulfone (6b)

Procedure C: Method as described above afforded de-protected hexyl sulfone **6b** (105 mg, 82%) as a waxy white solid, mp 66–67 °C; $[\alpha]_D^{25}$ +216 (*c,* 1.0 in acetone); δ_H (500 MHz, acetone-d_6) 0.89 (3H, t, *J* 7.1 Hz, CH_3), 1.28–1.37 (4H, m, CH_2), 1.45 (2H, quin., *J* 7.3 Hz, CH_2), 1.79 (2H, quin., *J* 7.8 Hz, CH_2), 3.10 (1H, dt, *J* 8.0 Hz, *J* 13.7 Hz, C*H*H′), 3.26 (1H, dt, *J* 7.8 Hz, *J* 13.7 Hz, CH*H*′), 3.76–3.86 (2H, m, H-5, H-5′), 4.06 (1H, aq, *J* 3.8 Hz, H-4), 4.29 (1H, aq, *J* 3.7 Hz, H-3), 4.41 (1H, t, $J_{5,5\text{-OH}}$ 5.4 Hz, $J_{5',5\text{-OH}}$ 5.4 Hz, 5-OH), 4.44 (1H, app. quin., *J* 3.5 Hz, H-2), 4.72 (1H, d, $J_{3,3\text{-OH}}$ 4.1 Hz, 3-OH), 4.83 (1H, d, $J_{1,2}$ 4.6 Hz, H-1), 5.07 (1H, d, $J_{2,2\text{-OH}}$ 7.4 Hz, 2-OH); δ_C (125 MHz, acetone-d_6) 14.2 (q, CH_3), 21.5, 23.1, 29.1, 32.1, 51.8 (5 × t, CH_2), 63.0 (t, C-5), 77.6, 78.2, 88.8, 94.7 (4 × d, C-3, C-2, C-4, C-1); ν_{max} (KBr disc) 3450–3500 (br s, OH), 1306 (s, S=O, asymm. stretch), 1135 (s, S=O, symm. stretch) cm^{-1}; *m/z* $(ESI)^+$ 869.3 (3M+Na^+, 17), 537.2 (2M+Na^+, 100), 532.2 (2M + NH_4^+, 53), 305.1 (M+Na^+, 68), 300.1 (M + NH_4^+, 77%). HRMS *m/z* calcd for $C_{11}H_{22}O_6S$ [M+Na]$^+$: 305.1035. Found: 305.1031.

3.21. β-D-Arabinofuranosyl octyl sulfone (6c)

Procedure C: Method as described above afforded de-protected octyl sulfone **6c** (137 mg, 80%) as a waxy white solid; mp 80–81 °C; $[\alpha]_D^{25}$ +207 (*c,* 1.0 in acetone); δ_H (500 MHz, acetone-d_6) 0.88 (3H, t, *J* 7.1 Hz, CH_3), 1.24–1.38 (8H, m, CH_2), 1.44 (2H, quin., *J* 7.4 Hz, CH_2), 1.79 (2H, quin., *J* 7.8 Hz, CH_2), 3.10 (1H, dt, *J* 8.0 Hz, *J* 13.7 Hz, C*H*H′), 3.25 (1H, dt, *J* 7.9 Hz, *J* 13.7 Hz, CH*H*′), 3.75–3.86 (2H, m, H-5, H-5′), 4.06 (1H, aq, *J* 3.8 Hz, H-4), 4.28 (1H, aq, *J* 3.7 Hz, H-3), 4.39 (1H, t, $J_{5,5\text{-OH}}$ 5.4 Hz, $J_{5',5\text{-OH}}$ 5.4 Hz, 5-OH), 4.44 (1H, ddd, $J_{1,2}$ 4.6 Hz, $J_{2\text{-OH},2}$ 7.4 Hz, $J_{2,3}$ 3.7 Hz, H-2), 4.71 (1H, d, $J_{3,3\text{-OH}}$ 4.1 Hz, 3-OH), 4.83 (1H, d, $J_{1,2}$ 4.6 Hz, H-1), 5.06 (1H, d,

$J_{2,2\text{-OH}}$ 7.4 Hz, 2-OH); δ_C (125 MHz, Acetone-d_6) 14.4 (q, CH_3), 21.5, 23.3, 29.4, 29.8, 30.1, 32.5, 51.8 (7 × t, CH_2), 63.0 (t, C-5), 77.7, 78.2, 88.8, 94.7 (4 × d, C-3, C-2, C-4, C-1); ν_{max} (KBr disc) 3450–3500 (br. s, OH), 1301 (s, S=O, asymm. stretch), 1135 (s, S=O, symm. stretch) cm^{-1}; *m/z* (ESI)$^+$ 953.4 (3M+Na^+, 29), 948.5 (3M+NH_4^+, 7), 643.3 (2M+Na^+, 94), 638.3 (2M+NH_4^+, 85), 333.1 (M+Na^+, 58), 328.2 (M+NH_4^+, 100%). HRMS *m/z* calcd for $C_{13}H_{26}O_6S$ [M+Na]$^+$: 333.1348. Found: 333.1340.

3.22. β-D-Arabinofuranosyl decyl sulfone (6d)

Procedure C: Method as described above, except flash column chromatography (chloroform/isopropyl alcohol, 9:1) afforded de-protected decyl sulfone **6c** (103 mg, 75%) as a waxy white solid, mp 92–93 °C; $[\alpha]_D^{25}$ +183 (*c*, 1.1 in acetone); δ_H (500 MHz, acetone-d_6) 0.88 (3H, t, *J* 6.8 Hz, CH_3), 1.25–1.37 (12H, m, CH_2), 1.44 (2H, quin., *J* 7.2 Hz, CH_2), 1.79 (2H, quin., *J* 7.8 Hz, CH_2), 3.10 (1H, dt, *J* 8.0 Hz, *J* 14.1 Hz, C*H*H′), 3.25 (1H, dt, *J* 7.9 Hz, *J* 14.1 Hz, CH*H*′), 3.76–3.86 (2H, m, H-5, H-5′), 4.06 (1H, aq, *J* 3.8 Hz, H-4), 4.28 (1H, aq, *J* 3.4 Hz, H-3), 4.39 (1H, t, $J_{5,5\text{-OH}}$ 5.3 Hz, $J_{5',5\text{-OH}}$ 5.3 Hz, 5-OH), 4.44 (1H, app. quin., *J* 3.3 Hz, H-2), 4.71 (1H, d, $J_{3,3\text{-OH}}$ 3.9 Hz, 3-OH), 4.83 (1H, d, $J_{1,2}$ 4.6 Hz, H-1), 5.06 (1H, d, $J_{2,2\text{-OH}}$ 7.3 Hz, 2-OH); δ_C (125 MHz, acetone-d_6) 14.4 (q, CH_3), 21.6, 23.4, 29.4, 30.0, 30.1, 30.3, 31.6, 32.7, 51.8 (9 × t, CH_2), 63.0 (t, C-5), 77.7, 78.2, 88.8, 94.7 (4 × d, C-3, C-2, C-4, C-1); ν_{max} (KBr disc) 3450–3500 (br s, OH), 1303 (s, S=O, asymm. stretch), 1135 (s, S=O, symm. stretch) cm^{-1}; *m/z* (ESI)$^+$ 699.3 (2M+Na^+, 77), 694.4 (2M + NH_4^+, 100), 361.2 (M+Na^+, 56), 356.2 (M + NH_4^+, 92%). HRMS *m/z* calcd for $C_{15}H_{30}O_6S$ [M+Na]$^+$: 316.1661. Found: 316.1653. (Found: C, 52.97; H, 8.78. $C_{15}H_{30}O_6S$ requires C, 53.23; H, 8.93%).

3.23. β-D-Arabinofuranosyl dodecyl sulfone (6e)

Procedure C: Method as described above afforded de-protected dodecyl sulfone **6e** (87 mg, 94%) as a waxy solid; $[\alpha]^{23}$ −15 (*c*, 1.0 CH_3OH); δ_H (400 MHz, DMSO-d_6) 0.85 (3H, t, *J* 6.6 Hz, alkyl CH_3), 1.22–1.38 (16H, m, alkyl CH_2) 1.62–1.69 (2H, m, alkyl CH_2), 3.01–3.22 (2H, m, alkyl CH_2), 3.52 (1H, dd, $J_{4,5}$ 6.6 Hz, $J_{5,5'}$ 11.4 Hz, H-5), 3.58 (1H, dd, $J_{4,5'}$ 4.3 Hz, $J_{5,5'}$ 11.4 Hz, H-5′), 3.77–3.81 (1H, m, H-4), 3.99 (1H, at, J_{3-4} 5.1, H-3), 4.29 (1H, at, J_{2-3} 5.3, H-2), 4.80 (1H, d, $J_{1,2}$ 5.6 Hz H-1); δ_C (100.6 MHz, $CDCl_3$) 14.8 (alkyl CH_3), 21.1, 23.0, 28.9, 29.4, 29.6, 29.6, 29.8, 29.9, 30.0, 32.2, 51.0 (11 × alkyl CH_2), 62.7 (C-5), 76.0 (C-3), 77.5 (C-2), 87.6 (C-4), 93.9 (C-1); *m/z* (ES$^+$) 389 (M+Na^+, 100%); HRMS (ES$^+$) Calculated $NaC_{17}H_{34}O_6S$ 389.1968. Found: 389.1973).

3.24. β-D-Arabinofuranosyl tetradecyl sulfone (6f)

Procedure C: Method as described above, except reaction solvent (MeOH/EtOAc, 1:1, v/v) and flash column chromatography (chloroform/isopropyl alcohol, 9:1) afforded de-protected tetradecyl sulfone **6f** (250 mg, 88%) as a waxy white solid, m.p. 103–104 °C; $[\alpha]_D^{25}$ +175 (*c*, 1.1 in acetone); ν_{max} (KBr disc) 3450–3500 (br s, OH), 1307 (s, S=O, asymm. stretch), 1135 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, acetone-d_6) 0.88 (3H, t, *J* 6.8 Hz, CH_3), 1.24–1.38 (20H, m, CH_2), 1.44 (2H, quin., *J* 7.7 Hz, CH_2), 1.79 (2H, quin., *J* 7.9 Hz, CH_2), 3.10 (1H, dt, *J* 8.0 Hz, *J* 14.0 Hz, C*H*H′), 3.25 (1H, dt, *J* 7.9 Hz, *J* 14.0 Hz, CH*H*′), 3.77–3.85 (2H, m, H-5, H-5′), 4.06 (1H, aq, *J* 3.8 Hz, H-4), 4.28 (1H, aq, *J* 3.7 Hz, H-3), 4.38 (1H, t, $J_{5,5\text{-OH}}$ 5.4 Hz, $J_{5',5\text{-OH}}$ 5.4 Hz, 5-OH), 4.44 (1H, app. quin., *J* 3.6 Hz, H-2), 4.71 (1H, d, $J_{3,3\text{-OH}}$ 4.1 Hz, 3-OH), 4.83 (1H, d, $J_{1,2}$ 4.7 Hz, H-1), 5.05 (1H, d, $J_{2,2\text{-OH}}$ 7.4 Hz, 2-OH); δ_C (125 MHz, acetone-d_6) 14.4 (q, CH_3), 21.6, 23.4, 29.4, 29.7, 29.8, 29.8, 29.9, 30.1, 30.3, 30.3, 30.4, 32.7, 51.8 (13 × t, CH_2), 63.0 (t, C-5), 77.7, 78.2, 88.8, 94.7 (4 × d, C-3, C-2, C-4, C-1); *m/z* (ESI)$^+$ 811.5 (2M+Na^+, 37), 806.5 (2M + NH_4^+, 95), 417.2 (M+Na^+, 31), 412.3 (M + NH_4^+, 86%). HRMS *m/z* calcd for $C_{19}H_{38}O_6S$ [M+Na]$^+$: 417.2287. Found: 417.2282. (Found: C, 57.83; H, 9.74. $C_{19}H_{38}O_6S$ requires C, 57.84; H, 9.71).

3.25. β-D-Arabinofuranosyl hexadecyl sulfone (6g)

Procedure C: Method as described above, except reaction solvent (EtOAc) and flash column chromatography (chloroform/isopropyl alcohol, 9:1) afforded de-protected sulfone **6g** (200 mg, 81%) as a waxy white solid, mp 110–111 °C; $[\alpha]_D^{25}$ +149 (*c*, 1.1 in acetone); ν_{max} (KBr disc) 3450–3500 (br s, OH), 1301 (s, S=O, asymm. stretch), 1135 (s, S=O, symm. stretch) cm^{-1}; δ_H (500 MHz, acetone-d_6) 0.88 (3H, t, *J* 6.7 Hz, alkyl CH_3), 1.22–1.39 (24H, m, alkyl CH_2), 1.45 (2H, quin., *J* 7.1 Hz, CH_2), 1.80 (2H, quin., *J* 7.7 Hz, CH_2), 3.10 (1H, dt, *J* 8.0 Hz, *J* 13.7 Hz, C*H*H′), 3.26 (1H, dt, *J* 7.4 Hz, *J* 13.7 Hz, CH*H*′), 3.77–3.86 (2H, m, H-5, H-5′), 4.06 (1H, aq, *J* 3.9 Hz, H-4), 4.29 (1H, aq, *J* 3.5 Hz, H-3), 4.39 (1H, t, $J_{5,5\text{-OH}}$ 5.4 Hz, $J_{5',5\text{-OH}}$ 5.4 Hz, 5-OH), 4.44 (1H, app. quin., *J* 3.6 Hz, H-2), 4.71 (1H, d, $J_{3,3\text{-OH}}$ 4.1 Hz, 3-OH), 4.83 (1H, d, $J_{1,2}$ 4.7 Hz, H-1), 5.05 (1H, d, $J_{2,2\text{-OH}}$ 7.3 Hz, 2-OH); δ_C (125 MHz, acetone-d_6) 14.4 (q, CH_3), 21.5, 23.3, 25.5, 30.0, 30.1, 30.1, 30.2, 30.3, 30.3, 30.4, 30.4, 30.4, 30.5, 32.7, 51.8 (15 × t, CH_2), 63.0 (t, C-5), 77.6, 78.8, 88.8, 94.6 (4 × d, C-3, C-2, C-4, C-1); *m/z* (ESI)$^+$ 867.5 (2M+Na^+, 44), 862.5 (2M + NH_4^+, 100), 445.3 (M+Na^+, 39), 440.3 (M + NH_4^+, 95%). HRMS *m/z* calcd for $C_{21}H_{42}O_6S$ [M+Na]$^+$: 445.2600. Found 445.2593. (Found: C, 59.70; H, 10.07. $C_{21}H_{42}O_6S$ requires C, 59.68; H, 10.02).

3.26. Spot culture method for testing of anti-mycobacterial activity

Purified test compounds **6a–g** were prepared in DMSO at a range of concentrations up to 100 mg/mL. These stock solutions were added into different wells of 6-well plates, with 5 μL DMSO alone added to control wells (0.1% v/v). Molten MB agar (5 mL) containing OADC (Oleic acid-Albumin-Dextrose-Catalase, Difco) was poured immediately into the wells of the 6-well plates containing the extracts with thorough mixing. Once solidified, the MB agar containing test reagents and controls was inoculated with 5 μL of a 10^5 dilution of a mid-log phase culture (OD 1.0) of *M. bovis* BCG Pasteur containing approximately 500 cells. The cells were allowed to soak onto MB agar before the plates were covered, sealed with parafilm, inverted and incubated at 37 °C for 7–14 days. The resulting circular spot cultures were photographed using a BioRad Gel-Doc 2000 system.

Acknowledgements

We gratefully acknowledge financial support from the EPSRC (Project Grant D051495/1) and the Leverhulme Trust (Project Grant F/08 341/E).

References

1. Dye, C.; Scheele, S.; Dolin, P.; Pathania, V.; Raviglione, M. C. *J. Am. Med. Assoc.* **1999**, *282*, 677–686.
2. Aziz, M. A.; Wright, A.; Laszlo, A.; De Muynck, A.; Portaels, F.; Van Deun, A.; Wells, C.; Nunn, P.; Blanc, L.; Raviglione, M. *Lancet* **2006**, *368*, 2142–2154.
3. See: http://www.taacf.org.
4. Lowary, T. L. *Mini Rev. Med. Chem.* **2003**, *3*, 689–702.
5. For some leading references see: (a) Maddy, J. A.; Bansal, N.; Bermudez, L. E.; Comber, R. N.; Orme, I. M.; Suling, W. J.; Wilson, L. N.; Reynolds, R. C. *Biorg. Med. Chem. Lett.* **1998**, *8*, 237–242; (b) Pathak, A. K.; Pathak, V.; Madry, J. A.; Suling, W. J.; Gurcha, S. S.; Besra, G. S.; Reynolds, R. C. *Bioorg. Med. Chem. Lett.* **2002**, *10*, 923–928; (c) Pathak, A. K.; Pathak, V.; Madry, J. A.; Suling, W. J.; Gurcha, S. S.; Besra, G. S.; Reynolds, R. C. *Bioorg. Med. Chem. Lett.* **2002**, *10*, 3145–3151; (d) Chaumontet, M.; Pons, V.; Marotte, K.; Prandi, J. *Tetrahedron Lett.* **2006**, *47*, 1113–1116.

6. For some leading references see: (a) Cren, S.; Gurcha, S. S.; Blake, A. J.; Besra, G. S.; Thomas, N. R. *Org. Biomol. Chem.* **2004**, *2*, 2418–2420; (b) Pathak, A. K.; Pathak, V.; Kulshrestha, M.; Kinnaird, D.; Suling, W. J.; Gurcha, S. S.; Besra, G. S.; Reynolds, R. C. *Tetrahedron* **2003**, *59*, 10239–10248; (c) Wen, X.; Crick, D. C.; Brennan, P. J.; Hultin, P. G. *Bioorg. Med. Chem. Lett.* **2003**, *11*, 3579–3587; (d) Burton, A.; Wyatt, P.; Boons, G.-J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2375–2382; (e) Dykhuizen, E. C.; May, J. F.; Tongpenyai, A.; Kiessling, L. L. *J. Am. Chem. Soc.* **2008**, *130*, 6706–6707.
7. For some leading references see: (a) Marotte, K.; Ayad, T.; Genisson, Y.; Besra, G. S.; Baltas, M.; Prandi, J. *Eur. J. Org. Chem.* **2003**, 2557–2565; (b) Pathak, A. K.; Pathak, V.; Maddry, J. A.; Suling, W. J.; Gurcha, S. S.; Besra, G. S.; Reynolds, R. C. *Bioorg. Med. Chem.* **2001**, *9*, 3145–3151; (c) Joe, M.; Lowary, T. L. *Carbohydr. Res.* **2006**, *341*, 2723–2730; (d) Cociorva, O. M.; Gurcha, S. S.; Besra, G. S.; Lowary, T. L. *Bioorg. Med. Chem.* **2005**, *13*, 1369–1379; (e) Cociorva, O. M.; Lowary, T. L. *Carbohydr. Res.* **2004**, *339*, 853–865; (f) Maddry, J. A.; Bansal, N.; Bermudez, L. E.; Comber, R. N.; Orme, I. M.; Suling, W. J.; Wilson, L. N.; Reynolds, R. C. *Bioorg. Med. Chem. Lett.* **2008**, *8*, 237–242; (g) Smellie, I. A.; Bhakta, S.; Sim, E.; Fairbanks, A. J. *Org. Biomol. Chem.* **2007**, *5*, 2257–2266.
8. (a) Centrone, C. A.; Lowary, T. L. *J. Org. Chem.* **2002**, *67*, 8862–8870; (b) Centrone, C. A.; Lowary, T. L. *Biorg. Med. Chem.* **2004**, *12*, 5495–5503.
9. (a) Davis, C. B.; Hartnell, R. D.; Madge, P. D.; Owen, D. J.; Thomson, R. J.; Chong, A. K. J.; Coppel, R. L.; von Itzstein, M. *Carbohydr. Res.* **2007**, *342*, 1773–1780; (b) Owen, D. J.; Davis, C. B.; Hartnell, R. D.; Madge, P. D.; Owen, D. J.; Thomson, R. J.; Chong, A. K. J.; Coppel, R. L.; von Itzstein, M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2274–2277.
10. Wilkinson, B. L.; Long, H.; Sim, E.; Fairbanks, A. J. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 6265–6267.
11. van der Klien, P. A. M.; de Nooy, A. E. J.; van der Marel, G. A.; van Boom, J. H. *Synthesis* **1991**, 347–349.
12. Mereyala, H. B.; Lingannagaru, S. R. *Tetrahedron* **1997**, *53*, 17501–17512.
13. Maryanoff, B. E.; Reitz, A. B.; Tutwiler, G. F.; Benkovic, S. J.; Benkovic, P. A.; Pilkis, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 7851–7853.
14. Acton, E. M.; Fujiwara, A. N.; Goodman, L.; Henry, D. W. *Carbohydr. Res.* **1974**, *33*, 135–151.
15. Hiranuma, S.; Kajimoto, T.; Wong, C.-H. *Tetrahedron Lett.* **1994**, *35*, 5257–5260.
16. For some previous examples of dithioacetal formation by reaction of thiols with furanose sugars see: (a) Blumberg, K.; Van Es, T. *S. Afr. J. Chem.* **1986**, *39*, 201–207; (b) Blumberg, K.; Van Es, T. *Carbohydr. Res.* **1981**, *88*, 253–266; (c) Hughes, N. A.; Robson, R.; Saeed, S. A. *J. Chem. Soc., Chem. Commun.* **1968**, 1381–1383.
17. (a) Anderton, M. C.; Bhakta, S.; Besra, G. S.; Jeavons, P.; Eltis, L. D.; Sim, E. *Mol. Microbiol.* **2006**, *59*, 181–192; (b) Madikane, V. E.; Bhakta, S.; Russell, A. J.; Campbell, W. E.; Claridge, T. D.; Elisha, B. G.; Davies, S. G.; Smith, P.; Sim, E. *Bioorg. Med. Chem.* **2007**, *15*, 3579–3586.
18. Collins, L. A.; Franzblau, S. G. *Antimicrob. Agents Chemother.* **1997**, *41*, 1004–1009.
19. The importance of lipophilic chain length for recognition of donor analogues of DPA by arabinosyltransferases has been reported previously: See Lee, R. E.; Brennan, P. J.; Besra, G. S. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 951–954.
20. We thank referees for pointing out this possibility to us.