A Practical Silicon-Free Strategy for Differentiation of Hydroxy Groups in Arabinofuranose Derivatives

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Dedicated to the memory of the late Professor Leon V. Backinowsky

Abstract: Effective differentiation of 3,5-diol system and 2-hydroxy group in arabinofuranose derivatives, which is required for the preparation of building blocks useful for the synthesis of nucleoside analogues and oligosaccharide fragments of mycobacterial arabinogalactan and lipoarabinomannan, was achieved by using 3,5-di-*O*-benzoyl-1,2-*O*-benzylidene-β-D-arabinofuranose or 3-*O*-(chloroacetyl)-β-D-arabinofuranose 1,2,5-orthobenzoate, both readily accessible from inexpensive methyl α-D-arabinofuranoside via the corresponding glycosyl bromides. The use of expensive organosilicon protecting groups is completely avoided in this novel strategy, a feature that makes it amenable to scale-up.

Key words: carbohydrates, protecting groups, acetals, oligosaccharides, nucleosides

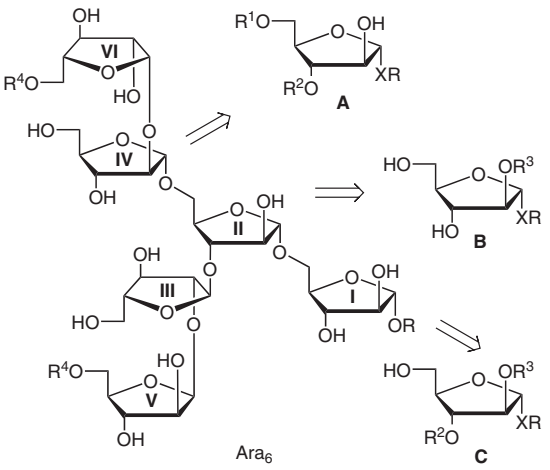
There has been a recent growth in interest in the synthesis of D-arabinofuranose (Ara) oligosaccharides related to the mycobacterial cell-wall components arabinogalactan, lipoarabinomannan, and arabinomannan of *Mycobacterium tuberculosis*,[1] because of the need to develop methods for the diagnosis, prevention, and treatment of human tuberculosis, which is a major health problem worldwide.[2] The nonreducing end of each of these polysaccharides consists of a common branched hexasaccharide motif (Ara_6) that plays an important role in the pathogenicity of mycobacteria (Scheme 1).[1]

Because the structure of Ara_6 contains both α-1–5-linkages (residue **I**) and β-1–2-linkages (residues **III** and **IV**) as well as a 3,5-branching (residue **II**), the building blocks **A**–**C**, selectively protected at O-2, O-3, and O-5 are required for the assembly of the hexasaccharide (Scheme 1). Various strategies have been developed for the preparation of selectively protected arabinofuranose monosaccharide building blocks (Scheme 2), none of which is free of problems.[1]

Building block **C** with a free 5-OH group can be prepared in a fairly straightforward manner by selective protection of the primary hydroxy group in the 2,3,5-triol **F** (Scheme 2) with one of several suitable protecting groups, such as benzoate,[3] trityl,[4] or *tert*-butyl(diphenyl)silyl,[1a] followed by blocking of the remaining secondary hydroxy groups and subsequent removal of the temporary protecting group from the primary hydroxy group. Alternatively, building block **C** can be prepared in one step by ring-opening of a 3-*O*-protected arabinose 1,2,5-orthobenzoate.[1h,5]

Arabinose thioglycosides with a nonprotected 2-hydroxy group (building block **A**) are accessible (Scheme 2) mainly through selective protection of the 3,5-diol function in arabinofuranose-based 2,3,5-triol **F** with cyclic organosilicon protecting groups such as 3,5-*O*-tetraisopropyldisiloxanylidene (TIPDS)[1c,e,i,j] or di-*tert*-butylsilyl (DTBS),[1a,b,e,g] which are introduced by using expensive reagents such as 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (**F** → **A1** or **A2**). Protection of the 2-OH group in building blocks **A1** or **A2** with an orthogonal protecting group gives rise to building blocks **D1** or **D2**, respectively, which are useful as glycosyl donors.[1a,b,e,i] Desilylation of building blocks **D1** or **D2** gives 3,5-diol **B** (**F** → **A** → **D** → **B**).[1a,g] Although this synthesis of building blocks **A** and **B** is very short and efficient, the preparative utility of this approach is somewhat restricted by the high cost of the reagents.

An alternative and more attractive approach (Scheme 2) for large-scale preparation of building block **A**, which is



Scheme 1 Structures of the common hexasaccharide moiety of mycobacterial arabinogalactan and lipoarabinomannan and of the key building blocks. R = aglycone; X = O or S; R^1, R^2, R^3 = protecting groups; R^4 = H or capping group.

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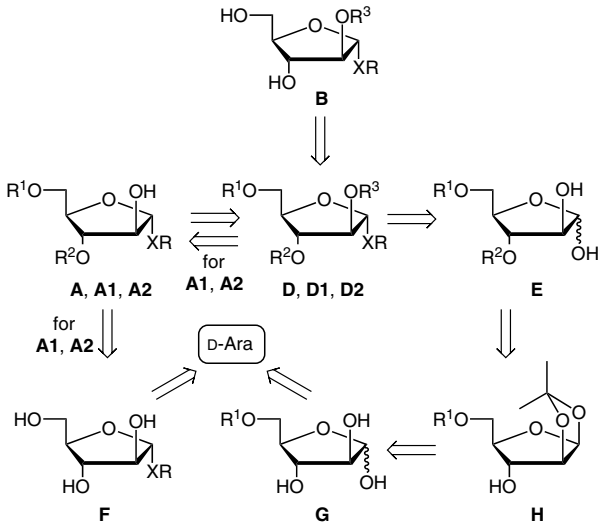
required for multistep syntheses of oligoarabinofuranosides,[6] relies on the introduction of a 1,2-*O*-isopropylidene group into the 5-*O*-silylated arabinose **G**[7] to give building block **H** followed by straightforward blocking of the 3-OH group with temporary protection and elaboration[1k] of the 1,2-diol **E**, obtained by removal of the 1,2-*O*-isopropylidene group (**G** → **H** → **E** → **D** → **A**). Selective protection of the 5-OH group of arabinose is vital for ensuring efficient formation of the furanose at the acetalization step (Scheme 2).



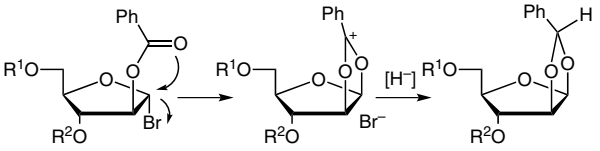
Scheme 2 Known approaches to the synthesis of building blocks **A** and **B**. R = aglycone; X = O or S; R^1,R^2,R^3 = protecting groups: for **A1** or **D1**, R^1R^2 = Si(*i*-Pr)$_2$OSi(*i*-Pr)$_2$ (TIPDS); for **A2** or **D2**, R^1R^2 = Si(*t*-Bu)$_2$ (DTBS); for **G** and **H**, R^1 = Si(*t*-Bu)Ph$_2$, Bz, Tr.

Here we describe an approach for the selective functionalization of arabinofuranose that extends the existing methodologies and which does not rely on the use of any organosilicon protecting groups.

We reasoned that the known problem of controlling the size of the sugar ring during formation of the 1,2-*O*-isopropylidene moiety in arabinose (the synthesis of building block **H** in Scheme 2) might be solved by the introduction of a cyclic 1,2-*O*-acetal moiety into a derivative with an existing furanose ring, rather than into an acyclic arabinose.

Such a cyclization is known in the pyranose series and is based on reductive debromination by sodium borohydride of glycopyranosyl bromides with a 2-*O*-benzoyl protecting group.[8] The reaction proceeds through neighboring-group participation of the acyl protecting group at the C-2 atom of the glycosyl bromide and it involves the generation of an acyloxonium ion. The ease of formation of this benzylic cation, which is stabilized by delocalization of the positive charge, is apparently the driving force for this reaction. Subsequent attack on the acyloxonium ion by a hydride anion leads to the 1,2-*O*-benzylidene derivative, which is the isolable product of the reaction.

We hypothesized that the reaction of 2-*O*-benzoylated glycosyl bromides with sodium borohydride might be extended to furanoses and might be used for the synthesis of 1,2-*O*-benzylidene derivatives of arabinofuranose (Scheme 3). Indeed, the related 3,5-di-*O*-(4-methylbenzoyl)-1,2-*O*-(4-methylbenzylidene)-β-L-arabinofuranose has been obtained (as an undesired product during the synthesis of 2-deoxy-L-ribose) by treatment of 2,3,5-tri-*O*-(4-methylbenzoyl)-α-L-arabinofuranosyl bromide with sodium cyanoborohydride.[9]



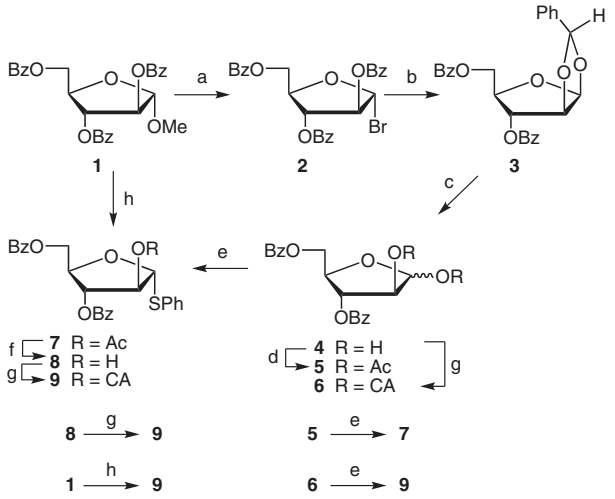
Scheme 3 Formation of 1,2-*O*-benzylidene acetal by reductive debromination of a 2-*O*-benzoylglycosyl bromide

The fully *O*-benzoylated arabinofuranosyl bromide **2**[10a] (Scheme 4), which is required for this transformation, can be prepared by treatment of readily available methyl tri-*O*-benzoyl-α-D-arabinofuranoside (**1**)[10] with hydrogen bromide in either acetic acid or dichloromethane.[5] Treatment of glycosyl bromide **2** with sodium borohydride in acetonitrile gave the desired 1,2-*O*-benzylidene acetal **3**, isolated as a single isomer in 90% yield. Acid hydrolysis removed the benzylidene function to give the 1,2-diol **4** (building block **E**) as a 1:1 anomeric mixture. The diol **4** was converted into the corresponding 1,2-di-*O*-acetate **5** or the 1,2-bis-*O*-chloroacetate **6** in high yields. Treatment of *O*-acetate **5** with benzenethiol and boron trifluoride etherate in dichloromethane gave thioglycoside **7** (building block **D**) with an orthogonal 2-*O*-acetyl protecting group as a single α-isomer in 85% yield. Similar treatment of 1,2-bis-*O*-chloroacetate **6** gave thioglycoside **9** with 2-*O*-chloroacetyl protecting groups as a single α-isomer in 83% yield.

The 2-*O*-acetyl protected derivative **7** was subjected to acid-catalyzed methanolysis under mild conditions;[11] this selectively cleaved the acetate esters, but did not affect the *O*-benzoyl groups, giving the 2-hydroxy derivative **8** (building block **A**) in 89% yield. The structure of the product **8** was supported by the upfield shift of the signal for H-2 in its ^{1}H NMR spectrum compared with that in the spectrum of the starting compound **7**. Chloroacetylation of the alcohol **8** by treatment with chloroacetic anhydride and 2,4,6-trimethylpyridine in dichloromethane gave thioglycoside **9**, identical to that described above, in 91% yield (Scheme 4).

As a result of the high efficiency of each step in the synthesis of phenyl thioglycoside **9** (building block **D**) in our approach, we developed a procedure for the preparation of **9** on a ~14-gram scale that involves only one chromatographic separation, that of purification of the final product **9**, which was obtained in 71% overall yield from the starting methyl glycoside **1** (Scheme 4, step *h*). Our procedure

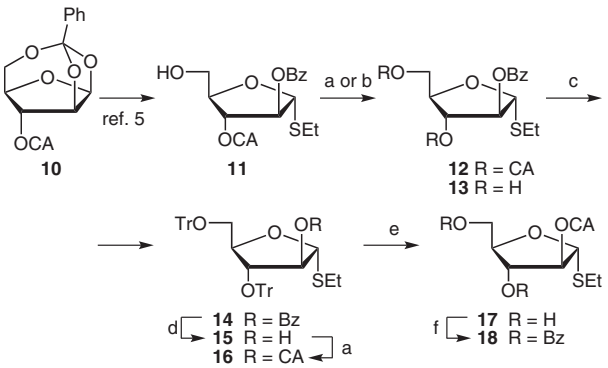
for the preparation of building blocks **A** and **D**, with a free or orthogonally protected hydroxy group at C-2, compares well with the protocols based on the use of organosilicon protecting groups (Scheme 2) in terms of both the overall efficiency and the cost of the reagents. The yield of thioglycoside **9** from commercially available D-arabinose is 32%, because methyl glycoside **1** can be easily prepared[10] in 45% yield and in multigram quantities from D-arabinose. The similar thioglycosides **D1** and **D2** (RX = TolS; R^3 = Bn), with much more expensive TIPDS and DTBS protecting groups (Scheme 2), were obtained from D-arabinose in 49%[1c] and 52%[1e] overall yields, respectively.



Scheme 4 *Reagents and conditions*: (a) 32% HBr/AcOH, CH_2Cl_2, ~20 °C; (b) $NaBH_4$, MeCN, ~20 °C (90%, two steps); (c) CH_2Cl_2–TFA–H_2O (100:10:1), ~20 °C (90%); (d) Ac_2O, py (93%); (e) PhSH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C → 20 °C (85% of **7**, 83% of **9**); (f) 4% HCl/MeOH, CH_2Cl_2, ~20 °C (89%); (g) $(ClCH_2CO)_2O$, 2,4,6-trimethylpyridine, CH_2Cl_2, 0 °C (76% of **6** from **3**, two steps; 91% of **9**); (h) 1. HBr, CH_2Cl_2, 0 °C; 2. $NaBH_4$, MeCN; 3. CH_2Cl_2–TFA–H_2O (100:10:1); 4. $(ClCH_2O)_2O$, 2,4,6-trimethylpyridine, CH_2Cl_2, 0 °C. 5. PhSH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C → 20 °C; 6. chromatography (silica gel) (71% of **9** with respect to **1** over five steps; ~14 g scale). CA = chloroacetyl.

The similar building block **D** with an ethanesulfenyl aglycon (compound **18** in Scheme 5) and building block **B** with two hydroxy groups at C-3 and C-5 (compound **13** in Scheme 5) can be prepared by another route that relies on the ready availability[1h] of 3-*O*-protected arabinose 1,2,5-orthobenzoates. We have recently studied the ring-opening reactions of 3-*O*-acyl-β-D-arabinofuranose 1,2,5-orthobenzoates with thiols and have demonstrated their synthetic utility.[5] In the context of this communication, it is important to note that a novel β-D-arabinofuranose 1,2,5-orthobenzoate with a 3-*O*-chloroacetyl group **10**[5] can be transformed into the corresponding ethyl thioglycoside **11** with a 5-hydroxy group in 94% yield.[5] Chloroacetylation of the single hydroxy group of **11** gave thioglycoside **12** (yield 88%) with selectively removable *O*-chloroacetyl groups at O-3 and O-5; this product is useful as glycosyl donor **D**, corresponding to the 3,5-diol building block **B**. Removal of the chloroacetyl groups from **11** by treatment with aqueous pyridine cleanly gave diol **13** (building block **B**) in 86% yield (Scheme 5), which corresponds to 53% yield of **13** from methyl glycoside **1** or 24% overall yield from D-arabinose. Compare the latter yield to the 49% overall yield of building block **B** (RX = TolS; R^3 = Bn) that is obtained by using the much more expensive TIPDS[1c] protecting group.

The diol **13** can be converted into compound **18** (building block **D**, similar to **9**) by the selective protection and deprotection operations outlined in Scheme 5. Although most steps proceed efficiently, the yield of thioglycoside **18** with the selectively removable 2-*O*-chloroacetyl group was only 34% from diol **13**. This value corresponds to 18% yield from methyl glycoside **1** or 8% overall yield from D-arabinose. The large number of steps and the overall inefficiency make this route less favorable for the preparation of building block **D** (compounds **9** and **18**) than the route via the 1,2-*O*-benzylidene derivative (Scheme 4).



Scheme 5 *Reagents and conditions*: (a) $(ClCH_2CO)_2O$, 2,4,6-trimethylpyridine, CH_2Cl_2 (88% **12**, 99% of **16**); (b) py–H_2O (2:1), 60 °C (86% of **13**); (c) $TrClO_4$, Et_3N, CH_2Cl_2 (90% of **14** from **13**); (d) NaOMe, MeOH, CH_2Cl_2 (84%); (e) AcOH, H_2O, 80 °C (54% of **17** from **16**); (f) BzCl, py (97%). CA = chloroacetyl.

Compounds **9**, **11**, and **12** have recently been used in the synthesis of spacer-containing glycosides of the hexaarabinofuranoside fragment of *M. tuberculosis* LAM, which after conjugation with recombinant mycobacterial proteins MPB-64 and Rv0934 produced artificial tuberculosis antigens.[12]

In conclusion, we achieved effective differentiation of 3,5-diol system and 2-hydroxy group in arabinofuranose derivatives by using 3,5-di-*O*-benzoyl-1,2-*O*-benzylidene-β-D-arabinofuranose or 3-*O*-chloroacetyl-β-D-arabinofuranose 1,2,5-orthobenzoate, both of which are readily accessible from cheap methyl α-D-arabinofuranoside via the corresponding glycosyl bromide. An appealing feature of this practical strategy is the complete avoidance of the use of expensive organosilicon protecting groups, which may prove to be essential for large-scale syntheses. The importance of our finding is not limited to oligosaccharide synthesis, because the known syntheses of various nucleoside analogues,[13] some of which are potential antivirals,[14] often rely on effective differentiation of the 3,5-diol

system[15] and the 2-hydroxy group in arabinofuranose derivatives.

The reactions were performed by using commercial reagents (Aldrich, Fluka, Acros Organics). Solvents were distilled, purified, and dried (where appropriate) by standard procedures. Column chromatography was performed on silica gel 60 (40–63 μm; Merck). TLC was carried out on plates of silica gel 60 on glass or aluminum foil (Merck). Spots were visualized under UV radiation or by heating the plates after immersion in a 1:10 (v/v) mixture of 85% aq H_3PO_4 and 95% aq EtOH. The ^1H and ^{13}C NMR spectra were recorded for solutions in $CDCl_3$ on a Bruker AC-200 instrument (200.13, and 50.32 MHz, respectively) or a Bruker AM-300 instrument (300.13, and 75.48 MHz, respectively). The ^1H NMR chemical shifts are referred to the residual signal of $CHCl_3$ (δ_H = 7.27 ppm), whereas the ^{13}C NMR shifts are referred to the $CDCl_3$ signal (δ_C = 77.0 ppm). Signals in the NMR spectra were assigned by means of 2D-spectroscopy (COSY, HSQC, NOESY, and HMBC) and by APT (DEPT-135 or JMODXH) experiments. High-resolution mass spectra (ESI) were recorded on a Bruker micrOTOF II mass spectrometer by using 2×10^{-5} M solns in MeCN or MeOH. Optical rotations were measured using a PU-07 automatic polarimeter (Russia). IR spectra were recorded on a Bruker ALPHA-T FTIR spectrometer over the 500–4000 cm^{-1} range by using KBr pellets.

3,5-Di-*O*-benzoyl-1,2-*O*-benzylidene-β-D-arabinofuranose (3)

Methyl 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranoside (**1**)[10] (10.0 g, 21.0 mmol) was dissolved in anhyd CH_2Cl_2 (21 mL) and the soln was cooled to 0 °C. A 32% soln of HBr in AcOH was prepared by dropwise addition a soln of H_2O (5 mL) in AcOH (18.3 mL) to a soln of AcBr (27.4 mL) in AcOH (15 mL) at 0 °C. The two solns were mixed and stirred at 0 °C for 30 min, then diluted with CH_2Cl_2 (500 mL), washed sequentially with ice-cold H_2O (2 × 500 mL) and ice-cold sat. aq $NaHCO_3$ (500 mL), filtered through a cotton-wool plug, concentrated under reduced pressure, and dried in vacuo to give 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl bromide (**2**).

The crude glycosyl bromide **2** was dissolved in anhyd MeCN (42 mL), and $NaBH_4$ (1.6 g, 42.0 mmol) was added. The mixture was stirred for 12 h at 20 °C then diluted with CH_2Cl_2 (500 mL), washed with H_2O (2 × 500 mL), filtered through Celite, and concentrated. The residue was dried in vacuo and crystallized from PE–EtOAc to give benzylidene derivative **3** as white crystals. Concentration of mother liquors and purification of the residue by column chromatography [silica gel, toluene–EtOAc (2:1)] gave an additional portion of **3** as a white solid; combined yield of **3**: 8.34 g (90%); mp 159–162 °C (PE–EtOAc); $[\alpha]_D^{22}$–2.2 (*c* 1.0, $CHCl_3$); R_f = 0.63 (toluene–EtOAc, 2:1).

IR (KBr): 1723, 1601, 1452, 1280, 1268 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 4.51–4.60 (m, 2 H, H-5a, H-5b), 4.63–4.75 (m, 1 H, H-4), 4.92 (d, *J* = 4.0 Hz, 1 H, H-2), 5.59 (s, 1 H, H-3), 6.05 (s, 1 H, PhC*H*), 6.25 (d, *J* = 4.0 Hz, 1 H, H-1), 7.35–7.65 (m, 11 H, Ph), 8.02–8.13 (m, 4 H, Ph).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 64.3 (C-5), 77.6 (C-3), 84.1 (C-2), 85.5 (C-4), 105.7 (Ph*C*H), 106.2 (C-1), 126.5, 127.9, 128.2, 128.3, 128.4, 128.5, 129.1, 129.2, 129.4, 129.6, 129.7, 129.8, 132.8, 133.0, 133.6, 135.5 (Ph), 165.3, 166.0 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{22}NaO_7$: 469.1258; found: 469.1263.

Anal. Calcd for $C_{26}H_{22}O_7$: C, 69.95; H, 4.97. Found: C, 69.55; H, 5.10.

3,5-Di-*O*-benzoyl-D-arabinofuranose (4)

A 9:1 mixture of TFA and H_2O (1.5 mL) was added to a soln of acetal **3** (1.03 g, 2.3 mmol) in CH_2Cl_2 (15 mL). The mixture was stirred for 4 h at 20 °C then diluted with CH_2Cl_2 (200 mL) and washed successively with H_2O (200 mL) and sat. aq $NaHCO_3$ (200 mL). The organic phase was filtered through a layer of a ~1:1 mixture of (v/v) Celite and powdered Na_2SO_4 then concentrated and dried in vacuo to give a white solid; yield: 0.74 g (90%; 1:1 mixture α- and β-anomers); R_f = 0.20 (toluene–EtOAc, 4:1).

IR (KBr): 3065, 2929, 1721, 1602, 1452, 1276 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 4.25–4.37 (m, 1.5 H, H-2β, H-4β, H-4α), 4.40–4.71 (m, 2.5 H, H-5aα, H-5bα, H-5aβ, H-5bβ, H-2α), 5.04 (dd, *J* = 5.1, 2.4 Hz, 0.5 H, H-3α), 5.03 (dd, *J* = 5.2, 2.3 Hz, 0.5 H, H-3β), 5.28 (m, 1 H, H-1α, H-1β), 7.22–7.56 (m, 4 H), 7.85–8.02 (m, 6 H).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 64.2 (C-5β), 65.5 (C-5α), 76.2 (C-2β), 78.9 (C-4β), 79.7 (C-2α), 80.4 (C-3β), 81.4 (C-4α), 81.7 (C-3α), 96.8 (C-1β), 102.8 (C-1α), 128.3, 128.4, 128.5, 129.7, 129.8, 133.2, 133.7 (Ph), 165.5, 165.8, 166.0, 166.1 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{18}O_7Na$: 381.0950; found: 381.0966.

1,2-Di-*O*-acetyl-3,5-di-*O*-benzoyl-D-arabinofuranose (5)

Ac_2O (0.5 mL, 1.27 mmol) was added to a soln of diol **4** (90.7 mg, 0.25 mmol) in pyridine (1 mL). After 30 min, the mixture was diluted with CH_2Cl_2 (50 mL) and washed successively with H_2O (50 mL), 1 M aq $KHSO_4$ (50 mL), H_2O (50 mL), and sat. aq $NaHCO_3$ (50 mL). The organic phase was concentrated and dried in vacuo to give a colorless syrup; yield: 104 mg, (93%; 1:1 mixture α- and β-anomers), R_f = 0.47 (toluene–EtOAc, 5:1).

^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.06 (s, 1.5 H, CH_3), 2.07 (s, 1.5 H, CH_3), 2.14 (s, 1.5 H, CH_3), 2.21 (s, 1.5 H, CH_3), 4.44–4.81 (m, 3 H, H-5aα, H-5bα, H-5aβ, H-5bβ, H-4α, H-4β), 5.41 (s, 0.5 H, H-2α), 5.46 (d, 0.5 H, *J* = 3.2 Hz, H-3α), 5.60 (dd, 0.5 H, *J* = 7.0, 4.7 Hz, H-2β), 5.83 (d, 0.5 H, *J* = 7.0 Hz, H-3β), 6.32 (s, 0.5 H, H-1α), 6.49 (d, 0.5 H, *J* = 4.7 Hz, H-1β), 7.34–7.50 (m, 4 H, Ph), 7.51–7.65 (m, 2 H, Ph), 7.99–8.11 (m, 4 H, Ph).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.8, 20.9 (*C*H_3CO), 63.4 (C-5β), 64.5 (C-5α), 75.1 (C-2β), 75.3 (C-3β), 77.4 (C-2α), 79.8 (C-4α), 80.4 (C-3α), 83.1 (C-4β), 93.5 (C-1β), 99.3 (C-1α), 128.2 (Ph), 129.7 (Ph), 133.1, 133.6 (Ph), 165.4, 165.7, 169.1, 169.6 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{22}NaO_9$: 465.1162; found: 465.1156.

3,5-Di-*O*-benzoyl-1,2-bis-*O*-(chloroacetyl)-D-arabinofuranose (6)

2,4,6-Trimethylpyridine (0.36 mL, 2.7 mmol) was added to a stirred soln of diol **4** (120 mg, 0.33 mmol) in anhyd CH_2Cl_2 (1.2 mL). The mixture was cooled to 0 °C, and a soln of $(ClCH_2CO)_2O$ (230 mg, 1.34 mmol) in CH_2Cl_2 (1.3 mL) was added dropwise. The mixture was stirred at 0 °C for 30 min, then diluted with CH_2Cl_2 (50 mL) and washed successively with H_2O (50 mL), 1 M aq $KHSO_4$ (50 mL), H_2O (50 mL), and sat. aq $NaHCO_3$ (50 mL). The organic phase was filtered through a layer of a ~1:1 (v/v) mixture of silica gel and powdered Na_2SO_4, concentrated, and dried in vacuo to give a white solid; yield: 130 mg (76% from **3** over two steps; 1:1.5 mixture α- and β-anomers); R_f = 0.59 (toluene–EtOAc, 5:1).

IR (KBr): 2958, 1769, 1719, 1275 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.84 (s, 1.6 H, CH_2Cl), 3.91 (s, 1.6 H, CH_2Cl), 4.01 (s, 2.4 H, CH_2Cl), 4.04 (s, 2.4 H, CH_2Cl), 4.42–4.71 (m, 3 H, H-5αa, H-5bα, H-5aβ, H-5bβ, H-4α, H-4β), 5.41 (s, 0.8 H, H-2α, H-3α), 5.60 (dd, *J* = 4.6, 2.2 Hz, 0.6 H, H-2β), 5.71–5.87 (m, 0.6 H, H-3β), 6.31 (s, 0.4 H, H-1α), 6.47 (d, *J* = 4.6 Hz, 0.6 H, H-1β), 7.27–7.56 (m, 12 H, Ph), 7.87–8.02 (m, 8 H, Ph).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 40.38, 40.42, 40.72, 40.80 (4 × CH_2Cl), 63.28 (C-5α), 64.4 (C-5β), 75.2 (C-3β), 76.9 (C-3α), 77.1 (C-2β), 80.8 (C-4β), 81.9 (C-2α), 83.9 (C-4α), 95.2 (C-1β), 100.4 (C-1α), 128.6, 128.7, 128.9, 123.0, 130.1, 133.56, 134.2 (Ph), 165.1, 165.4, 165.5, 165.7, 165.8, 165.9, 166.2 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{20}Cl_2NaO_9$: 533.0377; found: 533.0375.

Phenyl 2-*O*-Acetyl-3,5-di-*O*-benzoyl-1-thio-α-D-arabinofuranoside (7)

$BF_3{\cdot}Et_2O$ (30 μL, 0.24 mmol) was added to a stirred soln of acetate **5** (57 mg, 0.12 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The mixture was stirred for 10 min then PhSH (25 μL, 0.25 mmol) was added. After 1 h, the reaction was quenched by addition of Et_3N (50 μL). The mixture was diluted with CH_2Cl_2 (50 mL), washed with H_2O (50 mL), concentrated, and dried in vacuo. The residue was purified by column chromatography [silica gel, PE–EtOAc (9:1 to 5:1)] to give a colorless syrup; yield: 54 mg (85%); $[\alpha]_D^{22}$ +104.3 (*c* 1.0, $CHCl_3$); R_f = 0.60 (toluene–EtOAc, 10:1).

IR (KBr): 3062, 2960, 1749, 1723, 1602, 1452, 1273 cm^{-1}.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.06 (s, 3 H, CH_3), 4.71–4.91 (m, 2 H, H-5a, H-5b), 4.77–4.85 (m, 1 H, H-4), 5.50 (s, 2 H, H-2, H-3), 5.68 (s, 1 H, H-1), 7.22–7.69 (m, 11 H, Ph), 8.07–8.13 (m, 4 H, Ph).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6 (CH_3), 63.3 (C-5), 77.0 (C-3), 81.2 (C-2), 81.7 (C-4), 91.3 (C-1), 127.1, 127.8, 128.3, 128.5, 129.9, 130.6, 132.2, 133.1, 133.4, 133.7, 136.9 (Ph), 165.5, 166.0, 169.5 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{24}NaO_7S$: 515.1140; found: 515.1135.

Phenyl 3,5-Di-*O*-benzoyl-1-thio-α-D-arabinofuranoside (8)

A soln of HCl in MeOH [prepared by addition of AcCl (0.8 mL) to anhyd MeOH (20 mL) at 0 °C] was added to a soln of acetate **7** (0.42 g, 0.85 mmol) in CH_2Cl_2 (4 mL). After 12 h at 20 °C, the mixture was diluted with CH_2Cl_2 (100 mL) and washed successively with sat. aq $NaHCO_3$ (150 mL) and H_2O (100 mL). The organic phase was filtered through a layer of powdered Na_2SO_4, concentrated, and dried in vacuo to give a residue that was purified by column chromatography [silica gel, PE–EtOAc (6:1)] to give a colorless syrup; yield: 0.34 g (89%); $[\alpha]_D^{22}$ +187.2 (*c* 1.0, $CHCl_3$); R_f = 0.70 (toluene–EtOAc, 4:1).

IR (KBr): 3062, 2954, 1722, 1602, 1452, 1272 cm^{-1}.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.59 (d, *J* = 3.9 Hz, 1 H, OH), 4.50 (br s, 1 H, H-2), 4.63–4.79 (m, 2 H, H-5a, H-5b), 4.80–4.87 (m, 1 H, H-4), 5.20 (dd, *J* = 6.2, 3.3 Hz, 1 H, H-3), 5.66 (d, *J* = 3.1 Hz, 1 H, H-1), 7.21–7.65 (m, 11 H, Ph), 8.10–8.20 (m, 4 H, Ph).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 63.7 (C-5), 79.1 (C-4), 81.7 (C-2), 81.9 (C-3), 92.5 (C-1), 128.4, 129.0, 129.6, 130.0, 131.8, 133.2, 133.82 (Ph), 166.2, 167.8 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{22}NaO_6S$: 473.1035; found: 473.1029.

Phenyl 3,5-Di-*O*-benzoyl-2-*O*-(chloroacetyl)-1-thio-α-D-arabinofuranoside (9)

Method A

$BF_3{\cdot}Et_2O$ (30 μL, 0.2 mmol) was added to a stirred soln of bischloroacetate **6** (72.8 mg, 0.13 mmol) in CH_2Cl_2 (1 mL) at 0 °C. After 10 min, PhSH (25 μL, 0.6 mmol) was added and the mixture was stirred at 20 °C for 3 h. The reaction was then quenched by addition of sat. aq $NaHCO_3$ (1 mL) and the mixture was diluted with CH_2Cl_2 (50 mL), washed with sat. aq $NaHCO_3$ (50 mL), and concentrated. The residue was dried in vacuo then purified by column chromatography [silica gel, toluene–EtOAc (20:1)] to give a light yellow syrup; yield: 62.2 mg (83%); $[\alpha]_D^{22}$ +70.4 (*c* 1.0, $CHCl_3$); R_f = 0.68 (toluene–EtOAc, 10:1).

IR (KBr): 3062, 2956, 1771, 1723, 1602, 1584, 1452, 1271 cm^{-1}.

^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 4.00 (s, 2 H, CH_2Cl), 4.63–4.85 (m, 3 H, H-4, H-5a, H-5b), 5.51 (d, *J* = 4.5 Hz, 1 H, H-3), 5.58 (s, 1 H, H-2), 5.70 (s, 1 H, H-1), 7.28–7.66 (m, 11 H, Ph), 8.10 (s, 4 H, Ph).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 40.7 (CH_2Cl), 63.5 (C-5), 77.0 (C-3), 80.9 (C-2), 83.2 (C-4), 91.0 (C-1), 128.0, 128.3, 128.5, 128.7, 129.1, 129.7, 129.9 132.5, 132.6, 133.0, 133.2, 133.7 (Ph), 165.5, 166.1, 169.5 (CO).

HRMS–ESI: *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{23}ClNaO_7S$: 549.0751; found: 549.0655.

Method B

2,4,6-Trimethylpyridine (0.43 mL, 3.21 mmol) was added to a stirred soln of alcohol **8** (362 mg, 0.8 mmol) in anhyd CH_2Cl_2 (4 mL). The mixture was cooled to 0 °C and a soln of $(ClCH_2CO)_2O$ (275 mg, 1.61 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The mixture was stirred for 30 min at 0 °C then diluted with CH_2Cl_2 (75 mL) and washed successively with H_2O (75 mL), 1 M aq $KHSO_4$ (50 mL), H_2O (75 mL), and sat. aq $NaHCO_3$ (75 mL). The organic phase was filtered through a layer of a ~1:1 (v/v) mixture of Celite and powdered Na_2SO_4, concentrated, and dried in vacuo to give a colorless syrup; yield: 0.40 g (91%).

Method C

The arabinofuranosyl bromide **2** was prepared from arabinofuranoside **1** (20.0 g, 42.0 mmol) by treatment with HBr in CH_2Cl_2 according to the published procedure.[5] To a soln of the crude bromide **2** in anhyd MeCN (85 mL), $NaBH_4$ (3.2 g, 84.6 mmol) was added. The mixture was stirred for 48 h at 20 °C then concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (350 mL) and washed twice with H_2O (700 mL + 500 mL). The organic phase was filtered through a layer of anhyd Na_2SO_4, concentrated, and dried in vacuo to give benzylidene derivative **3** as a white solid; yield: 18.9 g (quant from **1**).

F_3CCO_2H (25 mL) and H_2O (2.5 mL) were added to a vigorously stirred soln of **3** (18.9 g) in CH_2Cl_2 (250 mL) at 0 °C and the mixture was allowed to warm to 20 °C and stirred for 4 h at 20 °C. The mixture was then diluted with CH_2Cl_2 (200 mL) and washed successively with H_2O (400 mL) and sat. aq $NaHCO_3$ (400 mL). The organic phase was filtered through a cotton-wool plug and concentrated. The syrupy residue was extracted with light petroleum (4 × 60 mL) to remove PhCHO and the insoluble product was dried in vacuo to give diol **4** as a white solid; yield: 11.2 g (74% from **1**).

2,4,6-Trimethylpyridine (26 mL, 194 mmol) was added to a stirred soln of diol **4** (10.6 g, 29.6 mmol) in anhyd CH_2Cl_2 (85 mL). The mixture was cooled to 0 °C and a soln of $(ClCH_2CO)_2O$ (15.22 g, 89 mmol) in CH_2Cl_2 (25 mL) was added. The mixture was stirred for 25 min at 0 °C then diluted with CH_2Cl_2 (350 mL) and washed successively with H_2O (300 mL), 1 M aq $KHSO_4$ (200 mL), H_2O (200 mL), and sat. aq $NaHCO_3$ (200 mL). The organic phase was filtered through a layer of a ~1:1 (v/v) mixture of silica gel and powdered Na_2SO_4, concentrated, and dried in vacuo to give the bischloroacetate **6** as a white solid; yield: 14.73 g (97%).

Bischloroacetate **6** (14.50 g, 28.36 mmol) was co-concentrated with toluene (50 mL), dried in vacuo, and dissolved in anhyd CH_2Cl_2 (285 mL). The soln was cooled to 0 °C and PhSH (3.21 mL, 31.2 mmol) and $BF_3{\cdot}Et_2O$ (3.5 mL, 28.4 mmol) were successively added. The mixture was stirred at 0 °C for 30 min then allowed to warm to 20 °C and stirred for an additional 3 h at 20 °C. It was then diluted with CH_2Cl_2 (200 mL), washed successively with H_2O (200 mL) and sat. aq $NaHCO_3$ (200 mL), and concentrated. The residue was dried in vacuo and purified by column chromatography [silica gel, PE–EtOAc (9:1 to 6:1)] to give thioglycoside **9** as a colorless syrup; yield: 14.61 g (71% with respect to **1** over 5 steps).

Ethyl 2-*O*-Benzoyl-3,5-bis-*O*-(chloroacetyl)-1-thio-α-D-arabinofuranoside (12)

2,4,6-Trimethylpyridine (4.0 mL, 30.2 mmol) was added to a stirred soln of **11**[5] (3.9 g, 10.3 mmol) in anhyd CH_2Cl_2 (12 mL). The mixture was cooled to 0 °C and a soln of $(ClCH_2CO)_2O$ (2.3 g, 13.7 mmol) in CH_2Cl_2 (7.5 mL) was added dropwise. The mixture was stirred for 30 min at 0 °C then diluted with CH_2Cl_2 (200 mL) and

washed successively with H_2O (150 mL), 1 M aq $KHSO_4$ (80 mL), H_2O (150 mL), and sat. aq $NaHCO_3$ (100 mL). The organic phase was filtered through a layer of ~1:1 (v/v) mixture of silica gel and powdered Na_2SO_4, concentrated, and dried in vacuo. The residue was purified by column chromatography [PE–EtOAc (9:1)] to give a colorless syrup; yield: 4.1 g (88%); $[\alpha]_D^{22}$ +85.4 (*c* 1.0, $CHCl_3$); R_f = 0.38 (PE–EtOAc, 5:1).

IR (KBr): 1766, 1727, 1270 cm^{-1}.

^1H NMR (200.13 MHz, $CDCl_3$): δ = 1.33 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2S), 2.57–2.84 (m, 2 H, CH_3CH_2S), 4.07 (s, 2 H, $ClCH_2CO$), 4.18 (s, 2 H, $ClCH_2CO$), 4.41–4.69 (m, 3 H, H-4, H-5a,b), 5.24–5.30 (m, 1 H, H-3), 5.38 (dd, *J* = 1.7, 1.5 Hz, 1 H, H-2), 5.54 (s, 1 H, H-1), 7.42–7.53 (m, 2 H, Ph), 7.56–7.67 (m, 1 H, Ph), 8.00–8.10 (m, 2 H, Ph).

^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 14.7 (SCH_2CH_3), 25.3 (SCH_2CH_3), 40.5, 40.6 ($ClCH_2CO$), 64.1 (C-5), 79.0, 79.4 (C-2, C-4), 82.2 (C-3), 87.8 (C-1), 128.6, 128.7, 129.8, 133.8 (Ph), 165.3, 166.7, 166.9 (CO).

HRMS–ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{20}Cl_2NaO_7S$: 473.0199; found: 473.0190.

Ethyl 2-*O*-Benzoyl-1-thio-α-D-arabinofuranoside (13)

Chloroacetate **11**[5] (6.11 g, 16.3 mmol) was dissolved in a 2:1 (v/v) mixture of pyridine and H_2O (45 mL) and the soln was stirred at 80 °C for 1 h, then concentrated, co-concentrated with toluene (500 mL), diluted with CH_2Cl_2 (500 mL), and washed successively with 1 M aq $KHSO_4$ (500 mL), H_2O (500 mL), and sat. aq $NaHCO_3$ (500 mL). The organic phase was filtered through a layer of powdered Na_2SO_4, concentrated, and dried in vacuo. The residue was purified by column chromatography [silica gel, PE–EtOAc (1:1)] to give a white foam; yield: 4.19 g (86%); $[\alpha]_D^{22}$ +154.6 (*c* 1.0, $CHCl_3$); R_f = 0.40 (toluene–EtOAc, 1:1).

IR (KBr): 2931, 1716, 1601, 1451, 1270 cm^{-1}.

^1H NMR (200.13 MHz, $CDCl_3$): δ = 1.35 (t, 3 H, *J* = 7.4 Hz, CH_3CH_2S), 1.92 (s, 1 H, OH), 2.54–2.89 (m, 2 H, CH_3CH_2S), 3.44 (d, *J* = 3.5 Hz, 1 H, OH), 3.82 (dd, $J_{5a,5b}$ = 12.1 Hz, $J_{5a,4}$ = 3.3 Hz, 1 H, H-5a), 3.95 (dd, $J_{5a,5b}$ = 12.1 Hz, $J_{5b,4}$ = 2.5 Hz,, 1 H, H-5b), 4.16–4.37 (m, 2 H, H-3, H-4), 5.05 (dd, $J_{2,3}$ = 2.6 Hz, $J_{1,2}$ = 2.5 Hz, 1 H, H-2), 5.56 (d, $J_{2,1}$ = 2.5 Hz, 1 H, H-1), 7.38–7.49 (m, 2 H, Ph), 7.55–7.66 (m, 1 H, Ph), 7.97–8.04 (m, 2 H, Ph).

^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 14.7 (SCH_2CH_3), 25.2 (SCH_2CH_3), 61.5 (C-5), 76.7 (C-3), 82.78 (C-4), 86.2 (C-2), 87.6 (C-1), 128.6, 129.8, 133.72 (Ph), 167.0 (CO).

HRMS–ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{18}NaO_5S$: 321.0767; found: 321.0763.

Ethyl 2-*O*-Benzoyl-1-thio-3,5-di-*O*-trityl-α-D-arabinofuranoside (14)

2,4,6-Trimethylpyridine (1.3 ml, 10 mmol) and $TrClO_4$ (1.3 g, 3.9 mmol) were added to a stirred soln of diol **13** (0.50 g, 1.7 mmol) in anhyd CH_2Cl_2 (7 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C before the reaction was quenched by addition of sat. aq $NaHCO_3$ (1 mL). The mixture was diluted with CH_2Cl_2 (200 mL) and washed successively with 1 M aq $KHSO_4$ (200 mL), H_2O (200 mL), and sat. aq $NaHCO_3$ (200 mL). The organic phase was filtered through a layer of powdered Na_2SO_4, concentrated, and dried in vacuo. The residue was purified by column chromatography (silica gel, PE + 1% Et_3N to PE–EtOAc (95:5) + 1% Et_3N] to give a white foam; yield: 1.21 g (90%); R_f = 0.33 (toluene).

IR (KBr): 3032, 2926, 1723, 1599, 1491, 1449, 1277 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2S), 2.68–2.82 (m, 2 H, CH_3CH_2S), 3.21 (dd, *J* = 10.2, 6.5 Hz, 1 H, H-5a), 3.37 (dd, 1 H, *J* = 10.2, 3.4 Hz, H-5b), 4.28 (d, *J* = 4.3 Hz, 1 H, H-3), 4.38 (s, 1 H, H-2), 4.77 (dt, *J* = 6.7, 3.4 Hz, 1 H, H-4), 5.26 (s, 1 H, H-1), 7.07–7.15 (m, 8 H, Ph), 7.20–7.33 (m, 12 H, Ph), 7.34–7.45 (m, 12 H, Ph), 7.50 (t, *J* = 7.38, 1 H, Ph), 7.65 (d, *J* = 7.52, 2 H, Ph).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 15.1 (CH_3CH_2S), 25.5 (CH_3CH_2S), 63.7 (C-5), 78.7 (C-3), 83.5 (C-2), 83.6 (C-4), 88.7 (C-1), 126.9, 127.3, 127.7, 128.0, 128.2, 128.9, 128.9, 132.9, 143.8, 143.9 (Ph).

HRMS–ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{52}H_{46}NaO_5S$: 805.2958; found: 805.2959.

Anal. Calcd for $C_{52}H_{46}O_5S$: C, 79.77; H, 5.92. Found: C, 80.05; H, 6.02.

Ethyl 1-Thio-3,5-di-*O*-trityl-α-D-arabinofuranoside (15)

MeOH (12 mL) and a 1 M soln of MeONa in MeOH (0.2 mL) were added successively to a stirred soln of benzoate **14** (0.70 g, 1.81 mmol) in anhyd CH_2Cl_2 (6 mL) and the mixture was stirred at 40 °C for 12 h. The reaction was quenched by addition of solid CO_2 and the mixture was diluted with CH_2Cl_2 (200 mL) and washed with H_2O (2 × 200 mL). The organic phase was filtered through a layer of powdered Na_2SO_4, concentrated, and dried in vacuo. The residue was purified by column chromatography [silica gel, PE + 1% Et_3N to PE–EtOAc (20:1) + 1% Et_3N) to give a white foam; yield: 1.04 g (84%); $[\alpha]_D^{22}$ +117.2 (*c* 1.6, $CHCl_3$); R_f = 0.70 (toluene–EtOAc, 10:1).

IR (KBr): 3058, 2926, 1491, 1448 cm^{-1}.

^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2S), 2.56–2.70 (m, 3 H, CH_3CH_2S, H-5a), 3.05 (d, *J* = 10.1 Hz, 1 H, OH), 3.29 (dd, *J* = 10.4, 1 H, 2.4 Hz, H-5b), 3.52 (d, *J* = 10.1 Hz, 1 H, H-2), 3.83 (d, *J* = 2.4 Hz, 1 H, H-3), 4.02–4.07 (m, 1 H, H-4), 5.16 (s, 1 H, H-1), 7.00–7.32 (m, 30 H, Ph).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.3 (SCH_2CH_3), 26.1 (SCH_2CH_3), 63.4 (C-5), 81.0 (C-3), 81.6 (C-2), 84.5 (C-4), 87.7, 88,3 (Ph_3C), 91.8 (C-1), 127.2, 127.2, 127.9, 128.8, 128.9, 143.1, 144.2 (Ph).

HRMS–ESI: *m*/*z* $[M + Na]^+$ calcd for $C_{45}H_{42}NaO_4S$: 701.2702; found: 701.2696.

Ethyl 2-*O*-(Chloroacetyl)-1-thio-α-D-arabinofuranoside (17)

2,4,6-Trimethylpyridine (0.8 mL, 5.8 mmol) was added to a stirred soln of alcohol **15** (0.99 g, 1.46 mmol) in anhyd CH_2Cl_2 (7 mL). The mixture was cooled to 0 °C and a soln of $(ClCH_2CO)_2O$ (0.5 g, 2.9 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The mixture was stirred at 0 °C for 30 min then diluted with CH_2Cl_2 (50 mL) and washed successively with H_2O (50 mL), 1 M $KHSO_4$ (50 mL), H_2O (50 mL), sat. aq $NaHCO_3$ (50 mL). The organic phase was filtered through a layer of ~1:1 (v/v) mixture of Celite and powdered Na_2SO_4 then concentrated and dried in vacuo to give chloroacetate **16** as a white foam; yield: (1.0 g, 99%).

The soln of chloroacetate **16** (0.54 g, 7.1 mmol) in AcOH (6 mL) and H_2O (3 mL) was heated at 80 °C for 2 h. The mixture was then co-concentrated with H_2O (2 × 3 mL) and the residue was purified by column chromatography [silica gel, benzene–acetone (1:4 to 2:3)] (**CAUTION:** *benzene is a carcinogen*) to give diol **17** as a light yellow syrup; yield: 380 mg (54%); $[\alpha]_D^{22}$ +167.2 (*c* 2.6, $CHCl_3$); R_f = 0.46 (toluene–EtOAc, 1:1).

^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2S), 2.30 (br s, 1 H, OH), 2.57–2.80 (m, 2 H, CH_3CH_2S), 3.42 (br s, 1 H, OH), 3.78 (dd, *J* = 12.3, 3.4 Hz, 1 H, H-5a), 3.91 (dd, *J* = 2.8, Hz, 1 H, H-5b), 4.11–4.24 (m, 2 H, H-3, H-4), 4.14 (s, 2 H, $COCH_2Cl$), 4.93 (t, *J* = 2.7, 2.3 Hz, 1 H, H-2), 5.39 (d, *J* = 2.3 Hz, 1 H, H-2).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 14.6 (CH_3CH_2S), 25.1 (CH_3CH_2S), 40.6 ($COCH_2Cl$), 61.2 (C-5), 76.2 (C-3), 82.8 (C-4), 85.9 (C-1), 87.9 (C-2), 167.7 (CO).

HRMS–ESI: *m*/*z* $[M + Na]^+$ calcd for $C_9H_{15}ClNaO_5S$: 293.0226; found: 293.0221.

Ethyl 3,5-Di-*O*-benzoyl-2-*O*-(chloroacetyl)-1-thio-α-D-arabinofuranoside (18)

BzCl (0.80 mL, 0.87 mmol) was added to the soln of diol **17** (59 mg, 0.218 mmol) in pyridine (2 mL) at 0 °C and the mixture was stirred at 0 °C for 0.5 h. The reaction was quenched by addition of sat. aq $NaHCO_3$ (1 mL) and the mixture was diluted with CH_2Cl_2 (50 mL) and washed successively with H_2O (50 mL) and sat. aq $NaHCO_3$ (50 mL). The organic phase was filtered through a layer of a ~1:1 (v/v) mixture of Celite and powdered Na_2SO_4 then concentrated and dried in vacuo. The residue was purified by column chromatography [silica gel, benzene–EtOAc (1:9)] to give a colorless syrup; yield: 102 mg (97%).

^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.4 Hz, 3 H, C*H*$_3$CH$_2$S), 2.63–2.87 (m, 2 H, CH$_3$C*H*$_2$S), 4.01 (s, 2 H, COC*H*$_2$Cl), 4.61–4.85 (m, 3 H, H-4, H-5a, H-5b), 5.40 (dd, *J* = 1.4, 1.5 Hz, 1 H, H-2), 5.44–5.53 (m, 2 H, H-1, H-3), 7.34–7.70 (m, 6 H, Ph), 8.02–8.13 (m, 4 H, Ph).

^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 14.8 (*C*H$_3$CH$_2$S), 25.3 (CH$_3$*C*H$_2$S), 40.3 (*C*H$_2$Cl), 63.2 (C-5), 77.8 (C-3), 80.5 (C-2), 83.6 (C-4), 87.7 (C-1), 128.3, 128.5, 128.8, 129.7, 130.0, 133.2, 133.7 (Ph), 165.5, 166.2 (CO).

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References

(1) (a) Joe, M.; Bai, Y.; Nacario, R. C.; Lowary, T. L. *J. Am. Chem. Soc.* **2007**, *129*, 9885. (b) Zhu, X.; Kawatkar, S.; Rao, Y.; Boons, G.-J. *J. Am. Chem. Soc.* **2006**, *128*, 11948. (c) Ishiwata, A.; Akao, H.; Ito, Y. *Org. Lett.* **2006**, *8*, 5525. (d) Lee, Y. J.; Lee, K.; Jung, E. H.; Jeon, H. B.; Kim, K. S. *Org. Lett.* **2005**, *7*, 3263. (e) Crich, D.; Pedersen, C. M.; Bowers, A. A.; Wink, D. J. *J. Org. Chem.* **2007**, *72*, 1553. (f) Fraser-Reid, B.; Lu, J.; Jayaprakash, K. N.; López, J. C. *Tetrahedron: Asymmetry* **2006**, *17*, 2449. (g) Liang, X.-Y.; Deng, L.-M.; Liu, X.; Yang, J.-S. *Tetrahedron* **2010**, *66*, 6687. (h) Marotte, K.; Sanchez, S.; Bamhaoud, T.; Prandi, J. *Eur. J. Org. Chem.* **2003**, 3587. (i) Yin, H.; D'Souza, F. W.; Lowary, T. L. *J. Org. Chem.* **2002**, *67*, 892. (j) Gadikota, R. R.; Callam, C. S.; Appelmelk, B. J.; Lowary, T. L. *J. Carbohydr. Chem.* **2003**, *22*, 459. (k) Mereyala, H. B.; Hotha, S.; Gurjar, M. K. *Chem. Commun. (Cambridge)* **1998**, 685. (l) Tam, P.-H.; Lowary, T. L. *Carbohydr. Chem.* **2010**, *36*, 38; and references cited therein.

(2) *Health Topics: Tuberculosis;* World Health Organization: Geneva, **2012**, http://www.who.int/topics/tuberculosis/en (accessed March 15, 2012).

(3) Pathak, A. K.; Pathak, V.; Bansal, N.; Maddry, J. A.; Reynolds, R. C. *Tetrahedron Lett.* **2001**, *42*, 979.

(4) Mei, X.; Ning, J. *Synlett* **2005**, 2267.

(5) Podvalnyy, N. M.; Sedinkin, S. L.; Abronina, P. I.; Zinin, A. I.; Fedina, K. G.; Torgov, V. I.; Kononov, L. O. *Carbohydr. Res.* **2011**, *346*, 7.

(6) Ishiwata, A.; Ito, Y. *J. Am. Chem. Soc.* **2011**, *133*, 2275.

(7) Dahlman, O.; Garegg, P. J.; Mayer, H.; Schramek, S. *Acta Chem. Scand., Ser. B* **1986**, *40*, 15.

(8) Kochetkov, N. K.; Byramova, N. É.; Tsvetkov, Y. E.; Backinowsky, L. V. *Tetrahedron* **1985**, *41*, 3363.

(9) Jung, M. E.; Xu, Y. *Org. Lett.* **1999**, *1*, 1517.

(10) (a) Ness, R. K.; Fletcher, H. G. *J. Am. Chem. Soc.* **1958**, *80*, 2007. (b) Callam, C. S.; Lowary, T. L. *J. Chem. Educ.* **2001**, *78*, 73.

(11) Byramova, N. É .; Ovchinnikov, M. V.; Backinowsky, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1983**, *124*, C8.

(12) Abronina, P. I.; Podvalnyy, N. M.; Melnikova, T. M.; Zinin, A. I.; Fedina, K. G.; Kachala, V. I.; Torgov, V. I.; Kononov, L. O.; Panferzev, E. A.; Baranova, E. V.; Mochalov, V. V.; Dyatlova, V. I.; Biketov, S. F. *Russ. Chem. Bull.* **2010**, *59*, 2333.

(13) (a) Pathak, T. *Chem. Rev.* **2002**, *102*, 1623. (b) Zatsepin, T. S.; Romanova, E. A.; Oretskaya, T. S. *Russ. Chem. Rev.* **2004**, *73*, 701.

(14) (a) *Antiviral Nucleosides: Chiral Synthesis and Chemotherapy;* Chu, C. K., Ed.; Elsevier: Amsterdam, **2003**. (b) De Clercq, E. *Antiviral Res.* **2005**, *67*, 56. (c) Mathéa, C.; Gosselin, G. *Antiviral Res.* **2006**, *71*, 276.

(15) (a) Wuts, P. G. M.; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; Wiley-Interscience: Hoboken, **2007**, 239. (b) Wuts, P. G. M.; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*, 4th ed.; Wiley-Interscience: Hoboken, **2007**, 353. (c) Kocieński, P. J. *Protecting Groups*, 3rd ed.; Thieme: Stuttgart, **2005**, 171.