Design, synthesis and activity of thio-linked arabinofuranosyl disaccharides against mycobacterial tuberculosis (MTB) and *Mycobacterium avium* complex (MAC)

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Dedicated to Professor Richard R. Schmidt on the occasion of his 78th anniversary

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Abstract

We report the chemical synthesis of a series of disaccharides of arabinofuranose with a glycosidic sulfur linker as mimics of the acceptor for arabinofuranosyltransferases with and without using any activator to avoid any complex reactions. These analogs were tested for *in vitro* activity against MTB strain H37Ra and 3 MAC clinical isolates. MICs were determined using a colorimetric microdilution broth assay. Bactericidal activity was studied with kill curves over a period of seven days. Intracellular activity against MTB H37Ra was determined in the Mono Mac 6 (MM6) human monocytic cell line.

Keywords: Arabinofuranosyl transferases, inhibitors, arabinofuranose, thio linked disaccharides, mycobacteria, bacterial cell walls

Introduction

The resurgence of tuberculosis in developed nations as well as the appearance of multiple drug resistant forms of the disease throughout the world has raised the concern that this disease may resurface as serious public health problem[1-3] and this attracted renewed attention in identifying the potent antimycobacterial agents. Also, the effective chemotherapy of persons with AIDS who are infected with *Mycobacterium avium* can be difficult due to the inherent resistance of this organism.[4] All *Mycobacterium* species share a characteristic cell wall, thicker than in many other bacteria, which is hydrophobic, waxy, and rich in mycolic acids/mycolates. The cell wall consists of the hydrophobic mycolate layer and a peptidoglycan layer held together by a

polysaccharide, arabinogalactan. The cell wall makes a substantial contribution to the hardiness of this genus. The biosynthetic pathways of cell wall components are potential targets for new drugs for tuberculosis. Much of the pathogenicity of *M. tuberculosis* results from its unique and complex cell envelope. The major components of this mycobacterial envelope are the mycolyl arabinogalactanpeptidoglycan complexes (mAGPs) and the lipoarabinomannan (LAM)-associated lipoglycans. The biosynthetic pathways of cell wall components are potential targets for new drugs for tuberculosis. The recent advances in the characterization of mycobacteria cell walls have led to the identification of a vast array of highly unique biochemical targets that could lead to a new generation of potent and selective anti tubercular agents.[5] Arabinogalactan, a major and essential component of the cell wall, is an attractive target for drug development as neither D-arabinofuranose nor D-galactofuranose, the monomers composing arabinogalactan, are found in mammalian cells.[6] The effectiveness of antituberculosis drug, Ethambutol,[7] which inhibits the synthesis of arabinan,[8] a cell envelope component, illustrates the importance of this structure to the survival of the organism. Since several natural and synthetic arabinosyl glycosides are known to be substrate of mycobacterial arabinosyl transferase,[9] we hypothesized that simple arabinosyl disaccharide incorporating a sulfur atom that could potentially chelate the putative cation might function as specific inhibitors.

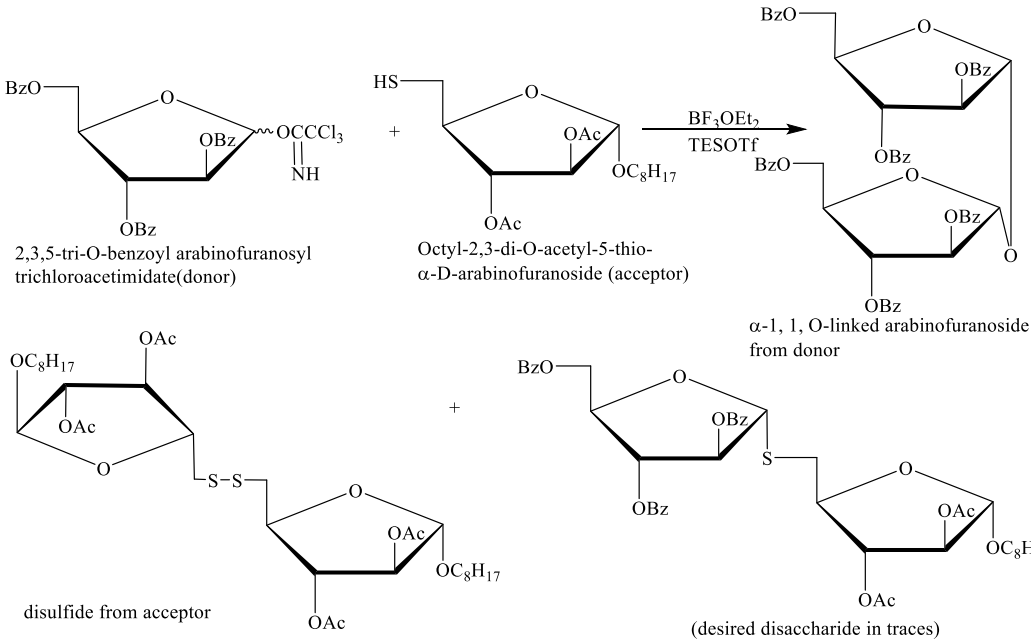
The inhibitors of mycobacterial arabinofuranosyl transferases could be the ideal synthetic targets as neither D-arabinofuranose nor D-galactofuranose, the monomer composing arabino-galactan are found in mammalian cells. Recently, several oligosaccharides with sulfur in the glycosidic linkage are investigated as potential inhibitors of glycosyltransferases. Such compounds should also reduce hydrophilicity and enhance hydrolytic and enzymatic stability.
We have initiated a program to synthesize a series of disaccharides with sulfur linkers as mimics of the acceptor for arabinofuranosyl transferase. Such compounds should also reduce hydrophilicity and enhance hydrolytic and enzymatic stability.

Herein we report for the first time the synthesis, characterization and biological evaluation of several regioselectively protected D-arabinofuranosyl-(1,5)-D-arabinofuranosides with thio-linked octyl groups. An octyl group has been shown to be suitable for studies of mycobacterial arabinosyltransferases and other glycosyltransferases.[6b,7b,9b,10]

Results and Discussion

Thio-linked oligosaccharides involving hexoses have been synthesized earlier by a variety of procedures, (a) a S_N2 type reaction involving the reaction of a thiolate anion on a glycosyl halide,[11] and (b) the displacement of a leaving group by a 1-thioglycose.[12] Initially our approach was based on the former procedure to yield thio-linked arabinofuranoside, **9a, b, c** but the latter procedure was applied in a modified displacement reaction for the synthesis of the rest of the disaccharides to avoid using the toxic mercury salts as an activator and also to avoid any complex side reactions. An attempt was also made to couple the 2,3,5-tri-*O*-benzoyl arabino-

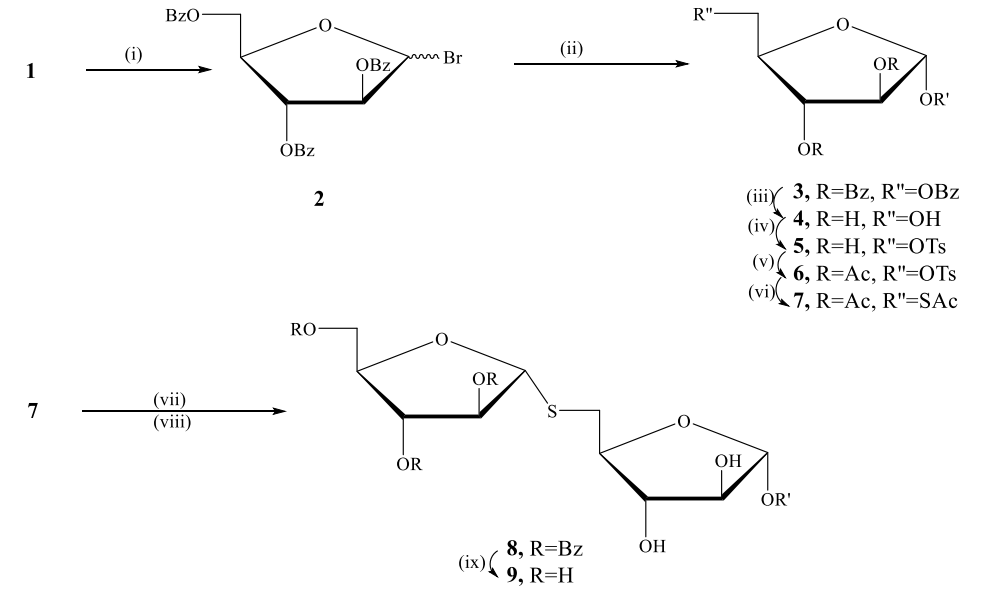
furanosyl trichloroacetimidate[13] with octyl-2,3-di-*O*-acetyl-5-thio-α-D-arabinofuranoside[13] using the promoters BF_3OEt_2 or TESOTfl[14] which resulted in an inseparable mixture of symmetric α,1-1, *O*-linked arabinofuranoside from donor, disulfide from acceptor and traces of the desired disaccharide (Scheme 1).



Scheme 1. Attempted synthesis of thio-linked disaccharides.

The octyl (**3a**), 1-methylpropyl (*sec*-butyl) (**3b**) and 3-phenylpropyl (**3c**) arabinosides were obtained separately from methyl-2,3,5-tri-*O*-benzoyl-α-D-arabinofuranoside[15] (**1**) through the glycosyl bromide (**2**)[16] with $SnCl_4$[17] (Scheme 2). Another two-step protection/deprotection sequence yielded **6** which on reaction with potassium thioacetate gave **7**. Compound **7** upon treatment with sodium methoxide and coupling with **2** using mercuric cyanide as an activator afforded **8** in good yield. The target compounds **9a-c** were obtained after debenzoylation of **8**.

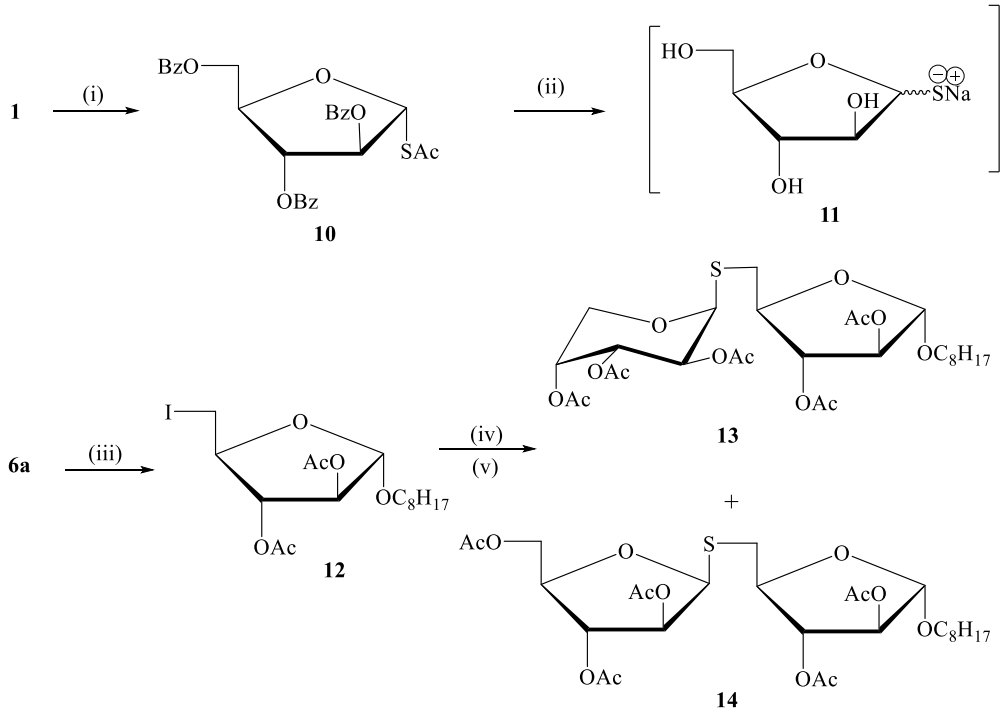
Compound **10** was obtained on treating **1**[15] with thiolacetic acid in boron trifluoride etherate which upon reaction with sodium methoxide gave **11** (Scheme 3). The coupling of **11** and **12** (obtained from **6a** on refluxing with sodium iodide in 2-butanone) on displacing the iodide of **12** without using any activator and followed by acetylation did not yield the expected α-linked thio disaccharide but β-linked ara*p*(S,1-5) ara*f* (**13**) and ara*f*(S,1-5) ara*f* (**14**).



a, R'=C_8H_{17}; b, R'=$CH(CH_3)CH_2CH_3$; c, R'=$CH_2CH_2CH_2C_6H_5$

Reagents & Conditions- (i) 30% HBr in glacial AcOH, RT, 1h; (ii) R'OH, $SnCl_4$, RT, 15h; (iii) NH_3, MeOH, RT, 22h; (iv) C_5H_5N, TsCl, 0°-RT, 24h; (v) C_5H_5N, Ac_2O, RT, 15h; (vi) KSAc, RT, 26h; (vii)

Scheme 2. Synthesis of the thio-linked disaccharides **9a-c.**

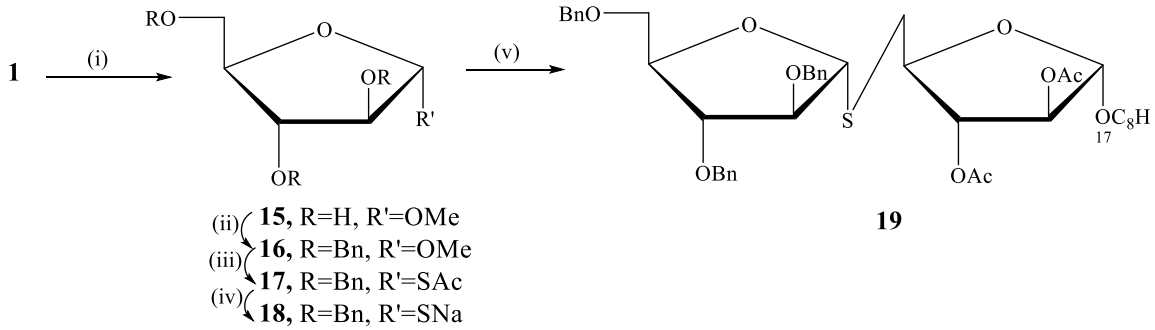


Reagents & Conditions: (i) AcSH, BF_3OEt_2, RT, 18h; (ii) MeONa, 0° to RT, 2h; (iii) NaI, 2-butanone, 85°, 18h; (iv) **11**, DMF, RT, 18h; (v) C_5H_5N, Ac_2O, RT, 18h.

Scheme 3. Synthesis of the thio-linked disaccharides **13** and **14**.

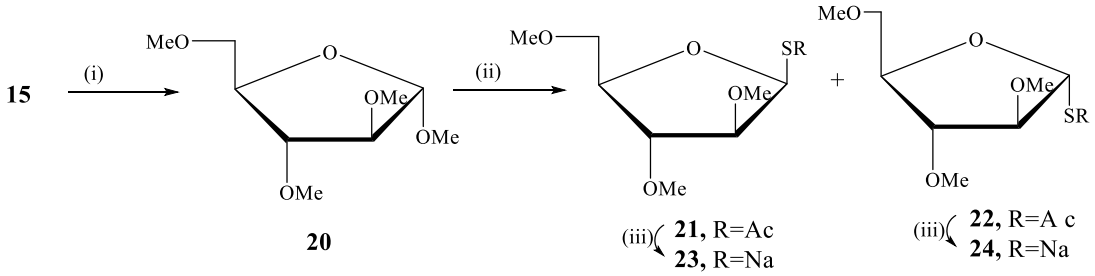
To obtain the desired α-linked disaccharide, compound **18** synthesized from **1**[15] after three steps of protection/deprotection techniques, on coupling with tosyl derivative(**6a**) yielded only the α-linked thiodisaccharide **19** (Scheme 4).

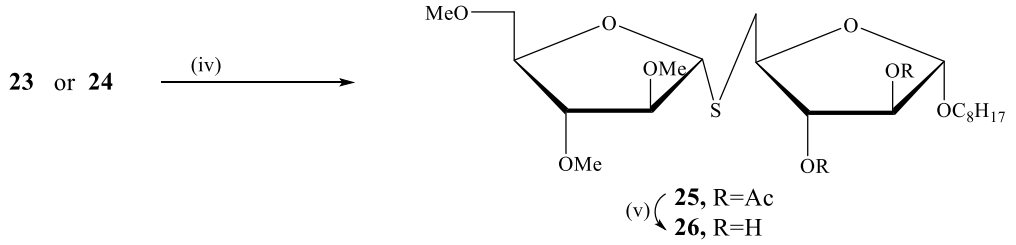
Similarly, the α-linked thiodisaccharide **26** was made from **15**[18] as follows. Compound **15**[18] upon methylation gave **20** followed by acetolysis with thiol acetic acid yielded β and α thioacetates **21** and **22**, respectively. After chromatographic separation, both the thiosodium derivatives **23** and **24** were reacted separately with **6a**, in absence of any activator, gave only α-linked thio disaccharide **25** irrespective of the anomeric configuration of starting thioacetates **21** and **22**, which on deacetylation gave **26** (Scheme 5).



Reagents & Conditions- (i) NH_3, MeOH, RT, 18h; (ii) NaH, BnBr, 0° to RT, 18h; (iii) AcSH, BF_3OEt_2, RT, 18h; (iv)NH_3, MeOH, RT, 18h; (v) **6a,** DMF, RT, 18h.

Scheme 4. Synthesis of the thio-linked disaccharide **19.**

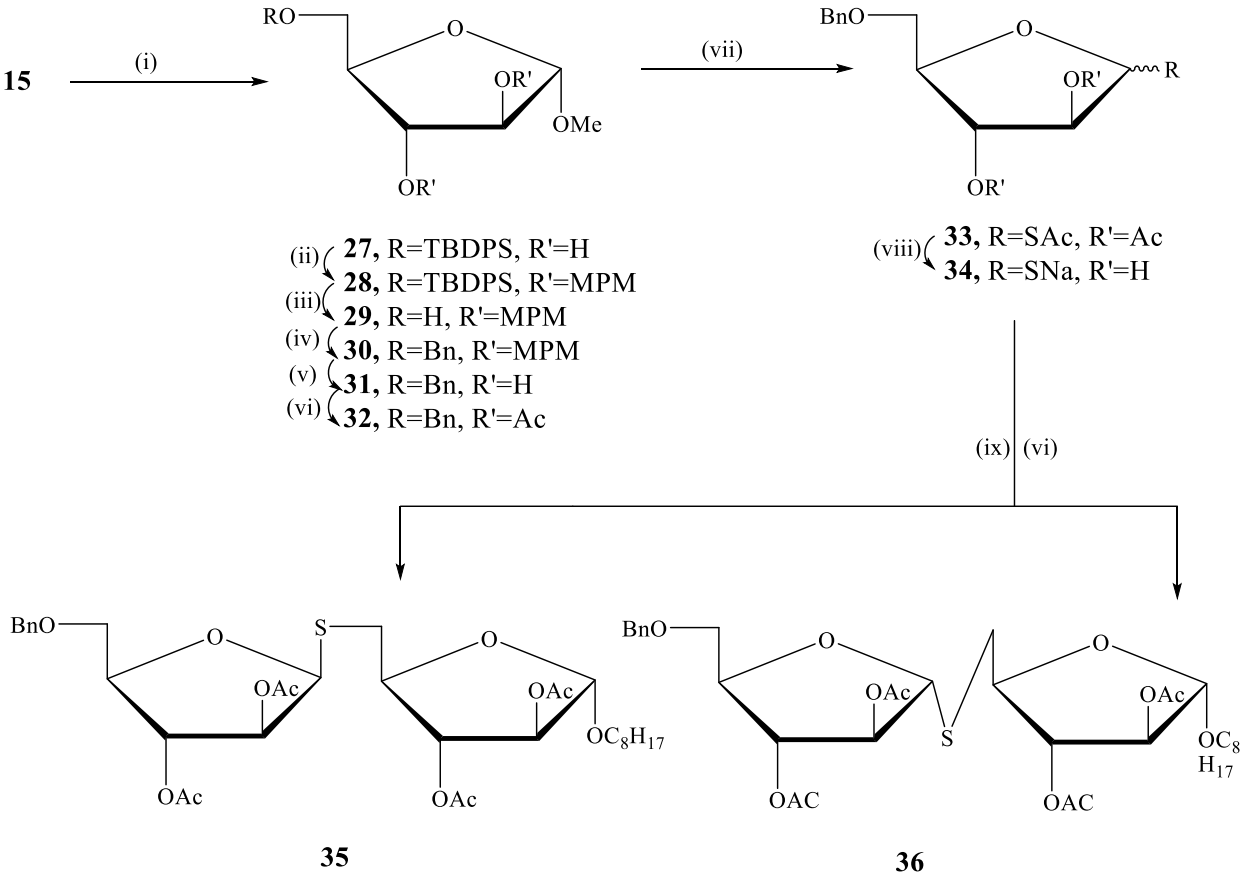




Reagents & Conditions- (i) NaH, MeI, 0° to RT, 18h; (ii) AcSH, BF_3OEt_2, RT, 18h; (iii) MeONa, 0° to RT, 2h; (iv) **6a,** DMF, RT, 48h; (v) NH_3/MeOH, RT, 18h.

Scheme 5. Synthesis of the thio-linked disaccharide **26**.

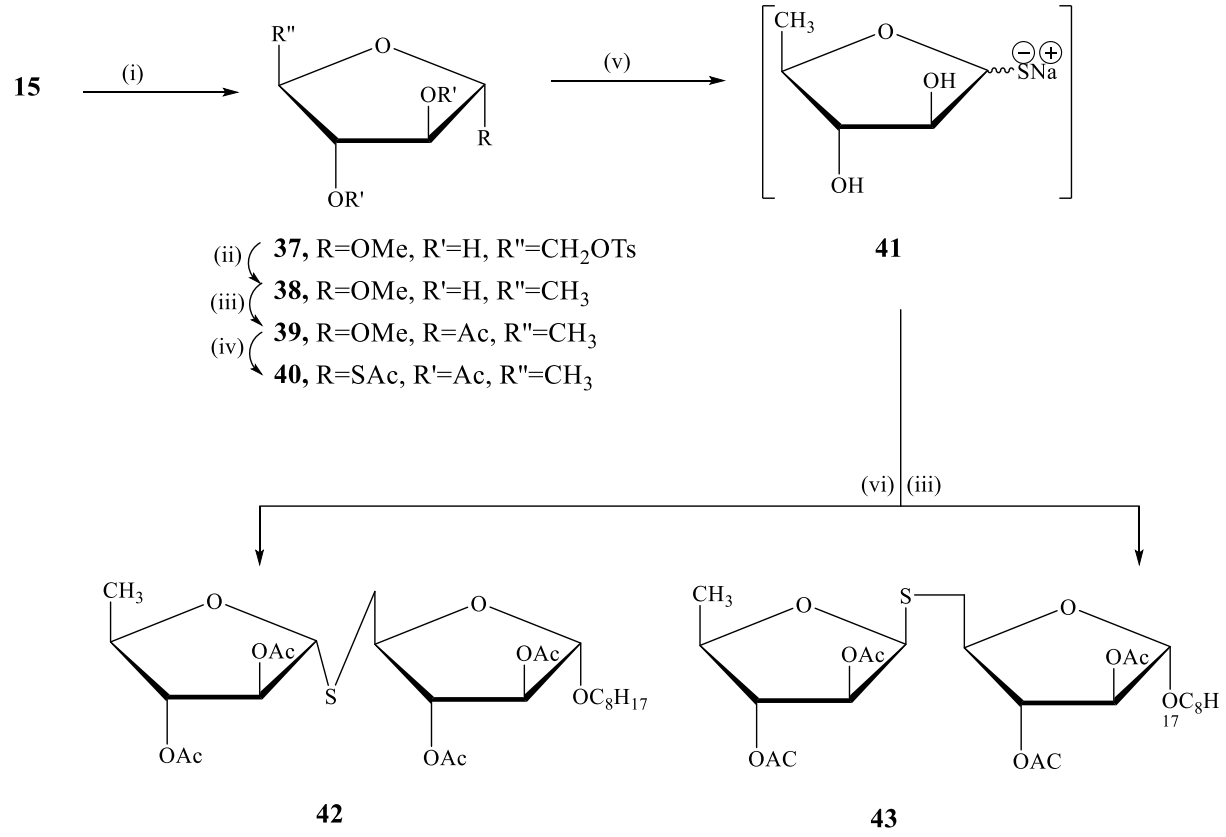
Compound **34** was obtained from **15**[18] on making the 5-*O*-TBDPS-derivative[19] (**27**) followed by alkylation to get 2,3-di-*O*-methoxybenzyl, **28**, which upon desilylation (**29**), benzylation (**30**), demethoxybenzylation (**31**) and acetylation gave **32**. Compound **32** on reaction with thiolacetic acid in boron trifluoride etherate yielded α-thioacetate **33** which ultimately gave the thiosodium **34** with sodium methoxide. Compound **34** was condensed with **6a** followed by acetylation resulted in thiodisaccharides **35** and **36** (Scheme 6).



Reagents & Conditions- (i) TBDPSCl**,** Imidazole, RT, 3h; (ii) NaH, MPMCl, TBABr, 0° to RT, 18h; (iii) TBAF,0° to RT, 18h; (iv) NaH, BnBr, 0° to RT, 18h; (v) CAN, RT, 4h; (vi) C_5H_5N, Ac_2O, RT, 18h; (vii) AcSH, BF_3OEt_2, RT, 18h; (viii) MeONa, 0° to RT, 2h; (ix) **6a,** DMF, RT, 48h.

Scheme 6. Synthesis of the thio-linked disaccharides **35** and **36**.

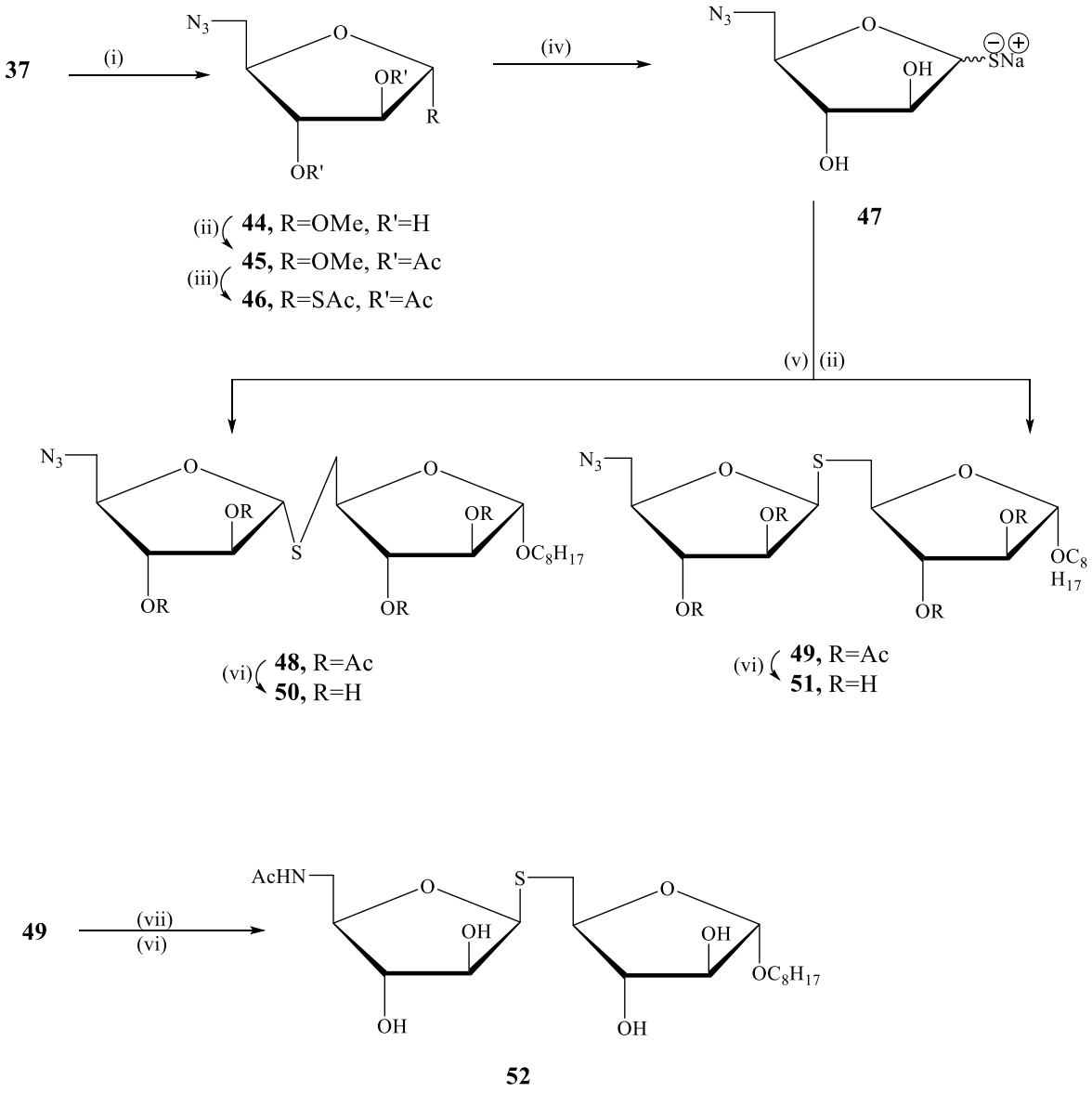
Likewise, 5-deoxyarabinose **39** was obtained from **15**[18] on tosylation (**37**), reduction with lithium aluminium hydride (**38**), and acetylation. Compound **39** was converted into α-thioacetate **40** as reported earlier and coupled with **6a** through **41** to give 5′-deoxythiodisaccharides **42** and **43** on acetylating the residue (Scheme 7).



Reagents & Conditions- (i) C_5H_5N, TsCl, 0° to RT, 48h, (ii) LAH, RT, 18h, (iii) C_5H_5N, Ac_2O, RT, 18h; (iv) AcSH, BF_3OEt_2, RT, 18h; (v) MeONa, 0° to RT, 2h; (vi) **6a,** DMF, RT, 48h.

Scheme 7. Synthesis of the thio-linked disaccharides **42** and **43**.

Compound **37** was refluxed with sodium azide to yield **44** which upon acetylation gave **45**. The α-thioacetate **46** was obtained from **45** with thiol acetic acid which ultimately yielded **47** with sodium methoxide. The coupling of **47** and **6a** gave the expected disaccharides **48** and **49** as octylglycosides after acetylating the residue. The deacetylation of isolated α- and β-linked thiodisaccharides **48** and **49** yielded **50** and **51** respectively. Compound **49** upon treatment with triphenylphosphine in water followed by deacetylation gave 5′-acetamidothiodisaccharide **52** (Scheme 8).



Reagents & Conditions- (i) NaN_3, 100°, 6h; (ii) C_5H_5N, Ac_2O, RT, 18h; (iii) AcSH, BF_3OEt_2, RT, 18h; (iv) MeONa, 0° to RT, 2h; (v) **6a,** DMF, RT, 48h; (vi) NH_3/MeOH, RT, 18h; (vii) Ph_3P, H_2O, 65°, 5.5h.

Scheme 8. Synthesis of the thio-linked disaccharides **50-52**.

Biological test data

Table 1. Antimycobacterial activity of thio-linked disaccharides against *Mycobacterium tuberculosis* (MTB) and *Mycobacterium avium* Complex (MAC)

Test Compound	MIC (μg/ml)			
	MTB H37Ra	MAC NJ 168	MAC NJ 211	MAC NJ 3404
8	128	>128	>128	
9	4	>128	128	>12.8≤128
13	>128	>128	>128	>128
14	>128	>128	>128	>128
19	>128	>128	>128	>128
25	>128	>128	>128	>128
26	>128	>128	>128	>128
35	>128	*a*	>128	*a*
36	>128	*a*	>128	*a*
42	>128	*a*	>128	*a*
43	>128	*a*	>128	*a*
48	>128	*a*	>128	*a*
49	>128	*a*	>128	*a*
50	128	*a*	>128	*a*
51	128	*a*	128	*a*
52	>128	*a*	>128	*a*
Ethambutol (ETB)	2-4	8	4-8	8

a – not determined.

Table 2. Activity of compound **9** against *Mycobacterium tuberculosis* H37Ra in infected human Mono Mac 6 macrophages [a]

μg/ml	μM	Log_{10} CFU (colony forming unit)	
		Day 0	Day 7
0.0	0.0	4.94	5.41
0.50	1.2	-	5.18
4.0	9.8	-	5.18
32[b]	78	-	4.34 [c]

[a] Rifamicin (positive control : Log_{10} CFU @ 16 ng/ml = <4. [b] The macrophage viability was reduced by 39% of the control at this concentration. The LD_{50} for uninfected macrophages was >48 μg/ml. [c] Significant response (P <0.001).

Compound **9** was active against *M. tuberculosis* with an MIC that was comparable to that observed with ethambutol. However, the thio-linked arabinofuranosyl disaccharide derivatives examined in this study tended to be less active against *M. avium*. Compound **9** was also bactericidal for *M. tuberculosis* and showed significant intracellular activity in a human macrophage cell line. However, the concentration of **9** that was active intracellularly also lowered the viability of the infected macrophages by 39%. The possible contribution of this loss of macrophage viability to the decrease in viability of the intracellular *M. tuberculosis* is unclear. We have observed that when there is significant decrease in macrophage viability, *M. tuberculosis* viability can also be affected. Therefore, the CFU reduction may not have been due to the drug alone.

Experimental Section

General. The general procedures were same as reported earlier.[20] The solvent used in NMR is $CDCl_3$ unless otherwise stated. The structures of disaccharides were assigned on the basis of decoupling experiments in ^{1}H NMR.

Octyl-α-D-arabinofuranoside (4a). To a solution of **2**[16] (19.0 g, 36.1 mM) obtained from **1**[15], in CH_3CN (600 mL) was added *n*-octanol (10 mL, 63.5 mM) and $SnCl_4$ (10 mL, 85.5 mM). The reaction mixture was stirred under argon at room temp. After 15h the reaction mixture was diluted with sat $NaHCO_3$ (127 mL) and filtered through a celite pad. To the filtrate was added $CHCl_3$ (260 mL) and water (260 mL). The aqueous layer was extracted thrice with $CHCl_3$. The combined organic layers were washed with aq. $NaHCO_3$, water, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give crude yellow oil. Purification through a short column of silica gel (cyclohexane : EtOAc, 4 : 1) gave **3a** (14 g) as a yellow oil.
A solution of **3a** (4.69 g, 8.17 mM) in dry MeOH (36 mL) was treated with methanolic ammonia (7N, 36 mL) under an atmosphere of argon. After 22 h at room temp the reaction mixture was concentrated under reduced pressure followed by column chromatography ($CHCl_3$: MeOH, 9.5 : 0.5) gave **4a,** (5.30 g, 56 % for the last two steps). FAB-MS : *m/z* 263$(M+H)^+$. ^{1}HNMR : δ 5.01 (1H, s, H-1), 4.16 (1H, dd, *J* 4.2, 1.9 Hz, H-4), 4.01 (2H, m, H-2, H-3), 3.89 (1H, dd, *J* 11.8, 2.4 Hz, H-5a), 3.82 (1H, dd, *J* 11.8, 1.76 Hz, H-5b), 3.71 (1H, m, OC*H*H-$(CH_2)_6CH_3$), 3.44 (1H, m, OCH*H*-$(CH_2)_6CH_3$), 1.59 (2H, m, OCHH-C*H*$_2(CH_2)_5CH_3$), 1.27 (10H, m, OCHH-$CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 7.0 Hz, OCHH-$CH_2(CH_2)_5CH_3$).
Octyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (**5a**). Compound **4a** (6.39 g, 24.4 mM) in anhydrous pyridine (30 mL) was cooled to 0 ºC and added drop wise a solution of *p*-toluenesulphonyl chloride (5.11 g, 26.8 mM). After 24 h at room temperature, the mixture was poured into ice water (83 mL), and extracted twice with CH_2Cl_2. The combined organic layers were washed successively with 1N HCl, aq. $NaHCO_3$, water, dried ($MgSO_4$), filtered, and concentrated to give crude yellow oil. Purification by silica gel chromatography (cyclohexane :

EtOAc, 1 : 1) gave **5a** (5.72 g, 57%) as a clear oil. FAB-MS *m/z* 417 $(M+H)^+$. ^{1}H NMR : δ 7.78 (2H, d, *J* 8.1 Hz, Ar*H*, ortho), 7.50 (2H, d, *J* 8.5 Hz, Ar*H*, meta), 5.42 (1H, d, *J* 5.3 Hz, 2-OH), 5.32 (1H, d, *J* 5.3 Hz, 3-OH), 4.64 (1H, d, *J* 0.8 Hz, H-1), 4.14 (1H, dd, *J* 11.0, 2.6 Hz, H-5a), 4.02 (1H, dd, *J* 11.0, 6.6 Hz, H-5b), 3.80 (1H, m, H-3), 3.72 (1H, m, H-2), 3.58 (1H, m, H-4), 3.48 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.40 (s, 3H, ArCH_3), 3.25 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 1.49 (2H, m, -$OCH_2CH_2(CH_2)$5CH3), 1.26 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.85 (3H, t, *J* 7.0 Hz, -$OCH_2CH_2(CH_2)_5CH_3$).

Octyl-2,3-di-*O*-acetyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (**6a**). To an ice cold solution of **5a** (4.93 g, 11.85 mM) in pyridine (21 mL) was added drop wise Ac_2O (15.2 mL) and allowed to equilibrate to room temp. Usual work up and purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave 4.0 g (68%) of **6a** as a clear oil. FAB-MS *m/z* 501 $(M+H)^+$; ^{1}H NMR : δ 7.80 (2H, d, *J* 8.3 Hz, Ar*H*, ortho), 7.35 (2H, d, *J* 8.5 Hz, Ar*H*, meta), 5.03 (1H, d, *J* 1.3 Hz, H-2), 4.96 (1H, s, H-1), 4.85 (1H, dd, *J* 4.8, 1.0 Hz, H-3), 4.27 (2H, m, H-5a,b), 4.15 (1H, m, H-4), 3.62 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.40 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 2.45 (s, 3H, ArCH_3), 2.07, 2.06 (3H each, s, 2 × OAc), 1.56 (2H, m, -$OCH_2CH_2(CH_2)$5CH3), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.87 (3H, t, *J* 7.0 Hz, -$OCH_2CH_2(CH_2)_5CH_3$).

Octyl-2,3-di-*O*-acetyl-5-deoxy-5-*S*-acetyl-5-thio-α-D-arabinofuranoside (**7a**). To a solution of **6a** (1.02 g, 2.04 mM) in DMF (4 mL) was added potassium thioacetate (0.60 g, 5.26 mM) under an atmosphere of argon. After 26 h at room temperature, the reaction mixture was diluted with ether (40 mL). The aqueous phase was extracted with ether and the combined organic layers were washed with water, dried (Na_2SO_4), filtered, and concentrated to give crude orange oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave 0.719 g (88%) of **7a** as a yellow oil. FAB-MS *m/z* 405 $(M+H)^+$; ^{1}HNMR : δ 5.03 (1H, d, *J* 1.9 Hz, H-2), 4.96 (1H, bs, H-1), 4.89 (1H, dd, *J* 5.7, 1.9 Hz, H-3), 4.16 (1H, m, H-4), 3.65 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.40 (2H, m, H-5a, -OCH*H*$(CH_2)_6CH_3$), 3.17 (1H, dd, *J* 15.8, 6.8 Hz, H-5b), 2.36 (s, 3H, -SAc), 2.109, 2.101 (3H, s, 2 × OAc), 1.56 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$).

Octyl-5-deoxy-5-*S*-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (8a). To a solution of **7a** (1.14 g, 2.8 mM) in dry MeOH (24 mL), cooled to -40ºC, was added a solution of sodium metal (65 mg) in dry MeOH (20 mL). The mixture was stirred for 1 h at -40 ºC, and then for 30 min at 0 ºC, the course of the reaction being monitored by T.L.C. The solvent was removed by passing argon into the mixture. To the residue was added dry benzene (34mL) and nitromethane (34 mL). The volume was reduced by half under reduced pressure. Then a solution of **2** (2.27 g, 4.3 mM) in benzene (5 mL) and nitromethane (5mL) was added, followed by $Hg(CN)_2$ (1.08 g, 4.3 mM) and 4 A^0 molecular sieves. The cloudy white reaction mixture was stirred for 40 h at 65 ºC, under an atmosphere of argon, with exclusion of moisture and light. The reaction mixture was allowed to cool, diluted with $CHCl_3$ (24mL), and filtered through a bed of celite. The filtrate was washed with water, aq. $NaHCO_3$, aq. NaCl, dried ($MgSO_4$), filtered, and concentrated to give crude yellow foam. Purification by silica gel chromatography (cyclohexane : EtOAc, 3 : 1) gave 0.28 g (15%) of **8a** as a yellow oil. FAB-MS

m/z 729 $(M+Li)^+$; ^{1}HNMR : δ 7.70 (15H, m, Ar*H*), 5.81, (1H, bs, H-1′), 5.65 (1H, d, *J* 4.6 Hz, H-2′), 5.50 (1H, dd, *J* 1.3, 1.1 Hz, H-3′), 4.98 (1H, bs, H-1), 4.77 (3H, m, H-4′, H-5′a,b), 4.32 (1H, m, H-4), 4.06 (1H, d, $J_{2,OH}$=9.0 Hz, H-2), 3.98 (1H, dd, $J_{3,4,OH}$=10.1, 2.9 Hz, H-3), 3.65 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.38 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.26 (1H, dd, *J* 14.7, 4.8 Hz, H-5a), 3.01 (2H, m, 2-OH, H-5b), 2.60 (1H, d, *J* 10.1 Hz, 3-OH), 1.52 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.25 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.86 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (HRMS calcd for $C_{39}H_{46}O_{11}S$: *m/z* $(M+Na)^+$ 745.2653. Found *m/z* 745.2678).

Octyl-5-deoxy-5-*S*-(α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (9a). To a solution of **8a** (0.18 g, 0.25 mM) in dry chloroform (2 mL) and dry methanol (1.5 mL) was added a solution of sodium metal (10 mg) in dry methanol (1 mL). The reaction mixture was stirred under an atmosphere of argon. After 36h at room temperature, the reaction mixture was diluted with water (6 mL) and neutralized with Dowex-50W (50X8-400) cation exchange resin. The mixture was filtered through a cintered glass funnel and the filtrate partitioned between chloroform and water. The aqueous layer was washed with chloroform and then concentrated under reduced pressure. The white residue was purified by silica gel chromatography ($CHCl_3$: MeOH, 9 : 1) to give 0.04 g (40%) of **9a** as a clear oil. FAB-MS *m/z* 417 $(M+Li)^+$; ^{1}HNMR (Me_2SO-d_6) : δ 5.53 (1H, d, *J* 5.5 Hz, OH), 5.37 (1H, d, *J* 4.8 Hz, OH), 5.23 (1H, d, *J* 5.1 Hz, OH), 5.19 (1H, d, *J* 5.5 Hz, OH), 4.96 (1H, d, *J* 3.7 Hz, H-1), 4.75 (1H, t, *J* 5.5 Hz, 5′-OH), 4.68 (1H, d, *J* 2.0 Hz, H-1′), 3.85 (1H, m, H-3), 3.65 (8H, m, H-5′a, H-4′, H-3′, H-2′, H-2, H-3, -OC*H*H$(CH_2)_6CH_3$), 3.44 (1H, m, H-5′b), 2.91 (1H, dd, *J* 13.8, 3.7 Hz, H-5a), 2.65 (1H, dd, *J* 13.8, 7.0 Hz, H-5b), 1.50 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.25 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.85 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (HRMS calcd for $C_{18}H_{34}O_8S$: *m/z* $(M+Na)^+$ 433.1866. Found *m/z* 433.1868).

1-Methylpropyl-2,3,5-tri-*O*-benzoyl-α-D-arabinofuranoside (**3b**). To a solution of **2**[16] (2.71 g, 5.17 mM) in CH_3CN (80 mL) was added n-octanol (0.81 mL, 8.9 mM) and $SnCl_4$ (1.38 mL, 11.8 mM) as done in **3a** to give an orange oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave of **3b** as diastereomers **(**2.0 g, 75%) as a clear oil. FAB-MS *m/z* 525 $(M+Li)^+$; ^{1}H NMR : δ 8.70 (15H, m, Ar*H*), 5.58 (1H, bs, H-3), 5.48 (1H, bs, H-2), 5.40 (1H, bs, H-1), 4.87 (1H, m, H-5a), 4.67 (1H, m, H-5b), 4.57 (1H, m, H-4), 3.81 (1H, m, OC*H*$(CH_3)CH_2CH_3$), 1.58 (2H, m, OCH$(CH_3)CH_2CH_3$), 1.26 (3H, d, OCH$(CH_3)CH_2CH_3$), 0.88 (3H, t, *J* 6.8 Hz, OCH$(CH_3)CH_2CH_3$).

1-Methylpropyl-α-D-arabinofuranoside (4b). A solution of **3b** (3.29 g, 6.35 mM) in dry methanol (28 mL) was treated with methanolic ammonia (7N, 28 mL) under an atmosphere of argon as reported earlier in **4a** to give **4b** (1.3 g) as a yellow oil. The material was used directly in the next step.

1-Methylpropyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (5b). Compound **4b** (1.3 g, 6.31 mM) in anhydrous pyridine (9.3 mL) was cooled to 0 °C and added drop wise a solution of *p*-toluenesulphonyl chloride (1.30 g, 6.82 mM) as mentioned earlier in **5a** to give a crude yellow oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 1 : 1) gave **5b** as diastereomers (1.4 g, 62%) as a clear oil. FAB-MS *m/z* 361 $(M+H)^+$. ^{1}HNMR : δ 7.80 (2H, d, *J*

8.3 Hz, Ar*H*, ortho), 7.35 (2H, d, *J* 8.3 Hz, Ar*H*, meta), 5.08 (1H, s, H-1), 4.22 (2H, m, H-5a,b), 4.05 (1H, m, H-2), 3.88 (1H, m, H-3), 3.70 (1H, m, -OC*H*(CH_3)CH_2CH_3), 2.87 (1H, *J* 10.7 Hz, 3-OH), 2.45 (3H, s, ArC*H*$_3$), 2.22 (1H, *J* 7.7 Hz, 2-OH), 1.46 (2H, m, -OCH(CH_3)C*H*$_2$$CH_3$), 1.12 (3H, m, OCH(C*H*$_3$)$CH_2CH_3$), 0.87 (3H, t, *J* 7.2 Hz, OCH(CH_3)CH_2C*H*$_3$).

1-Methylpropyl-2,3-di-*O*-acetyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (6b). To an ice cold solution of **5b** (1.62 g, 4.50 mM) in pyridine (8 mL) was added drop wise Ac_2O (7.3 mL) as done in **6a** to give a crude oil. Purification by silica gel chromatography (cyclohexane/EtOAc, 3 : 1) gave 1.48 g (74%) of **6b** as diastereomers. FAB-MS *m/z* 451 $(M+Li)^+$; ^{1}H NMR : δ 7.80 (2H, Ar*H*, ortho), 7.34 (2H, Ar*H*, meta), 5.07 (1H, s, H-1), 5.00 (1H, bs, H-3), 4.88 (1H, m, H-2), 4.26 (3H, m, H-4, H-5a,b), 3.65 (1H, m, -OC*H*(CH_3)CH_2CH_3), 2.45 (3H, s, ArC*H*$_3$), 2.07 (6H, s, 2 × OAc), 1.47 (2H, m, -OCH(CH_3)C*H*$_2$$CH_3$), 1.13 (3H, m, OCH(C*H*$_3$)$CH_2CH_3$), 0.90 (3H, t, *J* 7.2 Hz, OCH(CH_3)CH_2C*H*$_3$). Anal. Calcd. for $C_{20}H_{28}O_9S$. 0.1 $CHCl_3$: C, 52.89; H, 6.20. Found : C, 52.68; H, 6.19.

1-Methylpropyl-2,3-di-O-acetyl-5-deoxy-5-S-acetyl-5-thio-α-D-arabinofuranoside (7b). To a solution of **6b** (1.09 g, 2.18 mM) in DMF (4.3 mL) was added potassium thioacetate (0.64 g, 5.62 mM) as reported in **7a** to give a crude orange oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave 0.689 g (81%) of **7b** as a yellow oil (diastereomers). FAB-MS *m/z* 355 $(M+Li)^+$; ^{1}HNMR : δ 5.09 (1H, s, H-1), 5.00 (1H, s, H-3), 4.86 (1H, m, H-2), 4.23 (3H, m, H-4, H-5a,b), 3.63 (1H, m, -C*H*(CH_3)CH_2CH_3), 2.45 (3H, s, ArC*H*$_3$), 2.07 (6H, s, 2 × OAc), 1.47 (2H, m, -CH(CH_3)C*H*$_2$$CH_3$), 1.22 (6H, m, -CH(C*H*$_3$)$CH_2$C*H*$_3$). Anal. Calcd. for $C_{15}H_{24}O_7S$: C, 51.71; H, 6.94. Found : C, 51.37; H, 6.85.

1-Methylpropyl-5-deoxy-5-*S*-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (8b). To a solution of **7b** (0.868 g, 2.49mM) in dry MeOH (18 mL), cooled to -40 °C, was added a solution of sodium metal (60 mg) in dry MeOH (18 mL). The mixture was stirred at -40 °C, and slowly allowed to equilibrate to room temperature. After 20 h the solvent was removed by passing argon into the mixture, and then carefully under reduced pressure. To the residue was added dry benzene (30 mL) and nitromethane (30mL). The volume was reduced by half under reduced pressure. Then a solution of 3 (2.09 g, .3.97 mM) in benzene / nitromethane (4.5 mL each) was added, followed by $Hg(CN)_2$ (1.0 g, 3.97 mM) and 4 A^0 molecular sieves as mentioned in **8a** to give a crude yellow oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 3 : 1 to 100% EtOAc) gave 0.70 g (43%) of **8b** as a pale yellow oil (diastereomers). FAB-MS *m/z* 673 $(M+Li)^+$; ^{1}HNMR : δ 7.70 (15H, m, Ar*H*), 5.82 (1H, bs, H-1′), 5.65 (1H, d, *J* 4.6 Hz, H-3′), 5.50 (1H, dd, *J* 1.3, 1.1 Hz, H-2′), 5.11 (1H, bs, H-1), 4.77 (3H, m, H-4′, H-5′a,b), 4.32 (1H, m, H-4), 4.03 (1H, d, $J_{2,3,OH}$ = 9.2, 3.3Hz, H-2), 3.98 (1H, m, H-3), 3.65 (1H, m, -C*H*(CH_3)CH_2CH_3), 3.25 (1H, dd, *J* 14.5, 5.0 Hz, H-5a), 3.01 (2H, m, 2-OH, H-5b), 2.63 (1H, d, *J* 10.7 Hz, 3-OH), 1.52 (2H, m, -OCH(CH_3)C*H*$_2$$CH_3$), 1.25 (3H, m, -CH(C*H*$_3$)$CH_2CH_3$), 0.86 (3H, t, 6.8Hz, -CH(CH_3)CH_2C*H*$_3$). (HRMS calcd for $C_{35}H_{38}O_{11}S$: *m/z* $(M+Na)^+$ 689.2027. Found *m/z* 689.2033).

1-Methylpropyl-5-deoxy-5-*S*-(α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (9b). To a solution of **8b** (0.649 g, 0.97 mM) in dry chloroform (7 mL) and dry MeOH (7 mL) was

added a solution of sodium metal (60 mg) in dry MeOH (4 mL) as in **9a** followed by gel chromatography ($CHCl_3$: MeOH, 9 : 1) to give 0.209 g (61%) of **9b** as a clear oil (diastereomers). FAB-MS *m/z* 361 $(M+Li)^+$; ^{1}HNMR (Me_2SO-d_6) : δ 5.53 (1H, d, *J* 5.5 Hz, OH), 5.37 (1H, d, 5.0Hz, OH), 5.23 (1H, d, *J* 5.0 Hz, OH), 5.18 (1H, dd, *J* 5.7 Hz, OH), 4.96 (1H, d, *J* 1.7 Hz, H-1), 4.75 (1H, t, *J* 5.2 Hz, 5′-OH), 4.68 (1H, d, *J* 1.9 Hz, H-1′), 3.85 (1H, m, H-3), 3.65 (7H, m, H-5′a, H-4′, H-3′, H-2′, H-2, H-3, -C*H*$(CH_3)CH_2CH_3$), 3.44 (1H, m, H-5′b), 2.92 (1H, dd, *J* 13.4, 3.7 Hz, H-5a), 2.65 (1H, dd, *J* 13.4, 7.2 Hz, H-5b), 1.50 (2H, m, -OCH(CH_3)C*H*$_2CH_3$), 1.25 (3H, m, -CH(C*H*$_3)CH_2CH_3$), 0.85 (3H, t, *J* 7.2 Hz, -CH$(CH_3)CH_2$C*H*$_3$). (HRMS calcd for $C_{14}H_{26}O_8S$: *m/z* $(M+Na)^+$ 377.1240. Found *m/z* 377.1244).

3′-Phenylpropyl-2,3,5-tri-*O*-benzoylarabinofuranoside (3c). To a solution of **2**[16] (9.7 g, 18.5 mM) in CH_3CN (289 mL), was added 3-phenyl-1-propanol (4.3 mL, 31.5 mM) and $SnCl_4$ (4.8 mL, 40.8 mM) as done in **3a** to give a crude yellow oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave 6.72 g (63%) of **3c** as a clear oil. FAB-MS *m/z* 587 $(M+Li)^+$; ^{1}HNMR : δ 7.62 (20 H, m, Ar.*H*), 5.58 (1H, d, *J* 4.8 Hz, H-3), 5.54 (1H, d, *J* 1.3 Hz, H-2), 5.28 (1H, s, H-1), 4.82 (1H, dd, *J* 11.6, 3.5 Hz, H-5a), 4.67 (1H, dd, *J* 12.1, 5.1 Hz, H-5b), 4.58 (1H, m, H-4), 3.82 (1H, m, -OC*H*$HCH_2CH_2C_6H_5$), 3.57 (1H, m, -OCH*H*$CH_2CH_2C_6H_5$), 2.72 (2H, m, -OCH_2CH_2C*H*$_2C_6H_5$), 2.00 (2H, m, -OCH_2C*H*$_2CH_2C_6H_5$). Anal. Calcd. for $C_{35}H_{32}O_8.H_2O$: C, 70.23; H, 5.68. Found : C, 70.09; H, 5.58.

3′-Phenylpropyl-α-D-arabinofuranoside (**4c**)**.** A solution of **3c** (6.7 g, 11.5 mM) in 51 mL of dry MeOH was treated with methanolic ammonia (7N, 51 mL) as reported in **4a** to give 3.0 g (quant.) of **4c** as a yellow oil. The material was used directly in the next step.

3′-Phenylpropyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (**5c**). Compound **4c** (3.0 g, 11.5 mM) in anhydrous pyridine (14 mL) was cooled to 0 °C and added drop wise a solution of *p*-toluenesulphonyl chloride (2.42 g, 12.7 mM) as done in **5a** to give an orange-brown oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 1 : 1) gave 2.91 g (60%) of **5c** as a pale yellow oil. FAB-MS *m/z* 423 $(M+H)^+$; ^{1}HNMR : δ 7.80 (2H, d, *J* 8.6 Hz, Ar*H*), 7.32 (2H, d, *J* 8.6 Hz, Ar*H*), 7.25 (5H, m, -OCHH$CH_2CH_2C_6H_5$), 4.94 (1H, s, H-1), 4.27 (3H, m, H-4, H-5a,b), 3.92 (1H, m, H-3), 3.73 (1H, m, -OC*H*$HCH_2CH_2C_6H_5$), 3.43 (1H, m, -OCH*H*$CH_2CH_2C_6H_5$), 2.74 (1H, d, *J* 10.1 Hz, 3-OH), 2.65 (2H, t, *J* 7.9 Hz, -OCHHCH_2C*H*$_2C_6H_5$), 2.44 (3H, s, ArC*H*$_3$), 2.36 (1H, d, *J* 6.8 Hz, 2-OH), 1.90 (2H, m, -OCHHC*H*$_2CH_2C_6H_5$). Anal. Calcd. for $C_{21}H_{26}O_7S.0.1CHCl_3$: C, 60.82; H, 6.22. Found : C, 60.52; H, 6.11.

3′-Phenylpropyl-2,3-di-*O*-acetyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (**6c**). To an ice cold solution of **5c** (2.78 g, 6.59 mM) in pyridine (11.7 mL) was added drop wise Ac_2O (10.7 mL) as in **6a** to give a crude oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave 1.46 g (45%) of **6c** as a clear oil. FAB-MS *m/z* 507 $(M+H)^+$; ^{1}HNMR : δ 7.80 (2H, d, *J* 8.3 Hz, Ar*H*), 7.33 (2H, d, *J* 7.9 Hz, Ar*H*), 7.22 (5H, m, -OCHH$CH_2CH_2C_6H_5$), 5.05 (1H, d, *J* 1.3 Hz, H-2), 4.97 (1H, s, H-1), 4.88 (1H, dd, *J* 4.8, 0.9 Hz, H-3), 4.26 (2H, m, H-5a,b), 4.19 (1H, m, H-4), 3.65 (1H, m, -OC*H*$HCH_2CH_2C_6H_5$), 3.40 (1H, m, -OCH*H*$CH_2CH_2C_6H_5$),

2.65 (2H, m, -OCHHCH$_2$C*H*$_2$C$_6$*H*$_5$), 2.44 (3H, s, Ar.C*H*$_3$), 2.08 (6H, s, 2 × OAc), 1.88 (2H, m, -OCHHC*H*$_2$CH$_2$C$_6$*H*$_5$); Anal. Calcd. for $C_{25}H_{30}O_9S$: C, 59.29; H, 5.93. Found : C, 59.45; H, 6.30.

3′-Phenylpropyl-2,3-di-*O*-acetyl-5-deoxy-5-*S*-acetyl-α-D-arabinofuranoside (**7c**). To a solution of **6c** (1.41 g, 2.80 mM) in DMF (6.5 mL) was added potassium thioacetate (1.07 g, 9.38 mM) as reported in **7a** to give a crude orange oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 4 : 1) gave 0.904 g (79%) of **7c** as an orange oil. FAB-MS *m/z* 417 $(M+Li)^+$; ^{1}HNMR : δ 7.22 (5H, m, Ar.*H*), 5.06 (1H, d, *J* 1.5 Hz, H-2), 4.96 (1H, s, H-1), 4.90 (1H, dd, *J* 5.5, 1.5 Hz, H-3), 4.19 (1H, m, H-4), 3.69 (1H, m, -OC*H*HCH$_2$CH$_2$C$_6$*H*$_5$), 3.43 (1H, m, -OCH*H*CH$_2$CH$_2$C$_6$*H*$_5$), 3.36 (1H, dd, *J* 13.8, 4.8 Hz, H-5a), 3.16 (1H, dd, *J* 13.8, 6.8 Hz, H-5b), 2.69 (2H, m, -OCHHCH$_2$C*H*$_2$C$_6$*H*$_5$), 2.35 (3H, s, -SAc), 2.11 (6H, s, 2xOAc), 1.90 (2H, m, -OCHHC*H*$_2$CH$_2$C$_6$*H*$_5$). Anal. Calcd. for $C_{20}H_{26}O_7S$: C, 58.52; H, 6.38. Found : C, 58.79; H, 6.39.

3′-Phenylpropyl-5-deoxy-5-*S*-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (**8c**). To a solution of **7c** (0.848 g, 2.06 mM) in dry MeOH (15 mL), cooled to -40 ºC, was added a solution of sodium metal (70 mg) in dry MeOH (15 mL). The mixture was stirred at -40ºC, and slowly allowed to equilibrate to room temperature. After 18 h the solvent was removed by passing argon into the mixture, and then carefully under reduced pressure. To the residue was added dry benzene (25 mL) and nitromethane (25 mL). The volume was reduced by half under reduced pressure. Then a solution of **3** (1.92 g, 3.65 mM) in benzene/nitromethane (5 mL each) was added, followed by $Hg(CN)_2$ (0.92 g, 3.65 mM) and 4 A^0 molecular sieves as done in **8a** to give a crude orange oil. Purification by silica gel chromatography (cyclohexane : EtOAc, 2 : 1) gave 0.25 g (16%) of **8c** as a clear oil. FAB-MS *m/z* 735 $(M+Li)^+$; ^{1}HNMR : δ 7.60 (20H, m, Ar.*H*), 5.81, (1H, bs, H-1′), 5.65 (1H, dd, *J* 2.0, 0.9 Hz, H-3′), 5.50 (1H, t, *J* 1.3 Hz, H-2′), 4.97 (1H, s, H-1), 4.83 (1H, m, H-5′a), 4.77 (1H, m, H-4′), 4.71 (1H, m, H-5′b), 4.30 (1H, m, H-4), 4.06 (1H, bs, H-2), 4.05 (1H, bs, H-3), 3.69 (1H, m, OH), 3.62 (1H, m, -OC*H*HCH$_2$CH$_2$C$_6$H$_5$), 3.40 (1H, m, -OCH*H*CH$_2$CH$_2$C$_6$*H*$_5$), 3.25 (1H, dd, *J* 14.7, 4.8 Hz, H-5a), 2.97 (1H, dd, *J* 14.7, 3.9 Hz, H-5b), 2.96 (1H, m, OH), 2.64 (2H, t, *J* 7.9 Hz, -OCHHCH$_2$C*H*$_2$C$_6$*H*$_5$), 1.88 (2H, m, -OCHHC*H*$_2$CH$_2$C$_6$*H*$_5$). (HRMS calcd for $C_{40}H_{40}O_{11}S$: *m/z* $(M+Na)^+$ 751.2183. Found *m/z* 751.2195).

3′-Phenylpropyl-5-deoxy-5-*S*-(α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (**9c**). To a solution of **8c** (0.224 g, 0.30 mM) in dry $CHCl_3$ (2.2 mL) and dry MeOH (2.2 mL) was added a solution of sodium metal (20 mg) in dry MeOH (1.3 mL) as mentioned in **9a**. The residue was purified by silica gel chromatography ($CHCl_3$: MeOH, 9 : 1) to give 70 mg (55%) of **9c** as a clear oil. FAB-MS *m/z* 417 $(M+H)^+$; ^{1}H NMR (Me_2SO-d_6) : δ 7.22 (5H, m, -C$_6$*H*$_5$), 5.54 (1H, 2-OH), 5.40 (1H, 2′-OH), 5.24 (2H, 3-OH, 3′-OH), 4.98 (1H, d, *J* 3.7 Hz, H-1), 4.78 (1H, 5′-OH), 4.70 (1H, d, *J* 2.2 Hz, H-1′), 3.70 (5H, m, H-2, H-3, H-3′, H-4′, -OC*H*HCH$_2$CH$_2$C$_6$H$_5$), 3.45 (2H, m, H-5′a,b), 3.30 (1H, m, -OCH*H*CH$_2$CH$_2$C$_6$H$_5$), 2.92 (1H, dd, *J* 13.6, 3.9 Hz, H-5a), 2.65 (1H, dd, *J* 13.6, 6.8 Hz, H-5b), 2.62 (1H, t, *J* 8.1 Hz, -OCHHCH$_2$C*H*$_2$C$_6$H$_5$), 1.79 (1H, m, -OCHHC*H*$_2$CH$_2$C$_6$H$_5$). (HRMS calcd for $C_{19}H_{28}O_8S$: *m/z* $(M+Na)^+$ 439.1397. Found *m/z* 439.1396).

1-Thioacetyl-2,3,5-tri-*O*-benzoyl-1-thio-α-D-arabinofuranoside (**10**). Compound **1**[15] (500 mg, 1.05 mM) was dissolved in anhydrous CH_2Cl_2 (10 mL), thiolacetic acid (71 μL, 0.99 mM) was added drop wise followed by BF_3OEt_2 (0.66 mL, 5.25 mM) at room temperature under the atmosphere of argon. The reaction mixture was stirred overnight at room temperature. Aq. $NaHCO_3$ was added to it and reaction mixture was extracted twice with CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Column chromatography (cyclohexane : EtOAc, 9.5 : 0.5) of the residue gave **10** (464 mg, 85%) as a colorless syrup. FAB-MS *m/z* 527 $(M+Li)^+$; ^{1}HNMR δ 8.06 (6H, m, arom.*H*, ortho), 7.45 (9H, m, arom.*H*, meta, para), 6.32 (1H, d, *J* 0.6 Hz, H-1), 5.70 (1H, broad s, H-2), 5.63 (1H, m, H-3), 4.73 (2H, m, H-5a,b), 4.62 (1H, m, H-4), 2.45 (3H, s, -SAc).

Octyl-2,3-di-*O*-acetyl-5-deoxy-5-iodo-α-D-arabinofuranoside (**12**). A solution of NaI (840 mg, 5.6 mM) and **6a** (400 mg, 0.8 mM) in 2-butanone (10 mL) was refluxed for 5 h. The reaction mixture was cooled to ambient temperature and filtered through a pad of celite. The filtrate was concentrated in reduced pressure and residue was partitioned between CH_2Cl_2 and water. The organic layer was washed with aq. $Na_2S_2O_3$ (0.1N), water, dried over Na_2SO_4, filtered and concentrated to give a clear oil. Column chromatography (cyclohexane : EtOAc, 9.5 : 0.5) of oil resulted in **12** (205 mg, 56%). FAB-MS *m/z* 463 $(M+Li)^+$; ^{1}HNMR δ 5.09 (1H, d, *J* 1.3 Hz, H-2), 5.03 (1H, s, H-1), 4.87 (1H, dd, *J* 5.1, 1 Hz, H-3), 4.06 (1H, m, H-4), 3.68 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.45 (3H, m, H-5a,b, -OCH*H*$(CH_2)_6CH_3$), 2.11 (6H, s, 2 × OAc), 1.57 (2H, m, -OCH_2C*H*$_2(CH_2)_5CH_3$), 1.27 (10H, m, -$OCH_2CH_2(C$*H*$_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5C$*H*$_3$).

Octyl-2,3-di-*O*-acetyl-5-*S*-(2,3,4-tri-*O*-acetyl-β-D-arabinopyranosyl)-5-thio-α-D-arabino-furanoside (13) and **Octyl-2,3-di-*O*-acetyl-5-*S*-(2,3,5-tri-*O*-acetyl-β-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside** (**14**). To a solution of **10** (103 mg, 0.2 mM) in anhydrous MeOH (5 mL), freshly prepared solution of MeONa (1M, 0.2 mL) was added drop wise at –78 ^{0}C under argon. After 1h at room temperature, TLC confirmed the completion of the reaction. MeOH was evaporated off by gently passing the argon through the flask. The resulting residue **11** was dried overnight in vacuum pump.

The residue **11** and iodo sugar, **12** (76 mg, 0.16 mM) were dissolved separately in dry DMF (5mL each) and mixed together slowly at room temperature under the atmosphere of argon. The reaction mixture was stirred for 48 h at room temperature. DMF was evaporated off under reduced pressure. The residue was taken in CH_2Cl_2, washed with aq. $NaHCO_3$, water, dried over Na_2SO_4, filtered and concentrated to thick syrup. The syrup was acetylated with dry pyridine (3 mL) and Ac_2O (3 mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 9 : 1 to 8 : 2) gave **13** (30 mg, 25%) and **14** (20 mg, 16%).

13 : FAB-MS *m/z* 627 $(M+Li)^+$; ^{1}H NMR δ 5.83 (1H, d, *J* 5.3 Hz, H-1′), 5.31 (2H, m, H-2′, H-4′), 5.22 (1H, dd, *J* 10.3, 3.3 Hz, H-3′), 5.03 (1H, m, H-2), 4.97 (1H, s, H-1), 4.89 (1H, dd, *J* 5.5, 1.5H z, H-3), 4.30 (1H, dd, *J* 13.2, 1.5 Hz, H-5′a), 4.18 (1H, dd, *J* 11.6, 5.9 Hz, H-4), 3.67 (2H, m, H-5′b, -OC*H*H$(CH_2)_6CH_3$), 3.42 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 2.88 (2H, d, *J* 6.2 Hz, H-5a,b), 2.133, 2.096, 2.093, 2.075, 2.023 (3H, s, 5 × OAc), 1.58 (2H, m, -OCH_2C*H*$_2(CH_2)_5CH_3$), 1.27

(10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 54.56, H, 7.17. $C_{28}H_{44}O_{13}S$ required C, 54.18, H, 7.14).

14 : FAB-MS *m/z* 627 $(M+Li)^+$; ^{1}H NMR δ 5.63 (1H, d, *J* 5.3 Hz, H-1′), 5.39 (1H, dd, *J* 5.0, 1.1 Hz, H-2′), 5.22 (1H, t, *J* 4.2 Hz, H-3′), 5.03 (1H, m, H-2), 4.98 (1H, s, H-1), 4.91 (1H, dd, *J* 7.3, 1.5 Hz, H-3), 4.43 (1H, dd, *J* 11.6, 5.3 Hz, H-5′a), 4.24 (2H, m, H-4′, H-5′b), 4.10 (1H, m, H-4), 3.66 (H, m, -OC*H*H$(CH_2)_6CH_3$), 3.42 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 2.99 (2H, m, H-5a,b), 2.13, 2.12, 2.11, 2.10, 2.09 (3H, s, 5 × OAc), 1.59 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 54.07, H, 6.75. $C_{28}H_{44}O_{13}S$ required C, 54.18, H, 7.14).

1-Thioacetyl-2,3,5-tri-*O*-benzyl-1-thio-α-D-arabinofuranoside (**17**). Compound **16**[21] (1.79 g, 4.12 mM) obtained from **15**[18], was dissolved in anhydrous CH_2Cl_2 (20 ml), thiolacetic acid (392 μL, 5.44 mM) was added drop wise followed by BF_3OEt_2 (3.88m L, 31 mM) at room temperature as done in **10**. Column chromatography (cyclohexane : EtOAc, 9.5 : 0.5) of the residue gave **17** (340 mg, 29%) and its β-anomer (200 mg, 17%) as colorless syrups. FAB-MS *m/z* 485 $(M+Li)^+$; ^{1}HNMR δ 7.29 (15H, m, arom.*H*), 6.12 (1H, s, H-1), 4.54 (6H, m, -CH_2 of Bn), 4.23 (1H, m, H-4), 4.13 (1H, t, *J* 1.5 Hz, H-2), 3.98 (1H, m, H-3), 3.59 (2H, m, H-5a,b), 2.36 (3H, s, -SAc).

Octyl-2,3-di-*O*-acetyl-5-*S*-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)-5-thio-α-D-arabino-furanoside (**19**). To a solution of **17** (230 mg, 0.48 mM) in anhydrous MeOH (5 mL), freshly prepared solution of MeONa (1M, 0.5 mL) was added drop wise at –78^{0}C as reported in **13** and **14** to give thiosodium **18.**

The residue **18** and tosyl derivative **6a** (250 mg, 0.5 mM) were dissolved separately in dry DMF (5 mL each) and mixed together slowly at room temperature as done in **13** and **14.** Column chromatography (cyclohexane : EtOAc, 9.5 : 0.5 to 9 : 1) of the residue gave **19** (42 mg, 12%). FAB-MS *m/z* 771 $(M+Li)^+$; ^{1}HNMR δ 7.28 (15H, m, arom.*H*), 5.50 (1H, d, *J* 2.2 Hz, H-1′), 5.06 (2H, m, H-2, H-3), 4.96 (1H, s, H-1), 4.53 (6H, m, -CH_2 of Bn), 4.31 (2H, m, H-4, H-4′), 3.99 (2H, m, H-2′, H-3′), 3.64 (3H, m, H-5′a,b, -OC*H*H$(CH_2)_6CH_3$), 3.39 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.18 (1H, dd, *J* 14.1, 4.5 Hz, H-5a), 2.91 (1H, dd, *J* 14.1, 5.7 Hz, H-5b), 2.06, 2.03, (3H, s, 2 × OAc), 1.57 (2H, m, $OCH_2CH_2(CH_2)_5CH_3$), 1.26 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.87 (3H, t, *J* 6.3 Hz, $OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 66.91, H, 6.96. $C_{43}H_{56}O_{10}S$ required C, 66.51, H, 7.37).

Methyl-2,3,5-tri-*O*-methyl-α-D-arabinofuranoside (**20**). Compound **15**[18] (1.73 g, 10.59 mM) was dissolved in dry DMF (50 mL) and NaH (60% dispersion in mineral oil, 2.12 g, 53 mM) was added. The reaction mixture was stirred at room temperature for 30min followed by addition of iodomethane (3.62 mL, 58.24 mM) dropwise at 0 ºC and stirred for 4 h at room temperature. MeOH (20 mL) was added, the solution was concentrated to dryness, the oil was redissolved in CH_2Cl_2 and organic layer was washed with water, brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was chromatographed (cyclohexane : EtOAc, 9 : 1) to yield **20** (1.29 g, 60%). FAB-MS *m/z* 213 $(M+Li)^+$; ^{1}HNMR δ 4.92 (1H, s, H-1), 4.11

(1H, m, H-4), 3.70 (1H, dd, *J* 2.2, 0.7 Hz, H-2), 3.59 (3H, m, H-3, H-5a,b), 3.422 , 3.419, 3.409, 3.402 (3H, s, 4x -OMe).

1-Thioacetyl-2,3,5-tri-*O*-methyl-1-thio-β-D-arabinofuranoside (**21**) and **1-Thioacetyl-2,3,5-tri-*O*-methyl-1-thio-α-D-arabinofuranoside** (**22**). Compound **20** (1.28 g, 6.24 mM) was dissolved in anhydrous CH_2Cl_2 (15 ml), thiolacetic acid (585 μL, 8.11 mM) was added drop wise followed by BF_3OEt_2 (5.8 mL, 46.8 mM) as reported in **10** to give the thin oil which was column chromatographed (cyclohexane : EtOAc, 8.5 : 1.5) to give **21** (688 mg, 44%) and **22** (279 mg, 18%).

21 : FAB-MS *m/z* 257 $(M+Li)^+$; ^{1}HNMR δ 6.04 (1H, d, *J* 4.9 Hz, H-1), 4.05 (1H, m, H-4), 3.94 (1H, dd, *J* 4.9, 3.6 Hz, H-2), 3.71 (1H, t, *J* 3.8 Hz, H-3), 3.50 (2H, m, H-5a,b), 3.42, 3.41, 3.38 (3H, s, 3 × OMe), 2.37 (3H, s, SAc).

22 : FAB-MS *m/z* 257 $(M+Li)^+$; ^{1}HNMR δ 6.06 (1H, d, *J* 0.6 Hz, H-1), 4.09 (1H, dd, *J* 10.1, 4.9 Hz, H-4), 3.89 (1H, t, *J* 1.3 Hz, H-2), 3.64 (1H, m, H-3), 3.53 (2H, m, H-5a,b), 3.43, 3.40, 3.39 (3H, s, 3 × OMe), 2.36 (3H, s, -SAc).

Octyl-2,3-di-*O*-acetyl-5-*S*-(2,3,5-tri-*O*-methyl-α-D-arabinofuranosyl)-5-thio-α-D-arabino-furanoside (**25**). To a solution of **22** (275 mg, 1.1 mM) in anhydrous MeOH (5 mL), freshly prepared solution of MeONa (1M, 1.1 mL) was added drop wise at –78 ^{0}C as reported in **13** and **14** to give thiosodium **24.**

The residue **24** and tosyl derivative **6a** (550 mg, 1.1 mM) were dissolved separately in dry DMF (2mL each) and mixed together slowly at room temperature as done in **13** and **14.** Column chromatography (cyclohexane : EtOAc, 9 : 1 to 8.5 : 1.5) of the residue gave **25** (275 mg, 47%). Similarly, compound **21** (100 mg, 0.4 mM) was reacted with MeONa to give **23** which on coupling with **6a** (205 mg, 0.4 mM) followed by column chromatography (cyclohexane : EtOAc, 9 : 1 to 8 : 2) gave **25** (50 mg, 23 %). FAB-MS *m/z* 542.8 $(M+Li)^+$; ^{1}HNMR δ 5.43 (1H, d, *J* 1.9 Hz, H-1′), 5.04 (2H, m, H-2, H-3), 4.96 (1H, s, H-1), 4.30 (1H, m, H-4), 4.20 (1H, m, H-4′), 3.62 (5H, m, H-5′a,b, H-3′, H-2′, -OC*H*H$(CH_2)_6CH_3$), 3.42 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.412, 3.411, 3.399 (3H, s, 3 × OMe), 3.16 (1H, dd, *J* 14.1, 4.7 Hz, H-5a), 2.88 (1H, dd, *J* 14.1, 5.7 Hz, H-5b), 2.09, 2.08 (3H, s, 2 × OAc), 1.57 (2H, m, -$OCH_2CH_2$$(CH_2)_5CH_3$), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5$$CH_3$), 0.88 (3H, t, *J* 6.3 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 56.01, H, 8.12. $C_{25}H_{44}O_{10}S$ required C, 55.95, H, 8.26).

Octyl-5-*S*-(2,3,5-tri-*O*-methyl-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside. (**26**). Compound **25** (104 mg, 0.19 mM) was dissolved in dry MeOH (2mL) and methanolic ammonia (7N, 2 mL) was added to it. The reaction mixture was stirred overnight at room temperature and solvents were evaporated under reduced pressure. Column chromatography (cyclohexane : EtOAc, 7 : 3 to 6 : 4) of the residue gave **26** (61 mg, 70%). FAB-MS *m/z* 459 $(M+Li)^+$; ^{1}HNMR δ 5.43 (1H, d, *J* 1.9 Hz, H-1′), 4.95 (1H, s, H-1), 4.25 (2H, m, H-4, H-4′), 4.03 (1H, dd, *J* 8.5, 0.9 Hz, H-2), 3.96 (1H, m, H-3), 3.63 (5H, m, H-2′, H-3′, H-5′ab, -OC*H*H$(CH_2)_6CH_3$), 3.42 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.41, 3.40, 3.39 (3H, s, 3 × OMe), 3.21 (1H, dd, *J* 14.6, 5.1 Hz, H-5a), 2.99 (1H, d, *J* 8.5 Hz, 2-OH), 2.89 (1H, dd, *J* 14.6, 3.4 Hz, H-5b), 2.83 (1H, d, *J* 9.9 Hz, 3-OH), 1.59

(2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.3 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 55.67, H, 8.66. $C_{21}H_{40}O_8S$ required C, 55.72, H, 8.90).

Methyl-2,3-di-*O*-methoxybenzyl-5-*O*-*t*-butyldiphenylsily-α-D-arabinofuranoside (**28**). Compound **27**[19] (5.22 g, 12.97 mM) was added to a suspension of NaH (60% dispersion in mineral oil, 1.24 g, 31.05 mM) in dry DMF (40 mL) drop wise at 0 ^{0}C followed by methoxybenzylchloride (4.22 mL, 31.05 mM) and tetrabutylammonium bromide (1 g). The reaction mixture was stirred overnight at room temperature and was worked up as reported in **20.** The residue was column chromatographed (cyclohexane : EtOAc, 1 : 1) to yield **28** (3.7 g, 45%). FAB-MS *m/z* 665 $(M+Na)^+$; ^{1}HNMR δ 7.51 (10H, m, Ph*H* of TBDPS), 7.18 (4H, m, methoxy Bn*H*, ortho), 6.83 (4H, m, methoxyBn*H*, meta), 4.91 (1H, s, H-1), 4.43 (4H, m, -CH_2 of methoxyBn), 4.11 (1H, m, H-4), 3.94 (2H, m, H-5a,b), 3.80, 3.77 (3H, s, 2 × OMe), 3.79 (2H, m, H-2, H-3), 3.37 (3H, s, -OMe), 1.04 (9H, s, -CMe_3).

Methyl-2,3-di-*O*-methoxybenzyl-α-D-arabinofuranoside. (**29**). Tetrabutylammonium fluoride (8 mL, 7.95 mM) was added drop wise to a solution of **28** (3.65 g, 5.68 mM) in freshly distilled THF (50 mL) at 0 ^{0}C. The reaction was warmed upto room temperature and stirred for 3 h. Brine water was added to the reaction mixture and extracted with EtOAc twice. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was passed through a column (cyclohexane : EtOAc, 8 : 2 to 6 : 4) to yield **29** (1.63g, 76%). FAB-MS *m/z* 411 $(M+Li)^+$; ^{1}HNMR δ 7.23 (4H, m, methoxyBn*H*, ortho), 6.86 (4H, m, methoxyBn*H*, meta), 4.90 (1H, s, H-1), 4.47 (4H, m, -CH_2 of methoxyBn), 4.10 (1H, m, H-4), 3.93 (2H, m, H-2, H-3), 3.82 (1H, m, H-5a), 3.80, 3.79 (3H, s, 2 × OMe), 3.60 (1H, m, H-5b), 3.38 (3H, s, -OMe), 1.86 (1H, dd, *J* 7.9, 4.4 Hz, 5-OH).

Methyl-2,3-di-*O*-methoxybenzyl-5-*O*-benzyl-α-D-arabinofuranoside. (**30**). Compound **29** (500 mg, 1.23 mM) was added to a suspension of NaH (60% dispersion in mineral oil, 35.4 mg, 1.47 mM) in dry DMF (10 mL) drop wise at 0^{0}C followed by addition of benzyl bromide (204μL, 1.72 mM) as done in **20**. The residue was column chromatographed (hexane : EtOAc, 8 : 2) to give **30** (600 mg, 98%). FAB-MS *m/z* 501 $(M+Li)^+$; ^{1}HNMR δ 7.31 (5H, m, Bn*H*), 7.19 (4H, m, methoxyBn*H*, ortho), 6.84 (4H, m, methoxyBn*H*, meta), 4.92 (1H, s, H-1), 4.55 (2H, m, -CH_2 of Bn), 4.43 (4H, m, -CH_2 of Bn), 4.17 (1H, m, H-4), 3.94 (1H, dd, *J* 2.8, 1.1 Hz, H-2), 3.85 (1H, dd, *J* 6.4, 2.7 Hz, H-3), 3.80, 3.78 (3H, s, 2 × OMe), 3.58 (2H, m, H-5a,b), 3.38 (3H, s, -OMe).

Methyl-2,3-di-*O*-acetyl-5-*O*-benzyl-α-D-arabinofuranoside (**32**). Ceric ammonium nitrate (2.65 g, 4.84 mM) was added to **30** (600 mg, 1.21 mM) in CH_3CN : H_2O (9 : 1, 20 mL) at room temperature. After 4 h, the reaction was diluted with aq. $NaHCO_3$ and extracted with CH_2Cl_2 twice. The organic layer was washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to give **31**. Acetylation of **31** with pyridine (3 mL) and Ac_2O (3 mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 9 : 1 to 8 : 2) yielded **32** (280 mg, 91%). FAB-MS *m/z* 345 $(M+Li)^+$; ^{1}HNMR δ 7.30 (5H, m, Bn*H*), 5.08 (1H, m, H-3), 5.04 (1H, d, *J* 1.3 Hz, H-2), 4.94 (1H, s, H-1), 4.61 (2H, m, -CH_2 of Bn), 4.20 (1H, m, H-4), 3.77

(1H, dd, *J* 10.8, 3.3 Hz, H-5a), 3.70 (1H, dd, *J* 10.8, 5.3 Hz, H-5b), 3.40 (3H, s, -OMe), 2.08, 2.04 (3H, s, 2 × OAc).

1-Thioacetyl-2,3-di-*O*-acetyl-5-*O*-benzyl-1-thio-α-D-arabinofuranoside (**33**). Compound **32** (260mg, 0.76mM) was dissolved in anhydrous CH_2Cl_2 (10ml), thiolacetic acid (75μL, 1.01mM) was added drop wise followed by BF_3OEt_2 (0.71mL, 5.7mM) at room temperature as reported in **10.** The residue was column chromatographed (cyclohexane : EtOAc, 9.1) to give **33** (191mg, 65%) as a colorless syrup. FAB-MS *m/z* 389 $(M+Li)^+$; ^{1}HNMR δ 7.30 (5H, m, Bn*H*), 6.03 (1H, s, H-1), 5.22 (1H, t, *J* 1.43Hz, H-2), 5.16 (1H, dd, *J* 4.3, 1Hz, H-3), 4.59 (2H, m, -CH_2 of Bn), 4.22 (1H, m, H-4), 3.72 (2H, d, *J* 4.6Hz, H-5a,b), 2.38 (3H, s, -SAc), 2.11, 2.01 (3H, s, 2 × OAc).

Octyl-2,3-di-*O*-acetyl-5-S-(2,3-di-*O*-acetyl-5-*O*-benzyl-β-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (**35**) and **Octyl-2,3-di-*O*-acetyl-5-S-(2,3-di-*O*-acetyl-5-*O*-benzyl-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside** (**36**). To a solution of **33** (176 mg, 0.4 6mM) in anhydrous MeOH (5 mL), freshly prepared solution of MeONa (1M, 0.46 mL) was added drop wise at -78 ^{0}C as reported in **13** and **14** to yield **34**.

The residue **34** and tosyl derivative **6a** (230 mg, 0.46 mM) were dissolved separately in dry DMF (2 mL each) and mixed together slowly at room temperature as done in **13** and **14**. The syrup was acetylated with pyridine (3 ml) and Ac_2O (3 mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 9 : 1 to 8.5 : 1.5) gave **35** (47 mg, 15%) and **36** (36 mg, 12%).

35 : FAB-MS *m/z* 675 $(M+Li)^+$; ^{1}HNMR δ 7.33 (5H, m, arom.*H*), 5.58 (1H, d, *J* 5.2 Hz, H-1′), 5.36 (1H, dd, *J* 5.0, 3.6 Hz, H-2′), 5.24 (1H, t, *J* 4.0 Hz, H-3′), 5.02 (1H, d, *J* 1.5 Hz, H-2), 4.97 (1H, s, H-1), 4.91 (1H, dd, *J* 5.5, 1.3 Hz, H-3), 4.58 (2H, m, -CH_2 of Bn), 4.21 (1H, dd, *J* 10.5, 5.8 Hz, H-4), 4.09 (1H, m, H-4′), 3.75 (2H, m, H-5′a,b), 3.67 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.41 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.02 (2H, m, H-5a,b), 2.086, 2.084, 2.077, 2.041 (3H, s, 4 × OAc), 1.55 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.26 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 7.0 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 59.30, H, 7.09. $C_{33}H_{48}O_{12}S$ required C, 59.26, H, 7.23).

36 : FAB-MS *m/z* 675 $(M+Li)^+$; ^{1}HNMR δ 7.33 (5H, m, arom.*H*), 5.47 (1H, d, *J* 0.6 Hz, H-1′), 5.16 (1H, dd, *J* 5.7, 1.3 Hz, H-3′), 5.10 (1H, t, *J* 1.7 Hz, H-2′), 5.03 (1H, broad s, H-3), 5.01 (1H, m, H-2), 4.97 (1H, s, H-1), 4.61 (2H, m, -CH_2 of Bn), 4.32 (2H, m, H-4, H-4′), 3.70 (3H, m, H-5′a,b, -OC*H*H$(CH_2)_6CH_3$), 3.40 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.15 (1H, dd, *J* 14.1, 4.5 Hz, H-5a), 2.95 (1H, dd, *J* 14.1, 5.8 Hz, H-5b), 2.09, 2.08, 2.07, 2.03 (3H, s, 4 × OAc), 1.55 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.26 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.3 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 59.27, H, 7.16. $C_{33}H_{48}O_{12}S$ required C, 59.26, H, 7.23).

Methyl-5-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (**37**). To a dry pyridine (10 mL) containing **15**[18] (1.5 g, 9.15 mM) was added dropwise a solution of *p*-toluenesulfonyl chloride (1.92 g, 10.06mM) in pyridine (10 mL) at 0 ºC and the reaction mixture was stirred at room temperature overnight as mentioned earlier in **5** to give a crude pale oil. Purification by silica gel chromatography (CH_2Cl_2 : MeOH, 9.5 : 0.5 to 9 : 1) gave **37** (1.72 g, 59%) as a clear oil. FAB-MS *m/z* 319 $(M+H)^+$; ^{1}HNMR δ 7.80 (2H, d, *J* 8.3 Hz, arom.*H*, ortho), 7.35 (2H, d, *J* 8.2

Hz, arom.*H*, meta), 4.91 (1H, s, H-1), 4.22 (3H, m, H-4, H-5a,b), 4.06 (1H, dd, *J* 7.0, 0.8 Hz, H-2), 3.89, (1H, m, H-3), 3.37 (3H, s, -OMe), 2.60 (1H, d, *J* 10.3 Hz, 3-OH), 2.45 (3H, s, arom.Me), 2.12 (1H, d, *J* 7.5Hz, 2-OH).

Methyl-2,3-di-*O*-acetyl-5-deoxy-α-D-arabinofuranoside. (**39**). Lithium aluminium hydride (160 mg, 4 mM) in ether (25 mL) was added drop wise to **37** (636 mg, 2 mM) in ether (75 mL) over 30 min at room temperature. The reaction was stirred at room temperature overnight followed by addition of EtOAc and water. The suspension was filtered through celite and the resulting filtrate was evaporated to dryness by coevaporating with pyridine thrice to give **38**. Acetylation of **38** with pyridine (5 mL) and Ac_2O (5 mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 8 : 2) yielded **39** (224 mg, 48%). FAB-MS *m/z* 233 $(M+H)^+$; ^{1}HNMR δ 5.04 (1H, dd, *J* 2.1, 0.4 Hz, H-2), 4.85 (1H, s, H-1), 4.77 (1H, m, H-3), 4.13 (1H, m, H-4), 3.38 (3H, s, -OMe), 2.103, 2.100 (3H, s, 2 × OAc), 1.40 (3H, d, *J* 6.4 Hz, H-5).

1-Thioacetyl-2,3-di-*O*-acetyl-5-deoxy-1-thio-α-D-arabinofuranoside (**40**). Compound **39** (202 mg, 0.87 mM) was dissolved in anhydrous CH_2Cl_2 (10 mL), thiolacetic acid (93 μL, 1.25 mM) was added drop wise followed by BF_3OEt_2 (0.9 mL, 7.12 mM) at room temperature as done in **10**. Column chromatography (cyclohexane : EtOAc, 9 : 1) of the residue gave **40** (202 mg, 84%). FAB-MS *m/z* 283 $(M+Li)^+$; ^{1}HNMR δ 5.97 (1H, d, *J* 0.5 Hz, H-1), 5.23 (1H, t, *J* 1.5 Hz, H-2), 3.83 (1H, m, H-3), 4.14 (1H, m, H-4), 2.39 (3H, s, -SAc), 2.12 (6H, s, 2 × OAc), 1.41 (3H, d, *J* 6.4 Hz, H-5).

Octyl-2,3-di-*O*-acetyl-5-S-(2,3-di-*O*-acetyl-5-deoxy-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (42) and **Octyl-2,3-di-*O*-acetyl-5-S-(2,3-di-*O*-acetyl-5-deoxy-β-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside** (**43**). To a solution of **40** (238 mg, 0.86 mM) in anhydrous MeOH (5 mL), freshly prepared solution of MeONa (1M, 0.9 mL) was added drop wise at -78 ^{0}C as reported in **13** and **14** to yield **41**.

The resulting residue **41** and tosyl derivative **6a** (430 mg, 0.86 mM) were dissolved separately in dry DMF (5 mL each) and mixed together slowly at room temperature as done in **13** and **14** to give crude syrup which was acetylated with pyridine (3 ml) and Ac_2O (3 mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 9 : 1 to 8.5 : 1.5) gave **42** (45 mg, 9%) and **43** (76 mg, 16%).

42 : FAB-MS *m/z* 569 $(M+Li)^+$; ^{1}HNMR δ 5.38 (1H, d, *J* 0.7 Hz, H-1′), 5.08 (1H, dd, *J* 1.6, 1.2 Hz, H-2′), 5.04 (1H, s, H-2), 5.03 (1H, m, H-3), 4.98 (1H, s, H-1), 4.80 (1H, m, H-3′), 4.28 (2H, m, H-4, H-4′), 3.66 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.42 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.13 (1H, dd, *J* 14.0, 4.6 Hz, H-5a), 2.93 (1H, dd, *J* 14.0, 5.7 Hz, H-5b), 2.105, 2.104, (3H, s, 2 × OAc), 2.09 (6H, s, 2 × OAc), 1.55 (2H, m, -$OCH_2CH_2$$(CH_2)_5CH_3$), 1.40 (3H, d, *J* 6.4 Hz, H-5′), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 55.69, H, 7.38. $C_{26}H_{42}O_{11}S$ required C, 55.50, H, 7.52).

43 : FAB-MS *m/z* 569 $(M+Li)^+$; ^{1}HNMR δ 5.49 (1H, d, *J* 5.1 Hz, H-1′), 5.36 (1H, dd, *J* 5.1, 3.5 Hz, H-2′), 5.03 (1H, d, *J* 1.5 Hz, H-2), 4.98 (1H, s, H-1), 4.96 (1H, m, H-3′), 4.91 (1H, m, H-3), 4.23 (1H, m, H-4), 3.97 (1H, m, H-4′), 3.68 (1H, m, -OC*H*H$(CH_2)_6CH_3$), 3.42 (1H, m, -OCH*H*$(CH_2)_6CH_3$), 3.04 (2H, m, H-5a,b), 2.121 (3H, s, -OAc), 2.098 (6H, s, 2 × OAc), 2.096

(3H, s, -OAc), 1.56 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.46 (3H, d, *J* 6.6 Hz, H-5′), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 55.51, H, 7.38. $C_{26}H_{42}O_{11}S$ required C, 55.50, H, 7.52).

Methyl-2,3-di-*O*-acetyl-5-deoxy-5-azido-α-D-arabinofuranoside. (**45**). NaN_3 (572 mg, 8.8 mM) was added to a solution of **37** (700 mg, 2.2 mM) in dry DMF (10 mL) at room temperature. The reaction was heated to 100 ^{0}C for 6 h followed by evaporation of DMF under reduced pressure. The residue was extracted with acetone : ether (2 : 1, 10 mL) thrice and filtered. The filtrate was evaporated to dryness under reduced pressure by coevaporating with pyridine thrice to give **44**. Acetylation of **44** with pyridine (5 mL) and Ac_2O (5 mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 9 : 1 to 8 : 2) yielded **45** (420 mg, 70%). FAB-MS *m/z* 274 $(M+H)^+$; ^{1}HNMR δ 5.08 (1H, dd, *J* 1.6, 0.4 Hz, H-2), 4.97 (1H, m, H-3), 4.95 (1H, s, H-1), 4.17 (1H, m, H-4), 3.69 (1H, dd, *J* 13.2, 2.8 Hz, H-5a), 3.45 (1H, dd, *J* 13.2, 5.2Hz, H-5b), 3.41 (3H, s, -OMe), 2.12, 2.10 (3H, s, 2 × OAc).

1-Thioacetyl-2,3-di-*O*-acetyl-5-deoxy-5-azido-α-D-arabinofuranoside (**46**). Compound **45** (420 mg, 1.53 mM) was dissolved in anhydrous CH_2Cl_2 (10 mL), thiolacetic acid (150 μL, 2 mM) was added drop wise followed by BF_3OEt_2 (1.45 mL, 11.47 mM) at room temperature as done in **10**. Column chromatography (cyclohexane : EtOAc, 9 : 1 to 8.5 : 1.5) of the residue gave **46** (257 mg, 53%). FAB-MS *m/z* 318 $(M+H)^+$; ^{1}HNMR δ 6.05 (1H, d, *J* 0.7 Hz, H-1), 5.27 (1H, t, *J* 1.2 Hz, H-2), 5.04 (1H, m, H-3), 4.17 (1H, m, H-4), 3.66 (1H, dd, *J* 13.3, 3.5 Hz, H-5a), 3.46 (1H, dd, *J* 13.3, 4.9Hz, H-5b), 2.40 (3H, s, -SAc), 2.15, 2.13 (3H, s, 2 × OAc).

Octyl-2,3-di-*O*-acetyl-5-*S*-(2,3-di-*O*-acetyl-5-deoxy-5-azido-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside (48) and **Octyl-2,3-di-*O*-acetyl-5-S-(2,3-di-*O*-acetyl-5-deoxy-5-azido-β-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside** (**49**). To a solution of **46** (250 mg, 0.79 mM) in anhydrous MeOH (7 mL), freshly prepared solution of MeONa (1M, .0.8 mL) was added drop wise at -78^{0}C as reported in **13** and **14** to yield thiosodium **47**.

The resulting residue **47** and tosyl derivative **6a** (395 mg, 0.79 mM) were dissolved separately in dry DMF (5 mL each) and mixed together slowly at room temperature as done in **13** and **14** to give crude syrup which was acetylated with pyridine (3 mL) and Ac_2O (3mL) followed by usual work up and column chromatography (cyclohexane : EtOAc, 9 : 1 to 8.5 : 1.5) gave **48** (24 mg, 9%) and **49** (37 mg, 12%) beside recovering the tosyl derivative **6a** (168 mg).

48 : FAB-MS *m/z* 621 $(M+NH_4)^+$; ^{1}HNMR δ 5.48 (1H, s, H-1′), 5.14 (1H, t, *J* 1.4 Hz, H-2′), 5.05 (1H, s, H-2), 5.02 (2H, m, H-3, H-3′), 4.99 (1H, s, H-1), 4.33 (2H, m, H-4, H-4′), 3.67 (2H, m, H-5′a, -OC*H*H$(CH_2)_6CH_3$), 3.45 (2H, m, H-5′b, -OCH*H*$(CH_2)_6CH_3$), 3.16 (1H, dd, *J* 14.1, 4.4 Hz, H-5a), 2.94 (1H, dd, *J* 14.1, 5.6 Hz, H-5b), 2.12, 2.11, 2.10, 2.09 (3H, s, 4 × OAc), 1.58 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.27 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (Found : C, 51.50, H, 6.74, N, 7.10. $C_{26}H_{41}N_3O_{11}S$ required C, 51.73, H, 6.84, N, 6.96).

49 : FAB-MS *m/z* 621 $(M+NH_4)^+$; ^{1}HNMR δ 5.66 (1H, d, *J* 5.3 Hz, H-1′), 5.39 (1H, dd, *J* 5.2, 4.0 Hz, H-2′), 5.14 (1H, t, *J* 4.2 Hz, H-3′), 5.03 (1H, d, *J* 1.5 Hz, H-2), 4.98 (1H, s, H-1), 4.91 (1H, dd, *J* 5.4, 1.3 Hz, H-3), 4.21 (1H, m, H-4), 4.03 (1H, m, H-4′), 3.68 (2H, m, H-5′a, -

OC*H*H(CH_2)$_6$$CH_3$), 3.55 (1H, dd, *J* 13.0, 3.9 Hz, H-5′b), 3.42 (1H, m, -OCH*H*(CH_2)$_6$$CH_3$), 3.06 (2H, m, H-5a,b), 2.13, 2.10 (3H, s, 2 × OAc), 2.09 (6H, s, 2 × OAc), 1.58 (2H, m, -OCH_2C*H*$_2$(CH_2)$_5$$CH_3$), 1.27 (10H, m, -$OCH_2CH_2$($CH_2$)$_5$$CH_3$), 0.88 (3H, t, *J* 6.4 Hz, -OCH_2CH_2(CH_2)$_5$C*H*$_3$). (HRMS calcd for $C_{26}H_{41}N_3O_{11}S$: *m/z* (M+Na) 626.2354. Found *m/z* 626.2332).

Octyl-5-*S*-(5-deoxy-5-azido-α-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside. (**50**). Compound **48** (24 mg, 0.04 mM) was dissolved in dry MeOH (2 mL) and methanolic ammonia (7N, 2 mL) was added to it as done in **26** to give thick syrup which was column chromatographed (CH_2Cl_2 : MeOH, 97 : 3) to give **50** (15 mg, 88%). FAB-MS *m/z* 442 $(M+Li)^+$; ^{1}HNMR (DMSO-d_6) δ 5.68 (1H, d, *J* 5.3 Hz, 2′-OH), 5.46 (1H, d, *J* 5.2 Hz, 3′-OH), 5.38 (1H, d, *J* 5.1 Hz, 2-OH), 5.20 (1H, d, *J* 5.5 Hz, 3-OH), 5.03 (1H, d, *J* 3.9 Hz, H-1′), 4.68 (1H, d, *J* 2.2 Hz, H-1), 3.88 (2H, m, H-4, H-4′), 3.74 (2H, dd, *J* 4.5, 1.6 Hz, H-2, H-2′), 3.61 (4H, m, H-3, H-3′, H-5′a, -OC*H*H(CH_2)$_6$$CH_3$), 3.39 (1H, m, H-5′b), 3.31 (1H, m, -OCH*H*(CH_2)$_6$$CH_3$), 2.92 (1H, dd, *J* 13.5, 3.9 Hz, H-5a), 2.68 (1H, dd, *J* 13.5, 6.9 Hz, H-5b), 1.49 (2H, m, -OCH_2C*H*$_2$-(CH_2)$_5$$CH_3$), 1.25 (10H, m, -$OCH_2CH_2$($CH_2$)$_5$$CH_3$), 0.85 (3H, t, *J* 6.8 Hz, -OCH_2CH_2-(CH_2)$_5$C*H*$_3$). (Found : C, 49.44, H, 7.52, N, 9.86. $C_{18}H_{33}N_3O_7S$ required C, 49.64, H, 7.64, N, 9.65).

Octyl-5-*S*-(5-deoxy-5-azido-β-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside. (**51**). Compound **49** (24 mg, 0.04 mM) was dissolved in dry MeOH (2 mL) and methanolic ammonia (7N, 2 mL) was added to it as done in **26** to give crude syrup which was column chromatographed (CH_2Cl_2 : MeOH, 97 : 3) to give **51** (16 mg, 94%). FAB-MS *m/z* 442 $(M+Li)^+$; ^{1}HNMR (DMSO-d_6) δ 5.63 (1H, d, *J* 4.8 Hz, 2′-OH), 5.43 (1H, d, *J* 4.4 Hz, 3′-OH), 5.39 (1H, d, *J* 4.9 Hz, H-1′), 5.36 (1H, d, *J* 5.2 Hz, 2-OH), 5.22 (1H, d, *J* 5.5 Hz, 3′-OH), 4.67 (1H, d, *J* 1.8 Hz, H-1), 4.01 (1H, t, *J* 4.4 Hz, H-2′), 3.81 (3H, m, H-4, H-3′, H-4′), 3.73 (1H, dd, *J* 4.6, 1.9 Hz, H-2), 3.52 (3H, m, H-3, H-5′a, -OC*H*H(CH_2)$_6$$CH_3$), 3.32 (2H, m, H-5′b, -OCH*H*(CH_2)$_6$$CH_3$), 2.87 (1H, dd, *J* 13.5, 3.7 Hz, H-5a), 2.73 (1H, dd, *J* 13.5, 7.8 Hz, H-5b), 1.49 (2H, m, -OCH_2C*H*$_2$(CH_2)$_5$$CH_3$), 1.25 (10H, m, -$OCH_2CH_2$($CH_2$)$_5$$CH_3$), 0.86 (3H, t, *J* 6.8 Hz, -OCH_2CH_2(CH_2)$_5$C*H*$_3$). (HRMS calcd for $C_{18}H_{33}N_3O_7S$: *m/z* (M+Na) 458.1931. Found *m/z* 458.1944).

Octyl-5-*S*-(5-deoxy-5-acetamido-β-D-arabinofuranosyl)-5-thio-α-D-arabinofuranoside. (**52**). Ph_3P (11 mg, 0.04 mM) and water (4.6 μL, 0.25 mM) were added to compound **49** (10 mg. 0.016 mM) in freshly distilled THF (1 mL) and stirred overnight at 65 ^{0}C. The TLC showed the mixture of products of close mobility in reaction mixture. Solvents were evaporated off under vacuum to dryness and the residue was deacetylated with methanolic ammonia (7N, 2 mL) in dry MeOH (2 mL). Solvents were evaporated under reduced pressure. The residue was passed through short column (CH_2Cl_2 : MeOH, 99 : 1) to give **52** (5 mg, 42%). FAB-MS *m/z* 452 $(M+H)^+$; ^{1}HNMR (DMSO-d_6) δ 5.53 (1H, d, *J* 4.8 Hz, 2′-OH), 5.38 (1H, d, *J* 4.9 Hz, 2-OH), 5.29 (1H, d, *J* 4.7 Hz, H-1′), 5.28 (1H, d, *J* 3.5 Hz, 3′-OH), 5.23 (1H, d, *J* 5.3 Hz, 3-OH), 4.67 (1H, d, *J* 1.9 Hz, H-1), 3.96 (1H, t, *J* 4.0 Hz, H-2′), 3.83 (1H, m, H-4′), 3.78 (1H, t, *J* 4.1 Hz, H-3′), 3.74 (1H, dd, *J* 4.5, 2.1 Hz, H-2), 3.64 (1H, m, H-4′), 3.57 (1H, dd, *J* 6.9, 4.2 Hz, H-3), 3.53 (1H, m, -OC*H*H(CH_2)$_6$$CH_3$), 3.32 (2H, m, H-5′a, -OCH*H*(CH_2)$_6$$CH_3$), 3.16 (1H, dd, *J* 13.4, 6.9

Hz, H-5′b), 2.87 (1H, dd, *J* 13.6, 3.8 Hz, H-5a), 2.73 (1H, dd, *J* 13.6, 7.8 Hz, H-5b), 1.48 (2H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 1.25 (10H, m, -$OCH_2CH_2(CH_2)_5CH_3$), 0.85 (3H, t, *J* 6.8 Hz, -$OCH_2CH_2(CH_2)_5CH_3$). (HRMS calcd for $C_{20}H_{37}NO_8S$: *m/z* $(M+Na)^+$ 474.2132. Found *m/z* 474.2128).

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