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SYNTHESIS OF FRAGMENTS OF A *STREPTOCOCCUS PNEUMONIAE* TYPE-SPECIFIC CAPSULAR POLYSACCHARIDE

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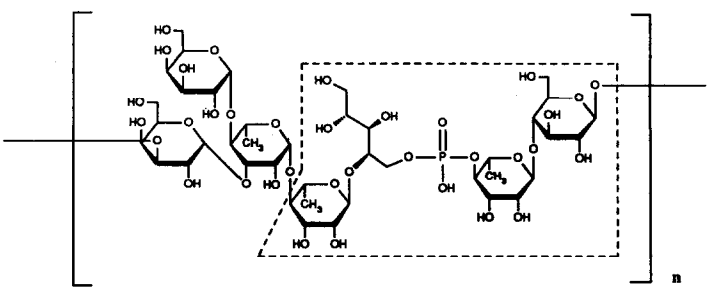
Abstract. Fragments of the teichoic acid-type polysaccharide of *Streptococcus pneumoniae* serotype 17F, containing a D-arabinitol phosphate moiety and a spacer, were synthesized. Starting from D-lyxose or D-mannose key intermediate 1-*O*-allyl-2,3-di-*O*-benzyl-5-*O*-benzoyl-D-arabinitol was prepared, which was condensed with tri-*O*-acetyl-α-L-rhamnosyl bromide. The resulting dimer was, after removal of the allyl group, phosphorylated with either *N*-benzyloxycarbonyl-3-aminopropyl(2-cyanoethyl)-*N,N*-diethylphosphoramidite or 2-cyanoethoxy(*N,N*-diethylamino)chlorophosphine, the latter reagent leading to a suitable phosphite-donor. The phosphite-acceptors *N*-benzyloxycarbonyl-3-aminopropyl 2,3-di-*O*-(2-methylbenzoyl)-α-L-rhamnopyranoside and *N*-benzyloxycarbonyl-3-aminopropyl 2,3-di-*O*-benzoyl-4-*O*-[2,3-di-*O*-(2-methylbenzoyl)-α-L-rhamnopyranosyl]-6-*O*-(2-methylbenzoyl)-β-D-glucopyranoside were prepared by selective removal of a 4-*O*-dichloroacetyl group from the fully protected monomer and dimer, respectively. Condensation of the phosphite-donor with the individual acceptors led to the isolation of spacer containing trimer and tetramer fragments of the title polysaccharide.

Streptococcus pneumoniae is the cause of lower respiratory tract infections in humans and is responsible for bacterial middle ear infections (otis media) in children[1]. At present 85 different serotypes, based on polysaccharide capsules, have been recognized[2]. The pneumococcal polysaccharides, which play a pivotal role in infections, have recently been attracting attention because of their use in a multivalent vaccine (Pneumovax^{R}) against pneumococcal diseases. However, the effect of this vaccine for patients with a high risk for pneumoniae and for small children is often unsatisfactory due to the inherent immunological character of polysaccharide antigens[3].

In order to facilitate mapping of the immunodominant region of these polysaccharides, chemical synthesis of well defined fragments is of great importance and may also open the way to construct more effective vaccines[4].

FIGURE 1

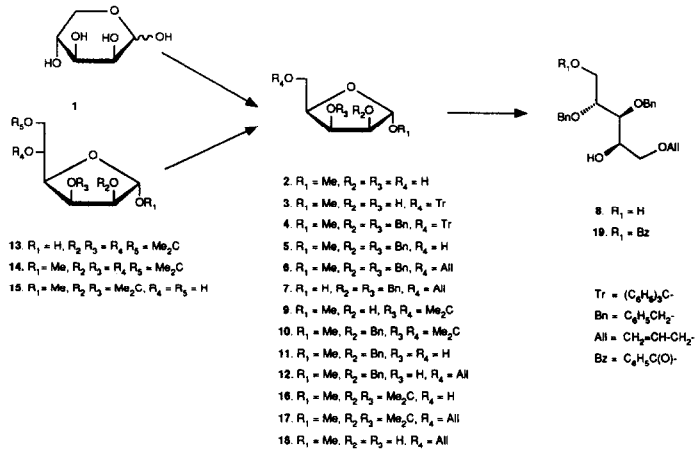


Recently, the structure of the capsular polysaccharide of serotype 17F has been elucidated[5]. It is composed (*Figure 1*) of a teichoic acid-type polymer of heptasaccharide repeating units linked by phosphodiester bonds.

We here report the synthesis of the di-, tri- and tetrasaccharide **28**, **46** and **48** which are fragments of the repeating unit (see dashed box in *Figure 1*) and covalently linked to a spacer suitable for conjugation to macromolecular carriers.

A key intermediate in the approach to fragments **28**, **46**, and **48** is the partially protected D-arabinitol **19** (see *Scheme 1*), which will not only allow the introduction of the required α-rhamnosidic linkage at C-2 but also, due to the nature of the protecting groups, of a phosphodiester bond between the hydroxy groups at C-1 and C-4 of the D-arabinitol and L-rhamnose units, respectively.

SCHEME 1



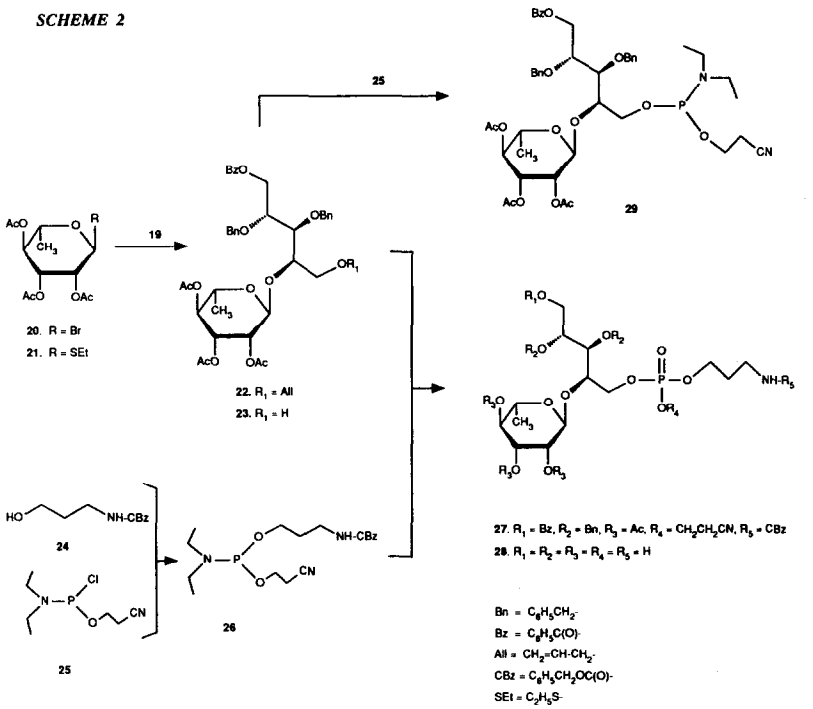
In the first approach to **19** (see *Scheme 1*), D-lyxose was converted into the known[6] methyl α-D-lyxofuranoside **2**. Treatment of crude **2** with triphenylchloromethane in pyridine gave, after purification, the trityl derivative **3**. Benzylation (BnBr/NaH) followed by detritylation of **4** with aq. acetic acid furnished **5**. Allylation (AllBr/NaH) gave **6** in an overall yield of 50% (based on **1**). Next, methyl glycoside **6** was treated with aq. acetic acid to produce **7** which was reduced with sodium borohydride in ethanol to give 1-*O*-allyl-3,4-di-*O*-benzyl-D-arabinitol **8** in 90% yield. Regioselective benzoylation of **8** with 1-*O*-(benzoyloxy)benzotriazole[7] in the presence of triethylamine resulted in the isolation of the benzoyl compound **19** in an excellent yield.

We further explored whether compound **6**, which plays a crucial role in the synthesis of **19**, was also accessible *via* the following modification of the D-lyxose route. Thus acetonation of **2** and subsequent conventional benzylation of **9** gave **10**, the 3,5-*O*-isopropylidene group of which was removed by acidic hydrolysis to yield diol **11**. Regioselective stannylidene-assisted[8] allylation of **11** furnished **12**, benzylation of which resulted in the isolation of **6** in an overall yield of 39% (based on **1**). Compound **6** thus obtained was in every aspect - ^{1}H- and ^{13}C NMR spectroscopy - identical with **6** prepared *via* the original approach.

In a second approach (see *Scheme 1*) to the crucial intermediate **6**, the easily accessible 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **13** (ref. 9) was methylated under phase-transfer conditions[10], followed by acidic hydrolysis of the 5,6-*O*-acetonide function in **14** to give diol **15**. Oxidation[11] of the latter with sodium periodate and subsequent reduction with sodium borohydride gave **16**, which was converted into **17** by allylation (AllBr/-

NaH). Unfortunately, removal of the 2,3-*O*-isopropylidene function in **17** with aq. acetic acid was accompanied by hydrolysis of the glycosidic bond. Best results were obtained by heating **17** with 1% HCl in methanol for 10 min followed by evaporation of the reaction mixture and repetition (4 x) of this procedure. Benzylation of **18** afforded **6** in an overall yield of 57% (based on **17**). Compound **6** thus isolated was identical - specific rotation, ^{1}H- and ^{13}C NMR spectroscopy - with **6** obtained *via* the D-lyxose approach. The above results indicate that the first D-lyxose approach to the pivotal intermediate **6** is, in terms of reproducibility and ease of performing the individual steps, superior over the *D*-mannose approach.

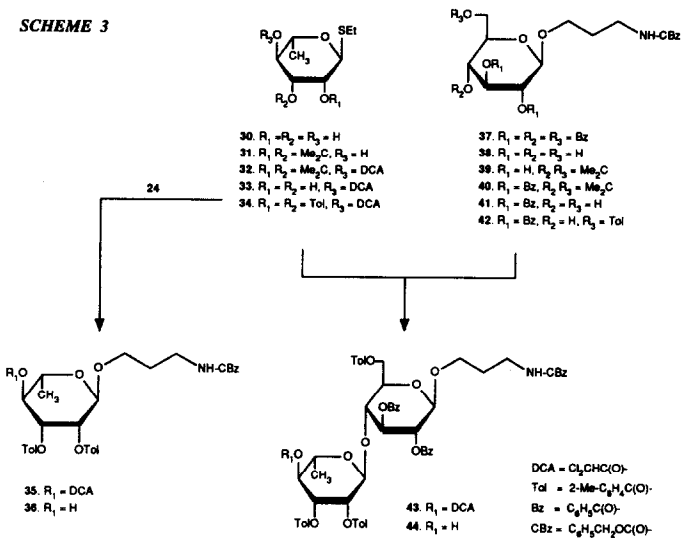
SCHEME 2



The assembly of dimer **28**, which entails the stereoselective formation of an α-glycosidic linkage and the introduction of a phosphodiester, could be realized as follows (see *Scheme 2*). Mercuric cyanide assisted glycosidation[12] of the donor 2,3,4-tri-*O*-acetyl-α-L-rhamnosyl bromide **20** (ref. 13) with acceptor **19** resulted in the isolation of the α-linked dimer **22** in 95% yield. On the other hand, coupling of **19** with the corresponding α-SEt donor **21** in the presence of methyl trifluoromethanesulfonate[14] afforded **22** in a yield of 85%. The allyl protecting group of dimer **22** could be removed conveniently by the two-step procedure of Oltvoort *et al.*[15] to give **23** (87% yield). 1-*H*-Tetrazole mediated phosphitylation[16] of **23** with reagent **26**, prepared *in situ* by reaction of *N*-(benzyloxycarbonyl)-3-aminopropanol **24** (ref. 17) with 2-cyanoethoxy(*N*,*N*-diethylamino)chlorophosphine **25** (ref. 18), afforded an intermediate phosphitetriester which was oxidised immediately with *tert*-butyl hydroperoxide[19] to give fully protected **27**. Crude **27** was, without further purification, deblocked by the following two-step procedure. Ammonolysis of the base-labile protecting groups (R_1, R_3 and R_4), followed by hydrogenolysis in the presence of 10% Pd-C of the benzyl (R_3) and benzyloxycarbonyl (R_5) groups, resulted, after purification (Sephadex LH-

20), in the isolation of homogeneous **28**. The identity of **28** (Na^+-salt) was firmly established by ^1H-, ^{13}C- and ^{31}P NMR spectroscopy (see *Table 1*). Further, phosphitylation of **23** with a slight excess of reagent **25** gave the phosphite-amidite **29** in an excellent yield. The latter derivative proved to be very convenient (see *Scheme 4*) for the preparation of the phosphate-diester containing trimer **46** and tetramer **48**.

SCHEME 3

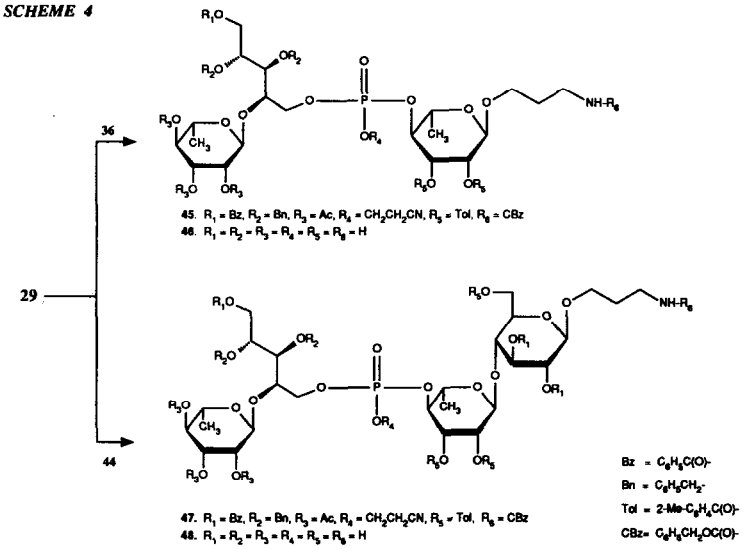


The synthetic route to the properly-protected rhamnosyl-donor **34** and glycosyl-acceptor **42** is illustrated in *Scheme 3*. Thus Zemplén deacetylation of **21** and subsequent acetonation of **30** gave **31** having a free hydroxyl at C-4. In order to meet the requirements of introducing stereoselectively the *trans*-glycosidic linkage in **35** and **43**, as well as removing selectively a protecting group at C-4 of the donor molecule, the following protecting-group-strategy was adopted. Thus compound **32** containing the rather base-labile dichloroacetyl (DCA) group was easily accessible[20] by treating **31** with dichloroacetic anhydride. The 2,3-*O*-isopropylidene group of **32** was removed by acidolysis, and the resulting free hydroxyl groups were protected with 2-methylbenzoyl (Tol) groups by treating **33** with excess 2-methylbenzoyl chloride in pyridine, to afford donor **34** in an overall yield of 53% (based on **21**). The exclusive formation of the α-linked product **35**, which was isolated in 72% yield, in the methylsulfenyl triflate mediated glycosidation[21] of spacer **25** with donor **34** nicely illustrated the neighbouring group participation of the 2-methylbenzoyl ester function. On the other hand, attempts to remove the DCA-group in **35** according to the literature procedure[22] was, in this particular case, not successful. However, treatment of **35** in methanol with a slight excess of aq. ammonia revealed rapid and selective hydrolysis of the DCA-group, and **36** could be isolated in 82% yield.

The glycosyl-acceptor **42** was now prepared by the following six-step procedure. Glycosidation of 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide[23] with spacer **24** afforded **37**. Zemplén debenzoylation and subsequent introduction of a 4,6-*O*-isopropylidene function in **38** gave **39**, which was treated with benzoyl chloride in pyridine followed by acidolysis of the acetonide function in **40** to yield diol **41** in an overall yield of 64% (based on **37**). Finally, regioselective 2-methylbenzoylation with 1-*O*-(2-methylbenzoyloxy)benzotriazole furnished acceptor **42** in an excellent yield. Glycosidation of donor **34** with acceptor **42**, followed by selective removal of the DCA-

group from the coupling product **43**, was performed in the same way as referenced for **35** and **36**, to give **44** in an overall yield of 66% (based on **34**). The ^{1}H- and ^{13}C NMR data of compounds **36** and **44** (see *Tables 1* and *2*) are in full accord with the proposed structures.

SCHEME 4



In the final stage of the synthesis the phosphite derivative **29** was now coupled (see *Scheme 4*), in a similar fashion as mentioned earlier for the preparation of **27** (see *Scheme 2*), with **36** and **44** to give the fully-protected fragments **45** and **47**, respectively. The crude fragments thus obtained were deblocked by the same two-step procedure used to convert **27** into **28**. Purification (Sephadex LH-20) of the crude products afforded homogeneous **46** and **48** in an overall yield of 72 and 61% (based on **36** and **44**), respectively. The ^{1}H- and ^{13}C NMR data of fragments **46** and **48** listed in *Tables 1* and *2* are in good agreement with those reported for saccharides containing α-linked L-rhamnopyranosyl residues.

In conclusion, the synthetic route described herein towards the preparation of fragments of the *Streptococcus pneumoniae* serotype 17F capsular polysaccharide illustrates that a phosphite-triester approach is very convenient to introduce the type of phosphate-diester present in this complex polysaccharide. Further, we believe that the up to now overlooked dichloroacetyl group, due to its stability under conditions of glycosidation, acylation and, particularly so, its selective removal in the presence of 2-methylbenzoyl groups in rhamnopyranosyl units, promises to be a very useful protecting group in future oligosaccharide synthesis.

Immunological results of compounds **28**, **46** and **48** will be published elsewhere. At present we are exploring the feasibility of preparing longer fragments of the repeating unit of the capsular polysaccharide of *S. pneumoniae* serotype 17F.

TABLE 1 ^{13}C NMR chemical shifts (δ, ppm) of compounds **28**, **46** and **48**

Residue	Compound	**28**	**46**	**48**
Rhamnose	C-1	100.4	100.3	100.4
	C-2	71.4	71.4	71.4
	C-3	71.0	71.0	71.0
	C-4	72.8	72.8	72.8
	C-5	70.2	70.1	70.1
	C-6	17.6	17.6	17.6
Arabinitol	C-1	66.4 ($^2J_{cp}$ 5.7 Hz)	66.5 ($^2J_{cp}$ 5.4 Hz)	66.5 ($^2J_{cp}$ 5.7 Hz)
	C-2	75.4 ($^3J_{cp}$ 8.2 Hz)	75.5 ($^3J_{cp}$ 8.1 Hz)	75.5 ($^3J_{cp}$ 8.3 Hz)
	C-3	70.6	70.7	70.6
	C-4	71.5	71.5	71.5
	C-5	63.9	63.9	63.9
Rhamnose	C-1		100.37	101.4
	C-2		71.0	71.3
	C-3		71.0	70.9 ($^3J_{cp}$<1 Hz)
	C-4		78.4 ($^2J_{cp}$ 6.23 Hz)	78.4 ($^2J_{cp}$ 6.4 Hz)
	C-5		68.4 ($^3J_{cp}$ 6.15 Hz)	68.9 ($^3J_{cp}$ 6.3 Hz)
	C-6		17.9	17.7
Glucose	C-1			103.1
	C-2			74.3
	C-3			75.3
	C-4			78.2
	C-5			76.0
	C-6			61.0
Spacer	C-1	64.2 ($^2J_{cp}$ 5.1 Hz)	66.0	68.8
	C-2	30.2 ($^3J_{cp}$ 7.3 Hz)	27.5	27.6
	C-3	39.6	38.5	38.5

TABLE 2 ^1H NMR chemical shifts (δ, ppm) of compounds **28**, **46** and **48**

Residue	Compound	**28**	**46**	**48**
Rhamnose	H-1	5.04 ($J_{1,2}$ 1.7 Hz)	5.05 ($J_{1,2}$ 1.4 Hz)	5.04 ($J_{1,2}$ 1.8 Hz)
	H-2	3.98	4.00	4.01
	H-3	3.76	3.76	3.78
	H-4	3.42	3.42	3.41
	H-5	3.80	3.80	3.81
	H-6	1.25	1.25	1.24
Arabinitol	H-1	4.02	4.06	66.5
	H-2	4.16	4.14	75.5
	H-3	3.65	3.66	70.6
	H-4	3.68	3.68	71.5
	H-5	3.65, 3.78	3.67, 3.76	3.67, 3.78
Rhamnose	H-1		4.77 ($J_{1,2}$ 1.5 Hz)	4.84 ($J_{1,2}$ 1.8 Hz)
	H-2		3.90	3.97
	H-3		3.95	3.87
	H-4		3.95	3.96
	H-5		3.76	4.10
	H-6		1.31	1.26
Glucose	H-1			4.43 ($J_{1,2}$ 8.0 Hz)
	H-2			3.24
	H-3			3.56
	H-4			3.52
	H-5			3.50
	H-6			3.73, 3.83
Spacer	H-1	3.96	3.55, 3.81	3.77, 4.01
	H-2	1.98	1.95	1.95
	H-3	3.06	3.08	3.10

Experimental

General methods. - Dioxane, pyridine and acetonitrile were dried by refluxing with CaH_2 (5g/l) and then distilled. Dichloromethane, 1,2 dichloroethane and toluene were distilled from P_2O_5. *N,N*-dimethylformamide was stirred with CaH_2 at room temperature and distilled under reduced pressure. Dioxane, pyridine and acetonitrile were stored over molecular sieves 4A (Aldrich), toluene over sodium wire and dichloromethane and 1,2 dichloroethane were stored over alumina. Reactions were performed at ambient temperature unless noted otherwise. Column chromatography was performed on columns of silica gel 60 (Merck 70-230 mesh). Gel filtration was performed on Sephadex LH-20 (Pharmacia). T.l.c. was conducted on DC Fertigfolien (Schleicher & Schüll F1500 LS254). Compounds were detected by charring with 20% sulfuric acid in methanol. Optical rotations were determined with a Perkin-Elmer Model 241 polarimeter, for solutions in $CHCl_3$ at 22° unless stated otherwise. NMR spectra were recorded with a Jeol JNM-FX200 (^{13}C, 50.1 MHz, internal Me_4Si or methanol; ^{31}P, 80.7 MHz, external 85% H_3PO_4). and a Brucker WM-300 spectrometer equipped with an Aspect-2000 computer (^1H, 300 MHz, internal Me_4Si).

Methyl α-D-lyxofuranoside (**2**). - A solution of D-lyxopyranose **1** (3 g, 20 mmole) in methanol (60 ml) was treated with acetyl chloride (0.3 ml) and left for 24 h at room temperature. The reaction mixture was neutralized with Amberlite IRA 400 (OH^--form, 15 g) and concentrated. T.l.c. analysis of the residue indicated the presence of a major product, which was established to be **2**, together with minor amounts of the other possible isomers. Crude **2** was used in the next step without further purification; R_F 0.71 in 11:7:2 ethylacetate-n-propanol-water; ^{13}C-n.m.r. data (CD_3O_3): δ 109.6 (C-1); 81.3 (C-4); 77.0 (C-2); 72.2 (C-3); 61.5 (C-5); 55.6 (OCH_3).

Methyl 5-O-triphenylmethyl-α-D-lyxofuranoside (**3**). - To a solution of crude **2** in pyridine (50 ml) was added chlorotriphenylmethane (6.7 g, 24 mmole). The reaction mixture was stirred for 17 h at 50°. The reaction was quenched by addition of water (5 ml). Evaporation of the solvent gave a residue which was redissolved in dichloromethane (50 ml) and extracted successively with H_2O, aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel in dichloromethane-methanol 98:2 to give pure **3** (8.5 g, 70%); $[\alpha]_D$ +103.3° (c 1); R_F 0.55 in 95:5 dichloromethane-methanol; ^1H-n.m.r. data ($CDCl_3$): δ 7.1-7.5 (m, 15 H, H-arom.); 4.89 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1); 4.35 (m, 1 H, H-2); 4.20 (m, 1 H, H-4); 3.97 (m, 1 H, H-3); 3.54 (dd, 1 H, $J_{5b,4}$ 3.6 Hz, $J_{5b,5a}$ 10.3 Hz, H-5b); 3.36 (s, 3 H, OCH_3); 3.29 (dd, 1 H, $J_{5a,4}$ 4.6 Hz; $J_{5a,5b}$ 10.3 Hz, H-6a); ^{13}C-n.m.r ($CDCl_3$): δ 108.1 (C-1); 87.8 ($(C_6H_5)_3C$); 77.8, 75.6 (C-2, C-4); 71.7 (C-3); 62.6 (C-5); 55.2 (OCH_3).

Anal. Calc. for $C_{25}H_{26}O_5$: C 73.5, H 6.5; found: C 73.2, H 6.4%.

Methyl 2,3-di-O-benzyl-α-D-lyxofuranoside (**5**). - Compound **3** (4.06 g, 10 mmole) was dissolved in DMF (50 ml). NaH (0.58 g, 24 mmole) and benzyl bromide (4.1 g, 24 mmole) were added and the reaction mixture was stirred for 3 h. Excess NaH was destroyed by addition of methanol (5 ml) and the mixture was evaporated, redissolved in dichloromethane (50 ml), extracted twice with water, dried ($MgSO_4$) and concentrated to give crude **4**; R_F 0.85 in 95:5 dichloromethane-acetone. Compound **4** was redissolved in acetic acid-H_2O 4:1 (50 ml) and heated at 70° for 1 h. Evaporation of the solvent and coevaporation with ethanol (3x25 ml) gave a residue which was chromatographed on silica gel with 98:2 dichloromethane-acetone to afford pure **5** (2.7 g, 79%); $[\alpha]_D$ -3.0° (c 1); R_F 0.65 in 95:5 dichloromethane-acetone; ^1H-n.m.r. data ($CDCl_3$): δ 7.26-7.33 (m, 10 H, H-arom.); 4.99 (d, $J_{1,2}$ 1.0 Hz, H-1); 4.60, 4.47 (2 x AB, 4 H, 2 x benzyl-CH_2); 4.35-4.15 (m, 3 H, H-2, H-3, H-4); 3.82 (m, 2 H, 2 x H-5); 3.31 (s, 3 H, OCH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 105.2 (C-1); 80.0, 78.3, 77.8 (C-2, C-3, C-4); 72.6, 72.3 (2 x benzyl-CH_2); 61.4 (C-5); 54.8 (OCH_3).

Anal. Calc. for $C_{20}H_{24}O_5$: C 69.7, H 7.0; found: C 69.5, H 7.1%.

Methyl 2,3-di-O-benzyl-5-O-allyl-α-D-lyxofuranoside (**6**). - To a mixture of **5** (2.7 g, 7.9 mmole) in DMF (50 ml) was added NaH (0.24 g, 10 mmole) and allyl bromide (1.2 g, 10 mmole). After stirring for 2 h at 22°, methanol (5 ml) was added and the reaction mixture was concentrated. The residue was redissolved in dichloromethane (50 ml) and extracted twice with water, dried

($MgSO_4$), concentrated and purified by column chromatography on silica gel with 99:1 dichloromethane-acetone to give **6** (2.7 g, 90%); $[\alpha]_D$ +16.6° (c 1); R_F 0.78 in 95:5 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.89 (m, 1 H, CH_2=C*H*-CH_2-); 5.18 (m, 2 H, CH_2=CH-CH_2-); 5.01 (d, 1 H, $J_{1,2}$ 2.3 Hz, H-1); 4.64, 4.56 (2 x AB, 4 H, 2 x benzyl-CH_2); 4.33 (dt, $J_{4,3}$ 5.4 Hz, $J_{4,5}$ 6.0 Hz, H-4); 4.19 (dd, 1 H, $J_{3,2}$ 4.6 Hz, $J_{3,4}$ 5.4 Hz, H-3); 4.01 (m, 2 H, CH_2=CH-CH_2-); 3.88 (dd, 1 H, $J_{2,1}$ 2.3 Hz, $J_{2,3}$ 4.6 Hz, H-2); 3.72 (d, 2 H, $J_{4,5}$ 6.0 Hz); 3.35 (s, 3 H, OCH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 134.6 (CH_2=*C*H-CH_2-); 116.8 (CH_2=CH-CH_2-); 106.2 (C-1); 82.3, 78.0, 77.8 (C-2, C-3, C-4); 73.1, 72.3 (2 x benzyl-CH_2); 72.2 (CH_2=CH-CH_2-); 69.5 (C-5); 55.3 (OCH_3).

Anal. Calc. for $C_{23}H_{28}O_5$: C 71.9, H 7.3; found: C 71.5, H 7.4%.

2,3-di-O-benzyl-5-O-allyl-D-lyxofuranose (**7**). - A solution of **6** (2.7 g, 7.1 mmole) in 4:1 acetic acid-H_2O (50 ml) was refluxed for 6 h. Evaporation of the solvent followed by coevaporation of the residue with toluene (3x 20 ml) gave hemiacetal **7** as a mixture of isomers which was used in the next step without further purification (2.0 g); R_F 0.45 in 95:5 dichloromethane-acetone.

1-O-allyl-3,4-di-O-benzyl-D-arabinitol (**8**). - Hemiacetal **7** (2.5 g, 6.75 mmole) was dissolved in ethanol and treated with $NaBH_4$ (0.45 g, 12 mmole). After stirring for 30 min, the reaction mixture was neutralized with acetic acid and concentrated. The residue was redissolved in dichloromethane and extracted with aq. NaCl and aq. $NaHCO_3$, dried ($MgSO_4$) and concentrated once more. Purification by chromatography on silica gel with 97:3 dichloromethane-acetone yielded **8** (2.25 g, 90%); $[\alpha]_D$ -16.0° (c 1); R_F 0.30 in 97:3 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.80 (m, 1 H, CH_2=C*H*-CH2-); 5.20 (m, 2 H, CH_2=CH-CH_2-); 4.0-3.6 (m, 7 H, H-2, H-3, H-4, 2 x H-5, CH_2=CH-CH_2-); 3.52 (dd, 1 H, $J_{1b,2}$ 5.9 Hz, $J_{1b,1a}$ 9.5 Hz, H-1b); 3.43 (dd, 1 H, $J_{1a,2}$ 6.2 Hz, $J_{1a,1b}$ 9.5 Hz, H-1a); ^{13}C-n.m.r ($CDCl_3$): δ 134.4 (CH_2=*C*H-CH_2-); 117.2 (CH_2=CH-CH_2-); 79.6 (C-4); 77.2 (C-3); 74.3, 72.3 (2 x benzyl-CH_2); 72.2 (CH_2=CH-CH_2-); 71.2 (C-1); 69.7 (C-2); 60.5 (C-5).

Anal. Calc. for $C_{22}H_{28}O_5$: C 71.0, H 7.6; found: C 70.9, H 7.6%.

Methyl 2-O-benzyl-3,5-O-isopropylidene-α-D-lyxofuranoside (**10**). - Crude **2** (1.64 g, 10 mmole) was dissolved in acetone (20 ml). Dimethoxypropane (6 ml, 50 mmole) and p-toluenesulphonic acid (30 mg) were added and the reaction mixture was stirred for 1 h, neutralized with Amberlite IRA-400 (OH^--form, 5 g) and methanol (20 ml), filtered and concentrated to give crude **9**; R_F 0.3 in 95:5 dichloromethane-methanol. Compound **9** was dissolved in DMF and treated with NaH (0.29 g, 12 mmole) and benzyl bromide (2.1 g, 12 mmole). After stirring for 2 h, methanol (5 ml) was added and the reaction mixture was concentrated, redissolved in dichloromethane (30 ml), extracted with H_2O and aq. NaCl, dried ($MgSO_4$) and concentrated to give a residue which was chromatographed on silica gel with 95:5 dichloromethane-acetone to afford **10** (1.5 g, 51%, based on **1**); $[\alpha]_D$ +62.4° (c 1); R_F 0.54 in 95:5 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.15 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1); 4.64 (s, 2 H, benzyl-CH_2); 4.18 (m, 1 H, H-4); 4.0-3.8 (m, 4 H, H-2, H-3, 2 x H-5); 3.39 (s, 3 H, OCH_3); 1.46, 1.38 (2 x s, 6 H, $(CH_3)_2C$); ^{13}C-n.m.r. ($CDCl_3$): δ 107.9 (C-1); 97.2 ($(CH_3)_2C$); 84.4, 71.1, 68.6 (C-2, C-3, C-4); 72.1 (benzyl-CH_2); 60.5 (C-5); 56.2 (OCH_3); 28.8, 18.6 ($(CH_3)_2C$).

Anal. Calc. for $C_{16}H_{22}O_5$: C 65.3, H 7.5; found: C 65.4, H 7.2%

Methyl 2-O-benzyl-α-D-lyxofuranoside (**11**). - Compound **10** (1.5 g, 5.1 mmole) was dissolved in 4:1 acetic acid-H_2O (50 ml) and stirred at 50° for 45 min. The mixture was concentrated followed by coevaporation of the remaining residue with toluene (3x 20 ml) to give **11** in quantitative yield (1.3 g, 100%); R_F 0.1 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 4.94 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1); 4.68 (s, 2 H, benzyl-CH_2); 4.14 (m, 1 H, H-4); 4.05-3.75 (m, 4 H, H-2, H-3, 2 x H-5); 3.35 (s, 3 H, OCH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 105.7 (C-1); 82.5, 79.0, 71.8 (C-2, C-3, C-4); 73.2 (benzyl-CH_2); 61.5 (C-5); 55.2 (OCH_3).

Methyl 2-O-benzyl-5-O-allyl-α-D-lyxofuranoside (**12**). - A mixture of **11** (1.27 g, 5 mmole) and dibutyltin oxide (1.24 g, 5 mmole) in methanol was refluxed for 1 h. Evaporation of the solvent yielded a residue which was coevaporated with toluene (2x 20 ml), redissolved in toluene (20 ml) and treated with allyl bromide (0.9 g, 7.5 mmole) and tetrabutylammonium bromide (0.24 g, 0.75 mmole) and heated at 60° for 17 h. The reaction mixture was concentrated, redissolved in dichloromethane (50 ml),

extracted with 1M aq. KF (2x 20 ml) and aq. NaCl (1x 20 ml), dried ($MgSO_4$) and concentrated. Purification of the residue by chromatography on silica gel with 97:3 dichloromethane-acetone gave **12** (1.19 g, 81%); $[\alpha]_D$ +79.3° (c 1); R_F 0.65 in 95:5 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.86 (m, 1 H, CH_2=C*H*-CH_2-); 5.18 (m, 2 H, CH_2=CH-CH_2-); 4.96 (d, 1 H, $J_{1,2}$ 2.3 Hz, H-1); 4.62 (AB, 2 H, benzyl-CH_2); 4.28 (m, 1 H, H-3); 4.18 (m, 1 H, H-4); 4.03 (m, 2 H, CH_2=CH-CH_2-); 3.92 (dd, 1 H, $J_{1,2}$ 2.3 Hz, $J_{2,3}$ 5.1 Hz, H-2); 3.79 (dd, 1 H, $J_{5b,4}$ 3.8 Hz, $J_{5b,5a}$ 10.5 Hz, H-5b); 3.66 (dd, 1 H, $J_{5a,4}$ 3.66 Hz, $J_{5a,5b}$ 10.5 Hz, H-5a); 3.55 (s, 3 H, OCH_3); ^{13}C-n.m.r. ($CDCl_3$): 134.3 (CH_2=*C*H-CH_2-); 116.9 (*C*H_2=CH-CH_2-); 106.5 (C-1); 83.6, 79.1, 70.6 (C-2, C-3, C-4); 68.4 (C-5); 55.2 (OCH_3).

Anal. Calc. for $C_{16}H_{22}O_5$: C 65.3, H 7.5; found: C 65.1, H 7.4%.

Methyl 2,3-di-O-benzyl-5-O-allyl-α-D-lyxofuranoside (**6**). - To a solution of **12** (1.17 g, 4 mmole) in DMF (20 ml) was added NaH (0.12 g, 5 mmole) and benzyl bromide (0.85 g, 5 mmole). After stirring for 2 h, methanol (5 ml) was added and the mixture was concentrated, redissolved in dichloromethane (50 ml), extracted with H_2O and aq. NaCl, dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with 99:1 dichloromethane-acetone to give **6** (1.4 g, 90%).

Methyl 2,3;5,6-di-O-isopropylidene-α-D-mannofuranoside (**14**). - To a suspension of **13** (5.2 g, 20 mmole) in dichloromethane (30 ml) and 10 M aq. NaOH (5 ml) was added methyl iodide (3.1 ml, 50 mmole) and tetrabutylammonium iodide (0.74 g, 2 mmole). The mixture was stirred vigorously for 24 h. The organic layer was separated, extracted with water (2x 25 ml), dried ($MgSO_4$) and concentrated to give **10** (5.0 g, 92%); $[\alpha]_D$ +81.9° (c 1); R_F 0.80 in 95:5 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 4.87 (s, 1 H, H-1); 4.77 (dd, 1 H, $J_{3,2}$ 5.9 Hz, $J_{3,4}$ 3.6 Hz, H-3); 4.56 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2); 4.42 (m, 1 H, H-4); 4.08 (m, 2 H, 2 x H-6); 3.90 (dd, $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 8.0 Hz, H-4); 3.31 (s, 3 H, OCH_3); 1.46, 1.45, 1.38, 1.32 (4 x s, 12 H, 2 x (CH_3)$_2$C)); ^{13}C-n.m.r. ($CDCl_3$): δ 112.5, 109.1 (2 x (CH_3)$_2$*C*); 107.2 (C-1); 84.9, 80.2, 79.4 (C-2, C-3, C-4); 73.1 (C-5); 66.9 (C-6); 54.9 (OCH_3); 26.8, 25.8, 25.1, 24.5 (4 x (CH_3)$_2$C).

Methyl 2,3-O-isopropylidene-α-D-mannofuranoside (**15**). - Compound **14** (4.9 g, 18 mmole) was dissolved in 4:1 acetic acid-water (100 ml) and stirred for 17 h at 20°. The reaction mixture was concentrated and coevaporated with toluene (3x 30 ml) to yield **15** (4.0 g, 95%); $[\alpha]_D$ +85.3° (c 1); R_F 0.45 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 4.88 (s, 1 H, H-1); 4.84 (dd, 1 H, $J_{3,2}$ 5.9 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.56 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2); 3.99 (dd, 1 H, $J_{3,4}$ 5.9 Hz, $J_{4,5}$ 2.7 Hz, H-4); 3.60-3.90 (m, 3 H, H-5, 2 x H-6); 3.30 (s, 3 H, OCH_3); 1.47, 1.33 (2 x s, 6 H, (CH_3)$_2$C); ^{13}C-n.m.r. ($CDCl_3$): δ 112.4 ((CH_3)$_2$*C*); 107.0 (C-1); 84.5, 79.8, 79.0 (C-2, C-3, C-4); 69.8 (C-5); 64.2 (C-6); 54.3 (OCH_3); 25.8, 24.6 ((CH_3)$_2$C).

Methyl 2,3-O-isopropylidene-α-D-lyxofuranoside (**16**). - A solution of **15** (4 g, 17.1 mmole) in 1:4 ethanol-water (80 ml) was treated with sodium periodate (4.75 g, 22 mmole). After stirring for 15 min, ethanol (100 ml) was added. The precipitated $NaIO_3$ was filtered and washed with ethanol (2x 25 ml). To the filtrate was added sodium borohydride (1.89 g, 50 mmole) and the reaction mixture was stirred for 30 min, neutralized with acetic acid and concentrated once more. The residue was redissolved in dichloromethane, extracted with H_2O and aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated. The remainder was chromatographed on silica gel in 98:2 dichloromethane-methanol to afford **16** (3.1 g, 89%); $[\alpha]_D$ +93.7° (c 1); R_F 0.55 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.08 (s, 1 H, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 112.0 ((CH_3)$_2$*C*); 106.5 (C-1); 84.4, 79.4, 79.2 (C-2, C-3, C-4); 60.0 (C-5); 54.0 (OCH_3); 25.3, 24.1 ((CH_3)$_2$C).

Anal. Calc. for $C_9H_{16}O_5$: C 73.1, H 6.8; C 73.0, H 6.8%.

Methyl 2,3-O-isopropylidene-5-O-allyl-α-D-lyxofuranoside (**17**). - To a mixture of **16** (3.06 g, 15 mmole) in DMF (30 ml) was added NaH (0.43 g, 18 mmole) and allyl bromide (2.2 g, 18 mmole). After stirring for 1 h, excess NaH was destroyed with methanol and the reaction mixture was concentrated. The residue was redissolved in dichloromethane, extracted with H_2O and aq. NaCl. The organic layer was dried (Na_2SO_4) and concentrated to give **17** (3.3 g, 90%) which was used in the next step without further purification; $[\alpha]_D$ +95.5° (c 1); R_F 0.70 in 95:5 dichloromethane-acetone; ^{13}C-n.m.r. data ($CDCl_3$): δ 134.8 (CH_2=*C*H-

CH_2-); 117.1 (CH_2=CH-CH_2-); 112.5 ((CH_3)$_2$*C*); 107.3 (C-1); 85.0, 80.0, 79.0 (C-2, C-3, C-4); 72.4 (CH_2=CH-CH_2-); 68.3 (C-5); 54.6 (OCH_3); 26.1, 25.0 ((CH_3)$_2$C).

Methyl 5-O-allyl-α-D-lyxofuranoside (**18**). - Derivative **17** (2.4 g, 10 mmole) was refluxed with methanol containing 0.3% HCl (w/v, 40 ml) for 15 min and concentrated. The above mentioned procedure was repeated four times. T.l.c. analysis indicated the formation of a major component which was established to be **18**, after purification by chromatography on silica gel with 96:4 dichloromethane-methanol. Yield 1.18 g, 60%; $[\alpha]_D$ +115.2° (c 1); R_F 0.52 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 4.82 (s, 1 H, H-1); 4.50 (m, 1 H, H-3); 4.23 (dt, 1 H, $J_{4,5}$ 2.6 Hz, $J_{4,3}$ 7.2 Hz, H-4); 3.90 (m, 1 H, H-2); 3.69 (d, 2 H, $J_{5,4}$ 2.6 Hz, 2 x H-5); 3.35 (s, 3 H, OCH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 133.4 (CH_2=*C*H-CH_2-); 118.0 (*C*H_2=CH-CH_2-); 107.5 (C-1); 77.5, 74.6, 71.3 (C-2, C-3, C-4); 72.5 (CH_2=CH-*C*H_2-); 68.0 (C-5); 54.9 (OCH_3).

Methyl 2,3-di-O-benzyl-5-O-allyl-α-D-lyxofuranoside (**6**). - A mixture of **18** (1.22 g, 6 mmole) in DMF (25 ml) was treated with NaH (0.36 g, 15 mmole) and benzyl bromide (2.56 g, 15 mmole). The reaction mixture was stirred for 3 h at 20°. Methanol (5 ml) was added to destroy excess NaH followed by evaporation of the solvents. The remainder was processed as described above for the preparation of **6**, starting from compound **5**, to give (2.0 g, 87%).

1-O-Allyl-3,4-di-O-benzyl-5-O-benzoyl-D-arabinitol (**19**). - 1-(Benzoyloxy)benzotriazole[7] (1.34 g, 5.75 mmole) and triethylamine (0.61 g, 6 mmole) were added to a solution of compound **8** (1.86 g, 5 mmole) in dry 1,2-dichloroethane (25 ml). After stirring for 17 h at 20° the reaction mixture was extracted with aq. $NaHCO_3$ (2x 10 ml), dried (Na_2SO_4) and concentrated to give a residue which was chromatographed on silica gel with 98:2 dichloromethane-acetone to afford pure **19** (1.92 g, 81%); $[\alpha]_D$ -2.7° (c 1); R_F 0.76 in 95:5 dichloromethane-acetone; ^{13}C-n.m.r. data ($CDCl_3$): δ 165.9 (C=O); 134.2 (CH_2=*C*H-CH_2-); 116.7 (*C*H_2=CH-CH_2); 77.3 (C-3); 76.9 (C-4); 73.9, 72.2 (2 x benzyl-*C*H_2); 71.8 (CH_2=CH-*C*H_2-); 70.7 (C-1); 69.2 (C-2); 63.3 (C-5).

Anal. Calc. for $C_{29}H_{32}O_6$: C 73.1, H 6.8; found: C 73.0, H 6.9%.

Ethyl 2,3,4-tri-O-acetyl-1-thio-α-L-rhamnopyranoside (**21**). - To a cooled (0°) solution of 1,2,3,4-tetra-O-acetyl-α/β-L-rhamnopyranose (6.6 g, 20 mmole) and ethanethiol (1.92 ml, 26 mmole) in dry dichloromethane (50 ml) was added tin(IV)chloride (0.23 ml, 2 mmole). After stirring for 1 h, the reaction mixture was extracted with aq. NaCl (2x 100 ml) and aq. $NaHCO_3$ (50 ml), dried (Na_2SO_4) and concentrated. Diethylether (150 ml) was added and the resulting solution was left for 17 h. The precipitated ethyl 2,3,4-tri-O-acetyl-β-L-rhamnopyranoside (0.6 g, 9% ; $[\alpha]_D$ +48.5° (c 1); R_F 0.55 in 1:1 ether-hexane) was filtered off and the filtrate was concentrated to give **21** which was sufficiently pure for further reactions. Yield (5.9 g, 88%); $[\alpha]_D$ +110.8° (c 1); R_F 0.62 in ether-hexane; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.33 (dd, 1 H, $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 3.3 Hz, H-2); 5.22 (dd, 1 H, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 10.0 Hz, H-3); 5.20 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1); 5.09 (t, 1 H, $J_{4,3}\approx J_{4,5}$ 10.0 Hz, H-4); 4.24 (m, 1 H, H-5); 2.65 (m, 2 H, S*C*H_2CH$_3$); 2.16, 2.06, 1.98 (3 x s, 9 H, *C*H_3COO); 1.30 (t, 3 H, *J* 7.5 Hz, SCH$_2$*C*H_3); 1.23 (d, 3 H, $J_{6,5}$ 6.2 Hz, 3 x H-6); ^{13}C-n.m.r. ($CDCl_3$): δ 168.8, 168.7 (3 x C=O); 81.1 (C-1); 70.7, 70.3 (C-2, C-4); 68.7 (C-3); 66.2 (C-5); 24.6 (S*C*H_2CH$_3$); 19.9, 19.8, 19.6 (3 x *C*H_3COO); 16.5 (C-6); 14.1 (SCH$_2$*C*H_3).

1-O-allyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-3,4-di-O-benzyl-5-O-benzoyl-D-arabinitol (**22**). - *a) From glycosyldonor* **20**. Arabinitol derivative **19** (0.95 g, 2 mmole) and mercuric cyanide (0.51 g, 2 mmole) were coevaporated with dry acetonitrile (3x 20 ml) and redissolved in the same solvent (15 ml). Tetra-O-acetyl-α-L-rhamnopyranosyl bromide (0.88 g, 2.5 mmole) in 1,2-dichloroethane (5 ml) was added dropwise. After stirring for 1 h under a N_2, atmosphere the reaction mixture was diluted with dichloromethane, extracted with aq. 1M KBr (2x 20 ml) and aq. $NaHCO_3$ (20 ml), dried (Na_2SO_4) and concentrated . The residue was chromatographed on Sephadex LH-20 with 1:1 dichloromethane-methanol to give **22** (1.42 g, 95%). *b) From glycosyl-donor* **21**. A mixture of **19** (0.48 g, 1 mmole) and **21** (0.40 g, 1.2 mmole) was coevaporated with 1,2 dichloroethane (3x 10 ml) an redissolved in the same solvent (10 ml). Powdered molecular sieves (4A, 1 g) was added and the mixture was stirred 30 min under a N_2 atmosphere. Methyl trifluoromethanesulphonate (0.28 ml, 2.5 mmole) was added. After stirring for 3 h, 1:1 pyridine-

water (1 ml) was added, the reaction mixture was filtered and the filtrate was extracted with aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated. Purification was performed as described above to give **22** (0.61 g, 82%); $[\alpha]_D$ -23.1° (c 1); R_F 0.68 in 1:1 ether-hexane; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.80 (m, 1 H, CH_2=C*H*-CH_2-); 5.02 (s, 1 H, H-1); 5.4-5.2 (m, 3 H, H-2^1, H-3^1, H-4^1); 5.2-5.0 (m, 2 H, CH_2=CH-CH_2-); 4.9-4.6 (m, 5 H, 2 x benzyl-CH_2, H-5b); 4.52 (dd, 1 H, $J_{5a,4}$ 5.7 Hz, $J_{5a,5b}$ 12.4 Hz, H-5a); 4.1-3.9 (m, 6 H, H-2, H-3, H-4, H-5^1, CH_2=CH-CH_2-); 3.59 (d, 2 H, $J_{1,2}$ 4.3 Hz, 2 x H-1); 2.13, 1.98, 1.94 (3 x s, 9 H, 3 x CH_3COO); 1.02 (d, 3 H, $J_{6,5}$ 6.2 Hz, 3 x H-6^1; ^{13}C-n.m.r. ($CDCl_3$): δ 169.8, 169.6 (3 x acetyl C=O); 166.1 (benzoyl C=O); 134.1 (CH_2=*C*H-CH_2-); 117.1 (*C*H_2=CH-CH_2-); 96.3 (C-1^1); 78.4, 77.1, 76.1 (C-2, C-3, C-4); 74.5, 72.1 (2 x benzyl-*C*H_2); 71.8 (CH_2=CH-*C*H_2-); 70.8 (C-4^1); 69.9 (C-3^1); 69.0 (C-2^1); 66.5 (C-5^1); 68.8 (C-1); 63.8 (C-5); 20.7, 20.5 (3 x *C*H_3COO); 17.1 (C-6^1).

O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-(1→2)-3,4-di-O-benzyl-5-O-benzoyl-D-arabinitol (**23**). - To a solution of compound **22** (1.5 g, 2 mmole) in 1,2 dichloroethane (10 ml) was added 1,6 cyclooctadiene-bis-[methyldiphenylphosphine]-iridium hexafluorophosphate (≈ 1 mg) under an atmosphere of nitrogen. The stirred solution was degassed and placed under an atmosphere of hydrogen, during which operation the catalyst was activated and the slightly red solution turned colorless. After 2 min, the mixture was degassed once more and placed under nitrogen. After stirring for 3 h, the reaction mixture was concentrated. The residue was redissolved in 10:1 acetone-water (20 ml) and treated with mercuric chloride (0.60 g, 2.2 mmole) and mercuric oxide (0.48 g, 2.2 mmole). The reaction mixture was stirred for 20 min, filtered over Celite, concentrated to a small volume, diluted with dichloromethane, extracted with aq. KBr (1M, 2x 20 ml) and aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel with 98:2 dichloromethane-acetone to give compound **23** (1.23 g, 87%); -59.4° (c 2); R_F 0.30 in 98:2 dichloromethane-acetone; ^{13}C-n.m.r. data ($CDCl_3$): δ 95.7 (C-1^1); 78.3, 77.4 (C-2, C-3, C-4); 74.5, 72.1 (2 x benzyl-CH_2); 70.6 (C-4^1); 69.9 (C-3^1); 69.1 (C-2^1); 66.6 (C-5^1); 63.6 (C-5); 60.5 (C-1); 17.1 (C-6^1).

Anal. Calc. for $C_{41}H_{48}O_{13}$: C 65.8, H 6.5; found: C 65.5, H 6.4%.

N-Benzyloxycarbonyl-3-aminopropyl-(2-cyanoethyl)-N,N-diethylphosphoramidite (**26**). - To a mixture of *N*-benzyloxycarbonyl-3-aminopropanol **24** (209 mg, 1 mmole) and diisopropylethylamine (0.31 ml, 1.8 mmole) in dichloromethane (5 ml) was added 2-cyanoethoxy(*N,N*-diethylamino)chlorophosphine (**25**) (0.29 g, 1.4 mmole). After stirring for 10 min, the reaction mixture was extracted with aq. NaCl (2x 10 ml) and aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated to give **26** (0.36 g, 94%); ^{31}P-n.m.r. data (CD_3CN): δ 140.23.

3-Aminopropyl O-(α-L-rhamnopyranosyl)-(1→2)-D-arabinitol-1-phosphate (**28**). - To a solution of compound **23** (177 mg, 0.25 mmole) and reagent **26** (133 mg, 0.35 mmole) in acetonitrile (3 ml) was added 1-*H*-tetrazole (70 mg, 1 mmole), and the mixture was stirred for 30 min when t.l.c. analysis showed all **23** to be consumed. *Tert.*-butyl hydroperoxide (0.1 ml, 1 mmole) was added and stirring was continued for 15 min. The reaction mixture was concentrated under reduced pressure to give **27** (R_F 0.45 in 95:5 dichloromethane-acetone) and redissolved in 2:1 methanol-25% ammonium hydroxide (10 ml) and stirred for 17 h at 60°. Evaporation of the solvents gave a residue which was chromatographed on Sephadex LH-20 with methanol. The appropriate fractions were collected, concentrated and converted into the Na^+ salt by passing it through a cation-exchanger column (Dowex W50) with methanol. The resulting product was redissolved in 50:47:3 methanol-water-acetic acid, and hydrogenated in the presence of 10% palladium on charcoal for 48 h. The catalyst was removed by filtration and the filtrate was concentrated. The residue was chromatographed on Sephadex LH-20 with methanol to give derivative **28** (87 mg, 81%); $[\alpha]_D$ -26.5° (c 1, H_2O); ^{31}P-n.m.r. data (D_2O): δ 1.057; ^{1}H- and ^{13}C-n.m.r. data: see *Tables 1* and *2*.

Anal. Calc. for $C_{14}H_{30}NO_{12}P$: C 38.6, H 6.9; found: C 38.2, H 7.2%

O-(2,3,4-tri-O-acetyl-α-L-rhamnosyl)-(1→2)-3,4-di-O-benzyl-5-O-benzoyl-D-arabinityl-N,N-diethyl-(2-cyanoethyl)-phosphoramidite (**29**). - To a stirred solution of **23** (0.70 g, 1 mmole) and diisopropylethylamine (0.34 ml, 2 mmole) in 1,2-dichloroethane (5 ml) was added reagent **25** (0.31 g, 1.5 mmole). After stirring for 15 min, the reaction mixture was successively extracted with aq.

NaCl (2x 15 ml) and aq. $NaHCO_3$, and concentrated to afford **29** (0.83 g, 94%) as a mixture of diasteriomers; R_F 0.65 in 95:5 dichloromethane-acetone; ^{31}P-n.m.r. data (CD_3CN): δ 149.1 and 149.4.

Ethyl 1-thio-α-L-rhamnopyranoside (**30**). - Compound **21** (5 g, 15 mmole) was dissolved in methanol (40 ml) and treated with $NaOCH_3$ (30 mg) for 1 h. The reaction mixture was neutralized with Dowex W50 (H^+-form, 2 g) filtered and concentrated to give **30** (3.1 g, quantitative); $[\alpha]_D$ -155.2° (c 1, MeOH); R_F 0.3 in 9:1 dichloromethane-methanol; ^{1}H-n.m.r. data (CD_3OD): δ 5.18 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1); 3.92 (m, 2 H, H-2, H-5); 3.60 (dd, 1 H, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz, H-3); 3.41 (t, 1 H, $J_{4,3}$≈$J_{4,5}$ 9.3 Hz, H-4); 2.62 (m, 2 H, S$CH_2$$CH_3$); 1.26 (m, 6 H, 3 x H-6, SCH_2CH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 86.0 (C-1); 74.1 (C-4); 73.7 (C-2); 72.8 (C-3); 69.9 (C-5); 25.9 (S$CH_2$$CH_3$); 17.8 (C-6); 15.4 ($SCH_2CH_3$).

Ethyl 2,3-O-isopropylidene-1-thio-α-L-rhamnopyranoside (**31**). - A mixture of **30** (3.1 g, 15 mmole), dimethoxypropane (7 ml) and acetone (25 ml) was treated with p-toluenesulphonic acid (30 mg) and stirred for 1 h. Amberlite (OH^--form, 5 g) and methanol (10 ml) was added and, after stirring for 10 min, the reaction mixture was filtered and concentrated to give **31** (3.7 g, 95%) which was used in the next step without further purification; $[\alpha]_D$ -96.8° (c 1); R_F 0.45 in 97:3 dichloromethane-methanol. ^{1}H-n.m.r. data ($CDCl_3$): δ 5.53 (s, 1 H, H-1); 4.17 (d, 1 H, $J_{2,3}$ 5.6 Hz, H-2); 4.06 (dd, 1 H, $J_{3,2}$ 5.6 Hz, $J_{3,4}$ 7.2 Hz, H-3); 3.96 (m, 1 H, H-4); 3.40 (dd, 1 H, $J_{4,3}$ 7.6 Hz, $J_{4,5}$ 9.8 Hz, H-4); 2.60 (m, 2 H, S$CH_2$$CH_3$); 1.54, 1.35 (2 x s, 6 H, $(CH_3)_2C$); 1.30 (m, 6 H, 3 x H-6, SCH_2CH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 109.1 ($(CH_3)_2C$); 86.0 (C-1); 78.2, 76.5, 74.8, 65.8 (C-2, C-3, C-4, C-5); 27.9, 26.1 ($(CH_3)_2C$); 24.1 (S$CH_2$$CH_3$); 17.0 (C-6); 14.4 ($SCH_2CH_3$).

Ethyl 4-O-dichloroacetyl-1-thio-α-L-rhamnopyranoside (**33**). - To a mixture of **31** (2.48 g, 10 mmole) in pyridine (25 ml) was added dichloroacetic anhydride (3.6 g, 15 mmole). After stirring for 1 h, water (1 ml) was added and the reaction mixture was concentrated. The residue was redissolved in dichloromethane, extracted with aq. $NaHCO_3$ and concentrated to give **32** (R_F 0.82 in 97:3 dichloromethane-acetone). Crude **32** was redissolved in 4:1 acetic acid-water and kept at 45° for 17 h. The reaction mixture was concentrated and the remaining was chromatographed on silica gel with 97:3 dichloromethane-methanol to give **33** (2.42 g, 76%); $[\alpha]_D$ -115.6° (c 1); R_F 0.40 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.30 (s, 1 H, H-1); 5.00 (t, 1 H, $J_{4,3}$≈$J_{4,5}$ 9.5 Hz, H-4); 6.04 (s, 1 H, Cl_2CH); ^{13}C-n.m.r. ($CDCl_3$): δ 163.5 (C=O); 84.2 (C-1); 76.2, 72.0, 69.3 (C-2, C-3, C-4); 65.8 (Cl_2CH); 16.6 (C-6).

Ethyl 2,3-di-O-(2-methylbenzoyl)-4-O-dichloroacetyl-1-thio-α-L-rhamnopyranoside (**34**). - 2-Methylbenzoyl chloride (2.3 g, 15 mmole) in dioxane (10 ml) was added dropwise to a solution of compound **33** (2.42 g, 7.6 mmole) in pyridine (25 ml). After stirring for 1 h water (1 ml) was added and the reaction mixture was concentrated, extracted with aq. $NaHCO_3$ (2x 20 ml), dried (Na_2SO_4) and concentrated. Chromatography on silica gel with 99:1 dichloromethane-acetone yielded **34** (3.1 g, 73%); $[\alpha]_D$ +39.5° (c 1); R_F 0.90 in 99:1 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.86 (s, 1 H, Cl_2CH); 5.73 (dd, 1 H, $J_{2,1}$ 1.3 Hz, $J_{2,3}$ 3.3 Hz, H-2); 5.60 (dd, 1 H, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 10.1 Hz, H-3); 5.46 (t, 1 H, $J_{4,3}$≈$J_{4,5}$ 10.0 Hz, H-4); 5.44 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1); 4.42 (m, 1 H, H-5); 2.69 (m, 2 H, S$CH_2$$CH_3$); 2.52, 2.54 (2 x s, 6 H, 2 x toluoyl-CH_3); 1.36 (d, 3 H, $J_{6,5}$ 6.1 Hz, 3 x H-6); 1.33 (t, 3 H, *J* 7.5 Hz, SCH_2CH_3); ^{13}C-n.m.r. ($CDCl_3$): δ 166.2, 165.9 (2 x toluoyl C=O); 163.6 (DCA C=O); 81.9 (C-1); 73.3 (C-4); 72.3 (C-2); 70.2 (C-3); 66.6 (C-5); 63.8 (Cl_2CH); 25.5 (S$CH_2$$CH_3$); 21.6, 21.2 (2 x toluoyl CH_3); 17.3 (C-6); 14.8 (SCH_2CH_3).

Anal. Calc. for $C_{26}H_{28}Cl_2O_7S$: C 56.2, H 5.1; found: C 56.0, H 5.1%

N-Benzyloxycarbonyl-3-aminopropyl 2,3-di-O-(2-methylbenzoyl)-4-O-dichloroacetyl-α-L-rhamnopyranoside (**35**). - To a stirred mixture of **34** (1.11 g, 2 mmole), **24** (0.42 g, 2 mmole), silver trifluoromethanesulphonate (0.56 g, 2.2 mmole), powdered molecular sieves (4A, 2 g) and 1,2-dichloroethane (8 ml) was added freshly prepared 1M methylsulfenyl bromide in 1,2-dichloroethane (2.2 ml). The reaction mixture was stirred for 2 h, filtered, extracted successively with aq. $NaHSO_3$ and aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated. The residue was chromatographed on a column of Sephadex-LH20 with 1:1 dichloromethane-methanol to give **35** (0.99 g, 71%); $[\alpha]_D$ +37.1° (c 1); R_F 0.72 in 95:5 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.86 (s, 1 H, Cl_2CH);

5.71 (dd, 1 H, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 10.0 Hz, H-3); 5.64 (dd, 1 H, $J_{2,1}$1.5 Hz, $J_{2,3}$ 3.3 Hz, H-2); 5.40 (t, 1 H, $J_{4,3}$≈$J_{4,5}$ 10.0 Hz, H-4); 5.12 (s, 2 H, benzyl-CH_2); 4.95 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1); 4.11 (m, 1 H, H-5); 3.82, 3.58 (2 x m, 2 H, H1a, H1b, spacer); 3.38 (m, 2 H, H-3, spacer); 2.52, 2.50 (2 x s, 6 H, toluoyl-CH_3); 1.89 (m, 2 H, H-2, spacer); 1.32 (d, 3 H, $J_{6,5}$ 6.2 Hz, 3 x H-6); ^{13}C-n.m.r. ($CDCl_3$): 166.3 (2 x C=O, Tol); 163.8 (C=O, DCA); 156.4 (C=O, CBz); 97.6 (C-1); 74.5, 70.4, 69.1 (C-2, C-3, C-4); 66.0 (C-5); 66.6 (C-1, spacer); 66.1 (benzyl-CH_2); 63.8 (Cl_2CH); 38.4 (C-3, spacer); 29.7 (C-2, spacer); 21.7 (2 x toluoyl-CH_3); 17.4 (C-6).

Anal. Calc. for $C_{35}H_{37}Cl_2NO_{10}$: C 59.8, H 5.3; found: C 60.1, H 5.6%

N-Benzyloxycarbonyl-3-aminopropyl 2,3-di-O-(2-methylbenzoyl)-α-L-rhamnopyranoside (**36**). - Aq. ammonia (25% w/v, 0.11 ml) was added to a solution of compound **35** (0.70 g, 1 mmole) in methanol (5 ml). After 1 h, the reaction mixture was neutralized with acetic acid and concentrated. The residue was redissolved in dichloromethane, extracted with aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated. The remaining redidue was purified by silica gel chromatography with 97:3 dichloromethane-acetone to yield **36** (0.58 g, 82%); $[\alpha]_D$ +39.5° (c 1); R_F 0.50 in 95:5 dichloromethane-acetone; ^{13}C-n.m.r. data ($CDCl_3$): δ 167.5, 166.4 (C=O, Tol); 156.5 (C=O, CBz); 97.5 (C-1); 72.7, 71.9, 70.6 (C-2, C-3, C-4); 68.9 (C-5); 66.6 (C-1, spacer); 65.3 (benzyl-CH_2); 38.3 (C-3, spacer);, 29.6 (C-2, spacer); 21.8, 21.7 toluoyl-CH_3); 17.7 (C-6).

N-Benzyloxycarbonyl-3-aminopropyl 2,3,4,6-tetra-O-benzoyl-β-D-glucopyranoside (**37**). - Tetra-O-benzoyl-α-D-glucopyranosyl bromide (6.59 g, 10 mmole) was added to a mixture of **24** (2.09 g, 10 mmole), mercuric bromide (3.60 g, 10 mmole) and mercuric cyanide (2.53 g, 10 mmole) and acetonitrile (40 ml). After stirring for 4 h, the reaction mixture was concentrated, redissolved in dichloromethane, extracted successively with aq. KBr (1M, 3x 25 ml) and aq. $NaHCO_3$ and concentrated. The residue was chromatographed on silica gel with 97:3 dichloromethane-acetone to give **37** (5.8 g, 74%); $[\alpha]_D$ +21.2° (c 1); R_F 0.65 in 97:3 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.93 (dd, 1 H, $J_{4,3}$≈$J_{4,5}$ 9.5 Hz, H-4); 5.70 (dd, 1 H, $J_{3,2}$≈$J_{3,4}$ 9.8 Hz, H-3); 5.54 (dd, 2 H, $J_{2,1}$ 8.0 Hz, $J_{2,3}$ 9.8 Hz, H-2); 5.04 (s, 2 H, benzyl-CH_2); 4.84 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1); 4.68 (dd, 1 H, $J_{6b,5}$ 3.1 Hz, $J_{6b,6a}$ 12.0 Hz, H-6b); 4.49 (dd, 1 H, $J_{6a,5}$ 4.9 Hz, $J_{6a,6b}$ 12.1 Hz, H-6a); 4.12 (m, 1 H, H-5); 3.95, 3.62 (2 x dt, 2 H, 2 x H-1, spacer); 3.18 (m, 2 H, H-3, spacer); 1.74 (m, 2 H, H-2, spacer); ^{13}C-n.m.r. ($CDCl_3$): δ 166.0, 165.7, 165.5 (4 x C=O, benzoyl); 156.3 (C=O, CBz); 101.1 (C-1); 72.7, 72.2, 71.8, 69.6 (C-2, C-3, C-4, C-5); 67.6 (C-1, spacer); 66.3 (benzyl-CH_2); 62.9 (C-6); 38.0 (C-3, spacer); 29.5 (C-2, spacer).

N-Benzyloxycarbonyl-3-aminopropyl β-D-glucopyranoside (**38**). - Compound **37** (5.8 g, 7.4 mmole) was dissolved in methanol (50 ml). Sodium methoxide (30 mg) was added and the reaction mixture was stirred for 17 h, neutralized with Dowex (H^+-form, 3 g) and concentrated to give **38** (2.7 g, 98%); $[\alpha]_D$ -23.8° (c 1, MeOH); R_F 0.43 in 85:15 dichloromethane-methanol; ^{13}C-n.m.r. data (CD_3OD): δ 158.8 (C=O, CBz); 104.2 (C-1); 77.9, 77.8 (C-3, C-5); 74.9 (C-2); 71.5 (C-5); 68.0 (benzyl-CH_2); 67.3 (C-1, spacer); 62.7 (C-6); 38.7 (C-3, spacer); 30.8 (C-2, spacer).

N-Benzyloxycarbonyl-3-aminopropyl 4,6-O-isopropylidene-β-D-glucopyranoside (**39**). - To a suspension of **38** (2.7 g, 7.3 mmole) in acetone (50 ml) was added 2,2-dimethoxypropane (8 ml) and p-toluenesulphonic acid (20 mg). After stirring for 4 h, Amberlite IRA-400 (OH^--form, 10 g) and methanol (25 ml) were added and, after stirring for 5 min, the reaction mixture was filtered and concentrated. The residue was redissolved in dichloromethane, extracted with aq. NaCl, dried (Na_2SO_4) and concentrated to afford **39** (2.37 g, 79%); R_F 0.50 in 95:5 dichloromethane-methanol; ^{13}C-n.m.r. data (CD_3OD): δ 105.0 (C-1); 100.7 (($CH_3)_2C$); 75.9, 75.0, 74.8, 68.5 (C-2, C-3, C-4, C-5); 63.2 (C-6); 69.6 (C-1, spacer); 38.5 (C-3, spacer); 30.1 (C-2, spacer); 29.4, 19.4 (($CH_3)_3C$)

N-Benzyloxycarbonyl-3-aminopropyl 2,3-di-O-benzoyl-β-D-glucopyranoside (**41**). - Benzoyl chloride (2.25 g, 16 mmole) was added dropwise to a stirred solution of **39** (2.26 g, 5.5 mmole) in pyridine (30 ml). After 2 h water (2 ml) was added and the reaction mixture was concentrated, redissolved in dichloromethane, extracted with aq. $NaHCO_3$ (2x 25 ml), dried (Na_2SO_4) and concentrated once more to yield **40** (R_F 0.75 in 95:5 dichloromethane-acetone) which was redissolved in 4:1 acetic acid-water

(40 ml), kept at 50° for 1 h, and concentrated. The residue was chromatographed on silica gel with 98:2 dichloromethane-methanol to give **41** (2.6 g, 82%); $[\alpha]_D$ +29.7° (c 1); R_F 0.40 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.47 (dd, 1 H, $J_{3,2}\approx J_{3,4}$ 9.0 Hz, H-3); 5.39 (dd, 1 H, $J_{2,1}$ 7.4 Hz, $J_{2,3}$ 9.0 Hz, H-2); 4.69 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1); ^{13}C-n.m.r. data ($CDCl_3$): 166.0, 165.3 (2 x C=O, benzoyl); 156.1 (C=O, CBz); 100.9 (C-1); 76.3, 76.1, 71.7, 69.3 (C-2, C-3, C-4, C-5); 67.4 (C-1, spacer); 66.4 (benzyl-CH_2); 62.3 (C-6); 37.9 (C-3, spacer); 29.4 (C-2, spacer).

Anal. Calc. for $C_{31}H_{33}NO_{10}$: C 64.2, H 5.7; found: C 64.1, H 5.5%.

1-O-(2-methylbenzoyloxy)benzotriazole - To a cooled (0°) mixture of 1-hydroxybenzotriazole (2.7 g, 20 mmole), triethylamine (2.02 g, 20 mmole) and dichloromethane (50 ml) was added dropwise 2-methylbenzoyl chloride (3.09 g ,20 mmole). After stirring for 30 min, the reaction mixture was extracted with water and aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated to give the title compound as a white solid (4.65 g, 92%).

N-Benzyloxycarbonyl-3-aminopropyl 2,3-di-O-benzoyl-6-O-(2-methylbenzoyl)-β-D-glucopyranoside (**42**). - Compound **41** (2.3 g, 4 mmole) was dissolved in 1,2-dichloroethane (20 ml). 1-(2-methylbenzoyloxy)benzotriazole (1.1 g, 4.3 mmole) and triethylamine (4.55 g, 4.5 mmole) were added and the reaction mixture was stirred for 17 h, extracted with aq. $NaHCO_3$) and concentrated. The residue was chromatographed on silica gel with 97:3 dichloromethane-acetone to give **42** (2.37 g, 85%); $[\alpha]_D$ +24.7° (c 1); R_F 0.89 in 95:5 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.51 (dd, 1 H, $J_{3,2}\approx J_{3,4}$ 9.8 Hz, H-3); 5.40 (dd, 1 H, $J_{2,1}$ 7.4 Hz, $J_{2,3}$ 9.8 Hz, H-2); 5.00 (s, 2 H, benzyl-CH_2); 4.72 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1); 4.0-3.7 (m, 5 H, H-4, H-5, 2 x H-6, H-1b, spacer); 3.58 (m, 1 H, H-1a, spacer); 3.15 (m, 2 H, H-3, spacer); 2.59 (s, 3 H, 3 x toluoyl-CH_3); 1.72 (m, 2 H, H-2, spacer); ^{13}C-n.m.r. ($CDCl_3$): δ 167.5 (C=O, Tol); 166.5, 165.2 (2 x C=O, benzoyl); 156.3 (C=O, CBz); 100.7 (C-1); 75.8, 74.2, 71.6, 69.3 (C-2, C-3, C-4, C-5); 63.2 (C-6); 67.3 (C-1, spacer); 66.1 (benzyl-CH_2); 63.2 (C-6); 37.9 (C-3, spacer); 29.2 (C-2, spacer); 21.6 (toluoyl-CH_3).

Anal. Calc. for $C_{39}H_{39}NO_{11}$: C 67.1, H 5.6; found: C 66.9, H 5.6%.

N-Benzyloxycarbonyl 2,3-di-O-benzoyl-4-O-[2,3-di-O-(2-methylbenzoyl)-4-O-dichloroacetyl-α-L-rhamnopyranosyl]-6-O-(2-methylbenzoyl)-β-D-glucopyranoside (**43**). - To a mixture of **42** (0.70 g, 1 mmole), **34** (0.83 g, 1.5 mmole), silver trifluoromethanesulphonate (0.38 g, 1.5 mmole), powdered molecular sieves (4A, 1 g) and 1,2-dichloroethane (5 ml) was added 1 M methylsulfenyl bromide in 1,2-dichloroethane (1.5 ml). After stirring for 2 h, the reaction mixture was filtered, successively extracted with aq. $NaHSO_3$ and aq. $NaHCO_3$, dried (Na_2SO_4) and concentrated. Purification of the residue by chromatography on Sephadex LH-20 with 1:1 dichloromethane-methanol led to the isolation of **43** (0.95 g, 80%); $[\alpha]_D$ +48.4° (c 1); R_F 0.55 in 97:3 dichloromethane-acetone; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.84 (dd, 1 H, $J_{3,2}\approx J_{3,4}$ 9.5 Hz, H-3); 5.75 (s, 1 H, Cl_2CH); 5.63 (dd, 1 H, $J_{3,2}$ 3.4 Hz, $J_{3,4}$ 10.0 Hz, H-3^1); 5.58 (dd, 1 H, $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 3.3 Hz, H-2^1); 5.39 (dd, 1 H, $J_{2,1}$ 8.0 Hz, $J_{2,3}$ 9.8 Hz, H-2); 5.25 (dd, 1 H, $J_{4,3}\approx J_{4,5}$ 9.9 Hz, H-4^1); 5.18 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1^1); 5.04 (s, 2 H, benzyl-CH_2); 4.78 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1); 4.64 (dd, 1 H, $J_{6b,5}$ 3.0 Hz, $J_{6b,6a}$ 12.5 Hz, H-6b); 4.29 (dd, 1 H, $J_{4,3}\approx J_{4,5}$ 9.5 Hz, H-4); 4.0-3.8 (m, 4 H, H-5, H-6a, H-5^1, H-1b spacer); 3.62 (m, 1 H, H-1a, spacer); 3.17 (m, 2 H, H-3, spacer); 2.58, 2.54, 2.38 (3 x s, 9 H, 3 x toluoyl-CH_3); 1.72 (m, 2 H, H-2, spacer); 0.73 (d, 3 H, $J_{6,5}$ 6.2 Hz, 3 x H-6^1); ^{13}C-n.m.r. ($CDCl_3$): δ 166.6, 166.1 (3 x C=O, toluoyl); 165.7, 165.2 (2 x C=O, benzoyl); 163.0 (C=O, DCA); 156.3 (C=O, CBz); 100.9 (C-1); 98.5 (C-1^1); 76.4, 73.9, 73.5, 73.4, 72.1, 70.6, 68.4, 66.9 (C-2, C-3, C-4, C-5, C-2^1, C-3^1, C-4^1, C-5^1); 67.6 (C-1, spacer); 66.2 (benzyl-CH_2); 63.7 (Cl_2CH); 61.9 (C-6); 38.0 (C-3, spacer); 29.4 (C-2, spacer).

N-Benzyloxycarbonyl 2,3-di-O-benzoyl-4-O-(2,3-di-O-(2-methylbenzoyl)-α-L-rhamnopyranosyl)-6-O-2-(methylbenzoyl)-β-D-glucopyranoside (**44**). - Aq. ammonium hydroxide (25% w/v; 0.13 ml) was added to a stirred mixture of **43** (0.95 g, 0.8 mmole) in methanol (8 ml). After stirring for 2 h, the reaction mixture was neutralized with acetic acid and concentrated. Purification by chromatography on silica gel with 96:4 dichloromethane-acetone gave **44** (0.70 g, 82%); $[\alpha]_D$ +45.1° (c 1); R_F 0.71 in 97:3 dichloromethane-methanol; ^{1}H-n.m.r. data ($CDCl_3$): δ 5.81 (dd, 1 H, $J_{3,2}\approx J_{3,4}$ 9.4 Hz, H-3); 5.49 (dd, 1 H, $J_{2,1}$ 1.5 Hz, $J_{2,3}$ 3.3 Hz, H-2^1); 5.45-5.30 (m, 2 H, H-2, H-3^1); 5.16 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1^1); 4.74 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1); 4.0-3.5 (m, 7 H, H-5, 2

x H-6, H-4, H-5, 2 x H-1 spacer); 0.80 (d, 3 H, $J_{4,5}$ 6.2 Hz; 3 x H-6^1); ^{13}C-n.m.r. ($CDCl_3$): 100.8 (C-1); 98.9 (C-1^1); 26.5, 73.4, 73.3, 72.2, 71.9, 71.4, 70.9, 69.9 (C-2, C-3, C-4, C-5, C-2^1, C-3^1, C-4^1, C-5^1); 61.9 (C-6), 17.0 (C-6^1).

Anal. Calc. for $C_{61}H_{91}NO_{17}$: C 67.8, H 5.7; found: C 67.9, H 5.9%.

3-Aminopropyl 4-O-{2-O-(α-L-rhamnopyranosyl)-D-arabinityl-1-phosphate}-α-L-rhamnopyranoside **46**. - 1-*H*-Tetrazole (70 mg, 1 mmole) was added to a stirred mixture of **36** (149 mg, 0.25 mmole), amidite **29** (264 mg, 0.30 mmole) and acetonitrile (4 ml). After 30 min, *tert.*-butyl hydroperoxide (0.1 ml, 1 mmole) was added and stirring was continued for 15 min. The reaction mixture was concentrated to give crude **45** (R_F 0.45 in 95:5 dichloromethane-acetone) which was redissolved in 2:1 methanol-25% ammonium hydroxide (15 ml) and processed as described for the preparation of **23** to give homogenous **46** (102 mg, 71%); $[\alpha]_D$ -58.6° (c 1, H_2O); ^{31}P-n.m.r. data (D_2O): δ 0.604; ^{1}H- and ^{13}C-n.m.r. data: see *Tables 1* and *2*.

Anal. Calc. for $C_{20}H_{40}NO_{16}P$: C 41.3, H 6.9; found: C 41.0, H 7.1%.

3-Aminopropyl 4-O-{4-O-{2-O-(α-L-rhamnopyranosyl)-D-arabinityl-1-phosphate}-α-L-rhamnopyranosyl}-β-D-glucopyranoside **48**. - To a mixture of **44** (151 mg, 0.14 mmole), amidite **29** (176 mg, 0.2 mmole) and acetonitrile (3 ml) was added 1-*H*-tetrazole (70 mg, 1 mmole). After stirring for 30 min, *tert.*-butyl hydroperoxide (0.08 ml 0.8 mmole) was added to give **47** (R_F 0.39 in 95:5 dichloromethane-acetone). The reaction mixture was processed as described for the preparation of **23** to give fully deblocked tetramer **48** (65 mg, 62%); $[\alpha]_D$ -57.8° (c 1, H_2O); ^{31}P-n.m.r. data (D_2O): δ 0.755; ^{1}H- and ^{13}C-n.m.r. data: see *Tables 1* and *2*.

Anal. Calc. for $C_{26}H_{50}NO_{21}P$: C 42.0, H 6.8; found: C 41.6, H 7.1%.

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