Parasite glycoconjugates. Part 11.[1] Preparation of phosphodisaccharide synthetic probes, substrate analogues for the elongating α-D-mannopyranosylphosphate transferase in the *Leishmania*

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Received (in Cambridge, UK) 12th June 2000, Accepted 10th November 2000
First published as an Advance Article on the web 11th December 2000

A set of phosphodisaccharides, substrate analogues, which will be used to study acceptor–substrate specificity of the *Leishmania* biosynthetic enzymes, are synthesized using the Koenigs–Knorr and trichloroacetimidate methods for the glycosylation reactions, S_N2 nucleophilic displacement of a triflic ester for epimerization, and the glycosyl hydrogenphosphonate method for phosphorylation.

Introduction

Throughout the tropics and subtropics *Leishmania* parasites cause a variety of diseases ranging from self-limiting skin lesions to the often fatal visceral leishmaniasis. The surface lipophosphoglycan (LPG) produced by the infectious promastigote stage of all species of the *Leishmania* contains a polymeric section consisting of (1→6)-linked β-D-galactosyl-(1→4)-α-D-mannosyl phosphate repeating units. The importance of the LPG for parasite infectivity and survival[2] makes the enzymes responsible for the biosynthesis of this glycoconjugate of great interest. Phospho-oligosaccharide fragments of the LPG of *L. donovani*, *L. mexicana* and *L. major* were synthesized[3–6] in our laboratory and tested as acceptor substrates (*in vitro*) for the *Leishmania* α-D-mannopyranosylphosphate transferase (MPT) responsible for the transfer of α-D-Man*p* phosphate from GDP-Man to the growing phosphoglycan chain. It was shown[7] that the phosphodisaccharide **1**[4,8] (representing one repeating unit of the phosphoglycan) is the minimal structure exhibiting acceptor substrate activity for the MPT.

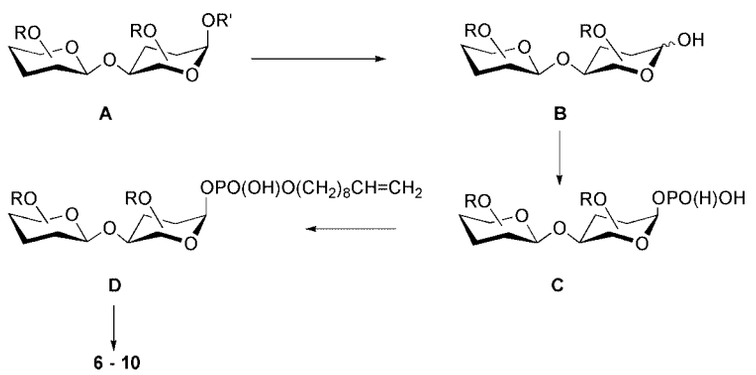
In Part 9[8] of this series, we disclosed our interest in the design and synthesis of various structural analogues of compound **1** to test the fine acceptor substrate specificity of the MPT and to gain more information about enzyme–substrate recognition. Thus, phosphodisaccharides **2–5**, which are epimers of the substrate **1** at C-1′, C-2′, C-3′ or C-4′, respectively, have been synthesized.

We now report the chemical synthesis of the disaccharide phosphates **6–10**. Compounds **6** and **7** are epimers of the substrate **1** at C-2 and C-3, respectively, of the D-mannopyranose moiety. Compounds **8** and **9** are substrate analogues deoxygenated at positions C-6 and C-6′, respectively. In this context, the preparation of the analogue **10**, which is an epimer of compound **9** at C-1′ and could be (as well as the analogue **9** itself) a potential inhibitor of the enzyme, is also described. The information obtained from testing the acceptor activity of the substrate analogues **2–10** will be used to predict which sugar hydroxy groups of compound **1** are involved in enzyme–substrate recognition events and to design potential enzyme inhibitors.

Results and discussion

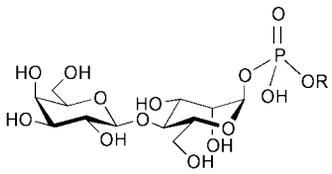
The synthetic schemes for the preparation of the phosphodisaccharides **6–10** consist of a few general steps (Scheme 1): 1) synthesis of fully protected disaccharide derivatives **A**; 2) anomeric de-*O*-protection (⟶ **B**); 3) H-phosphonylation at position O-1 (⟶ **C**); 4) coupling of the H-phosphonates **C** with dec-9-en-1–ol (using the glycosyl H-phosphonate method)[9] to furnish the protected glycosyl phosphodiesters **D**; 5) total de-*O*-protection.

The octa-*O*-acetyl-α,β-lactose **11** (α : β = 7 : 1; which is a precursor of the phosphodisaccharide **6**; Scheme 2) was prepared by conventional acetylation of α-lactose and then converted to the hemiacetal **12** (83%; α : β = 4 : 1) by anomeric de-*O*-acylation[3–6,8–10] with dimethylamine in CH_3CN–THF. H-Phosphonylation[3–6,8–10] of compound **12** with triimidazolylphosphine (prepared *in situ* from PCl_3, imidazole and Et_3N) followed by mild hydrolysis produced a mixture of α- and β-linked

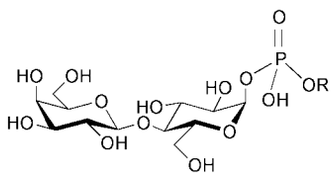


Scheme 1 R = Ac, or Bz; R′ = Ac, or Bz, or Bn.

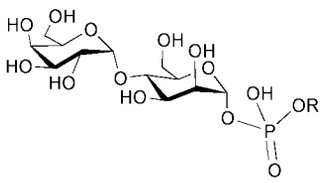
 DOI: 10.1039/b0046531



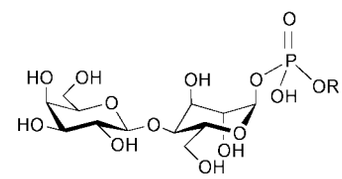
β-D-Gal*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **1**



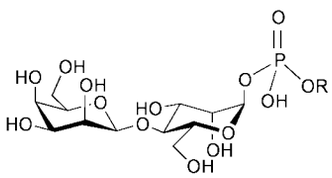
β-D-Gal*p*-(1→4)-α-D-Glc*p*-1-PO_3H-OR **6**



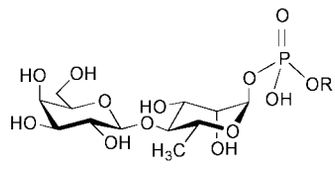
α-D-Gal*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **2**



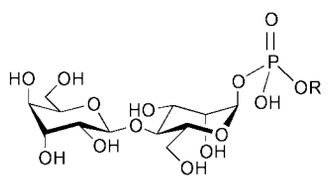
β-D-Gal*p*-(1→4)-α-D-Alt*p*-1-PO_3H-OR **7**



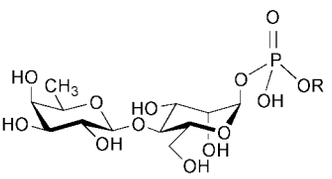
β-D-Tal*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **3**



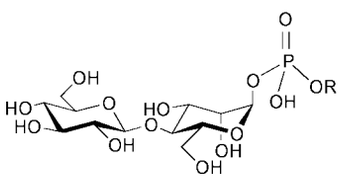
β-D-Gal*p*-(1→4)-α-D-Rha*p*-1-PO_3H-OR **8**



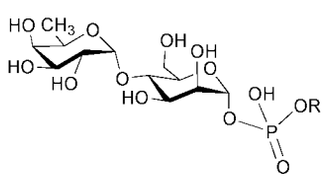
β-D-Gul*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **4**



β-D-Fuc*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **9**



β-D-Glc*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **5**



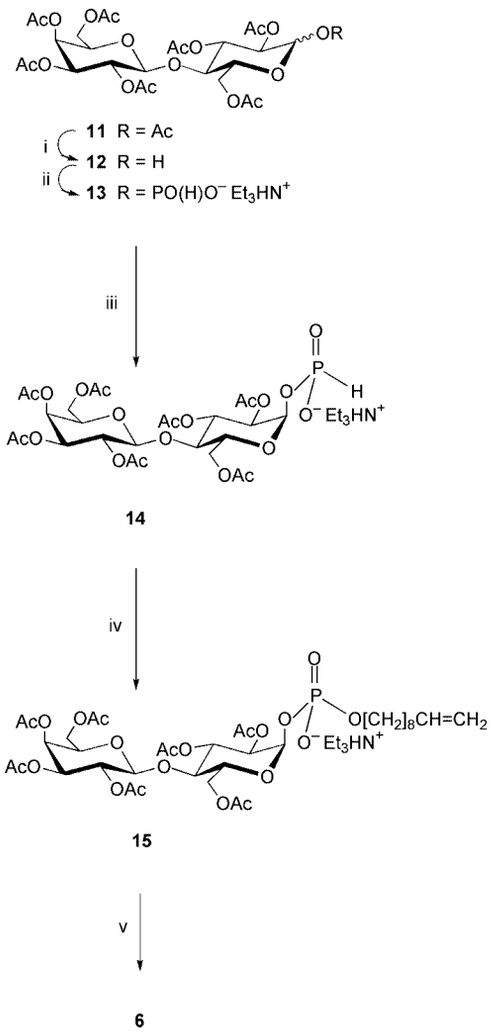
α-D-Fuc*p*-(1→4)-α-D-Man*p*-1-PO_3H-OR **10**

R = $[CH_2]_8CH{=}CH_2$

H-phosphonates **13** (α : β = 4 : 1, as evinced from ^1H and ^{31}P NMR spectra, see Experimental section), which were not separable by flash-column chromatography. This mixture was converted to the pure α-(H-phosphonate) **14** (48% based on the hemiacetal **12**) by treatment with H_3PO_3 in acetonitrile. This procedure was developed first for the preparation[10] of pure 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl H-phosphonate and utilizes the higher reactivity of the β-linked glycosyl H-phosphonate, converting it to either the α-linked isomer (as a result of S_N2-attack), or easily separable hemiacetal derivative (product of acid-catalyzed cleavage of the H-phosphonate group).

Synthesis of the protected benzyl β-D-galactopyranosyl-(1→4)-α-D-altropyranoside **22** (which is a precursor of the phosphodisaccharide **7**; Scheme 3) was performed from benzyl 2,3,6-tri-*O*-benzoyl-α-D-altropyranoside **20** and acetobromogalactose **21**. The altropyranoside **20** in turn was prepared starting from benzyl α-D-mannopyranoside, which was converted first to the 2-*O*-benzoate **17** (65%) by 4,6-*O*-isopropylidenation[11] with 2-methoxypropene (⟶ **16**) followed by selective benzoylation[12] with benzoyl cyanide in the presence of Et_3N. Successive reaction with triflic anhydride in CH_2Cl_2 in the presence of pyridine led to the triflate **18**, which reacted with tetrabutylammonium benzoate (Bu_4NOBz) in toluene (60 °C) to give the altroside **19** (73%). The D-*altro*-configuration of the derivative **19** was confirmed by the characteristic values of $J_{2,3} = J_{3,4} = 3.0$ Hz in ^1H NMR spectrum. Further, compound **19** was converted to the glycosyl acceptor **20** (67%) by acid hydrolysis followed by selective 6-*O*-benzoylation with benzoyl cyanide.

Glycosylation of the acceptor **20** with the bromide **21** in the presence of silver triflate (AgOTf), silver carbonate and molecular sieves 4 Å in dichloromethane provided the disaccharide **22** in 52% yield. Hydrogenolysis of compound **22** over $Pd(OH)_2/C$ afforded a mixture of α- and β-hemiacetals **24** in the ratio α : β = 0.8 : 1 (confirmed by ^1H NMR data, see Experimental section). Probably, the mutarotation was facilitated because of unfavourable 1,3-synaxial interaction between 1-OH and 3-benzoate in the α-hemiacetal. The anomeric mixture **24** was converted to the pure α-(H-phosphonate) **23** using the same procedure as described for the H-phosphonate **14**: *i.e.*, the reaction with triimidazolylphosphine and mild hydrolysis (⟶ **25**) followed by treatment with H_3PO_3 in CH_3CN. This produced the H-phosphonate **23** (35% based on the disaccharide **22**) along with the recovered hemiacetal **24** (49%).

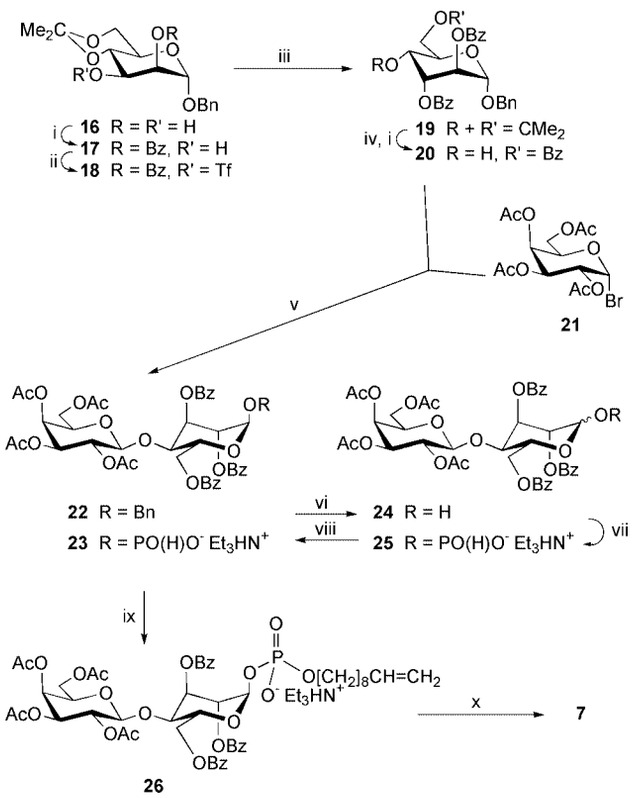


Scheme 2 *Reagents*: i, Me_2NH, MeCN–THF; ii, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); iii, H_3PO_3, MeCN; iv, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; v, NaOMe, MeOH.

The hepta-*O*-acetyl-β-D-galactopyranosyl-(1→4)-α-D-rhamnopyranose **29** (which is a precursor of the phosphodisaccharide **8**; Scheme 4) was synthesized using acetobromogalactose **21** and methyl 2,3-*O*-isopropylidene-α-D-rhamnopyranoside[13] **27** as starting materials. Their coupling in the presence of $Hg(CN)_2$–$HgBr_2$ in acetonitrile–toluene gave the disaccharide **28** (74%), which was converted to the crystalline heptaacetate **29** in 69% yield by acid hydrolysis followed by acetolysis/acetylation[14] with 1.32% (v/v) H_2SO_4 in acetic anhydride.

The hepta-*O*-benzoyl-β-D-fucopyranosyl-(1→4)-α-D-mannopyranose **37** (which is a precursor of the phosphodisaccharide **9**; Scheme 5) was prepared in 62% yield by the glycosylation of the D-mannose tetrabenzoate[3] **36** with the α-D-fucosyl trichloroacetimidate **35** in the presence of trimethylsilyl (TMS) triflate. A small proportion of the isomeric α-linked disaccharide **40** (13%; a precursor of the phosphodisaccharide **10**; Scheme 6) was also isolated from the reaction mixture. The trichloroacetimidate **35** in turn was synthesized from D-fucose by consecutive standard benzoylation (⟶ **33**), anomeric deprotection with Me_2NH (⟶ **34**; 61%) and the reaction (93% yield) with trichloroacetonitrile in the presence of 1,8–diazabicyclo[5.4.0]undec-7-ene (DBU).[15]

The β-configuration of newly formed glycosidic linkages in the disaccharides **22**, **28** and **37** followed from the characteristic values of $J_{1',2'}$ (7.5–8.0 Hz) in ^{1}H NMR spectra. For the α-D-fucoside **40** the corresponding value is $J_{1',2'}$ = 3.0 Hz.

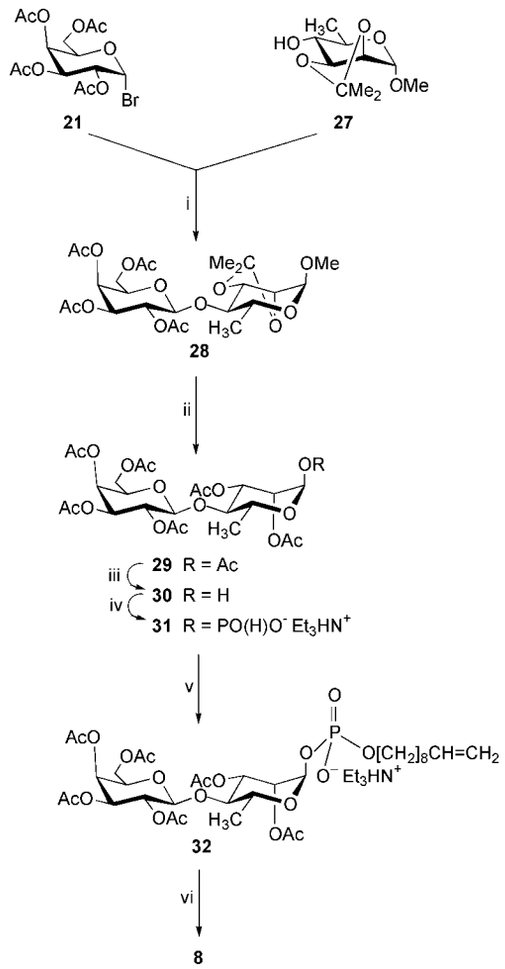


Scheme 3 *Reagents*: i, BzCN, Et_3N, MeCN; ii, Tf_2O, CH_2Cl_2–pyridine; iii, Bu_4NOBz, toluene; iv, 80% AcOH; v, AgOTf, Ag_2CO_3, MS 4 Å, CH_2Cl_2; vi, H_2, $Pd(OH)_2$/C, THF; vii, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); viii, H_3PO_3, MeCN; ix, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; x, NaOMe, MeOH.

In contrast to the anomeric de-*O*-acylation of the peracetylated lactose **11** (see above), similar reaction of the disaccharide heptaacetate **29** and heptabenzoates **37** and **40** with dimethylamine in CH_3CN–THF afforded the pure α-hemiacetal derivatives **30**, **38** and **42** (66–90%), respectively. Compounds **30**, **38** and **42** were then treated with triimidazolylphosphine followed by mild hydrolysis to produce the α-linked glycosyl H-phosphonates **31**, **39** and **43**, respectively, in 70–97% yield.

The structures of all the prepared disaccharide H-phosphonates were confirmed by NMR and mass spectrometric data (see Experimental section). For example, signals characteristic of the H-phosphonate group [δ_P 0.77; δ_H 5.67 (dd, $J_{1,2}$ 3.4, $J_{1,P}$ 8.8, 1-H), 6.89 (d, $^1J_{H,P}$ 637.8, HP)] were present in the ^{31}P and ^{1}H NMR spectra of the derivative **14**. The α-configuration of the D-glucopyranosyl residue followed from the characteristic value of $J_{1,2}$. The main signal in the (electrospray) ES(−) mass spectrum corresponded to the pseudomolecular ion (*m*/*z* 698.9, $[M - Et_3N - H]^-$) for the compound. The structures **23**, **31**, **39** and **43** were established in similar manner apart from that the α-configuration of the D-Alt*p* (in compound **23**), D-Rha*p* (in compound **31**) and D-Man*p* (in compounds **39** and **43**) residues followed from the characteristic positions of the 3- and 5-H resonances in ^{1}H NMR spectra. The chemical shifts of these signals were close to those of 3- and 5-H of the disaccharide derivatives **22** (containing a benzyl 2,3,6-tri-*O*-benzoyl-α-D-altropyranoside moiety), **29** (containing a 1,2,3-tri-*O*-acetyl-α-D-rhamnopyranose moiety) and **37** and **40** (both containing 1,2,3,6-tetra-*O*-benzoyl-α-D-mannopyranose moieties), respectively.

The glycosyl H-phosphonates **14**, **23**, **31**, **39** and **43** were converted to the protected phosphodiesters **15**, **26**, **32**, **41** and **44** (75-96% yield), respectively, by their condensation with dec-9-en-1-ol in pyridine in the presence of trimethylacetyl chloride followed by oxidation of the resulting H-phosphonic diesters with iodine in aq. pyridine. The deprotected phosphodi-



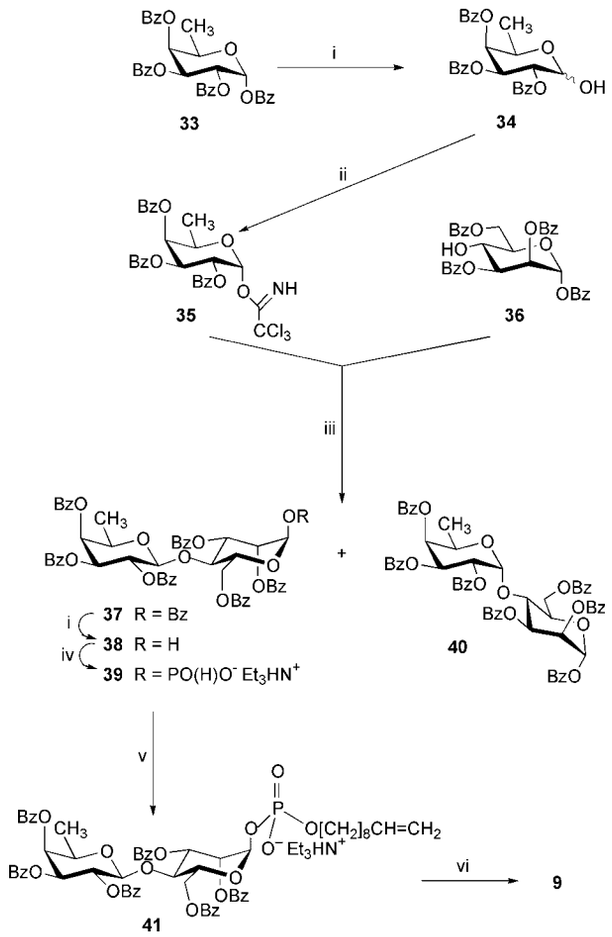
Scheme 4 *Reagents*: i, $Hg(CN)_2$, $HgBr_2$, MeCN–PhMe; ii, (a) aq. TFA, $CHCl_3$; (b) H_2SO_4, Ac_2O; iii, Me_2NH, MeCN–THF; iv, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); v, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; vi, NaOMe, MeOH.

saccharides **6–10** were prepared from the derivatives **15**, **26**, **32**, **41** and **44**, respectively, by de-*O*-acylation with 0.05 mol dm^{-3} methanolic sodium methoxide in 88–100% yield.

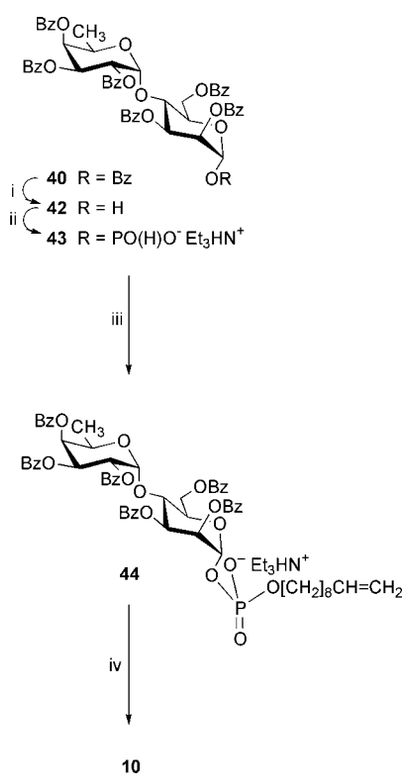
The structures of the compounds **6–10** and the protected phosphodiesters **15**, **26**, **32**, **41** and **44** were confirmed by NMR and mass spectrometric data. The ^{31}P NMR spectra exhibited single signals [δ_P between −1.35 and −1.96 for the deprotected compounds **6–10** (in D_2O) and between −1.67 and −3.12 for the protected phosphodiesters (in $CDCl_3$)], which are characteristic for glycoside-linked phosphodiesters.[3–6,8–10] The presence of a (1→1)-phosphodiester linkage at the reducing terminus of each of the disaccharides **6–10** was confirmed by the C-1 and C-2 signals of the corresponding monosaccharide residue and the dec-9-enyl unit in the ^{13}C NMR spectra (Table 1). These signals were shifted as a result of the α- and β-effects of phosphorylation and were coupled with phosphorus (or broadened).

The α-configuration of the D-glucopyranosyl phosphate fragments in compounds **6** and **15** was evident from the characteristic values of $J_{1,2}$ = 3.4–3.5 Hz in the ^1H NMR spectra (see Experimental section). The α-configuration of the D-altropyranosyl residue in the phosphodisaccharide **7** followed from the characteristic value† of $^1J_{C,H}$ = 171.3 Hz for the signal of C-1 and the characteristic position of the C-5 resonance of D-Alt*p* in the ^{13}C NMR spectrum (Table 1). The chemical shift

† The value of $^1J_{C1,H1} \approx 170$ Hz is typical for α-D-derivatives. For the β-D-glycosyl residues the value is about 160 Hz: for β-D-Gal*p* in compound **7**, $^1J_{C1',H1'}$ = 162.5 Hz (Table 1) (see also refs. 3, 4, 9 and 16).



Scheme 5 *Reagents*: i, Me_2NH, MeCN–THF; ii, CCl_3CN, DBU, CH_2Cl_2; iii, TMS triflate, MS 4 Å, CH_2Cl_2; iv, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); v, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; vi, NaOMe, MeOH.



Scheme 6 *Reagents*: i, Me_2NH, MeCN–THF; ii, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); iii, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; iv, NaOMe, MeOH.

Table 1 ^{13}C and ^{31}P NMR data [δ_C and δ_P in ppm; $J_{C,P}$ and $J_{C,H}$ in Hz; spectra recorded in D_2O] and ESMS(−) data (*m*/*z*) for the phosphodisaccharides **6**–**10**

Residue	Atom	**6**[a]	**7**[a]	**8**[b]	**9**[a]	**10**[a]
Dec-9-enyl	OCH_2CH_2	67.20d $J_{C,P}$ 4.0	67.82d $J_{C,P}$ ≈6	67.76d $J_{C,P}$ ≈6	67.45br	67.01br
	OCH_2CH_2	31.15d $J_{C,P}$ 9.0	30.96d $J_{C,P}$ 8.8	30.87d $J_{C,P}$ 5.9	30.95br	31.03d $J_{C,P}$ 8.3
	–CH=	140.32	141.64	141.54	140.87	141.52
	$=CH_2$	115.10	115.09	115.00	115.00	114.98
Aldose	C-1	95.71d $J_{C,P}$ 6.9 $J_{C,H}$ 171.3	96.76br $J_{C,H}$ 169.7	96.70br $J_{C,H}$ 171.0	96.69br $J_{C,H}$ 170.5	96.78d $J_{C,P}$ 5.8
	C-2	72.10d $J_{C,P}$ 7.7	71.54d $J_{C,P}$ 10.0	71.18d $J_{C,P}$ 6.9	70.89d $J_{C,P}$ 7.2	71.29d $J_{C,P}$ 7.5
	C-3	72.23	70.95	69.61	69.76	70.54
	C-4	78.77	74.38	82.62	77.20	76.98
	C-5	72.39	69.78	69.44	73.12	73.30
	C-6	60.65	61.53	17.82	61.10	61.30
Aldose′	C-1′	103.85 $J_{C,H}$ 162.5	105.04 $J_{C,H}$ 161.0	104.27 $J_{C,H}$ 160.5	103.87 $J_{C,H}$ 160.5	102.08 $J_{C,H}$ 171.0
	C-2′	71.83	71.96	72.09	71.45	69.64
	C-3′	73.58	73.67	73.61	73.71	71.23
	C-4′	69.51	69.96	69.72	72.12	72.57
	C-5′	76.25	76.21	76.37	72.01	68.22
	C-6′	61.93	62.20	62.18	16.34	16.42
Phosphate	P	−1.96	−1.35	−1.50	−1.41	−1.66
	m/*z*[c]	559.34	558.90	543.25	543.10	543.10

[a] Additional signals of Et_3NH^+ [δ_C 9.20–9.37 (CH_3) and δ_C 47.41–47.63 (CH_2)] were present. [a,b] Additional signals of CCH_2C [δ_C 25.95–26.26, 29.19–30.09 and 34.16–34.44] were present. [c] Corresponds to the pseudomolecular ions $[M - Et_3N - H]^-$. For compounds **6** and **7** (triethylammonium salt), $C_{28}H_{56}NO_{14}P$ requires *M*, 661.34 (expected *m*/*z*, 559.14); for compounds **8**–**10** (triethylammonium salt), $C_{28}H_{56}NO_{13}P$ requires *M*, 645.35 (expected *m*/*z*, 534.15).

of the C-5 signal (δ_C 69.78) is fairly close to that of C-5 (δ_C 70.00)‡ of methyl α-D-altropyranoside.[17]

The α-configuration of the D-mannopyranosyl phosphate fragments in compounds **9** and **10** and of the D-rhamnopyranosyl phosphate in compound **8** was confirmed by 1) the characteristic values† of $^1J_{C,H}$ for the signals of C-1 and 2) the characteristic positions of the C-3 and C-5 resonances of D-Man*p* and D-Rha*p* residues, respectively, in the ^{13}C NMR spectra (see Table 1). The chemical shifts of the signals of C-3 and -5 of D-Man*p* and C-3 of D-Rha*p* (*i.e.*, 6-deoxy-D-mannose) are close to those of C-3 and C-5 of α-D-mannopyranosyl phosphate[18] taking into account the influence of the glycosyl substituents at position 4. The chemical shift of C-5 resonance (δ_C 69.44) of D-Rha*p* in compound **8** is very close to that of C-5 (δ_C 69.40)§ of methyl α-D-rhamnopyranoside.[17]

The α-configuration of the glycosyl phosphate linkages in the protected derivatives **26**, **32**, **41** and **44** followed from the characteristic positions of 1-, 3- and 5-H resonances in their ^1H NMR spectra (see Experimental section).

The molecular masses of the phosphodiesters **6–10**, **15**, **26**, **32**, **41** and **44** were confirmed by electrospray mass spectrometry. The signals in the ES(−) mass spectra corresponded to the pseudomolecular ions for the disaccharide phosphates (see Table 1 and Experimental section). A biochemical evaluation of compounds **6–10** will be published elsewhere[19] in due course.

Experimental

General procedures

Optical rotations were measured with a Perkin-Elmer 141 polarimeter; $[a]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. NMR spectra (^1H at 200 and 500 MHz, $^{13}C\{^1H\}$ at 50.3 and 125 MHz, and $^{31}P\{^1H\}$ at 81 and 202.5 MHz) were recorded with Bruker AM-200 and AM-500 spectrometers for solutions in $CDCl_3$, unless otherwise indicated. Chemical shifts (δ in ppm) are given relative to those for Me_4Si (for ^1H and ^{13}C) and external aq. 85% H_3PO_4 (for ^{31}P); *J*-values are given in Hz. ES mass spectra were recorded with a Micromass Quattro system (Micromass Biotech, UK). TLC was performed on Kieselgel 60 F_{254} (Merck) with *A*, toluene–ethyl acetate (95:5); *B*, toluene–ethyl acetate (9:1); *C*, toluene–ethyl acetate (7:3); *D*, toluene–ethyl acetate (3:7); *E*, dichloromethane–methanol (95:5); *F*, chloroform–methanol (8:2); and *G*, chloroform–methanol–water (10:10:3) as developers and detection under UV light or by charring with sulfuric acid–water–ethanol (15:85:5). Flash-column chromatography (FCC) was performed on Kieselgel 60 (0.040–0.063 mm) (Merck). Dichloromethane, acetonitrile and toluene were freshly distilled from CaH_2. Solutions worked up were concentrated under reduced pressure at < 40 °C.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α,β-D-glucopyranose 12

To a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-1,2,3,6-tetra-*O*-acetyl-α,β-D-glucopyranose **11** (1 g, 1.47 mmol) [prepared by standard acetylation of α-lactose with Ac_2O in pyridine at 0 °C; δ_H (200 MHz) (*inter alia*) 1.94, 1.98, 2.10, 2.13 and 2.15 (15 H, 5 × s, 5 × Ac), 2.03 (9 H, s, 3 × Ac), 3.79 (t, $J_{3,4} = J_{4,5} = 9.6$, 4-H$^{\alpha}$), 3.86 (1 H, dt, $J_{5',6'}$ 6.6, 5′-H), 3.93–4.17 (4 H, m, 5-H, 6-H^a and 6′-H_2), 4.42 (1 H, dd, $J_{5,6b}$ 1.6, $J_{6a,6b}$ 12.4, 6-H^b), 4.45 (d, $J_{1',2'}$ 7.9, 1′-H$^{\alpha}$), 4.54 (d, $J_{1',2'}$ 8.2, 1′-H$^{\beta}$), 4.94 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 4.98 (dd, $J_{2,3}$ 9.9, 2-H$^{\alpha}$), 5.10 (dd, $J_{2',3'}$ 10.6, 2′-H$^{\alpha}$), 5.33 (1 H, dd, $J_{4',5'}$ 0.5, 4′-H), 5.44 (dd, 3-H$^{\alpha}$), 5.65 (d, $J_{1,2}$ 7.1, 1-H$^{\beta}$) and 6.22 (d, $J_{1,2}$ 3.6, 1-H$^{\alpha}$); α:β ≈ 7:1] in acetonitrile (6 cm^3) was added 2 mol dm^{-3} Me_2NH in THF (4 cm^3; 7.96 mmol) and the mixture was kept at rt with monitoring by TLC (solvent *D*). After 4–9 h the mixture was concentrated to dryness and acetonitrile was evaporated off from the residue. FCC [ethyl acetate–toluene, (2:8) ⟶ (8:2)] of the residue gave the *disaccharide α,β-hemiacetal* **12**

‡ For methyl β-D-altropyranoside, $\delta_{C\text{-}5}$ = 75.60.[17]
§ For methyl β-D-rhamnopyranoside, $\delta_{C\text{-}5}$ = 73.60.[17]

(0.779 g, 83%) as an amorphous solid, $[\alpha]_D^{25}$ +35.2 (*c* 1.06, $CHCl_3$) (Found: C, 48.8; H, 5.6. $C_{26}H_{36}O_{18}$ requires C, 49.1; H, 5.7%); δ_H (200 MHz) (*inter alia*) 1.96, 2.03, 2.04, 2.05, 2.07, 2.12 and 2.15 (21 H, 7 × s, 7 × Ac), 3.75 (dd, $J_{4,5}$ 9.3, 4-H$^{\alpha}$), 3.86 (1 H, dt, $J_{5',6'}$ 6.3, 5′-H), 4.00–4.22 (4 H, m, 5-H, 6-H^a and 6′-H$_2$), 4.47 (d, $J_{1',2'}$ 7.7, 1′-H$^{\beta}$), 4.48 (1 H, dd, $J_{5,6b}$ 3.4, $J_{6a,6b}$ 11.2, 6-H^b), 4.49 (d, $J_{1',2'}$ 7.9, 1′-H$^{\alpha}$), 4.76 (m, 1- and 2-H$^{\beta}$), 4.81 (dd, 2-H$^{\alpha}$), 4.94 (1 H, dd, $J_{3',4'}$ 3.2, 3′-H), 5.09 (dd, $J_{2',3'}$ 10.6, 2′-H$^{\beta}$), 5.11 (dd, $J_{2',3'}$ 10.5, 2′-H$^{\alpha}$), 5.22 (t, $J_{2,3} = J_{3,4} = 9.3$, 3-H$^{\beta}$), 5.34 (1 H, dd, $J_{4',5'}$ 0.5, 4′-H), 5.36 (d, $J_{1,2}$ 3.4, 1-H$^{\alpha}$) and 5.51 (t, $J_{2,3} = J_{3,4} = 9.7$, 3-H$^{\alpha}$); α:β = 4:1.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl hydrogenphosphonate, triethylammonium salt 14

To a stirred solution of imidazole (0.65 g, 9.56 mmol) in acetonitrile (10 cm^3) at 0 °C was added phosphorus trichloride (0.25 cm^3, 2.87 mmol) followed by Et_3N (1.4 cm^3, 10.04 mmol). The mixture was stirred for 20 min, after which a solution of compound **12** (0.304 g, 0.478 mmol) in MeCN (10 cm^3) was added dropwise over a period of 10–15 min at 0 °C. The mixture was stirred at rt for 30–40 min and quenched with 1 mol dm^{-3} triethylammonium (TEA) hydrogen carbonate (pH 7; 4 cm^3). The clear solution was stirred for 15 min, CH_2Cl_2 (100 cm^3) was added and the organic layer was washed in turn with ice-cold water (2 × 40 cm^3) and cold 0.5 mol dm^{-3} TEA hydrogen carbonate (2 × 40 cm^3), dried by filtration through cotton wool, and concentrated to give the α,β-(H-phosphonate) **13**, δ_P 0.43 (P$^{\alpha}$) and 1.20 (P$^{\beta}$); δ_H (200 MHz) (*inter alia*) 5.20 (dd, $J_{1,2}$ 7.7, $J_{1,P}$ 9.1, 1-H$^{\beta}$), 5.67 (dd, $J_{1,2}$ 3.4, $J_{1,P}$ 8.8, 1-H$^{\alpha}$), 6.88 (d, $^1J_{H,P}$ 644.0, H-P$^{\beta}$) and 6.91 (d, $^1J_{H,P}$ 637.8, H-P$^{\alpha}$); α:β = 4:1.

The residue was dissolved in CH_3CN (15 cm^3) and anhydrous H_3PO_3 (0.67 g, 8.17 mmol) was added. The mixture was stirred at rt for 19 h, then diluted with CH_2Cl_2 (100 cm^3) and washed successively with cold saturated aq. $NaHCO_3$ (2 × 40 cm^3) and cold 0.5 mol dm^{-3} aq. TEA hydrogen carbonate (2 × 40 cm^3). The organic phase (containing the hemiacetal **12**) was discarded. The aqueous washings were then combined, and extracted with CH_2Cl_2 (4 × 40 cm^3). The combined organic washings were dried by filtration through cotton wool, and concentrated to produce the α-hydrogenphosphonate **14** (0.184 g, 48%) as a chromatographically homogeneous amorphous solid, $[\alpha]_D^{26}$ +41.8 (*c* 0.97, $CHCl_3$); δ_H (200 MHz) 1.32 (9 H, t, 3 × *Me*CH_2), 1.92, 2.00, 2.02, 2.07 and 2.10 (15 H, 5 × s, 5 × Ac), 1.99 (6 H, s, 2 × Ac), 3.04 (6 H, q, 3 × MeCH_2), 3.74 (1 H, t, $J_{3,4} = J_{4,5} = 9.6$, 4-H), 3.84 (1 H, t, $J_{5',6'}$ 6.7, 5′-H), 3.97–4.20 (4 H, m, 5-H, 6-H^a and 6′-H$_2$), 4.41 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.42 (1 H, br d, $J_{6a,6b}$ 10.9, 6-H^b), 4.84 (1 H, dd, $J_{1,2}$ 3.4, 2-H), 4.90 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.06 (1 H, dd, $J_{2',3'}$ 10.3, 2′-H), 5.30 (1 H, d, 4′-H), 5.44 (1 H, t, $J_{2,3}$ 9.6, 3-H), 5.67 (1 H, dd, $J_{1,P}$ 8.8, 1-H) and 6.89 (1 H, d, $J_{H,P}$ 637.8, HP); δ_P 0.77; ESMS(−) data: *m*/*z* 698.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 699.08. $C_{32}H_{52}NO_{20}P$ requires *M*, 801.28).

Dec-9-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl phosphate, triethylammonium salt 15

A mixture of the H-phosphonate **14** (126 mg, 0.16 mmol) and dec-9-en-1-ol (0.056 cm^3, 0.31 mmol) was dried by evaporation of pyridine (3 × 2 cm^3) therefrom. The residue was dissolved in pyridine (1 cm^3), trimethylacetyl chloride (0.048 cm^3, 0.39 mmol) was added, and the mixture was stirred at rt for 10–15 min, whereafter a freshly prepared solution of iodine (80 mg, 0.314 mmol) in pyridine–water (95:5; 2 cm^3) was added. After 30 min, CH_2Cl_2 was added and the solution was washed successively with ice-cold 1 mol dm^{-3} aq. $Na_2S_2O_3$ and cold 0.5 mol dm^{-3} aq. TEA hydrogen carbonate, dried by filtration through cotton wool, and concentrated. FCC [CH_2Cl_2–MeOH–Et_3N, (99:0:1) ⟶ (89:10:1)] of the residue gave the phosphodiester **15** (144 mg, 96%) as an amorphous solid, $[\alpha]_D^{25}$ +37 (*c* 0.96, $CHCl_3$); δ_H (200 MHz) 1.20–1.32 (10 H, m, 5 × CH_2), 1.29 (9 H, t, 3 × *Me*CH_2), 1.57 (2 H, tt, *J* 6.9, OCH$_2$C*H*$_2$CH$_2$), 1.93, 2.01, 2.02, 2.09 and 2.12 (15 H, 5 × s, 5 × Ac), 2.00 (8 H, s, 2 × Ac and m, CH_2CH_2CH=), 3.03 (6 H, q, 3 × MeCH_2), 3.76 (1 H, t, $J_{3,4} = J_{4,5} = 9.6$, 4-H), 3.83 (1 H, t, $J_{5',6'}$ 6.7, 5′-H), 3.85 (2 H, m, OCH_2CH$_2$), 3.98–4.12 (3 H, m, 6-H^a and 6′-H$_2$), 4.17 (1 H, ddd, $J_{5,6a}$ 2.4, 5-H), 4.41 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.45 (1 H, dd, $J_{5,6b}$ 1.3, $J_{6a,6b}$ 12.0, 6-H^b), 4.83 (1 H, ddd, $J_{1,2}$ 3.4, $J_{2,P}$ 1.9, 2-H), 4.90 (1 H, dd, 3′-H), 4.86 (1 H, dd, $^2J_{H,H}$ 1.4, $^3J_{H,H\text{-}Z}$ 10.3, *H*CH=CH), 4.95 (1 H, dd, $^3J_{H,H\text{-}E}$ 17.0, HC*H*=CH), 5.07 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.31 (1 H, d, $J_{3',4'}$ 3.2, 4′-H), 5.45 (1 H, t, $J_{2,3}$ 9.6, 3-H), 5.63 (1 H, dd, $J_{1,P}$ 8.0, 1-H) and 5.77 (1 H, ddt, J_{H,CH_2} 6.7, CH_2CH=CH_2); δ_P −1.67; ESMS(−): *m*/*z* 853.0 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 853.22. $C_{42}H_{70}NO_{21}P$ requires *M*, 955.42).

Dec-9-enyl β-D-galactopyranosyl-(1→4)-α-D-glucopyranosyl phosphate, triethylammonium salt 6

To a solution of compound **15** (138 mg) in MeOH (15 cm^3) was added 0.5 mol dm^{-3} methanolic NaOMe (1.7 cm^3). The mixture (now 0.05 mol dm^{-3} in NaOMe) was kept at room temperature for 1 h, whereafter it was deionized with Dowex 50W-X4 (H^+) resin, filtered, and immediately neutralized with Et_3N. The solution was concentrated and methanol was evaporated off from the residue. The phosphodiester **6** (96 mg, 100%) was thereby obtained as an amorphous solid, $[\alpha]_D^{25}$ +54.5 (*c* 1, MeOH); δ_H (200 MHz; D_2O) (*inter alia*) 1.16 (9 H, t, 3 × *Me*CH_2), 1.19 (10 H, m, 5 × CH_2), 1.48 (2 H, tt, *J* 6.9, OCH$_2$C*H*$_2$CH$_2$), 1.91 (2 H, dt, *J* 6.6, CH_2CH_2CH=), 3.06 (6 H, q, 3 × MeCH_2), 4.34 (1 H, d, $J_{1',2'}$ 7.6, 1′-H), 5.33 (1 H, dd, $J_{1,2}$ 3.5, $J_{1,P}$ 7.1, 1-H) and 5.71 (1 H, ddt, J_{H,CH_2} 6.6, $J_{H,H\text{-}Z}$ 10.2, $J_{H,H\text{-}E}$ 17.0, CH_2-C*H*=CH_2); δ_C, δ_P and ESMS(−) data: see Table 1.

Benzyl 2-*O*-benzoyl-4,6-*O*-isopropylidene-α-D-mannopyranoside 17

To a stirred solution of *benzyl* 4,6-*O*-*isopropylidene*-α-D-*mannopyranoside* **16** (3.1 g, 10 mmol) [prepared from benzyl α-D-mannopyranoside and 2-methoxypropene in 85% yield, $[\alpha]_D^{25}$ +85 (*c* 1, $CHCl_3$), R_f 0.3 (solvent *E*) (Found: C, 61.8; H, 7.2. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.1%) as described for the preparation of methyl 4,6-*O*-isopropylidene-α-D-mannopyranoside [11]] and BzCN (1.57 g, 12 mmol) in acetonitrile (20 cm^3) was added Et_3N (0.025 cm^3). After 30 min, methanol was added, the reaction mixture was concentrated, and toluene was evaporated off from the residue. FCC (solvent *A*) gave the *monobenzoate* **17** (3.15 g, 76%) as an amorphous solid, $[\alpha]_D^{25}$ +48 (*c* 1, $CHCl_3$); R_f 0.2 (solvent *B*) (Found: C, 66.25; H, 6.3. $C_{23}H_{26}O_7$ requires C, 66.65; H, 6.3%); δ_H (200 MHz) 1.49 and 1.61 (6 H, 2 × s, 2 × Me), 3.73-3.93 (3 H, m, 5-H and 6-H$_2$), 4.07 (1 H, t, $J_{3,4} = J_{4,5} = 9.0$, 4-H), 4.26 (1 H, dd, $J_{2,3}$ 3.4, 3-H), 4.53 and 4.73 (2 H, AB q, *J* 11.7, C*H*$_2$Ph), 5.00 (1 H, d, $J_{1,2}$ 1.3, 1-H), 5.50 (1 H, dd, 2-H) and 7.15–8.15 (10 H, m, 2 × Ph).

Benzyl 2,3-di-*O*-benzoyl-4,6-*O*-isopropylidene-α-D-altropyranoside 19

Triflic anhydride (2.05 cm^3, 12.2 mmol) was added dropwise to a cooled (0 °C) stirred solution of compound **17** (2.53 g, 6.11 mmol) in CH_2Cl_2 (50 cm^3) containing pyridine (3.85 cm^3, 48.9 mmol), and then the reaction mixture was allowed to warm to rt. After 1 h, the mixture was diluted with CH_2Cl_2, washed successively with ice-cold 0.1 mol dm^{-3} HCl, ice-cold saturated aq. $NaHCO_3$ and water, and dried by filtration through cotton wool. The filtrate was concentrated to dryness and toluene was evaporated off from the residue to produce the triflate **18** [R_f 0.5 (solvent *B*), δ_H (200 MHz) 1.45 and 1.58 (6 H, 2 × s, 2 × Me), 3.83–3.93 (3 H, m, 5-H and 6-H$_2$), 4.28 (1 H, t, $J_{3,4} = J_{4,5} = 9.1$, 4-H), 4.57 and 4.72 (2 H, AB q, *J* 11.7, C*H*$_2$Ph), 5.02 (1 H, d,

$J_{1,2}$ 1.1, 1-H), 5.25 (1 H, dd, $J_{2,3}$ 3.6, 3-H), 5.65 (1 H, dd, 2-H) and 7.10–8.10 (10 H, m, 2 × Ph)].

A solution of tetrabutylammonium benzoate (3.63 g, 10 mmol; dried beforehand by evaporation of anhydrous toluene therefrom) in toluene (20 cm^3) was added to a solution of the triflate **18** in the same solvent (30 cm^3). The reaction mixture was stirred at 60 °C for 7 h, then diluted with CH_2Cl_2, washed successively with saturated aq. $NaHCO_3$ and water, dried by filtration through cotton wool and concentrated. FCC (solvent *A*) gave the *altroside* **19** (2.3 g, 73%), mp 142–144 °C (from diethyl ether–hexane); $[\alpha]_D^{25}$ +16 (*c* 1, $CHCl_3$); R_f 0.5 (solvent *B*) (Found: C, 69.8; H, 5.9. $C_{30}H_{30}O_8$ requires C, 69.5; H, 5.8%); δ_H (200 MHz) 1.35 and 1.61 (6 H, 2 × s, 2 × Me), 3.90 (1 H, t, $J_{5,6a} = J_{6a,6b} = 9.6$, 6-H^a), 3.98 (1 H, dd, $J_{5,6b}$ 5.7, 6-H^b), 4.26 (1 H, dd, $J_{4,5}$ 9.6, 4-H), 4.43 (1 H, dt, 5-H), 4.53 and 4.82 (2 H, AB q, *J* 11.1, C*H*$_2$Ph), 5.03 (1 H, d, $J_{1,2}$ 1.1, 1-H), 5.39 (1 H, dd, 2-H), 5.55 (1 H, t, $J_{2,3} = J_{3,4} = 3.0$, 3-H) and 7.15–8.15 (15 H, m, 3 × Ph).

Benzyl 2,3,6-tri-*O*-benzoyl-α-D-altropyranoside 20

A solution of the altroside **19** (2.49 g, 4.8 mmol) in 80% aq. acetic acid (50 cm^3) was heated at 60 °C for 1 h, whereafter the mixture was concentrated and toluene was twice evaporated off from the residue. The residue was dissolved in acetonitrile (50 cm^3) and BzCN (0.63 g, 4.82 mmol) and Et_3N (0.025 cm^3) were added to the solution. After 30 min, methanol was added, the reaction mixture was concentrated, and toluene was evaporated off from the residue. FCC (solvent *A*) gave the *tribenzoate* **20** (1.87 g, 67%), mp 140–142 °C (from diethyl ether–hexane); $[\alpha]_D^{25}$ −6.5 (*c* 1, $CHCl_3$); R_f 0.25 (solvent *B*) (Found: C, 70.4; H, 5.1. $C_{34}H_{30}O_9$ requires C, 70.1; H, 5.2%); δ_H (200 MHz; $CDCl_3$ + D_2O) 4.28 (1 H, dd, $J_{4,5}$ 9.7, 4-H), 4.48 (1 H, ddd, $J_{5,6a}$ 2.3, 5-H), 4.58 and 4.83 (2 H, AB q, *J* 10.8, C*H*$_2$Ph), 4.66 (1 H, dd, $J_{6a,6b}$ 12.0, 6-H^a), 4.78 (1 H, dd, $J_{5,6b}$ 4.0, 6-H^b), 5.10 (1 H, d, $J_{1,2}$ 1.0, 1-H), 5.42 (1 H, dd, 2-H), 5.62 (1 H, t, $J_{2,3} = J_{3,4} = 3.2$, 3-H) and 7.15–8.15 (20 H, m, 4 × Ph).

Benzyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-Dl-altropyranoside 22

A solution of acetobromogalactose **21** (1.03 g, 2.5 mmol) in CH_2Cl_2 (15 cm^3) was added dropwise to a stirred mixture of the altroside **20** (0.73 g, 1.25 mmol), Ag_2CO_3 (1.37 g, 5.0 mmol), AgOTf (0.64 g, 2.5 mmol) and freshly activated molecular sieves 4 Å (powder, 5 g) in boiling dichloromethane (30 cm^3). The reaction mixture was stirred under reflux for 2.5 h and then at rt for 20 h. The solids were filtered off and the filtrate was concentrated. FCC [diethyl ether–hexane, (1 : 1) ⟶ (2 : 1)] gave the *disaccharide* **22** (0.59 g, 52%) as an amorphous solid, $[\alpha]_D^{25}$ +12 (*c* 1, $CHCl_3$); R_f 0.45 (solvent *C*) (Found: C, 63.1; H, 5.4. $C_{48}H_{48}O_{18}$ requires C, 63.15; H, 5.3%); δ_H (200 MHz) 1.91 (6 H, s, 2 × Ac), 1.93 and 2.01 (6 H, 2 × s, 2 × Ac), 3.82–3.99 (3 H, m, 5′-H and 6′-H$_2$), 4.32 (1 H, dd, $J_{4,5}$ 9.5, 4-H), 4.44 (1 H, dd, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 12.5, 6-H^a), 4.52 and 4.81 (2 H, AB q, *J* 11.6, C*H*$_2$Ph), 4.58–4.70 (3 H, m, 1′-, 5-H and 6-H^b), 4.91 (1 H, dd, $J_{2',3'}$ 10.5, 3′-H), 5.02 (1 H, br s, 1-H), 5.15 (1 H, dd, $J_{1',2'}$ 7.5, 2′-H), 5.25 (1 H, d, $J_{3',4'}$ 3.5, 4′-H), 5.46 (1 H, d, 2-H), 5.66 (1 H, t, $J_{2,3} = J_{3,4} = 3.3$, 3-H) and 7.15–8.15 (20 H, m, 4 × Ph).

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-altropyranosyl hydrogenphosphonate, triethylammonium salt 23

A solution of the disaccharide **22** (0.455 g, 0.499 mmol) in THF (5 cm^3) containing 20% $Pd(OH)_2/C$ (200 mg) was shaken under a slight overpressure of H_2 at rt for 2 h. The catalyst was filtered off through a Celite pad and the filtrate was concentrated to give the α,β-hemiacetal **24** (0.39 g, 95%) as an amorphous solid [R_f 0.3 (solvent *C*); δ_H (500 MHz) 1.89–2.03 (12 H, m, 4 × Ac), 3.78–3.92 (3 H, m, 5′-H and 6′-H$_2$), 4.30 (dd, $J_{4,5}$ 8.5, 4-H$^\beta$), 4.39 (dd, $J_{4,5}$ 8.5, 4-H$^\alpha$), 4.42 (dt, $J_{5,6a} = J_{5,6b} = 3.0$, 5-H$^\beta$), 4.52 (dd, $J_{5,6a}$ 3.0, $J_{6a,6b}$ 11.7, 6-H^a), 4.61 (d, $J_{1',2'}$ 7.0, 1′-H$^\alpha$), 4.67 (d, $J_{1',2'}$ 7.0, 1′-H$^\beta$), 4.70–4.78 (m, 5-H$^\alpha$ and 6-H^b), 4.92 (dd, $J_{3',4'}$ 3.0, 3′-H$^\alpha$), 4.95 (dd, $J_{3',4'}$ 3.0, 3′-H$^\beta$), 5.13 (dd, $J_{2',3'}$ 9.0, 2′-H$^\alpha$), 5.17 (dd, $J_{2',3'}$ 9.0, 2′-H$^\beta$), 5.22 (d, 4′-H$^\alpha$), 5.26 (d, 4′-H$^\beta$), 5.30 (br s, 1-H$^\beta$), 5.39 (br s, 1-H$^\alpha$), 5.46 (d, 2-H$^\beta$), 5.51 (d, 2-H$^\alpha$), 5.69 (t, $J_{2,3} = J_{3,4} = 2.8$, 3-H$^\beta$), 5.79 (t, $J_{2,3} = J_{3,4} = 2.8$, 3-H$^\alpha$) and 7.20–8.20 (15 H, m, 3 × Ph); α : β = 0.8 : 1].

The reaction of the compound **24** (0.39 g, 0.474 mmol) with PCl_3 (0.165 cm^3, 1.89 mmol), imidazole (0.45 g, 6.62 mmol) and Et_3N (0.99 cm^3, 7.09 mmol) in CH_3CN (10 cm^3), followed by hydrolysis with 1 mol dm^{-3} aq. TEA hydrogen carbonate (2.5 cm^3), was accomplished as described for the preparation of the disaccharide H-phosphonate **13**. After work-up, the solution was concentrated and acetonitrile was evaporated off from the residue. The residue was dissolved in the same solvent (5 cm^3) and anhydrous H_3PO_3 (0.39 g, 4.73 mmol) was added to the solution. The reaction mixture was kept at rt for 20 h, then diluted with CH_2Cl_2 (50 cm^3) and washed successively with saturated aq. $NaHCO_3$ and 0.5 mol dm^{-3} aq. TEA hydrogen carbonate, dried by filtration through cotton wool, and concentrated. FCC [CH_2Cl_2–MeOH, (99 : 1) ⟶ (80 : 20)] gave the H-phosphonate **23** (0.175 g, 35% from the disaccharide **22**) as an amorphous solid, $[\alpha]_D^{25}$ +1 (*c* 1, $CHCl_3$); R_f 0.35 (solvent *F*); δ_H (200 MHz) 1.20 (9 H, t, 3 × *Me*CH$_2$), 1.91, 1.92, 1.93 and 2.02 (12 H, 4 × s, 4 × Ac), 2.91 (6 H, q, 3 × MeC*H*$_2$), 3.80–3.88 (2 H, m, 5′-H and 6′-H^a), 3.93 (1 H, dd, $J_{5',6b'}$ 7.8, $J_{6a',6b'}$ 13.5, 6′-H^b), 4.35 (1 H, dd, $J_{4,5}$ 9.6, 4-H), 4.46 (1 H, dd, $J_{6a,6b}$ 11.6, 6-H^a), 4.64 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.71 (1 H, dd, $J_{5,6b}$ 1.0, 6-H^b), 4.88 (1 H, ddd, $J_{5,6a}$ 3.7, 5-H), 4.91 (1 H, dd, $J_{3',4'}$ 3.2, 3′-H), 5.13 (1 H, dd, $J_{2',3'}$ 10.6, 2′-H), 5.23 (1 H, d, 4′-H), 5.44 (1 H, d, 2-H), 5.67 (1 H, t, $J_{2,3} = J_{3,4} = 2.8$, 3-H), 5.72 (1 H, d, $J_{1,P}$ 8.5, 1-H), 7.02 (1 H, d, $J_{H,P}$ 640.0, HP) and 7.40–8.20 (15 H, m, 3 × Ph); δ_P 0.58; ESMS(−): *m*/*z* 884.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 885.008. $C_{47}H_{58}NO_{20}P$ requires *M*, 987.208). Also isolated was the disaccharide hemiacetal **24** (0.2 g, 49% recovery).

Dec-9-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-altropyranosyl phosphate, triethylammonium salt 26

This compound was prepared by condensation of the glycobiosyl H-phosphonate **23** (98 mg, 0.10 mmol) and dec-9-en-1-ol (0.053 cm^3, 0.30 mmol) in pyridine (1 cm^3) in the presence of trimethylacetyl chloride (0.037 cm^3, 0.30 mmol), followed by oxidation with iodine (51 mg, 0.20 mmol) in pyridine–water (95 : 5; 2 cm^3) as described for the synthesis of the phosphodiester **15**. FCC [CH_2Cl_2–MeOH, (99 : 1) ⟶ (80 : 20)] gave the phosphodiester **26** (85 mg, 75%) as an amorphous solid, $[\alpha]_D^{25}$ +2 (*c* 1, $CHCl_3$); R_f 0.5 (solvent *F*); δ_H (200 MHz) 1.25 (19 H, m, 3 × *Me*CH$_2$ and 5 × CH$_2$), 1.48 (2 H, tt, *J* 6.9, OCH$_2$C*H*$_2$CH$_2$), 1.95 (6 H, s, 2 × Ac), 1.97 and 2.00 (6 H, 2 × s, 2 × Ac), 2.03 (2 H, m, CH$_2$C*H*$_2$CH=), 2.95 (6 H, q, 3 × MeC*H*$_2$), 3.74–3.96 (5 H, m, 5′-H, 6′-H$_2$ and OC*H*$_2$CH$_2$), 4.38 (1 H, dd, $J_{4,5}$ 9.6, 4-H), 4.46 (1 H, dd, $J_{5,6a}$ 3.0, $J_{6a,6b}$ 11.8, 6-H^a), 4.64 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.72 (1 H, dd, $J_{5,6b}$ 1.0, 6-H^b), 4.87–4.95 (3 H, m, 3′-, 5-H and *H*CH=CH), 4.98 (1 H, dd, $^2J_{H,H}$ 1.6, $^3J_{H,H\text{-}E}$ 16.8, HC*H*=CH), 5.12 (1 H, dd, $J_{2',3'}$ 10.1, 2′-H), 5.23 (1 H, d, $J_{3',4'}$ 3.1, 4′-H), 5.50 (1 H, d, $J_{2,3}$ 3.0, 2-H), 5.64 (1 H, d, $J_{1,P}$ 7.7, 1-H), 5.68 (1 H, dd, $J_{3,4}$ 3.5, 3-H), 5.80 (1 H, ddt, J_{H,CH_2} 6.6, $^3J_{H,H\text{-}Z}$ 10.9, CH$_2$C*H*=CH$_2$) and 7.40–8.25 (15 H, m, 3 × Ph); δ_P −2.79; ESMS(−): *m*/*z* 1039.0 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 1039.14. $C_{57}H_{76}NO_{21}P$ requires *M*, 1141.344).

Dec-9-enyl β-D-galactopyranosyl-(1→4)-α-D-altropyranosyl phosphate, triethylammonium salt 7

To a solution of compound **26** (50 mg) in MeOH (1.8 cm^3) was added 0.5 mol dm^{-3} methanolic NaOMe (0.2 cm^3). The mixture (now 0.05 mol dm^{-3} in NaOMe) was kept at 0 °C for 16 h and then at room temperature for 8 h, whereafter it was deionized

with Dowex 50W-X4(H^+) resin, filtered and immediately neutralized with Et_3N. After concentration, water (3 × 5 cm^3) was evaporated off from the residue to remove methyl benzoate. The phosphodiester **7** (28 mg, 96%) was thereby obtained as an amorphous solid, $[\alpha]_D^{25}$ +36 (*c* 1, MeOH); R_f 0.65 (solvent *G*); δ_H (200 MHz; D_2O) (*inter alia*) 1.15 (9 H, t, 3 × *Me*CH_2), 1.23 (10 H, m, 5 × CH_2), 1.52 (2 H, tt, *J* 6.9, $OCH_2CH_2CH_2$), 1.94 (2 H, dt, *J* 6.7, CH_2CH_2CH=), 3.10 (6 H, q, 3 × $MeCH_2$), 4.41 (1 H, d, $J_{1',2'}$ 7.0, 1′-H), 5.21 (1 H, br d, $J_{1,P}$ 6.6, 1-H) and 5.83 (1 H, ddt, J_{H,CH_2} 6.7, $J_{H,H\text{-}Z}$ 10.1, $J_{H,H\text{-}E}$ 18.0, CH_2-CH=CH_2); δ_C, δ_P and ESMS(−) data: see Table 1.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-D-rhamnopyranoside 28

A solution of acetobromogalactose **21** (1.49 g, 3.58 mmol) in acetonitrile–toluene (10 : 3; 13 cm^3) was added to a stirred mixture of methyl 2,3-*O*-isopropylidene-α-D-rhamnopyranoside[13] **27** (0.318 g, 1.45 mmol), $Hg(CN)_2$ (0.9 g, 3.58 mmol) and $HgBr_2$ (0.64 g, 1.79 mmol) in the same mixed solvent (5 cm^3). After being stirred at rt for 16 h, the reaction mixture was diluted with CH_2Cl_2 (50 cm^3), washed successively with 1 mol dm^{-3} aq. KBr, saturated aq. $NaHCO_3$, and water, dried by filtration through cotton wool, and concentrated. FCC [toluene–ethyl acetate, (8 : 2)] of the residue gave the *disaccharide derivative* **28** (0.59 g, 74%), mp 126–129 °C (from ethanol); $[\alpha]_D^{22}$ +25.7 (*c* 1, $CHCl_3$) (Found: C, 52.5; H, 6.6. $C_{24}H_{36}O_{14}$ requires C, 52.6; H, 6.6%); δ_H (200 MHz) 1.23 (3 H, d, $J_{5,6}$ 6.3, 6-H_3), 1.32 and 1.50 (6 H, 2 × s, CMe_2), 2.00, 2.05, 2.07 and 2.15 (12 H, 4 × s, 4 × Ac), 3.34 (3 H, s, OMe), 3.36 (1 H, dd, $J_{3,4}$ 7.2, 4-H), 3.63 (1 H, dq, $J_{4,5}$ 9.8, 5-H), 3.88 (1 H, t, $J_{5',6'}$ 6.6, 5′-H), 4.06 (1 H, d, $J_{2,3}$ 5.7, 2-H), 4.14 (2 H, d, 6′-H_2), 4.24 (1 H, dd, 3-H), 4.65 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.81 (1 H, s, 1-H), 5.00 (1 H, dd, $J_{3',4'}$ 3.2, 3′-H), 5.21 (1 H, dd, $J_{2',3'}$ 10.3, 2′-H) and 5.36 (1 H, d, 4′-H).

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-1,2,3-tri-*O*-acetyl-α-D-rhamnopyranose 29

To a stirred solution of the disaccharide **28** (0.728 g) in chloroform (36 cm^3) was added 90% aq. trifluoroacetic acid (4 cm^3). Stirring was continued for 2 h, whereafter the solution was concentrated and toluene was twice evaporated off from the residue. The residue was then dissolved in Ac_2O (5 cm^3) and a sulfuric acid–acetic anhydride mixture [1 : 50 (v/v); 10.2 cm^3] was added. The solution was stirred at rt for 2 h, whereafter it was diluted with CH_2Cl_2 (100 cm^3), washed successively with water, saturated aq. $NaHCO_3$, and water, dried by filtration through cotton wool, and concentrated. Toluene was twice evaporated off from the residue. FCC (solvent *B* ⟶ solvent *C*) of the residue gave the *heptaacetate* **29** (0.57 g, 69%), mp 145–148 °C (from ethanol); $[\alpha]_D^{21}$ +36.8 (*c* 0.99, $CHCl_3$) (Found: C, 50.6; H, 5.9. $C_{26}H_{36}O_{17}$ requires C, 50.3; H, 5.9%); δ_H (200 MHz) 1.30 (3 H, d, $J_{5,6}$ 6.1, 6-H_3), 1.96, 2.02, 2.03, 2.04 and 2.14 (15 H, 5 × s, 5 × Ac), 2.13 (6 H, s, 2 × Ac), 3.63 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.4, 4-H), 3.82 (1 H, dq, 5-H), 3.87 (1 H, ddd, $J_{5',6a'}$ 7.1, 5′-H), 4.02 (1 H, dd, $J_{6a',6b'}$ 11.0, 6′-H^a), 4.16 (1 H, dd, $J_{5',6b'}$ 6.4, 6′-H^b), 4.58 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.97 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.14 (1 H, dd, $J_{2',3'}$ 10.3, 2′-H), 5.19 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 5.28 (1 H, dd, 3-H), 5.33 (1 H, dd, $J_{4',5'}$ 0.5, 4′-H) and 5.94 (1 H, d, $J_{1,2}$ 1.9, 1-H).

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-D-rhamnopyranose 30

This compound was prepared from compound **29** (0.307 g) as described for the hemiacetal derivative **12**. Two consecutive FCC separations [toluene–ethyl acetate, (55 : 45) ⟶ (8 : 2) and solvent *B* ⟶ solvent *D*] gave the *disaccharide* α-*hemiacetal* **30** (0.19 g, 66%) as an amorphous solid, $[\alpha]_D^{21}$ +11 (*c* 0.97, $CHCl_3$) (Found: C, 49.4; H, 6.0. $C_{24}H_{34}O_{16}$ requires C, 49.8; H, 5.9%); δ_H (200 MHz) 1.28 (3 H, d, $J_{5,6}$ 6.2, 6-H_3), 1.96, 2.01, 2.03, 2.04, 2.12 and 2.14 (18 H, 6 × s, 6 × Ac), 3.59 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.4, 4-H), 3.87 (1 H, t, $J_{5',6a'} = J_{5',6b'}$ = 6.5, 5′-H), 4.00 (1 H, dq, 5-H), 4.01 (1 H, dd, 6′-H^a), 4.16 (1 H, dd, $J_{6a',6b'}$ 11.0, 6′-H^b), 4.57 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.97 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.08 (1 H, d, $J_{1,2}$ 1.9, 1-H), 5.13 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.21 (1 H, dd, $J_{2,3}$ 3.5, 2-H), 5.32 (1 H, d, 4′-H) and 5.33 (1 H, dd, 3-H).

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-D-rhamnopyranosyl hydrogenphosphonate, triethylammonium salt 31

This compound was prepared by the reaction of the hemiacetal **30** (0.184 g, 0.32 mmol) with PCl_3 (0.166 cm^3, 1.91 mmol), imidazole (0.433 g, 6.36 mmol) and Et_3N (0.93 cm^3, 6.7 mmol) in acetonitrile (15 cm^3) followed by hydrolysis as described for the H-phosphonate **13**. For work-up, the reaction mixture was diluted with CH_2Cl_2 (100 cm^3) and washed successively with cold saturated aq. $NaHCO_3$ (2 × 40 cm^3) and cold 0.5 mol dm^{-3} aq. TEA hydrogen carbonate (2 × 40 cm^3). The organic phase was discarded. The aqueous washings were combined, and extracted with CH_2Cl_2 (4 × 20 cm^3). The combined organic washings were dried by filtration through cotton wool, and concentrated to produce the H-phosphonate **31** (0.165 g, 70%) as a chromatographically homogeneous amorphous solid, $[\alpha]_D^{25}$ +23.1 (*c* 1.06, $CHCl_3$); δ_H (200 MHz) 1.27 (3 H, d, $J_{5,6}$ 6.3, 6-H_3), 1.30 (9 H, t, 3 × *Me*CH_2), 1.94, 1.95, 2.00, 2.02, 2.08 and 2.11 (18 H, 6 × s, 6 × Ac), 3.03 (6 H, q, 3 × $MeCH_2$), 3.56 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.4, 4-H), 3.83 (1 H, t, $J_{5',6a'} = J_{5',6b'}$ = 6.6, 5′-H), 3.98 (1 H, dq, 5-H), 3.99 (1 H, dd, 6′-H^a), 4.12 (1 H, dd, $J_{6a',6b'}$ 11.0, 6′-H^b), 4.54 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.94 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.10 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.21 (1 H, dd, $J_{1,2}$ 1.8, 2-H), 5.30 (1 H, d, 4′-H), 5.31 (1 H, dd, $J_{2,3}$ 3.6, 3-H), 5.44 (1 H, dd, $J_{1,P}$ 8.8, 1-H) and 5.44 (1 H, d, $J_{H,P}$ 642.0, HP); δ_P −0.10; ESMS(−): *m*/*z* 641.0 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 641.07. $C_{30}H_{50}NO_{18}P$ requires *M*, 743.27).

Dec-9-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-D-rhamnopyranosyl phosphate, triethylammonium salt 32

This compound was prepared by condensation of the H-phosphonate **31** (0.14 g, 0.19 mmol) and dec-9-en-1-ol (0.067 cm^3, 0.38 mmol) in pyridine (1 cm^3) in the presence of trimethylacetyl chloride (0.058 cm^3, 0.47 mmol) followed by oxidation with iodine (0.096 g, 0.376 mmol) in pyridine–water (95 : 5; 2 cm^3) as described for the synthesis of the phosphodiester **15**. FCC [CH_2Cl_2–MeOH–Et_3N, (99 : 0 : 1) ⟶ (89 : 10 : 1)] gave the phosphodiester **32** (0.148 g, 88%) as an amorphous solid, $[\alpha]_D^{27}$ +12.4 (*c* 1.09, $CHCl_3$); δ_H (200 MHz) 1.18 (3 H, d, $J_{5,6}$ 6.0, 6-H_3), 1.24 (9 H, t, 3 × *Me*CH_2), 1.25 (10 H, m, 5 × CH_2), 1.53 (2 H, tt, *J* 6.9, $OCH_2CH_2CH_2$), 1.89, 1.90, 1.97, 1.98, 2.03 and 2.07 (18 H, 6 × s, 6 × Ac), 1.96 (2 H, dt, *J* 6.8, CH_2CH_2CH=), 3.00 (6 H, q, 3 × $MeCH_2$), 3.51 (1 H, dd, $J_{4,5}$ 9.7, 4-H), 3.71–3.86 (4 H, m, 5′-H, 6′-H^a and OCH_2CH_2), 3.97 (1 H, dq, 5-H), 4.08 (1 H, dd, $J_{5',6b'}$ 6.6, $J_{6a',6b'}$ 11.2, 6′-H^b), 4.52 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.84 (1 H, dd, $^2J_{H,H}$ 1.6, $^3J_{H,H\text{-}Z}$ 9.3, *H*CH=CH), 4.90 (1 H, dd, $^3J_{H,H\text{-}E}$ 17.0, HC*H*=CH), 4.92 (1 H, dd, 3′-H), 5.08 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.19 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 5.25 (1 H, d, $J_{3',4'}$ 4.0, 4′-H), 5.26 (1 H, dd, $J_{3,4}$ 9.4, 3-H), 5.34 (1 H, dd, $J_{1,2}$ 1.5, $J_{1,P}$ 8.8, 1-H) and 5.73 (1 H, ddt, J_{H,CH_2} 6.8, CH_2CH=CH_2); δ_P −3.12; ESMS(−): *m*/*z* 795.3 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 795.21. $C_{40}H_{68}NO_{19}P$ requires *M*, 897.41).

Dec-9-enyl β-D-galactopyranosyl-(1→4)-α-D-rhamnopyranosyl phosphate, ammonium salt 8

De-*O*-acetylation of compound **32** (74 mg) with 0.05 mol dm^{-3} NaOMe in methanol (3 h at rt) followed by work-up, as described in the preparation of the phosphodiester **6**, produced a crude product, which then was applied to a column (18 × 1.5 cm) of Fractogel TSK DEAE-650 (S) (HCO_3^--form) (Merck)

eluted with a linear gradient of NH_4HCO_3 (0 ⟶ 0.1 mol dm^{-3}) in 3:2 water–propan-2-ol at 1 cm^3 min^{-1} to afford the phosphodiester **8** (41 mg, 88%) as an amorphous solid, $[\alpha]_D^{26}$ +22.4 (*c* 0.99, MeOH); δ_H (200 MHz; D_2O) (*inter alia*) 1.22–1.45 (13 H, m, 6-H_3 and 5 × CH_2), 1.63 (2 H, tt, *J* 6.9, OCH_2-CH_2CH_2), 2.05 (2 H, dt, *J* 6.9, CH_2CH_2CH=), 4.48 (1 H, d, $J_{1',2'}$ 7.0, 1′-H), 5.32 (1 H, br d, $J_{1,P}$ 6.3, 1-H) and 5.91 (1 H, m, CH_2CH=CH_2); δ_C, δ_P and ESMS(−) data: see Table 1.

2,3,4-Tri-*O*-benzoyl-α,β-D-fucopyranose 34

To a solution of 1,2,3,4-tetra-*O*-benzoyl-α-D-fucopyranose **33** (0.5 g, 0.861 mmol) [prepared by standard benzoylation of α-D-fucose with benzoyl chloride in pyridine–chloroform; δ_H (200 MHz) 1.34 (3 H, d, $J_{5,6}$ 6.4, 6-H_3), 4.67 (1 H, q, 5-H), 5.92 (1 H, d, 4-H), 6.01 (1 H, dd, $J_{2,3}$ 10.8, 2-H), 6.14 (1 H, dd, $J_{3,4}$ 3.0, 3-H), 6.91 (1 H, d, $J_{1,2}$ 3.3, 1-H) and 7.17–8.28 (20 H, m, 4 × Ph)] in acetonitrile (3 cm^3) was added 2 mol dm^{-3} Me_2NH in THF (4.3 cm^3; 8.61 mmol) and the mixture was kept at rt with monitoring by TLC (solvents *B* and *C*). After 16–24 h, the mixture was concentrated to dryness and acetonitrile was evaporated off from the residue. FCC [toluene–ethyl acetate, (99:1) ⟶ (85:15)] gave the unchanged starting material **33** (0.079 g, 16% recovery) and the *hemiacetal* **34** (0.25 g, 61%; amorphous solid), $[\alpha]_D^{22}$ +247.4 (*c* 1, $CHCl_3$) (Found: C, 68.3; H, 5.1. $C_{27}H_{24}O_8$ requires C, 68.1; H, 5.1%); δ_H (200 MHz; $CDCl_3$ + D_2O) 1.26 (d, $J_{5,6}$ 6.4, 6-H^{α}), 1.35 (d, $J_{5,6}$ 6.3, 6-H^{β}), 4.12 (dq, $J_{4,5}$ 0.8, 5-H^{β}), 4.67 (q, H-5$^{\alpha}$), 5.06 (d, $J_{1,2}$ 6.8, 1-H^{β}), 5.66–5.85 (m, 1-H^{α}, 2-H, 3-H^{β} and 4-H), 6.09 (dd, $J_{2,3}$ 10.6, $J_{3,4}$ 3.2, 3-H^{α}) and 7.01–8.40 (15 H, m, 3 × Ph); α : β = 5 : 1.

2,3,4-Tri-*O*-benzoyl-α-D-fucopyranosyl trichloroacetimidate 35

To a stirred solution of the hemiacetal **34** (0.228 g, 0.48 mmol) and CCl_3CN (2 cm^3, 20 mmol) in dichloromethane (4 cm^3) cooled to 0 °C was added DBU (0.072 cm^3, 0.48 mmol) under argon. The mixture was stirred for 2 h at 0 °C and then concentrated. FCC (solvent *A*) of the residue gave the α-fucopyranosyl trichloroacetimidate **35** (0.277 g, 93%) as an amorphous solid, $[\alpha]_D^{22}$ +209.4 (*c* 1, $CHCl_3$); δ_H (200 MHz) 1.34 (3 H, d, $J_{5,6}$ 6.5, 6-H_3), 4.66 (1 H, dq, 5-H), 5.89 (1 H, dd, $J_{4,5}$ 0.5, 4-H), 5.92 (1 H, dd, $J_{2,3}$ 10.5, 2-H), 6.06 (1 H, dd, $J_{3,4}$ 3.2, 3-H), 6.86 (1 H, d, $J_{1,2}$ 3.3, 1-H), 7.10–8.23 (15 H, m, 3 × Ph) and 8.60 (1 H, s, HN); δ_C 16.19 (C-6), 67.95 (C-5), 68.05 (C-2), 68.66 (C-3), 71.29 (C-4), 90.91 (CCl_3), 94.11 (C-1), 128.30–133.48 (Ph), 160.78 (C=NH) and 165.62–165.83 (C=O); ESMS(+): *m*/*z* 459.2 (100%, $[M - CCl_3CONH]^+$) (expected *m*/*z*, 459.47. $C_{29}H_{24}Cl_3NO_8$ requires *M*, 620.86).

2,3,4-Tri-*O*-benzoyl-β-D-fucopyranosyl-(1→4)-1,2,3,6-tetra-*O*-benzoyl-α-D-mannopyranose 37 and 2,3,4-tri-*O*-benzoyl-α-D-fucopyranosyl-(1→4)-1,2,3,6-tetra-*O*-benzoyl-α-D-mannopyranose 40

A mixture of the trichloroacetimidate **35** (0.554 g, 0.89 mmol), 1,2,3,6-tetra-*O*-benzoyl-α-D-mannopyranose[3] **36** (0.638 g, 1.07 mmol) and freshly activated molecular sieves 4 Å (powder, 1 g) in dry dichloromethane (5 cm^3) was stirred under argon for 30 min. TMS triflate (0.046 cm^3, 0.22 mmol) was then added and the mixture was cooled to −70 °C. Stirring was continued for a further 1.5 h, while the mixture slowly warmed to −10 °C. The reaction was quenched with a few drops of *N*,*N*-diisopropylethylamine, the solids were filtered off, and the solvent was removed under reduced pressure. FCC (toluene ⟶ solvent *B*) of the residue gave a mixture of the disaccharides **37** and **40**, which were then separated by further FCC [dichloromethane–ethyl acetate, (100:0) ⟶ (98:2)]. That provided, first, the *β-linked disaccharide* **37** (0.582 g, 62%) as an amorphous solid, $[\alpha]_D^{23}$ +118 (*c* 1.03, $CHCl_3$) (Found: C, 69.6; H, 4.7. $C_{61}H_{50}O_{17}$ requires C, 69.4; H, 4.8%); δ_H (200 MHz) 0.82 (3 H, d, $J_{5',6'}$ 6.3, 6′-H_3), 3.56 (1 H, q, 5′-H), 4.27 (1 H, ddd, $J_{5,6a}$ 2.6, 5-H), 4.45 (1 H, dd, $J_{6a,6b}$ 12.7, 6-H^a), 4.68 (1 H, dd, $J_{5,6b}$ 1.8, 6-H^b), 4.69 (1 H, $J_{3,4} = J_{4,5} = 9.7$, 4-H), 4.96 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.39 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.48 (1 H, d, 4′-H), 5.70 (1 H, dd, $J_{2',3'}$ 10.3, 2′-H), 5.85 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 5.99 (1 H, dd, 3-H), 6.48 (1 H, d, $J_{1,2}$ 1.7, 1-H) and 7.08–8.22 (35 H, m, 7 × Ph). Continued elution gave the *α-linked disaccharide* **40** (0.126 g, 13%) as an amorphous solid, $[\alpha]_D^{23}$ +124 (*c* 0.93, $CHCl_3$) (Found: C, 69.9; H, 5.1%); δ_H (200 MHz) 1.13 (3 H, d, $J_{5',6'}$ 6.6, 6′-H_3), 4.42–4.56 (2 H, m, 5- and 5′-H), 4.66 (1 H, dd, $J_{5,6a}$ 2.7, $J_{6a,6b}$ 12.3, 6-H^a), 4.91 (1 H, $J_{3,4} = J_{4,5} = 9.3$, 4-H), 4.93 (1 H, dd, $J_{5,6b}$ 0.5, 6-H^b), 5.67–5.94 (6 H, 1′-, 2-, 2′-, 3-, 3′- and 4′-H), 6.55 (1 H, d, $J_{1,2}$ 2.0, 1-H) and 7.05–8.28 (35 H, m, 7 × Ph).

2,3,4-Tri-*O*-benzoyl-β-D-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-mannopyranose 38

This compound was prepared from compound **37** (0.307 g) as described for the hemiacetal derivative **34**. FCC [toluene ⟶ solvent *C*] gave the *disaccharide α-hemiacetal* **38** (0.25 g, 90%) as an amorphous solid, $[\alpha]_D^{25}$ +123.3 (*c* 1.06, $CHCl_3$) (Found: C, 68.1; H, 5.0. $C_{54}H_{46}O_{16}$ requires C, 68.2; H, 4.9%); δ_H (200 MHz) 0.83 (3 H, d, $J_{5',6'}$ 6.2, 6′-H_3), 3.53 (1 H, q, 5′-H), 4.07 (1 H, d, $J_{1,OH}$ 4.1, 1-OH), 4.33–4.46 (2 H, m, 5-H and 6-H^a), 4.58 (1 H, $J_{3,4} = J_{4,5} = 9.6$, 4-H), 4.77 (1 H, dd, $J_{5,6b}$ 0.6, $J_{6a,6b}$ 12.5, 6-H^b), 4.95 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.35 (1 H, d, $J_{1,2}$ 1.8, 1-H), 5.42 (1 H, dd, $J_{2',3'}$ 10.2, 3′-H), 5.46 (1 H, d, $J_{3',4'}$ 3.2, 4′-H), 5.62–5.75 (2 H, m, 2- and 2′-H), 5.95 (1 H, dd, $J_{2,3}$ 3.0, 3-H) and 6.98–8.22 (30 H, m, 6 × Ph).

2,3,4-Tri-*O*-benzoyl-β-D-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 39

This compound was prepared from the hemiacetal **38** (0.208 g, 0.219 mmol) as described for the H-phosphonate derivative **13**. This produced the disaccharide hydrogenphosphonate **39** (0.232 g, 95%) as a chromatographically homogeneous amorphous solid, $[\alpha]_D^{25}$ +102.4 (*c* 0.96, $CHCl_3$); δ_H (200 MHz) 0.81 (3 H, d, $J_{5',6'}$ 6.3, 6′-H_3), 1.27 (9 H, t, 3 × *Me*CH_2), 3.01 (6 H, q, 3 × MeCH_2), 3.49 (1 H, q, 5′-H), 4.37 (1 H, ddd, $J_{5,6a}$ 2.7, 5-H), 4.43 (1 H, dd, $J_{6a,6b}$ 12.9, 6-H^a), 4.53 (1 H, $J_{3,4} = J_{4,5} = 9.5$, 4-H), 4.65 (1 H, dd, $J_{5,6b}$ 1.4, 6-H^b), 4.87 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.34 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.42 (1 H, d, 4′-H), 5.64 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.67 (1 H, dd, $J_{1,2}$ 2.0, 2-H), 5.70 (1 H, dd, $J_{1,P}$ 7.7, 1-H), 5.88 (1 H, dd, $J_{2,3}$ 3.3, 3-H), 7.01 (1 H, d, $J_{H,P}$ 636.9, HP) and 7.05–8.15 (30 H, m, 6 × Ph); δ_P 0.11; ESMS(−): *m*/*z* 1012.8 (100%, $[M - Et_3N - H]^-$) (expected *m*/*z*, 1013.17. $C_{60}H_{62}NO_{18}P$ requires *M*, 1115.37).

Dec-9-enyl 2,3,4-tri-*O*-benzoyl-β-D-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-mannopyranosyl phosphate, triethylammonium salt 41

This compound was prepared by condensation of the H-phosphonate **39** (0.12 g, 0.107 mmol) and dec-9-en-1-ol (0.038 cm^3, 0.215 mmol) in pyridine (1 cm^3) in the presence of trimethylacetyl chloride (0.033 cm^3, 0.268 mmol) followed by oxidation with iodine (0.055 g, 0.215 mmol) in pyridine–water (95:5; 2 cm^3) as described for the synthesis of the phosphodiester **15**. FCC [CH_2Cl_2–MeOH–Et_3N, (99:0:1) ⟶ (89:10:1)] gave the phosphodiester **41** (0.108 g, 80%) as an amorphous solid, $[\alpha]_D^{25}$ +82.2 (*c* 1, $CHCl_3$); δ_H (200 MHz) 0.84 (3 H, d, $J_{5',6'}$ 6.3, 6′-H_3), 1.24 (10 H, m, 5 × CH_2), 1.30 (9 H, t, 3 × *Me*CH_2), 1.58 (2 H, tt, *J* 6.9, OCH_2CH_2), 1.97 (2 H, dt, *J* 6.9, CH_2CH_2CH=), 3.05 (6 H, q, 3 × MeCH_2), 3.47 (1 H, q, 5′-H), 3.90 (2 H, m, OCH_2CH_2), 4.37–4.49 (2 H, m, 5-H and 6-H^a), 4.55 (1 H, $J_{3,4} = J_{4,5} = 9.4$, 4-H), 4.64 (1 H, dd, $J_{5,6b}$ 1.1, $J_{6a,6b}$ 11.7, 6-H^b), 4.87 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.89 (1 H, dd, $^2J_{H,H}$ 1.3, $^3J_{H,H\text{-}Z}$ 10.4, *H*CH=CH), 4.95 (1 H, dd, $^3J_{H,H\text{-}E}$ 17.2, HC*H*=CH), 5.33 (1 H, dd, $J_{2',3'}$ 10.4, 3′-H), 5.43 (1 H, d, $J_{3',4'}$ 3.3, 4′-H), 5.65 (1 H, dd, $J_{1,P}$ 8.3, 1-H), 5.66 (1 H, dd, 2′-H), 5.74 (1 H, dd, $J_{1,2}$ 2.5, 2-H), 5.78 (1 H, ddt,

J_{H,CH_2} 6.9, $CH_2CH{=}CH_2$), 5.91 (1 H, dd, $J_{2,3}$ 3.4, 3-H) and 7.05–8.10 (30 H, m, 6 × Ph); δ_P −2.83; ESMS(−): *m*/*z* 1166.9 (100%, $[M - Et_3N - H]^-$) (expected *m*/*z*, 1167.31. $C_{70}H_{80}NO_{19}P$ requires *M*, 1269.51).

Dec-9-enyl β-D-fucopyranosyl-(1→4)-α-D-mannopyranosyl phosphate, triethylammonium salt 9

De-*O*-benzoylation of compound **41** (101 mg) with 0.05 mol dm^{-3} NaOMe in methanol (16 h at rt) followed by work-up, as described in the preparation of the phosphodiester **7**, gave the phosphodiester **9** (51 mg, 99%) as an amorphous solid, $[\alpha]_D^{28}$ +22.5 (*c* 0.99, MeOH); δ_H (D_2O) (*inter alia*) 1.22–1.39 (22 H, m, 6′-H_3, 3 × *Me*CH_2 and 5 × CH_2), 1.58 (2 H, tt, *J* 6.9, $OCH_2CH_2CH_2CH_2$), 2.01 (2 H, dt, *J* 6.9, $CH_2CH_2CH{=}$), 3.15 (6 H, q, 3 × MeCH_2), 4.38 (1 H, d, $J_{1',2'}$ 7.6, 1′-H), 5.37 (1 H, br d, $J_{1,P}$ 7.1, 1-H) and 5.83 (1 H, m, $CH_2CH{=}CH_2$); δ_C, δ_P and ESMS(−) data: see Table 1.

2,3,4-Tri-*O*-benzoyl-α-D-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-mannopyranose 42

This compound was prepared from compound **40** (160 mg) as described for the hemiacetal derivative **34**. FCC [toluene ⟶ solvent *C*] gave the *disaccharide α-hemiacetal* **40** (99 mg, 69%) as an amorphous solid, $[\alpha]_D^{26}$ +54.7 (*c* 1.02, $CHCl_3$) (Found: C, 68.0; H, 5.0. $C_{54}H_{46}O_{16}$ requires C, 68.2; H, 4.9%); δ_H (200 MHz) 1.13 (3 H, d, $J_{5',6'}$ 6.4, 6′-H_3), 3.83 (1 H, d, $J_{1,OH}$ 4.3, 1-OH), 4.52 (1 H, q, 5′-H), 4.60 (1 H, ddd, $J_{5,6b}$ 0.7, 5-H), 4.65 (1 H, dd, $J_{5,6a}$ 2.6, 6-H^a), 4.81 (1 H, $J_{3,4} = J_{4,5} = 9.6$, 4-H), 5.01 (1 H, dd, $J_{6a,6b}$ 11.2, 6-H^b), 5.40 (1 H, d, $J_{1,2}$ 1.8, 1-H), 5.68 (1 H, dd, 2-H), 5.75 (1 H, dd, $J_{2,3}$ 3.4, 3-H), 5.76–5.85 (4 H, m, 1′-, 2′-, 3′- and 4′-H) and 7.10–8.25 (30 H, m, 6 × Ph).

2,3,4-Tri-*O*-benzoyl-α-D-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 43

This compound was prepared from the hemiacetal **42** (88 mg, 0.092 mmol) as described for the H-phosphonate derivative **13**. This produced the disaccharide hydrogenphosphonate **43** (100 mg, 97%) as a chromatographically homogeneous amorphous solid, $[\alpha]_D^{21}$ +61 (*c* 1.06, $CHCl_3$); δ_H (200 MHz) 1.08 (3 H, d, $J_{5',6'}$ 6.3, 6′-H_3), 1.29 (9 H, t, 3 × *Me*CH_2), 3.01 (6 H, q, 3 × MeCH_2), 4.47 (1 H, q, 5′-H), 4.57–4.68 (2 H, m, 5-H and 6-H^a), 4.79 (1 H, $J_{3,4} = J_{4,5} = 9.4$, 4-H), 4.93 (1 H, dd, $J_{5,6b}$ 2.8, $J_{6a,6b}$ 12.9, 6-H^b), 5.67 (1 H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.0, 2-H), 5.70–5.82 (6 H, m, 1-, 1′-, 2′-, 3-, 3′- and 4′-H), 7.10 (1 H, d, $J_{H,P}$ 640.4, HP) and 6.92–8.23 (30 H, m, 6 × Ph); δ_P 0.57; ESMS(−): m/z 1013.0 (100%, $[M - Et_3N - H]^-$) (expected *m*/*z*, 1013.17. $C_{60}H_{62}NO_{18}P$ requires *M*, 1115.37).

Dec-9-enyl 2,3,4-tri-*O*-benzoyl-α-D-fucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-mannopyranosyl phosphate, triethylammonium salt 44

This compound was prepared by condensation of the H-phosphonate **43** (100 mg, 0.09 mmol) and dec-9-en-1-ol (0.035 cm^3, 0.197 mmol) in pyridine (1 cm^3) in the presence of trimethylacetyl chloride (0.03 cm^3, 0.246 mmol) followed by oxidation with iodine (50 mg, 0.197 mmol) in pyridine–water (95 : 5; 2 cm^3) as described for the synthesis of the phosphodiester **15**. FCC [CH_2Cl_2–MeOH–Et_3N, (99 : 0 : 1) ⟶ (87 : 12 : 1)] gave the phosphodiester **44** (95 mg, 78%) as an amorphous solid, $[\alpha]_D^{26}$ +46 (*c* 0.99, $CHCl_3$); δ_H (200 MHz) 1.04 (3 H, d, $J_{5',6'}$ 6.3, 6′-H_3), 1.23 (10 H, m, 5 × CH_2), 1.31 (9 H, t, 3 × *Me*CH_2), 1.64 (2 H, tt, *J* 6.9, $OCH_2CH_2CH_2$), 1.99 (2 H, dt, *J* 6.9, $CH_2CH_2CH{=}$), 3.10 (6 H, q, 3 × MeCH_2), 4.00 (2 H, m, $OCH_2CH_2CH_2$), 4.44 (1 H, q, 5′-H), 4.57–4.70 (2 H, m, 5-H and 6-H^a), 4.79 (1 H, $J_{3,4} = J_{4,5} = 9.8$, 4-H), 4.89 (2 H, br d, 6-H^b and *H*CH=CH), 4.96 (1 H, dd, $^2J_{H,H}$ 1.9, $^3J_{H,H\text{-}E}$ 17.0, HC*H*=CH), 5.65–5.83 (8 H, m, 1-, 1′-, 2-, 2′-, 3-, 3′-, 4′-H and $CH_2CH{=}CH_2$) and 7.00–8.25 (30 H, m, 6 × Ph); δ_P −2.60; ESMS(−): *m*/*z* 1166.9 (100%, $[M - Et_3N - H]^-$) (expected *m*/*z*, 1167.31. $C_{70}H_{80}NO_{19}P$ requires *M*, 1269.51).

Dec-9-enyl α-D-fucopyranosyl-(1→4)-α-D-mannopyranosyl phosphate, triethylammonium salt 10

De-*O*-benzoylation of compound **44** (95 mg) with 0.05 mol dm^{-3} NaOMe in methanol (16 h at rt) followed by work-up, as described in the preparation of the phosphodiester **7**, gave the phosphodiester **10** (48 mg, 100%) as an amorphous solid, $[\alpha]_D^{28}$ +69.8 (*c* 0.98, MeOH); δ_H (200 MHz; D_2O) (*inter alia*) 1.23 (3 H, d, $J_{5',6'}$ 6.6, 6′-H_3), 1.26-1.40 (19 H, m, 3 × *Me*CH_2 and 5 × CH_2), 1.61 (2 H, tt, *J* 6.5, $OCH_2CH_2CH_2CH_2$), 2.04 (2 H, dt, *J* 7.0, $CH_2CH_2CH_2CH{=}$), 3.20 (6 H, q, 3 × MeCH_2), 5.20 (1 H, br s, 1′-H), 5.42 (1 H, br d, $J_{1,P}$ 7.6, 1-H) and 5.83 (1 H, m, $CH_2CH{=}CH_2$); δ_C, δ_P and ESMS(−) data: see Table 1.

Acknowledgements

This work and I. A. I. were supported by a Wellcome Trust International Grant. The research of A. V. N. was supported by an International Research Scholar's award from the Howard Hughes Medical Institute. One of us (A. J. R.) thanks the BBSRC for the award of a studentship.

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