Parasite glycoconjugates. Part 12.[1] Synthesis of deoxy, fluorodeoxy and aminodeoxy disaccharide phosphates, substrate analogues for the elongating α-D-mannopyranosylphosphate transferase in the *Leishmania*

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A set of phosphodisaccharides, structural analogues of the β-D-galactosyl-(1⟶4)-α-D-mannosyl phosphate **1**, are synthesized using the Koenigs–Knorr method for the glycosylation reactions and the glycosyl hydrogenphosphonate method for phosphorylation. The compounds were tested as acceptor substrates/putative inhibitors for the *Leishmania* α-D-mannosylphosphate transferase.

Introduction

The *Leishmania* are sandfly-transmitted protozoan parasites that cause a variety of debilitating and often fatal diseases throughout the tropics and sub-tropics. One of the major molecules forming the glycocalyx of the *Leishmania* is the lipophosphoglycan (LPG), which is produced by the infectious promastigote stage of all species of the parasite. The LPG has been shown to be essential for parasite infectivity and survival[2] thus making the enzymes responsible for its biosynthesis of great interest. It contains a polymeric phosphoglycan region consisting of (1⟶6)-linked β-D-galactosyl-(1⟶4)-α-D-mannosyl phosphate repeating units, which has been shown[3] to be assembled *in vitro* by the sequential action of the *Leishmania* α-D-mannopyranosylphosphate transferase (MPT) and β-D-galactopyranosyl transferase. Phospho-oligosaccharide fragments of the LPG of *L. donovani*, *L. mexicana* and *L. major* were synthesized[4–7] in our laboratory and tested as acceptor substrates (*in vitro*) for the *Leishmania* MPT responsible for the transfer of α-D-Man*p* phosphate from GDP-Man to the growing phosphoglycan chain. It was reported[8] that the phosphodisaccharide **1**[5,9] (representing one repeating unit of the phosphoglycan) is the minimal structure exhibiting acceptor substrate activity for the MPT. Biosynthetic transfer of α-D-Man*p* phosphate from GDP-Man to compound **1** produced the expected trisaccharide diphosphate **1a** (Scheme 1, top).

In Parts 9[9] and 11[1] 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**–**7** (which are epimers of the substrate **1** at C-1′, C-2′, C-3′, C-4′, C-2 or C-3, respectively) and **8** and **9** (which are analogues of compound **1** deoxygenated at C-6 or C-6′, respectively) have been synthesized and tested as acceptor substrates for the enzyme. Preliminary biosynthetic experiments[10] showed that the epimerization at C-2, C-2′, C-3′ or C-4′ does not strongly affect the substrate activity of the corresponding phosphodisaccharides: compounds **6**, **3**, **4** and **5** were all substrates for the MPT but with reduced kinetics relative to compound **1**. In contrast, the epimers at C-1′ (compound **2**), at C-3 (compound **7**) and the 6-deoxy (**8**) and 6′-deoxy (**9**) analogues exhibited neither acceptor nor inhibitory activity, suggesting the β-configuration of D-galactose residue and the hydroxy groups at C-3, C-6 and C-6′, respectively, are the most essential for the enzyme–substrate binding.

We now report the chemical synthesis of the disaccharide phosphates **10**–**16** (Scheme 1), which are particular deoxy, fluorodeoxy and aminodeoxy analogues of compound **1** and designed in order to further refine the true acceptor substrate specificity of the enzyme. The information obtained from testing the acceptor (or inhibitory) activity of these compounds will be used to confirm which sugar hydroxy groups of compound **1** are involved in enzyme–substrate recognition events. Thus, the ability/inability of the 3-deoxy analogue **10** to act as a substrate for the MPT will confirm whether the 3-OH group is vital for the enzyme binding. The ability/inability of the fluorinated disaccharide phosphates **11** and **12** to act as substrates may discriminate between essential hydrogen bond acceptor and donor functionality of hydroxy groups at C-3 and C-6, respectively. The 6′-fluoro analogue **13** and 6′-amino analogue **16** may act as inhibitors for the MPT. The 2-amino and 2-acetamido derivatives **14** and **15** are expected to be acceptors for the MPT, since the epimer at C-2 (compound **6**) did work as an acceptor.[10] Both compounds should be quite lipophilic (the amino phosphate **14** will form a zwitterion) and may penetrate cell membranes. This property will be tested using living *Leishmania* promastigotes. The results will help to design potential inhibitors of the MPT.

Results and discussion

The synthetic schemes for the preparation of the phosphodisaccharides **10**–**16** include a few general steps: (1) synthesis of appropriately protected and functionalized disaccharide derivatives; (2) anomeric de-O-protection followed by H-phosphonylation at position O-1; (3) the preparation of O-protected disaccharide phosphates using the glycosyl H-phosphonate method;[11] (4) total de-O-protection (⟶ **10**–**13**). For the synthesis of the amino and acetamido derivatives **14**–**16**, additional steps: reduction of the azido group (⟶ **14** and **16**) and N-acetylation (⟶ **15**), were required.

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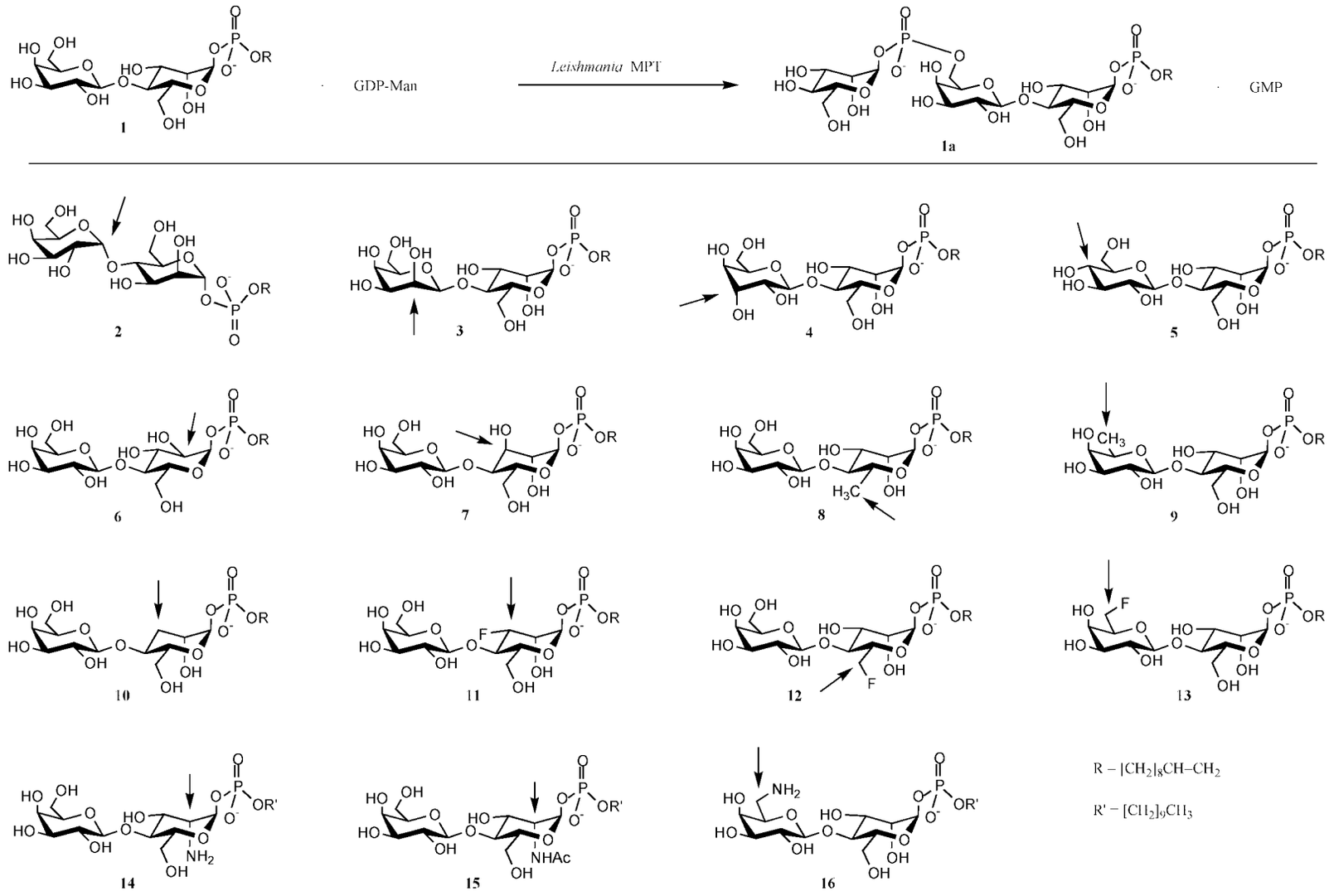
1
GDP-Man
Leishmania MPT
1a
GMP
2
3
4
5
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11
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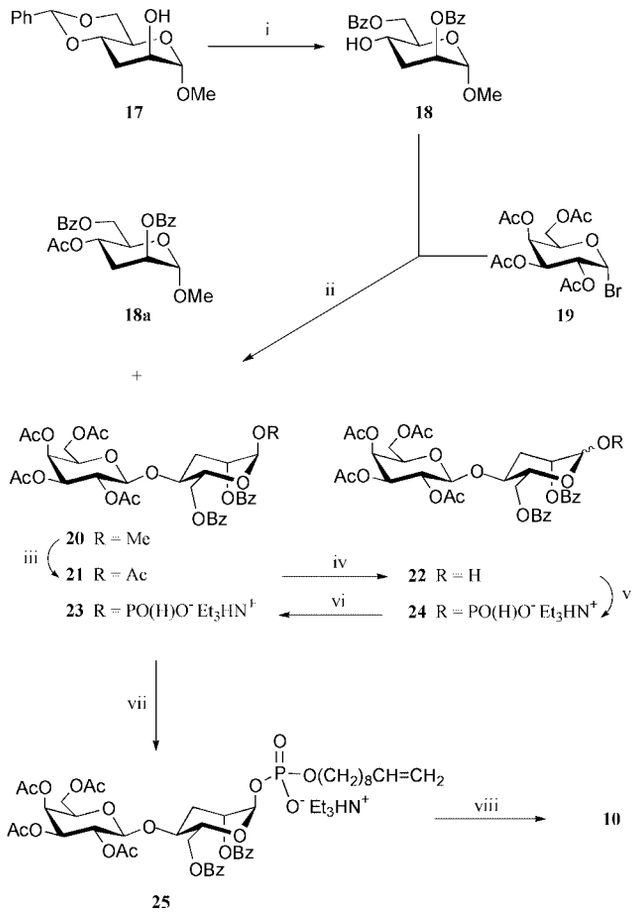
15
16
R – [CH2]8CH–CH2
R' – [CH2]9CH3

Scheme 1



Scheme 2 *Reagents*: i, (a) BzCl, pyridine; (b) I_2, MeOH; (c) BzCN, Et_3N, MeCN; ii, $AgSO_3CF_3$, 2,4,6-collidine, CH_2Cl_2; iii, H_2SO_4, Ac_2O; iv, Me_2NH, MeCN–THF; v, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); vi, H_3PO_3, MeCN; vii, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; viii, NaOMe, MeOH.

The 3-deoxydisaccharide derivative **21** (which is a precursor of the phosphodisaccharide **10**; Scheme 2) was prepared by the glycosylation of the 2,6-di-O-benzoyl-3-deoxy derivative **18** with acetobromogalactose **19** (⟶ **20**) followed by protective group modification at O-1. The glycosyl acceptor **18** was synthesized starting from the known 3-deoxy-α-D-*arabino*-hexopyranoside **17**[12] in an overall yield of 69% by successive benzoylation, benzylidene acetal cleavage[13] with iodine in MeOH, and selective 6-O-benzoylation[14] with benzoyl cyanide. Silver triflate (AgOTf)-assisted base-deficient glycosylation[15] reaction gave the β-linked disaccharide **20** (60%). The process was accompanied by the formation of the 4-O-acetate **18a** (37%) that decreased the efficiency of the glycosylation. Compound **18a** was shown to be easily converted back to the glycosyl acceptor **18** by de-O-acetylation[16] with HCl–MeOH in 89% yield. The disaccharide derivative **20** was converted to the crystalline penta-acetate **21** in 79% yield by acetolysis with H_2SO_4 in acetic anhydride.

Anomeric de-O-acylation[1,4–7,9,11] of compound **21** with dimethylamine in CH_3CN–THF afforded the hemiacetal **22** (90%; α : β = 9 : 1). H-Phosphonylation[1,4–7,9,11] of this derivative with triimidazolylphosphine (prepared *in situ* from PCl_3, imidazole and Et_3N) followed by mild hydrolysis gave an inseparable mixture of α- and β-linked H-phosphonates **24** [α : β = 9 : 1; δ_P 0.50 (P^α) and 1.26 (P^β)], which was treated with H_3PO_3 in CH_3CN to provide the pure α-(H-phosphonate) **23** (70% based on the hemiacetal **22**). This procedure was developed[1,17] for the 'correction' of the anomeric configuration of glycosyl H-phosphonates and utilizes the higher reactivity of the β-linked glycosyl H-phosphonate, converting them 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).

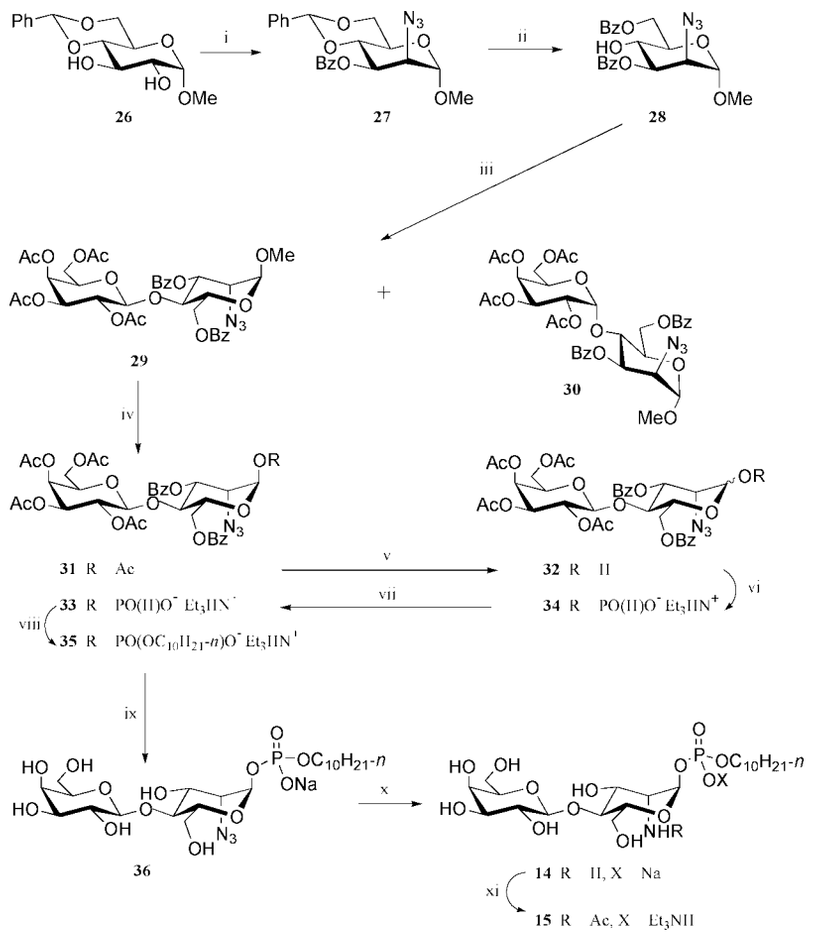
Synthesis of the protected 2-azido-2-deoxydisaccharide derivative **31** (which is a precursor of the phosphodisaccharides **14** and **15**; Scheme 3) was performed from the 2-azido-2-deoxy-α-D-mannoside **28** and acetobromogalactose **19** (⟶ **29**) followed by reprotection at O-1. The glycosyl acceptor **28** in turn was prepared starting from 4,6-O-benzylidene-α-D-glucopyranoside **26**,[18] which was converted first to the 2-azido-3-O-benzoate **27** (89%) by selective 2-O-triflylation with triflic anhydride followed by benzoylation and nucleophilic replacement of the triflate with NaN_3 in the presence of *n*-Bu_4NCl.[19] Successive benzylidene acetal cleavage[13] with iodine and selective 6-O-benzoylation with *N*-benzoylimidazole gave the mannoside **28** in 87% yield. The D-*manno*-configuration of the derivative **28** followed from the characteristic values of $J_{1,2}$ = 1.6 and $J_{2,3}$ = 3.8 Hz in the ^{1}H NMR spectrum. Glycosylation of the acceptor **28** with the bromide **19** in the presence of AgOTf (as described for the disaccharide **20**) produced the β-linked disaccharide **29** (75%) and some of the α-linked isomer **30** (13%). Compound **29** was further converted to the 1-O-acetate **31** (quantitatively) by treatment with H_2SO_4–Ac_2O.

Anomeric de-O-acetylation of the disaccharide **31** with Me_2NH (as above) gave a complex mixture of products, where the desired hemiacetal **32** was a minor component. Alternatively, the reaction with *tert*-butylamine in CH_3CN–MeOH[17] proceeded smoothly and provided the hemiacetal **32** as a mixture of anomers (α : β = 5 : 1). Compound **32** was converted to the pure α-(H-phosphonate) **33** by using the same procedure as described for the H-phosphonate **23**: *i.e.*, the reaction with triimidazolylphosphine and mild hydrolysis [⟶ **34**; α : β = 5 : 1; δ_P 0.28 (P^α) and 0.74 (P^β)] followed by treatment with H_3PO_3 in CH_3CN. This produced the H-phosphonate **33** (58% based on the 1-O-acetate **31**) along with the recovered hemiacetal **32** (35%).

The 3-deoxy-3-fluorodisaccharide derivative **42** (which is a precursor of the phosphodisaccharide **11**; Scheme 4) was synthesized starting from known 1,6-anhydro-3-deoxy-3-fluoro-β-D-mannopyranose[20] **37**, which was converted to the 2-O-benzoyl derivative **38** (46%) by selective benzoylation with *N*-benzoylimidazole. The isomeric 4-benzoate **39** (14%) and the dibenzoate **40** (9.5%) were also isolated from the reaction mixture. Glycosylation of the acceptor **38** with acetobromogalactose **19** in the presence of AgOTf (as above) gave the disaccharide **41** (48%), which was transformed to the crystalline hexa-acetate **42** in 83% yield by routine acetolysis procedure (as described for the preparation of the disaccharides **21** and **31**).

To prepare the 6-deoxy-6-fluorodisaccharide derivative **51** (which is a precursor of the phosphodisaccharide **12**; Scheme 5), the 6-deoxy-6-fluoro-2,3-O-isopropylidene-α-D-mannopyranoside **49** was synthesized starting from benzyl α-D-mannopyranoside **46**. Consecutive 6-O-tritylation, benzoylation and acid hydrolysis provided the 6-hydroxy mannoside **47** (60%), which was fluorinated[21] with diethylaminosulfur trifluoride (DAST) to form the 6-fluoride **48** (44%). The presence and the position of the fluorine atom in the molecule were confirmed by the characteristic signal at δ_F −231 (dt) in ^{19}F NMR spectrum, and by the characteristic values of $J_{5,F}$ = 22.9 and $J_{6,F}$ = 47.5 Hz in ^{1}H NMR spectrum (see Experimental section). The fluoride **48** was further converted to compound **49** (85%) by conventional debenzoylation followed by acetonation with 2,2-dimethoxypropane. Glycosylation of the acceptor **49** with acetobromogalactose **19** in the presence of AgOTf (as above) afforded the crystalline disaccharide **50** (80%), which was transformed to the derivative **51** in 90% yield by isopropylidene acetal cleavage[22] with pyridinium perchlorate followed by benzoylation.

The 6′-deoxy-6′-fluorodisaccharide derivative **61** (which is a precursor of the phosphodisaccharide **13**), was synthesized



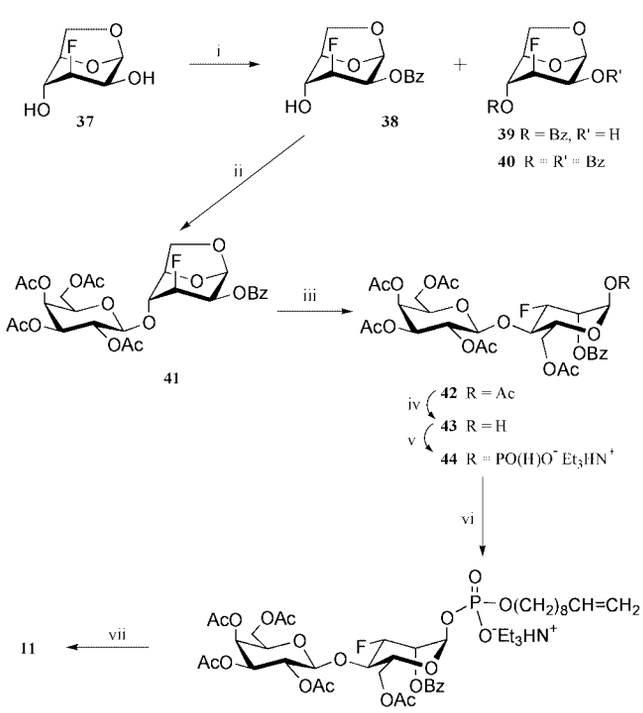
Scheme 3 *Reagents*: i, (a) Tf_2O, pyridine, CH_2Cl_2; (b) BzCl, pyridine; (c) NaN_3, *n*-Bu_4NCl, PhMe; ii, (a) I_2, MeOH; (b) *N*-benzoylimidazole, CH_2Cl_2; iii, **19**, $AgSO_3CF_3$, 2,4,6-collidine, CH_2Cl_2; iv, H_2SO_4, Ac_2O; v, *t*-$BuNH_2$, MeCN–MeOH; vi, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); vii, H_3PO_3; MeCN, viii, (a) decan-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; ix, (a) NaOMe, MeOH; (b) Dowex 50 (Na^+); x, H_2, $Pd(OH)_2$/C, MeOH; xi, (a) Ac_2O, MeOH; (b) Dowex 50 (H^+); (c) Et_3N.

from the 6-deoxy-6-fluoro-α-D-galactosyl bromide **57** and the 6-O-benzoyl-2,3-O-isopropylidene-α-D-mannopyranoside **59**, as shown in Scheme 6. The glycosyl donor **57** resulted from acetylation of the known 6-deoxy-6-fluorogalactoside **55**[23] followed by acetolysis (⟶ **56**) and 1-bromination with HBr in acetic acid in 81% overall yield. The glycosyl acceptor **59** was prepared from benzyl α-D-mannoside **46** via bisisopropylidenation with 2,2-dimethoxypropane followed by controlled hydrolysis[24] (⟶ **58**; 72%) and selective benzoylation[14] with benzoyl cyanide (82%). Glycosylation of the acceptor **59** with the bromide **57** in the presence of AgOTf (as above) gave the disaccharide **60** (88%), which was converted to the pentabenzoate **61** (97%) by isopropylidene acetal cleavage[22] with pyridinium perchlorate followed by benzoylation.

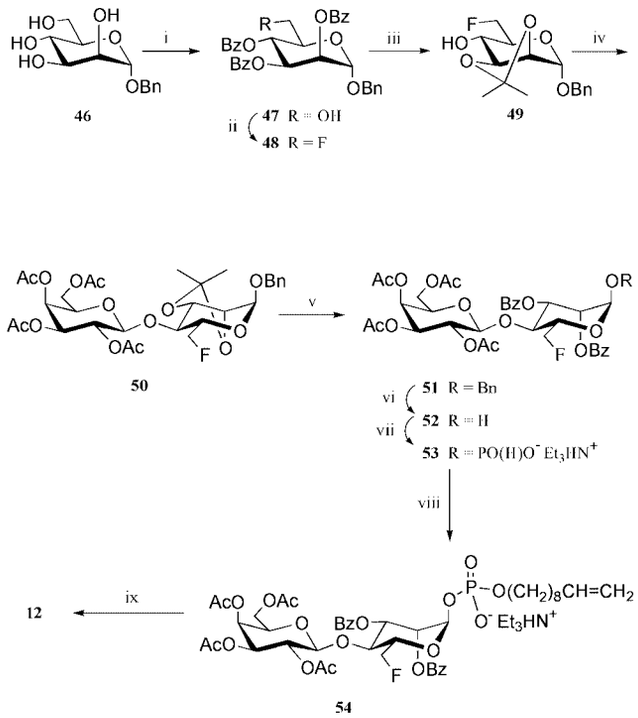
The 6′-azido-6′-deoxydisaccharide derivative **67** (which is a precursor of the phosphodisaccharide **16**; Scheme 7) was prepared starting from the known disaccharide **65**,[4] which was converted first to the 6′-hydroxy derivative **66** (76%) by consecutive de-O-acetylation[16] with HCl in MeOH, tritylation with dimethoxytrityl chloride (DMTCl) in pyridine, benzoylation and detritylation under mildly acidic conditions. Treatment of compound **66** with the NaN_3–Ph_3P–CCl_4 system[25] provided the 6′-azido-6′-deoxy derivative **67** in 60% yield.

The β-configuration of newly formed glycosidic linkages in the disaccharides **20**, **29**, **41**, **50** and **60** followed from the characteristic values of the $J_{1',2'}$ (7.7–8.1 Hz) in ^1H NMR spectra. For the α-D-galactoside **30** the corresponding value is $J_{1',2'} = 3.7$ Hz.

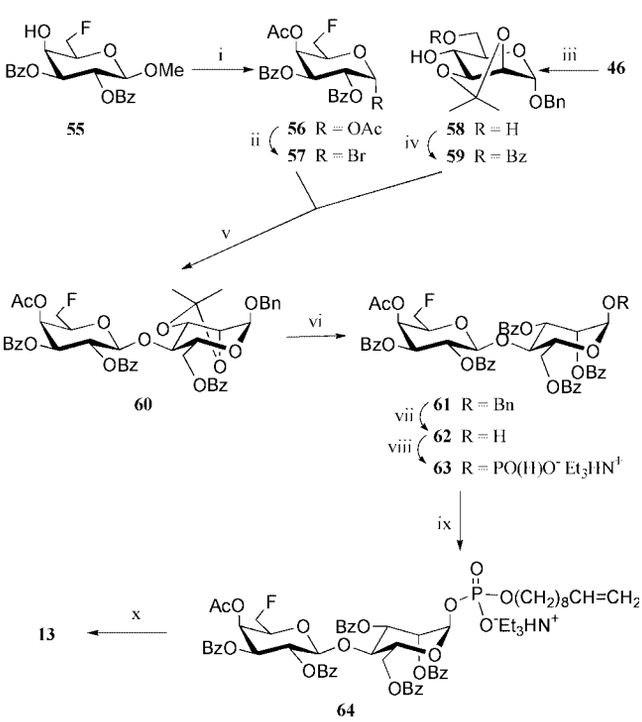
In contrast to the anomeric de-O-acylation of the 3-deoxy- (**21**) and 2-azido-2-deoxy- (**31**) disaccharide derivatives (see above), similar reaction of the 3-deoxy-3-fluoro (**42**) and



Scheme 4 *Reagents*: i, *N*-benzoylimidazole, CH_2Cl_2; ii, **19**, $AgSO_3CF_3$, 2,4,6-collidine, CH_2Cl_2; iii, H_2SO_4, Ac_2O; iv, Me_2NH, MeCN–THF; v, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); vi, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine, (b) I_2, pyridine–water; vii, NaOMe, MeOH.



Scheme 5 *Reagents*: i, (a) TrCl, pyridine; (b) BzCl, pyridine; (c) 80% aq. AcOH; ii, DAST, CH_2Cl_2; iii, (a) NaOMe, MeOH; (b) 2,2-dimethoxypropane, acetone, $TsOH{\cdot}H_2O$; iv, **19**, $AgSO_3CF_3$, 2,4,6-collidine, CH_2Cl_2; v, (a) $C_5H_5N{\cdot}HClO_4$, MeCN–water; (b) BzCl, pyridine; vi, H_2, $Pd(OH)_2$/C, EtOAc–MeOH; vii, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); viii, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; ix, NaOMe, MeOH.



Scheme 6 *Reagents*: i, (a) Ac_2O, pyridine; (b) H_2SO_4, Ac_2O; ii, HBr, AcOH; iii, 2,2-dimethoxypropane, acetone, $TsOH{\cdot}H_2O$; then water; iv, BzCN, Et_3N, MeCN; v, $AgSO_3CF_3$, 2,4,6-collidine, CH_2Cl_2; vi, (a) $C_5H_5N{\cdot}HClO_4$, MeCN–water; (b) BzCl, pyridine; vii, H_2, $Pd(OH)_2$/C, THF–MeOH; viii, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); ix, (a) dec-9-en-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; x, NaOMe, MeOH.

6′-azido-6′-deoxy (**67**) derivatives with dimethylamine in CH_3CN–THF afforded the pure α-hemiacetal disaccharides derivatives **43** (88%) and **68** (79%), respectively. Anomeric de-O-benzylation of the 6-fluoro-6-deoxy (**51**) and 6′-fluoro-6′-deoxy (**61**) disaccharides was achieved by catalytic hydrogenation over palladium(II) hydroxide to give smoothly the α-hemiacetal derivatives **52** and **62** in 90% and 81% yield, respectively. Compounds **43**, **52**, **62** and **68** then were treated with triimidazolylphosphine followed by mild hydrolysis to produce the α-glycosyl H-phosphonates **44**, **53**, **63** and **69**, respectively, in excellent yields.

The disaccharide H-phosphonates **23**, **44**, **53** and **63** were converted to the protected phosphodiesters **25**, **45**, **54** and **64** (74–90% 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. Similar condensation of the H-phosphonates **33** and **69** (containing azido groups) with decan-1-ol provided the phosphodiesters **35** (95%) and **70** (90%), respectively.

The deprotected phosphodisaccharides **10**–**13** were prepared from the derivatives **25**, **45**, **54** and **64**, respectively, by de-O-acylation with 0.05 mol dm^{-3} methanolic sodium methoxide in 97–100% yield. The preparation of the aminodeoxy phosphodisaccharides **14** (95%) and **16** (44%)† was performed from compounds **35** and **70**, respectively, by de-O-acylation followed by reduction of azido groups in intermediates **36** and **71**, respectively, by hydrogenation over palladium catalyst. N-Acetylation[26] of compound **14** with acetic anhydride in MeOH gave the phosphosaccharide **15** (91%).

The structures of the phosphodisaccharides **10**–**16** were confirmed by NMR and mass spectrometric data (see Table 1). The ^{31}P NMR spectra exhibited single signals [δ_P between −0.72 and −2.71], which are characteristic for glycosidically linked phosphodiesters.[1,4–7,9,11,17] The presence of a (1⟶1)-phosphodiester linkage at the reducing terminus of each of the disaccharides **10**–**16** was clearly indicated by the C-1 and C-2 signals of the corresponding monosaccharide residue and either the dec-9-enyl (for compounds **10**–**13**) or the decyl unit (for compounds **14**–**16**) in the ^{13}C NMR spectra. These signals were shifted as a result of the α- and β-effects of phosphorylation and were coupled with phosphorus (or broadened).

The position of the fluorine atom in compound **11** (at C-3) was confirmed by the chemical shift of the C-3 signal (which was strongly down-shifted as a result of fluorination) and the characteristic values[21] of $J_{C2,F}$ = 16.0, $J_{C3,F}$ = 185.0, $J_{C4,F}$ = 18.0 and $J_{C5,F}$ = 6.7 Hz in the ^{13}C NMR spectrum (signal of C-1 appeared as a broadened unresolved triplet because of C–P and C–F couplings). The position of the fluorine atom in compounds **12** and **13** was confirmed in a similar manner.

The α-configuration of the D-glycopyranosyl phosphate fragments in the disaccharide phosphates **10**–**16** was evident from the characteristic values of $^1J_{C,H}$ = 168.9–173.3 Hz for the signal of C-1 in the ^{13}C NMR spectra (it should be taken into account that compound **15** was prepared from compound **14**). The value of $^1J_{C1,H1}$ ≈170 Hz is typical for α-D-derivatives. For β-D-glycosyl residues the value is about 160 Hz: for β-D-Gal*p* in compounds **10**–**12** and **14**, $^1J_{C1',H1'}$ = 158.6–162.6 Hz (Table 1; see also refs. 1, 4, 5, 11 and 27).

The molecular masses of the phosphodiesters **10**–**16** were confirmed by electrospray mass spectrometry (ESMS). The signals in the ES(−) mass spectra corresponded to the pseudomolecular ions for the disaccharide phosphates (Table 1).

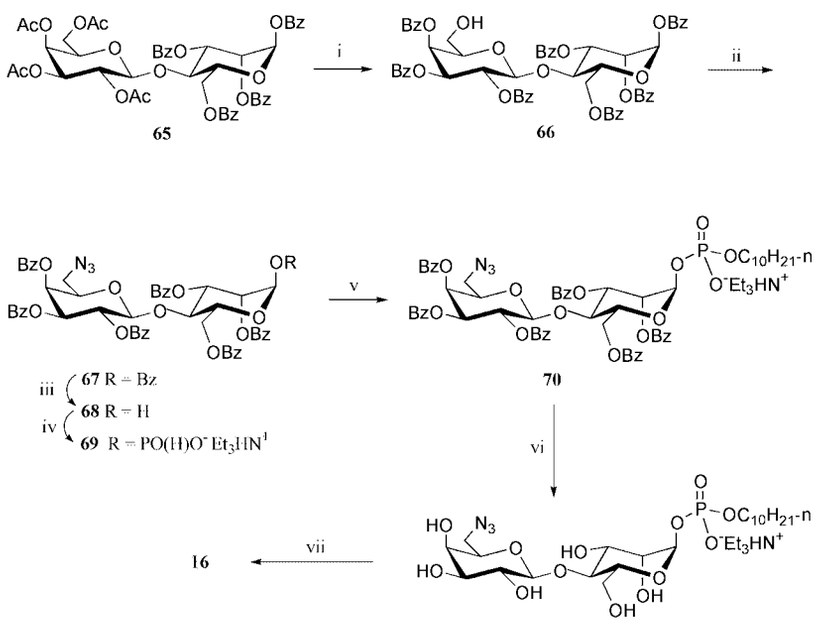
Compounds **10**–**16** were tested in a biochemical assay in a cell-free system[28] as substrate analogues/possible inhibitors for the MPT in the *Leishmania*. The phosphodisaccharides **10** and **11** (modified at C-3) showed increased (to about 130–140%) acceptor substrate activity relative to compound **1**, showing that the affinity of the substrate for the MPT can be improved

† Crude product **16** was obtained in 94% yield, but required additional purification (see Experimental section), which led to a moderate final yield.

Table 1 ^{13}C and ^{31}P NMR data [δ_C and δ_P in ppm; $J_{C,P}$(in parentheses), $J_{C,F}$ and $J_{C,H}$ in Hz; spectra recorded in D_2O] and ESMS(−) data (*m*/*z*) for the phosphodisaccharides **10**–**16**

Residue	Atom	**10**[a,b]	**11**[a,b]	**12**[a,b]	**13**[a,b]	**14**[a,c]	**15**[a–d]	**16**[a,c]
Dec-9-enyl	OCH_2CH_2	67.7d (5.8)	67.0d (5.8)	66.9d (5.7)	67.0d (5.6)	67.0d (5.1)	67.2d (6.6)	67.2d (5.8)
(or *n*-decyl	OCH_2CH_2	30.7d (7.3)	30.3d (6.7)	30.3d (6.6)	30.4d (6.7)	30.4d (6.5)	30.2d (6.5)	30.3d (5.8)
for **14**–**16**)	$CH{=}CH_2$	141.4	140.5	140.3	140.4			
	$CH{=}CH_2$	115.0	114.5	114.4	114.4			
Aldose	C-1	95.5d (5.1)	96.2br	96.2d (5.1)	96.1d (5.1)	96.8br	95.1d (4.1)	96.4d (5.1)
		$J_{C,H}$ 171.6	$J_{C,H}$ 173.3	$J_{C,H}$ 168.9	$J_{C,H}$ 169.3	$J_{C,H}$ 170.7		$J_{C,H}$ 171.0
	C-2	68.8d (8.7)	69.4dd (8.0)	70.4d (8.1)	70.4d (8.5)	54.4d (8.0)	53.0d (9.4)	70.9d (8.7)
			$J_{C,F}$ 16.0					
	C-3	34.1	90.4d	69.0	69.2	68.9	67.2	69.0
			$J_{C,F}$ 185.0					
	C-4	74.0	73.3d	75.2d	77.3	76.2	75.9	73.9
			$J_{C,F}$ 18.0	$J_{C,F}$ 5.1				
	C-5	71.9	72.5d	71.5d	72.5	72.5	72.3	72.6
			$J_{C,F}$ 6.7	$J_{C,F}$ 18.0				
	C-6	61.5	60.1	82.1d	60.6	60.4	60.0	60.2
				$J_{C,F}$ 168.0				
Aldose′	C-1′	104.8	103.5	103.5	103.5	103.5	103.4	102.8
		$J_{C,H}$ 158.6	$J_{C,H}$ 160.9	$J_{C,H}$ 159.6	$J_{C,H}$ 161.7	$J_{C,H}$ 162.6		$J_{C,H}$ 151.4
	C-2′	71.9	71.4	71.3	71.0	71.2	71.3	71.2
	C-3′	73.6	73.0	72.9	72.8	72.9	72.8	71.4
	C-4′	69.5	68.9	69.0	68.4d	68.9	69.0	69.5
					$J_{C,F}$ 7.1			
	C-5′	76.1	75.6	75.8	73.9d	75.7	75.7	73.0
					$J_{C,F}$ 19.6			
	C-6′	62.0	61.3	61.5	83.5d	61.4	61.5	40.7
					$J_{C,F}$ 165.8			
Phosphate	P	−1.44	−1.98	−0.79	−0.72	−2.71	−1.96	−1.91
	m/*z*[e]	542.94	561.08	561.10	561.10	560.31	602.25	559.79

[a] Additional signals of CCH_2C (δ_C 22.4–25.9, 28.7–29.6 and 31.6–33.7) were present. [b] Additional signals of Et_3NH^+ [δ_C 8.6–9.2 (CH_3) and δ_C 47.0–47.6 (CH_2)] were present. [c] Additional signals of CH_2CH_3 (δ_C 13.8–14.0) were present. [d] Additional signal of $COCH_3$ (δ_C 22.3) was present. [e] Corresponds to the pseudomolecular ions: $[M - Et_3N - H]^-$ for compounds **10** ($C_{28}H_{56}NO_{13}P$ requires *M*, 645.35; expected *m*/*z*, 543.23), **11**–**13** ($C_{28}H_{55}FNO_{13}P$ requires *M*, 663.34; expected *m*/*z*, 561.22) and **15** ($C_{30}H_{61}N_2O_{14}P$ requires *M*, 704.38; expected *m*/*z*, 602.27); $[M - Na]^-$ for compound **14** ($C_{22}H_{44}NaO_{13}P$ requires *M*, 583.24; expected *m*/*z*, 560.26); and $[M - NH_3 - H]^-$ for compound **16** ($C_{22}H_{47}N_2O_{13}P$ requres *M*, 578.28; expected *m*/*z*, 560.26).



Scheme 7 *Reagents*: i, (a) HCl, MeOH; (b) DMTCl, pyridine; (c) BzCl, pyridine; (d) TFA, CH_2Cl_2; ii, NaN_3, Ph_3P, CCl_4, DMF; iii, Me_2NH, MeCN–THF; iv, (a) triimidazolylphosphine, MeCN; (b) Et_3NHHCO_3, water (pH 7); v, decan-1-ol, trimethylacetyl chloride, pyridine; (b) I_2, pyridine–water; vi, NaOMe, MeOH; vii, (a) Dowex 50 (Na^+); (b) H_2, $Pd(OH)_2$/C, MeOH.

by manipulating the C-3 position and suggesting that the epimer (of compound **1**) at C-3 **7** did not work (see Introduction), probably due to a steric clash between the enzyme and the axial 3-OH group.

The phosphodisaccharide **12** (fluorinated at C-6) showed reduced (to about 30%) acceptor substrate activity compared with compound **1**. Taking into account that the 6-deoxy analogue **8** exhibited no acceptor activity at all (see Introduction), this result suggests that the 6-OH group in the acceptor **1** acts principally as a hydrogen-bond acceptor. Compounds **14** and **15** (modified at C-2) were found to be substrates for the MPT, but with reduced kinetics relative to compound **1**.

Compounds **13** and **16** (modified at C-6′) exhibited (as well as the 6′-deoxy analogue **9**) neither acceptor nor inhibitory activity, suggesting that 1) there is no MPT activity can act at sites other than the C-6′ hydroxy group and 2) this hydroxy group seems to be essential for enzyme recognition as well as for catalysis. A comprehensive characterization of the elongating MPT in the *Leishmania* using synthetic acceptor substrate analogues (a set of 25 phosphosaccharides) was recently published.[28]

Experimental

General procedures

Optical rotations were measured with a Perkin-Elmer 141 polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. NMR spectra (^{1}H at 300 MHz, ^{13}C{^{1}H} at 75 MHz, ^{31}P{^{1}H} at 121 MHz, and ^{19}F at 282 MHz) were recorded with a Bruker AM-300 spectrometer for solutions in $CDCl_3$, unless otherwise indicated. Chemical shifts (δ in ppm) are given relative to those for Me_4Si for (^{1}H and ^{13}C), external aq. 85% H_3PO_4 (for ^{31}P), and $CFCl_3$ (for ^{19}F); *J*-values are given in Hz. ES mass spectra were recorded with a Micromass Quattro system (Micromass Biotech, UK). IR spectra were recorded with a Nicolet 205 FT-IR spectrometer. TLC was performed on Kieselgel 60 F_{254} (Merck) with *A*, toluene–ethyl acetate (9 : 1); *B*, toluene–ethyl acetate (7 : 3); *C*, toluene–ethyl acetate (1 : 1); *D*, dichloromethane–methanol (9 : 1); and *E*, 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, pyridine and toluene were freshly distilled from CaH_2. Solutions worked up were concentrated under reduced pressure at <40 °C.

Methyl 2,6-di-O-benzoyl-3-deoxy-α-D-*arabino*-hexopyranoside 18

(a) To a stirred solution of the 3-deoxy derivative **17**[12] (818 mg, 3.07 mmol) in pyridine (7 cm^3) was added benzoyl chloride (0.5 cm^3, 4.31 mmol, 1.4 eq.) at 0 °C. After 2 h at rt, the reaction mixture was diluted with dichloromethane and washed successively with saturated aq. $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The residue was dissolved in methanol (15 cm^3) and a 2% solution of iodine in methanol (15 cm^3) was added. The reaction mixture was refluxed for 30 min, cooled, quenched with saturated aq. $Na_2S_2O_3$, and extracted with dichloromethane (2 × 30 cm^3). The combined organic extracts were washed with water, dried (Na_2SO_4), and concentrated. The residue was dissolved in acetonitrile (10 cm^3) and benzoyl cyanide (386 mg, 2.95 mmol) was added along with some triethylamine (0.06 cm^3). The resulting mixture was stirred at rt for 10 min, quenched with methanol (2 cm^3), concentrated, and methanol (2 × 5 cm^3) was evaporated off from the residue. FCC [toluene-ethyl acetate, (80 : 20)⟶(70 : 30)] gave the *monohydroxy derivative* **18** (819 mg, 69%) as an amorphous solid; $[\alpha]_D^{24}$ +29 (*c* 1, $CHCl_3$); R_f 0.43 (solvent *B*) (Found: C, 65.15; H, 5.7. $C_{21}H_{22}O_7$ requires C, 65.3; H, 5.7%); δ_H 2.12 (1 H, ddd, $J_{2,3ax}$ 2.9, $J_{3ax,4}$ 9.8, $J_{3ax,3eq}$ 13.7, 3-H^{ax}), 2.46 (1 H, dt, $J_{2,3eq}$ = $J_{3eq,4}$ = 3.5, 3-H^{eq}), 3.49 (3 H, s, OMe), 3.90 (1 H, ddd, $J_{4,5}$ 9.0, $J_{5,6a}$ 2.0, $J_{5,6b}$ 3.4, 5-H), 3.98 (1 H, ddd, 4-H), 4.48 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H^a), 4.77 (1 H, br s, 1-H), 4.99 (1 H, dd, 6-H^b), 5.20 (1 H, m, 2-H) and 7.20–8.20 (10 H, 2 × Ph).

(b) A solution of HCl in MeOH [prepared at 0 °C from acetyl chloride (0.6 cm^3) and methanol (14 cm^3)] was added to a solution of the acetate **18a** (672 mg, 1.472 mmol) in dichloromethane (5 cm^3), the resulting solution was kept at rt for 20 h, concentrated, and toluene (3 × 10 cm^3) was evaporated off from the residue. A solution of the residue in toluene–ethyl acetate (80 : 20) was filtered through a pad of silica and the filtrate was concentrated to give pure compound **18** (506 mg, 89%), identical with that obtained above.

Methyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,6-di-O-benzoyl-3-deoxy-α-D-*arabino*-hexopyranoside 20

Silver triflate (1.31 g, 5.10 mmol, 1.73 eq.) was dried by evaporation of anhydrous toluene (2 × 15 cm^3) therefrom. A solution of acetobromogalactose **19** (1.82 g, 4.425 mmol, 1.5 eq.), the dibenzoate **18** (1.14 g, 2.95 mmol) and 2,4,6-collidine (2,4,6-trimethylpyridine) (0.5 cm^3, 3.835 mmol, 1.3 eq.) in dichloromethane (30 cm^3) was added dropwise to a stirred suspension of silver triflate in dichloromethane (10 cm^3) at −20 to −30 °C. Cooling was discontinued after the addition was complete, and, after 30 min, the mixture (which became slightly acidic) was neutralized with pyridine (1 cm^3), filtered through a Celite pad, and the filtrate was concentrated. FCC (toluene–ethyl acetate, 85 : 15) of the residue gave, first, the acetate **18a** (463 mg, 37%); R_f 0.63 (solvent *B*); δ_H 1.99 (3 H, s, Ac), 2.07 (1 H, ddd, $J_{2,3ax}$ 3.1, $J_{3ax,4}$ 11.4, $J_{3eq,3ax}$ 13.8, 3-H^{ax}), 2.33 (1 H, ddd, $J_{2,3eq}$ 1.5, $J_{3eq,4}$ 4.0, 3-H^{eq}), 3.40 (3 H, s, OMe), 4.07 (1 H, ddd, $J_{4,5}$ 10.2, $J_{5,6a}$ 5.0, $J_{5,6b}$ 2.4, 5-H), 4.37 (1 H, dd, $J_{6a,6b}$ 12.0, 6-H^a), 4.59 (1 H, dd, 6-H^b), 4.71 (1 H, d, $J_{1,2}$ 1.5, 1-H), 5.12 (1 H, dt, 2-H), 4.72 (1 H, ddd, 4-H) and 7.20–8.10 (10 H, 2 × Ph). Continued elution with toluene–ethyl acetate (80 : 20) gave the desired *disaccharide* **20** (1.256 g, 60%) as an amorphous solid; $[\alpha]_D^{24}$ +28 (*c* 1, $CHCl_3$); R_f 0.40 (solvent *B*) (Found: C, 58.9; H, 5.7. $C_{35}H_{40}O_{16}$ requires C, 58.7; H, 5.6%); δ_H 1.85, 1.89, 2.00, and 2.08 (12 H, 4 s, 4 × Ac), 2.18–2.30 (1 H, m, 3-H^{ax}), 2.40 (1 H, br d, $J_{3eq,3ax}$ 13.8, 3-H^{eq}), 3.38 (3 H, s, OMe), 3.81 (1 H, t, $J_{5',6'}$ 6.2, 5′-H), 3.95–4.05 (4 H, m, 4-H, 5-H and 6′-H$_2$), 4.35 (1 H, dd, $J_{5,6a}$ 3.7, $J_{6a,6b}$ 11.8, 6-H^a), 4.49 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.50 (1 H, d, 6-H^b), 4.65 (1 H, br s, 1-H), 4.88 (1 H, dd, $J_{3',4'}$ 3.4, $J_{2',3'}$ 10.4, 3′-H), 5.11 (1 H, m, 2-H), 5.14 (1 H, dd, 2′-H), 5.11 (1 H, br d, 4′-H) and 7.20–8.10 (10 H, m, 2 × Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-1-O-acetyl-2,6-di-O-benzoyl-3-deoxy-α-D-*arabino*-hexopyranose 21

To a stirred solution of the disaccharide **20** (145 mg, 0.203 mmol) in acetic anhydride (1 cm^3) was added sulfuric acid (0.03 cm^3) at 0 °C. After stirring for 1 h at 0 °C, the reaction mixture was diluted with dichloromethane, washed successively with saturated aq. $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. FCC (toluene–ethyl acetate, 80 : 20) of the residue gave the *penta-acetate* **21** (119 mg, 79%); $[\alpha]_D^{24}$ +30 (*c* 1, $CHCl_3$); mp 121–122 °C (from EtOH); R_f 0.35 (solvent *B*) (Found: C, 57.4; H, 5.5. $C_{36}H_{40}O_{17}\cdot C_2H_5OH$ requires C, 57.7; H, 5.9%); δ_H 1.95, 1.98, 2.09, 2.17 and 2.18 (15 H, 5 s, 5 × Ac), 2.34 (1 H, ddd, $J_{2,3ax}$ 2.8, $J_{3ax,4}$ 10.5, $J_{3ax,3eq}$ 13.7, 3-H^{ax}), 2.64 (1 H, dt, $J_{2,3eq} = J_{3eq,4} = 3.3$, 3-H^{eq}), 3.90 (1 H, ddd, $J_{4',5'}$ 1.1, $J_{5',6a'}$ 5.7, $J_{5',6b'}$ 7.1, 5′-H), 4.05–4.23 (4 H, m, 4-H, 5-H and 6′-H$_2$), 4.46 (1 H, dd, $J_{5,6a}$ 3.2, $J_{6a,6b}$ 12.0, 6-H^a), 4.55 (1 H, d, 6-H^b), 4.58 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.97 (1 H, dd, $J_{2',3'}$ 10.4, $J_{3',4'}$ 3.4, 3′-H), 5.23 (1 H, m, 2-H), 5.24 (1 H, dd, 2′-H), 5.37 (1 H, dd, 4′-H), 6.15 (1 H, br s, 1-H) and 7.30–8.20 (10 H, m, 2 × Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,6-di-O-benzoyl-3-deoxy-α/β-D-*arabino*-hexopyranose 22

To a solution of the 1-O-acetate **21** (200 mg, 0.269 mmol) in MeCN (3 cm^3) was added 2 mol dm^{-3} dimethylamine in THF (1.0 cm^3, 2 mmol, 7.4 eq.), and the mixture was kept at rt with monitoring by TLC (solvent *C*). After 10 h, the mixture was concentrated and MeCN was evaporated off from the residue. FCC (toluene–ethyl acetate, 70 : 30) of the residue gave the *disaccharide α,β-hemiacetal* **22** (170 mg, 90%) as an amorphous solid; $[\alpha]_D^{24}$ +22 (*c* 1, $CHCl_3$); R_f 0.53 (solvent *C*) (Found: C, 57.8; H, 5.6. $C_{34}H_{38}O_{16}$ requires C, 58.1; H, 5.45%); δ_H (*inter alia*) 1.85, 1.88, 1.97 and 2.07 (12 H, 4 s, 4 × Ac), 4.43 (d, $J_{1',2'}$ 7.8, 1′-H$^\beta$), 4.50 (d, $J_{1',2'}$ 7.9, 1′-H$^\alpha$) and 7.20–8.20 (10 H, m, 2 × Ph); α : β = 9 : 1.

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,6-di-O-benzoyl-3-deoxy-α-D-*arabino*-hexopyranosyl hydrogenphosphonate, triethylammonium salt 23

To a stirred solution of imidazole (296 mg, 4.36 mmol, 5.5 eq.) in MeCN (10 cm^3) at 0 °C was added phosphorus trichloride (0.115 cm^3, 1.32 mmol, 5 eq.) and then triethylamine (0.65 cm^3, 4.54 mmol, 5.7 eq.). The mixture was stirred for 15 min, after which a solution of the hemiacetal derivative **22** (185 mg, 0.264 mmol) in MeCN (8 cm^3) was added dropwise during 15 min at 0 °C. The mixture was stirred at rt for 30 min and quenched with 1 mol dm^{-3} triethylammonium (TEA) hydrogen carbonate (pH 7; 6 cm^3). The clear solution was stirred for 15 min, dichloromethane (50 cm^3) was added, and the organic layer was washed in turn with ice–water and cold 0.5 mol dm^{-3} TEA hydrogen carbonate, dried by filtration through cotton wool, and concentrated to give the α,β-(H-phosphonate) **24** [δ_P 0.50 (P^α) and 1.26 (P^β); α : β = 9 : 1]. The residue was dissolved in MeCN (5 cm^3) and H_3PO_3 (368 mg, 4.49 mmol, 17 eq.) was added. The mixture was kept at rt for 64 h, diluted with dichloromethane, and the organic layer was washed with cold 0.5 mol dm^{-3} TEA hydrogen carbonate, dried by filtration through cotton wool, and concentrated. FCC [CH_2Cl_2–MeOH–Et_3N, (98.8 : 0.2 : 1)⟶(91 : 8 : 1)] of the residue gave, first, the hemiacetal derivative **22** (46 mg, 25%) and then the H-phosphonate **23** (158 mg, 70%) as an amorphous solid; $[\alpha]_D^{24}$ +24 (*c* 1, $CHCl_3$); R_f 0.18 (solvent *D*); δ_H 1.10 (9 H, t, *J* 7.3, 3 × C$H_3$$CH_2$N), 1.84, 1.88, 1.98 and 2.08 (12 H, 4 s, 4 × Ac), 2.38 (1 H, m, 3-H^{ax}), 2.65 (7 H, q, 3 × CH_3CH_2N and 3-H^{eq}), 3.75 (1 H, t, $J_{5',6a'} = J_{5',6b'}$ = 6.3, 5′-H), 3.95–4.10 (3 H, m, 4-H, and 6′-H_2), 4.26 (1 H, br d, $J_{4,5}$ 9.9, 5-H), 4.35 (1 H, dd, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 11.8, 6-H^a), 4.47 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.49 (1 H, br d, 6-H^b), 4.85 (1 H, dd, $J_{3',4'}$ 3.4, $J_{2',3'}$ 10.4, 3′-H), 5.12 (1 H, dd, 2′-H), 5.15 (1 H, m, 2-H), 5.25 (1 H, d, 4′-H), 5.55 (1 H, br d, $J_{1,P}$ 8.5, 1-H), 6.97 (1 H, d, $J_{H,P}$ 634.3, HP) and 7.25–8.10 (10 H, m, 2 × Ph); δ_P 0.50; ESMS(−) data: *m*/*z* 764.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 765.19 $C_{40}H_{54}NO_{18}P$ requires *M*, 867.31).

Dec-9-enyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,6-di-O-benzoyl-3-deoxy-α-D-*arabino*-hexopyranosyl phosphate, triethylammonium salt 25

A mixture of the H-phosphonate **23** (140 mg, 0.164 mmol) and dec-9-en-1-ol (0.058 cm^3, 0.32 mmol, 1.95 eq.) was dried by evaporation of pyridine (3 × 2 cm^3) therefrom. The residue was dissolved in pyridine (2 cm^3), trimethylacetyl chloride (0.06 cm^3, 0.487 mmol, 2.97 eq.) was added, and the mixture was stirred at rt for 30 min, whereafter a freshly prepared solution of iodine (80 mg, 0.315 mmol, 1.92 eq.) in pyridine–water (95 : 5; 2.3 cm^3) was added. After 30 min, dichloromethane 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, (98.9 : 0.1 : 1)⟶(91 : 8 : 1)] of the residue gave the phosphodiester **25** (148 mg, 90%) as an amorphous solid; $[\alpha]_D^{24}$ +16 (*c* 1, $CHCl_3$); R_f 0.43 (solvent *D*); δ_H 1.10–1.30 (10 H, m, CH_2=CHCH_2CH_2CH_2CH_2CH_2CH_2), 1.20 (9 H, t, *J* 7.3, 3 × C$H_3$$CH_2$N), 1.51 (2 H, quintet, *J* 7.0, OCH_2CH_2), 1.84, 1.88, 1.96 and 2.08 (12 H, 4 s, 4 × Ac), 1.95 (2 H, m, CH_2=CHCH_2), 2.10–2.45 (2 H, m, 3-H_2), 2.91 (6 H, q, 3 × CH_3CH_2N), 3.77 (1 H, t, $J_{5',6'}$ 6.4, 5′-H), 3.85 [2 H, q, $J_{P,H}$ = J(CH_2,CH_2) = 6.6, CH_2CH_2OP], 4.00 (2 H, d, 6′-H_2), 4.07 (1 H, dt, $J_{3eq,4}$ 5.6, $J_{3ax,4} = J_{4,5}$ = 10.4, 4-H), 4.27 (1 H, br d, 5-H), 4.36 (1 H, dd, $J_{5,6a}$ 3.0, $J_{6a,6b}$ 11.8, 6-H^a), 4.46 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.49 (1 H, br d, 6-H^b), 4.85 (1 H, dd, J_{gem} 1.3, J_{cis} 10.2, *H*CH=CH), 4.85 (1 H, m, 3′-H), 4.91 (1 H, dd, J_{trans} 16.9, HC*H*=CH), 5.12 (1 H, dd, $J_{1',2'}$ 8.1, $J_{2',3'}$ 10.3, 2′-H), 5.19 (1 H, m, 2-H), 5.25 (1 H, d, $J_{3',4'}$ 3.3, 4′-H), 5.49 (1 H, br d, $J_{1,P}$ 7.8, 1-H), 5.73 [1 H, ddt, J(H,CH_2) 6.7, CH_2=C*H*CH_2] and 7.25–8.0 (10 H, m, 2 × Ph); δ_P −2.14; ESMS(−) data: *m*/*z* 919.10 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 919.32; $C_{50}H_{72}NO_{19}P$ requires *M*, 1021.44).

Methyl 2-azido-3-O-benzoyl-4,6-O-benzylidene-2-deoxy-α-D-mannopyranoside 27

Triflic anhydride (0.35 cm^3, 2.08 mmol, 1.4 eq.) was added to a cooled (−30 °C) solution of the diol **26**[18] (423 mg, 1.5 mmol) in CH_2Cl_2 (7 cm^3) and pyridine (2 cm^3). The mixture was stirred at −30 °C for 1 h, whereafter benzoyl chloride (0.25 cm^3, 2.15 mmol, 1.43 eq.) was added. Cooling was discontinued and, after 15 min at rt, the reaction mixture was quenched with saturated aq. $NaHCO_3$ and extracted with dichloromethane (2 × 30 cm^3). The combined organic extracts were washed successively with water, 1 mol dm^{-3} aq. HCl, water, and brine, dried (Na_2SO_4), and concentrated. The residue was dissolved in toluene (25 cm^3), and NaN_3 (650 mg, 10 mmol, 6.7 eq.) and *n*-Bu_4NCl (1.4 g, 5 mmol, 3.35 eq.) were added. The reaction mixture was stirred at rt for 12 h, then refluxed for 30 min, cooled, washed with water, dried (Na_2SO_4), and concentrated. FCC [toluene–ethyl acetate, (99 : 1)⟶(95 : 5)] of the residue gave the *azido derivative* **27** (549 mg, 89%) as an amorphous solid; $[\alpha]_D^{24}$ +61 (*c* 1, $CHCl_3$); R_f 0.50 (solvent *A*) (Found: C, 61.2; H, 5.2; N, 10.3. $C_{21}H_{21}N_3O_6$ requires C, 61.3; H, 5.15; N, 10.2%); ν_{max} (film)/cm^{-1} (*inter alia*) 1724 (C=O), 2108 (–N_3); δ_H 3.47 (3 H, s, OMe), 3.92 (1 H, dd, $J_{5,6a}$ 9.8, $J_{6a,6b}$ 10.2, 6-H^a), 4.01 (1 H, dt, $J_{4,5} = J_{5,6a}$ = 9.8, $J_{5,6b}$ 4.4, 5-H), 4.26 (1 H, t, $J_{3,4}$ 10.0, 4-H), 4.31 (1 H, br d, $J_{2,3}$ 4.0, 2-H), 4.34 (1 H, dd, 6-H^b), 4.80 (1 H, br s, 1-H), 5.65 (1 H, s, PhC*H*), 5.78 (1 H, dd, 3-H) and 7.20–8.20 (10 H, 2 × Ph).

Methyl 2-azido-3,6-di-O-benzoyl-2-deoxy-α-D-mannopyranoside 28

To a stirred solution of the azido derivative **27** (510 mg, 1.24 mmol) in methanol (15 cm^3) was added a 2% solution of iodine in methanol (15 cm^3). The reaction mixture was refluxed for 30 min, cooled, quenched with saturated aq. $Na_2S_2O_3$, and extracted with dichloromethane (2 × 30 cm^3). The combined organic extracts were washed with water, dried (Na_2SO_4), and concentrated. The residue was dissolved in dichloromethane (10 cm^3) and imidazole (440 mg, 6.43 mmol, 5.18 eq.) was added followed by addition of benzoyl chloride (0.375 cm^3, 3.22 mmol, 2.6 eq.). The resulting mixture was stirred at rt for 20 h, quenched with saturated aq. $NaHCO_3$, and extracted with dichloromethane. The extracts were washed with water, dried (Na_2SO_4), and concentrated. FCC [toluene–ethyl acetate, (99 : 1)⟶(90 : 10)] of the residue gave the *monohydroxy derivative* **28** (461 mg, 87%) as an amorphous solid; $[\alpha]_D^{24}$ +110 (*c* 1, $CHCl_3$); R_f 0.60 (solvent *B*) (Found: C, 59.4; H, 5.2; N, 9.9. $C_{21}H_{21}N_3O_7$ requires C, 59.0; H, 4.95; N, 9.8%); ν_{max} (film)/cm^{-1} (*inter alia*) 1724 (C=O), 2108 (–N_3); δ_H 2.94 (1 H, d, $J_{4,OH}$ 5.0, OH), 3.37 (3 H, s, OMe), 3.91 (1 H, ddd, $J_{4,5}$ 9.7, $J_{5,6a}$ 2.1, $J_{5,6b}$ 4.4, 5-H), 4.03 (1 H, dt, $J_{3,4}$ 9.7, 4-H), 4.05 (1 H, dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.8, 2-H), 4.52 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H^a), 4.68 (1 H, dd, 6-H^b), 4.73 (1 H, d, 1-H), 5.50 (1 H, dd, 3-H) and 7.30–8.10 (10 H, 2 × Ph).

Methyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2-azido-3,6-di-O-benzoyl-2-deoxy-α-D-mannopyranoside 29

The reaction of the dibenzoate **28** (213 mg, 0.498 mmol) and acetobromogalactose **19** (309 mg, 0.751 mmol, 1.51 eq.) in CH_2Cl_2 (7 cm^3) in the presence of AgOTf (225 mg, 0.875 mmol, 1.76 eq.) and 2,4,6-collidine (0.085 cm^3, 0.642 mmol, 1.29 eq.) was performed as described for the preparation of the disaccharide **20**. FCC [toluene–ethyl acetate, (90 : 10)⟶(75 : 25)] gave, first, the *α-linked disaccharide* **30** (49 mg, 13%) as an amorphous solid; $[\alpha]_D^{24}$ +115 (*c* 1, $CHCl_3$); R_f 0.38 (solvent *B*) (Found : C, 55.7; H, 5.2; N, 5.2. $C_{35}H_{39}N_3O_{16}$ requires C, 55.5; H, 5.2; N, 5.5%); ν_{max} (film)/cm^{-1} (*inter alia*) 1721 and 1750

(C=O), 2106 (–N_3); δ_H 1.73, 1.85, 1.92 and 2.01 (12 H, 4 s, 4 × Ac), 3.40 (3 H, s, OMe), 3.84 (1 H, dd, $J_{5',6a'}$ 6.5, $J_{6a',6b'}$ 11.2, 6′-H^a), 3.96 (1 H, dd, $J_{5',6b'}$ 6.7, 6′-H^b), 4.06 (1 H, $J_{1,2}$ 2.1, $J_{2,3}$ 3.6, 2-H), 4.07 (1 H, m, 5-H), 4.26 (1 H, t, 5′-H), 4.32 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.3, 4-H), 4.48 (1 H, dd, $J_{5,6a}$ 5.1, $J_{6a,6b}$ 12.1, 6-H^a), 4.65 (1 H, dd, $J_{5,6b}$ 2.1, 6-H^b), 4.73 (1 H, d, 1-H), 5.10 (1 H, dd, $J_{1',2'}$ 3.7, $J_{2',3'}$ 11.0, 2′-H), 5.20 (1 H, dd, $J_{3',4'}$ 3.0, 3′-H), 5.35 (1 H, br d, 4′-H), 5.46 (1 H, d, 1′-H), 5.56 (1 H, dd, 3-H) and 7.10–8.10 (10 H, m, 2 × Ph). Continued elution provided the *β-linked disaccharide* **29** (283 mg, 75%); $[\alpha]_D^{24}$ +150 (*c* 1, $CHCl_3$); mp 165–167 °C (from EtOH); R_f 0.28 (solvent *B*) (Found : C, 55.2; H, 5.1; N, 5.4. $C_{35}H_{39}N_3O_{16}$ requires C, 55.5; H, 5.2; N, 5.5%); ν_{max} (film)/cm^{-1} (*inter alia*) 1729 and 1752 (C=O), 2108 (–N_3); δ_H 1.86, 1.89, 1.90 and 1.96 (12 H, 4 s, 4 × Ac), 3.46 (3 H, s, OMe), 3.50–3.75 (3 H, m, 5′-H and 6′-H_2), 4.10 (1 H, m, 5-H), 4.16 (1 H, $J_{1,2}$ 1.9, $J_{2,3}$ 3.6, 2-H), 4.31 (1 H, t, $J_{4,5} = J_{3,4}$ = 9.5, 4-H), 4.45 (1 H, dd, $J_{5,6a}$ 5.2, $J_{6a,6b}$ 11.9, 6-H^a), 4.63 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 4.70 (1 H, br d, 6-H^b), 4.79 (1 H, br s, 1-H), 4.90 (1 H, dd, $J_{3',4'}$ 3.2, $J_{2',3'}$ 10.5, 3′-H), 5.13 (1 H, dd, 2′-H), 5.20 (1 H, br d, 4′-H), 5.75 (1 H, dd, 3-H) and 7.40–8.20 (10 H, m, 2 × Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-1-O-acetyl-2-azido-3,6-di-O-benzoyl-2-deoxy-α-D-mannopyranose 31

To a stirred solution of the disaccharide **29** (180 mg, 0.238 mmol) in acetic anhydride (2 cm^3) was added sulfuric acid (0.05 cm^3) at 0 °C. After stirring for 1 h at 0 °C, the reaction mixture was diluted with dichloromethane, washed successively with saturated aq. $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. FCC (toluene–ethyl acetate, 60 : 40) of the residue gave the *penta-acetate* **31** (186 mg, quant.) as an amorphous solid; $[\alpha]_D^{24}$ +90 (*c* 1, $CHCl_3$); R_f 0.63 (solvent *C*) (Found: C, 54.8; H, 5.1; N, 5.7. $C_{36}H_{39}N_3O_{17}$ requires C, 55.0; H, 5.0; N, 5.35%); ν_{max} (film)/cm^{-1} (*inter alia*) 1747 (C=O), 2111 (–N_3); δ_H 1.86, 1.89 (× 2), 1.97 and 2.13 (15 H, 4 s, 5 × Ac), 3.45–3.68 (3 H, m, 5′-H and 6′-H_2), 4.00–4.10 (2 H, m, 2- and 5-H), 4.32 (1 H, t, $J_{4,5} = J_{3,4}$ = 9.2, 4-H), 4.32 (1 H, dd, $J_{5,6a}$ 4.3, $J_{6a,6b}$ 12.2, 6-H^a), 4.55 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.58 (1 H, br d, 6-H^b), 4.80 (1 H, dd, $J_{3',4'}$ 3.4, $J_{2',3'}$ 10.3, 3′-H), 5.04 (1 H, dd, 2′-H), 5.11 (1 H, br d, 4′-H), 5.67 (1 H, dd, 3-H), 6.08 (1 H, d, $J_{1,2}$ 1.9, 1-H) and 7.40–8.20 (10 H, m, 2 × Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2-azido-3,6-di-O-benzoyl-2-deoxy-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 33

To a solution of the 1-O-acetate **31** (260 mg, 0.331 mmol) in 1 : 3 MeOH–MeCN (12 cm^3) was added *tert*-butylamine (0.4 cm^3, 3.79 mmol, 10 eq.) and the mixture was kept at rt. After 17 h (about 90% conversion by TLC), the mixture was diluted with dichloromethane, washed with water, dried (Na_2SO_4), and concentrated. A solution of the residue in toluene–ethyl acetate (60 : 40) was filtered through a pad of silica gel to give a crude product (250 mg), containing mainly the disaccharide α,β-hemiacetal derivative **32** [δ_H (*inter alia*) 1.85, 1.89, 1.90 and 1.94 (12 H, 4 s, 4 × Ac), 5.42 (dd, $J_{2,3}$ 3.6, $J_{3,4}$ 9.5, 3-H$^\beta$), 5.75 (dd, $J_{2,3}$ 3.7, $J_{3,4}$ 8.7, 3-H$^\alpha$) and 7.40–8.20 (10 H, m, 2 × Ph); α : β = 5 : 1] and the starting material (about 10% recovery). This crude product was used without further purification.

The reaction of compound **32** (250 mg, <0.331 mmol) with PCl_3 (0.15 cm^3, 1.72 mmol, 5.2 eq.), imidazole (450 mg, 6.62 mmol, 6.7 eq.) and Et_3N (1.3 cm^3, 9.1 mmol, 9.2 eq.) in CH_3CN (18 cm^3) followed by hydrolysis with 1 mol dm^{-3} aq. TEA hydrogen carbonate (6 cm^3), was accomplished as described for the preparation of the disaccharide H-phosphonate **24**. After work-up, the solution was concentrated and acetonitrile was evaporated off from the residue to give the α,β-(H-phosphonate) **34** [δ_P 0.28 (P$^\alpha$) and 0.74 (P$^\beta$); α : β = 5 : 1]. The residue was dissolved in MeCN (10 cm^3) and H_3PO_3 (461 mg, 5.63 mmol, 17 eq.) was added. The mixture was kept at rt for 72 h, diluted with dichloromethane, and the organic layer was washed successively with water and 0.5 mol dm^{-3} TEA hydrogen carbonate, dried by filtration through cotton wool, and concentrated. FCC [CH_2Cl_2–MeOH–Et_3N, (98.8 : 0.2 : 1) ⟶ (91 : 8 : 1)] of the residue gave, first, the hemiacetal derivative **32** (87 mg, 35% recovery) and then the H-phosphonate **33** (175 mg, 58%) as an amorphous solid; $[\alpha]_D^{24}$ +66 (*c* 1, $CHCl_3$); R_f 0.18 (solvent *D*); ν_{max} (film)/cm^{-1} (*inter alia*) 1727 and 1750 (C=O), 2110 (–N_3); δ_H 1.24 (9 H, t, *J* 7.3, 3 × CH_3CH$_2$N), 1.91, 1.93, 1.97 and 2.02 (12 H, 4 s, 4 × Ac), 2.92 (6 H, q, 3 × CH$_3$CH_2N), 3.40–3.70 (3 H, m, 5′-H and 6′-H_2), 4.23 (1 H, dd, $J_{1,2}$ 2.0, $J_{2,3}$ 3.8, 2-H), 4.30–4.45 (3 H, m, 4-H, 5-H and 6-H^a), 4.58 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 4.67 (1 H, br d, $J_{6a,6b}$ 11.6, 6-H^b), 4.84 (1 H, dd, $J_{3',4'}$ 3.4, $J_{2',3'}$ 10.3, 3′-H), 5.08 (1 H, dd, 2′-H), 5.17 (1 H, br d, 4′-H), 5.66 (1 H, dd, $J_{1,P}$ 8.7, 1-H), 5.79 (1 H, dd, $J_{3,4}$ 9.1, 3-H), 7.01 (1 H, d, $J_{H,P}$ 636.4, HP) and 7.40–8.20 (10 H, m, 2 × Ph); δ_P 0.28; ESMS(−) data: *m*/*z* 805.93 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 806.19; $C_{40}H_{53}N_4O_{18}P$ requires *M*, 908.31).

Decyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2-azido-3,6-di-O-benzoyl-2-deoxy-α-D-mannopyranosyl phosphate, triethylammonium salt 35

A mixture of the H-phosphonate **33** (160 mg, 0.176 mmol) and decan-1-ol (0.07 cm^3, 0.366 mmol, 2.1 eq.) was dried by evaporation of pyridine (3 × 2 cm^3) therefrom. The residue was dissolved in pyridine (1 cm^3), trimethylacetyl chloride (0.06 cm^3, 0.487 mmol, 2.8 eq.) was added, and the mixture was stirred at rt for 30 min, whereafter a freshly prepared solution of iodine (93 mg, 0.366 mmol, 2.8 eq.) in pyridine–water (95 : 5; 2.7 cm^3) was added. After 30 min, dichloromethane 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, (98.9 : 0.1 : 1) ⟶ (87 : 12 : 1)] of the residue gave the phosphodiester **35** (178 mg, 95%) as an amorphous solid; $[\alpha]_D^{24}$ +72 (c 1, $CHCl_3$); R_f 0.33 (solvent *D*); ν_{max} (film)/cm^{-1} (*inter alia*) 1734 and 1754 (C=O), 2110 (–N_3); δ_H 0.88 (3 H, t, *J* 6.9, CH_3CH$_2$CH$_2$), 1.23 (14 H, m, 7 × CH$_2$), 1.33 (9 H, t, *J* 7.3, 3 × CH_3CH$_2$N), 1.60 (2 H, quintet, *J* 6.9, OCH$_2$CH_2CH$_2$), 1.92, 1.94, 1.98 and 2.03 (12 H, 4 s, 4 × Ac), 3.05 (6 H, q, 3 × CH$_3$CH_2N), 3.50–3.75 (3 H, m, 5′-H and 6′-H_2), 3.92 (2 H, m, CH$_2$CH_2OP), 4.31 (1 H, dd, $J_{1,2}$ 2.1, $J_{2,3}$ 3.9, 2-H), 4.35–4.45 (3 H, m, 4-H, 5-H and 6-H^a), 4.58 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.66 (1 H, br d, $J_{6a,6b}$ 11.3, 6-H^b), 4.83 (1 H, dd, $J_{3',4'}$ 3.5, $J_{2',3'}$ 10.4, 3′-H), 5.08 (1 H, dd, 2′-H), 5.17 (1 H, br d, 4′-H), 5.60 (1 H, dd, $J_{1,P}$ 7.7, 1-H), 5.81 (1 H, dd, $J_{3,4}$ 8.9, 3-H) and 7.40–8.20 (10 H, m, 2 × Ph); δ_P −2.66; ESMS(−) data: *m*/*z* 962.04 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 962.34; $C_{50}H_{73}N_4O_{19}P$ requires *M*, 1064.46).

Decyl β-D-galactopyranosyl-(1⟶4)-2-azido-2-deoxy-α-D-mannopyranosyl phosphate, sodium salt 36

To a solution of compound **35** (170 mg, 0.16 mmol) in MeOH (5.0 cm^3) was added 4.6 mol dm^{-3} methanolic NaOMe (0.5 cm^3). The mixture was kept at rt for 4 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 residue was dissolved in water (50 cm^3), treated with Dowex 50W–X4 (Na^+) resin for 19 h and filtered. The filtrate was concentrated to give the phosphodiester **36** (98 mg, quant.) as an amorphous solid; $[\alpha]_D^{24}$ +18 (c 1, MeOH); R_f 0.83 (solvent *E*); ν_{max} (film)/cm^{-1} (*inter alia*) 2114 (–N_3), 3426 (OH); δ_C (D_2O) 14.2, 22.9, 25.9, 29.6 (2 C), 29.8 (2 C), 32.1 (*C*H$_3$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$CH$_2$O), 30.7 (d, $J_{C,P}$ 6.5, *C*H$_2$CH$_2$OP), 60.5 (C-6), 61.1 (C-6′), 64.4 (d, $J_{C,P}$ 8.0, C-2), 66.9 (d, $J_{C,P}$ 5.8, CH$_2$*C*H$_2$OP), 68.8 (C-4′), 69.3 (C-3), 71.3 (C-2′), 72.7 (C-5), 72.9 (C-3′), 75.6 (C-5′), 76.6 (C-4), 94.3 (br s, C-1), 103.5 (C-1′); δ_P −2.12; ESMS(−) data: *m*/*z* 585.74 (100%,

[M − Na]$^-$), (expected *m*/*z*, 586.25; $C_{22}H_{41}N_3NaO_{13}P$ requires *M*, 609.23).

1,6-Anhydro-2-O-benzoyl-3-deoxy-3-fluoro-β-D-mannopyranose 38

To a solution of the diol **37**[20] (2.05 g, 12.5 mmol) and imidazole (2.21 g, 32.5 mmol, 2.6 eq.) in dichloromethane (40 cm^3) was added benzoyl chloride (1.74 cm^3, 15 mmol, 1.2 eq.) and the mixture was stirred for 2.5 h at rt. After the addition of several drops of water, the mixture was diluted with dichloromethane, washed successively with 0.5 mol dm^{-3} aq. HCl, water, and saturated aq. $NaHCO_3$, and concentrated. FCC (toluene–ethyl acetate, 75 : 25) of the residue gave, in order of elution, the known 2,4-di-O-benzoate **40**[20] (0.44 g, 9.5%); the 4-*O-benzoate* **39** (0.45 g, 14%); $[\alpha]_D^{24}$ −153 (*c* 2, $CHCl_3$); mp 142–143 °C (from diethyl ether–hexane); R_f 0.46 (solvent *B*) (Found : C, 58.5; H, 4.9. $C_{13}H_{13}FO_5$ requires C, 58.2; H 4.9%); δ_H 2.97 (1 H, dd, $J_{OH,F}$ 3.6, 2-OH), 3.82 (1 H, dddd, $J_{1,2}$ 2.0, $J_{2,3}$ 4.6, $J_{2,F}$ 23.4, $J_{2,OH}$ 12.3, 2-H), 3.89 (1 H, ddd, $J_{5,6a}$ 5.9, $J_{6a,F}$ 3.5, 6-H^a), 4.18 (1 H, dt, $J_{5,6b} = J_{6b,F}$ = 1.2, $J_{6a,6b}$ 7.8, 6-H^b), 4.75 (1 H, br d, 5-H), 4.88 (1 H, ddt, $J_{1,3} = J_{3,4}$ = 1.8, $J_{3,F}$ 46.9, 3-H), 5.32 (1 H, dt, $J_{4,5}$ 1.8, $J_{4,F}$ 13.1, 4-H), 5.50 (1 H, br s, 1-H) and 7.28–8.30 (5 H, m, Ph); and the required 2-*O-benzoate* **38** (1.53 g, 46%); $[\alpha]_D^{24}$ −106 (*c* 1, $CHCl_3$); mp 109–110 °C (from diethyl ether–hexane); R_f 0.38 (solvent *B*) (Found: C, 58.6; H, 5.0. $C_{13}H_{13}FO_5$ requires C, 58.2; H, 4.9%); δ_H 3.18 (1 H, br s, 4-OH), 3.93 (1 H, ddd, $J_{5,6a}$ 5.9, $J_{6a,F}$ 3.8, 6-H^a), 4.10 (1 H, br d, $J_{4,F}$ 10.2, 4-H), 4.43 (1 H, dt, $J_{5,6b} = J_{6b,F}$ = 1.2, $J_{6a,6b}$ 7.8, 6-H^b), 4.66 (1 H, br d, 5-H), 5.02 (1 H, dddd, $J_{3,4}$ 2.1, $J_{3,F}$ 48.5, 3-H), 5.17 (1 H, ddd, $J_{2,3}$ 4.3, $J_{2,F}$ 25.1, 2-H), 5.64 (1 H, t, $J_{1,2} = J_{1,3}$ = 1.8, 1-H) and 7.38–8.25 (5 H, m, Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1→4)-1,6-anhydro-2-O-benzoyl-3-deoxy-3-fluoro-β-D-mannopyranose 41

The reaction of the alcohol **38** (1.27 g, 4.73 mmol) and acetobromogalactose **19** (2.92 g, 7.1 mmol, 1.5 eq.) in CH_2Cl_2 (40 cm^3) in the presence of AgOTf (2 g, 7.8 mmol, 1.65 eq.) and 2,4,6-collidine (0.84 cm^3, 6.4 mmol, 1.35 eq.) was performed as described for the preparation of the disaccharide **20**. FCC (toluene–ethyl acetate, 75 : 25) afforded the *β-linked disaccharide* **41** (1.36 g, 48%) as an amorphous solid; $[\alpha]_D^{24}$ −64 (*c* 2, $CHCl_3$); R_f 0.49 (solvent *C*) (Found: C, 54.5; H, 5.3. $C_{27}H_{31}FO_{14}$ requires C, 54.2; H, 5.2%); δ_H 1.93, 1.96, 2.03 and 2.12 (12 H, 4 s, 4 × Ac), 3.82 (1 H, ddd, $J_{5,6a}$ 5.9, $J_{6a,F}$ 3.8, 6-H^a), 3.87 (1 H, dt, $J_{5',6a'} = J_{5',6b'}$ = 6.7, 5′-H), 4.01 (1 H, dt, $J_{4,5}$ 1.8, $J_{4,F}$ 12.5, 4-H), 4.04 (1 H, dd, $J_{6a',6b'}$ 11.3, 6′-H^a), 4.11 (1 H, dt, $J_{5,6b} = J_{6b,F}$ = 1.2, $J_{6a,6b}$ 7.7, 6-H^b), 4.12 (1 H, dd, 6′-H^b), 4.53 (1 H, br d, 5-H), 4.63 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 4.94 (1 H, ddd, $J_{2,3}$ 4.3, $J_{2,F}$ 25.5, 2-H), 4.97 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.09 (1 H, dddd, $J_{3,4}$ 1.9, $J_{3,F}$ 48.0, 3-H), 5.19 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.33 (1 H, dd, $J_{4',5'}$ 1.2, 4′-H), 5.52 (1 H, t, $J_{1,2} = J_{1,3}$ = 1.7, 1-H) and 7.33–8.08 (5 H, m, Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1→4)-1,6-di-O-acetyl-2-O-benzoyl-3-deoxy-3-fluoro-α-D-mannopyranose 42

To a solution of the disaccharide **41** (1.25 g, 2.09 mmol) in acetic anhydride (15 cm^3) was added sulfuric acid (0.06 cm^3) at 0 °C. The solution was kept at rt for 2 h, then poured into ice–water, and the mixture was stirred for 2 h. The precipitate formed was filtered off and the filtrate was extracted with dichloromethane (2 × 50 cm^3). A solution of the precipitate in dichloromethane and the combined extracts were washed successively with water, saturated aq. $NaHCO_3$, and water, and concentrated. Crystallization of the residue from ethanol afforded the *hexa-acetate* **42** (1.22 g, 83%); $[\alpha]_D^{24}$ +30 (*c* 2, $CHCl_3$); mp 191–193 °C; R_f 0.54 (solvent *C*) (Found : C, 53.2; H, 5.25. $C_{31}H_{37}FO_{17}$ requires C, 53.1; H, 5.3%); δ_H 1.99, 2.00, 2.09, 2.15 and 2.17 (× 2) (18 H, 5 s, 6 × Ac), 3.93 (1 H, ddd, $J_{5',6a'}$ 6.1, 5′-H), 3.99 (1 H, ddd, $J_{5,6a}$ 4.1, 5-H), 4.10 (1 H, dd, $J_{6a',6b'}$ 11.3, 6′-H^a), 4.18 (1 H, ddd, $J_{4,5}$ 9.8, $J_{4,F}$ 14.9, 4-H), 4.21 (1 H, dd, $J_{6a,6b}$ 12.0, 6-H^a), 4.24 (1 H, dd, $J_{5',6b'}$ 7.0, 6-H^b), 4.42 (1 H, ddd, $J_{5,6b}$ 2.1, $J_{6b,F}$ 1.9, 6-H^b), 4.64 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 5.02 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.17 (1 H, ddd, $J_{3,4}$ 8.6, $J_{3,F}$ 46.9, 3-H), 5.26 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.39 (1 H, dd, $J_{4',5'}$ 1.1, 4′-H), 5.58 (1 H, ddd, $J_{2,3}$ 3.8, $J_{2,F}$ 6.2, 2-H), 6.23 (1 H, dd, $J_{1,2}$ 2.3, $J_{1,F}$ 4.7, 1-H) and 7.43–8.13 (5 H, m, Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1→4)-6-O-acetyl-2-O-benzoyl-3-deoxy-3-fluoro-α-D-mannopyranose 43

To a solution of the 1-O-acetate **42** (960 mg, 1.37 mmol) in acetonitrile (10 cm^3) was added 2 mol dm^{-3} dimethylamine in THF (4.11 cm^3, 8.22 mmol, 6 eq.); the mixture was kept at rt for 3 h and then concentrated. The residue was dissolved in chloroform and the solution was washed successively with 0.5 mol dm^{-3} aq. HCl, water, saturated aq. $NaHCO_3$, and water, and concentrated. FCC (toluene–ethyl acetate, 60 : 40) of the residue gave the *hemiacetal* **43** (790 mg, 88%) as an amorphous solid; $[\alpha]_D^{24}$ +16 (*c* 2, $CHCl_3$); R_f 0.34 (solvent *C*) (Found: C, 52.7; H, 5.5. $C_{29}H_{35}FO_{16}$ requires C, 52.9; H, 5.4%); δ_H 1.99 (× 2), 2.09, 2.13 and 2.17 (15 H, 4 s, 5 × Ac), 3.93 (1 H, ddd, $J_{5',6a'}$ 6.1, 5′-H), 4.10 (1 H, dd, $J_{6a',6b'}$ 11.3, 6′-H^a), 4.08–4.23 (3 H, m, 4-H, 5-H and 6-H^a), 4.21 (1 H, dd, $J_{5',6b'}$ 6.7, 6′-H^b), 4.32 (1 H, br s, 1-OH), 4.49 (1 H, br d, $J_{6a,6b}$ 11.9, 6-H^b), 4.65 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 5.02 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.22 (1 H, ddd, $J_{3,4}$ 7.7, $J_{3,F}$ 47.0, 3-H), 5.25 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.36 (1 H, br s, 1-H), 5.38 (1 H, dd, $J_{4',5'}$ 0.9, 4′-H), 5.56 (1 H, ddd, $J_{1,2}$ 2.1, $J_{2,3}$ 3.7, $J_{2,F}$ 6.7, 2-H) and 7.46–8.11 (5 H, m, Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1→4)-6-O-acetyl-2-O-benzoyl-3-deoxy-3-fluoro-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 44

This compound was prepared by the reaction of the hemiacetal **43** (344 mg, 0.52 mmol) with PCl_3 (0.21 cm^3, 2.39 mmol, 4.6 eq.), imidazole (550 mg, 8.1 mmol, 5.2 eq.) and Et_3N (1.19 cm^3, 8.53 mmol, 5.5 eq.) in CH_3CN (24 cm^3) followed by hydrolysis with 1 mol dm^{-3} TEA hydrogen carbonate (5 cm^3) as described for the preparation of the disaccharide H-phosphonate **24**. FCC [CH_2Cl_2–MeOH–Et_3N, (95 : 4.9 : 0.1) → (85 : 14.9 : 0.1)] gave the H-phosphonate **44** (326 mg, 76%) as an amorphous solid; $[\alpha]_D^{24}$ +21 (*c* 1, $CHCl_3$); R_f 0.14 (solvent *D*); δ_H 1.32 (9 H, t, *J* 7.3, 3 × CH_3CH$_2$N), 1.97, 1.98, 2.07, 2.12 and 2.16 (15 H, 5 s, 5 × Ac), 3.05 (6 H, q, 3 × CH$_3$CH_2N), 3.84 (1 H, $J_{5',6a'}$ 6.1, 5′-H), 4.02 (1 H, dd, $J_{6a',6b'}$ 11.3, 6′-H^a), 4.09 (1 H, dd, $J_{5',6b'}$ 7.1, 6′-H^b), 4.09–4.17 (3 H, m, 4-H, 5-H and 6-H^a), 4.38 (1 H, br d, $J_{6b,6a}$ 10.2, 6-H^b), 4.56 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.93 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.16 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.18 (1 H, ddd, $J_{3,4}$ 8.1, $J_{3,F}$ 47.3, 3-H), 5.30 (1 H, dd, $J_{4',5'}$ 1.0, 4′-H), 5.53 (1 H, ddd, $J_{2,3}$ 3.7, $J_{2,F}$ 6.0, 2-H), 5.65 (1 H, ddd, $J_{1,2}$ 2.2, $J_{1,F}$ 4.9, $J_{1,P}$ 7.0, 1-H), 6.97 (1 H, d, $J_{H,P}$ 638.0, HP) and 7.37–8.02 (5 H, m, Ph); δ_P −0.30; ESMS(−) data: *m*/*z* 720.96 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 721.16; $C_{35}H_{51}FNO_{18}P$ requires *M*, 823.28).

Dec-9-enyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1→4)-6-O-acetyl-2-O-benzoyl-3-deoxy-3-fluoro-α-D-mannopyranosyl phosphate, triethylammonium salt 45

This compound was prepared by condensation of the disaccharide H-phosphonate **44** (287 mg, 0.35 mmol) and dec-9-en-1-ol (0.125 cm^3, 0.7 mmol, 2 eq.) in pyridine (2 cm^3) in the presence of trimethylacetyl chloride (0.11 cm^3, 0.88 mmol, 2.5 eq.) followed by oxidation with iodine (177 mg, 0.7 mmol, 2 eq.) in pyridine–water (95 : 5; 4 cm^3) as described for the synthesis of the phosphodiester **25**. FCC [CH_2Cl_2–MeOH–Et_3N, (95 : 4.9 : 0.1) → (90 : 9.9 : 0.1)] afforded the phosphodiester **45** (261 mg, 77%) as an amorphous solid; $[\alpha]_D^{24}$ +14 (*c* 2, $CHCl_3$); R_f 0.31 (solvent *D*); δ_H (*inter alia*) 1.19 (9 H, t, *J* 7.4, 3 × CH_3CH$_2$N), 1.96, 1.97, 2.06, 2.13 and 2.16 (15 H, 5 s, 5 × Ac),

3.07 (6 H, q, 3 × CH_3CH_2N), 3.85–3.93 (3 H, m, 5′-H and CH_2CH_2OP), 4.10 (1 H, dd, $J_{5',6a'}$ 6.3, $J_{6a',6b'}$ 11.2, 6′-H[a]), 4.16 (1 H, dd, $J_{5',6b'}$ 6.9, 6′-H[b]), 4.16–4.26 (3 H, m, 4-H, 5-H and 6-H[a]), 4.61 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.99 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.23 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.25 (1 H, ddd, $J_{2,3}$ 3.7, $J_{3,4}$ 8.2, $J_{3,F}$ 47.2. 3-H), 5.36 (1 H, dd, $J_{4',5'}$ 0.9, 4′-H), 5.62–5.68 (2 H, m, 1-H and 2-H), 5.79 [1 H, ddt, J(H, CH_2) 6.7, J_{cis} 10.2, J_{trans} 16.9, CH_2=C*H*CH_2] and 7.41–8.08 (5 H, m, Ph); δ_P −2.67; ESMS(−) data: *m*/*z* 874.92 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 875.30; $C_{45}H_{69}FNO_{19}P$ requires *M*, 977.42).

Benzyl 2,3,4-tri-O-benzoyl-α-D-mannopyranoside 47

The *tribenzoate* **47** was prepared from benzyl α-D-mannopyranoside **46** in 60% yield by conventional tritylation (trityl chloride in pyridine) followed by benzoylation (benzoyl chloride in pyridine) and detritylation (80% aq. AcOH), as an amorphous solid; $[\alpha]_D^{24}$ −104 (*c* 2, $CHCl_3$); R_f 0.31 (solvent *A*) (Found: C, 70.3; H, 5.2. $C_{34}H_{30}O_9$ requires C, 70.1; H, 5.2%); δ_H 2.71 (1 H, t, $J_{6,OH}$ 5.3, 6-OH), 3.79 (2 H, m, 6-H_2), 4.11 (1 H, dt, $J_{5,6}$ 3.0, 5-H), 4.73 and 4.87 (2 H, AB q, J_{gem} 12.0, C*H*$_2$Ph), 5.23 (1 H, d, $J_{1,2}$ 1.9, 1-H), 5.77 (1 H, dd, $J_{2,3}$ 3.4, 2-H), 5.88 (1 H, t, $J_{3,4} = J_{4,5}$ = 10.1, 4-H), 6.06 (1 H, dd, 3-H) and 7.15–8.17 (20 H, m, 4 × Ph).

Benzyl 2,3,4-tri-O-benzoyl-6-deoxy-6-fluoro-α-D-mannopyranoside 48

To a solution of the tribenzoate **47** (800 mg, 1.37 mmol) in dichloromethane (10 cm^3) was added DAST (0.27 cm^3, 2.05 mmol, 1.5 eq.) at −25 °C. The mixture was kept at rt overnight and then refluxed for 8 h. Methanol (0.5 cm^3) was added, the mixture was diluted with dichloromethane (100 cm^3), washed successively with saturated aq. $NaHCO_3$ and water, and concentrated. FCC (toluene–ethyl acetate, 98 : 2) of the residue gave the *fluoride* **48** (354 mg, 44%) as an amorphous solid; $[\alpha]_D^{24}$ −111 (*c* 2, $CHCl_3$); R_f 0.76 (solvent *A*) (Found: C, 70.3; H, 5.05. $C_{34}H_{29}FO_8$ requires C, 69.9; H, 5.0%); δ_H 4.23 (1 H, dddd, $J_{5,6a}$ 2.3, $J_{5,F}$ 22.9, 5-H), 4.49 (1 H, ddd, $J_{6a,6b}$ 10.4, $J_{6a,F}$ 47.5, 6-H[a]), 4.55 (1 H, ddd, $J_{5,6b}$ 4.7, $J_{6b,F}$ 47.5, 6-H[b]), 4.62 and 4.78 (2 H, AB q, J_{gem} 11.9, C*H*$_2$Ph), 5.11 (1 H, d, $J_{1,2}$ 1.9, 1-H), 5.67 (1 H, dd $J_{2,3}$ 3.0, 2-H), 5.82 (1 H, t, $J_{3,4} = J_{4,5}$ = 10.1, 4-H), 5.88 (1 H, dd, 3-H) and 7.05–8.20 (20 H, m, 4 × Ph); δ_F −231.0 (dt, *J* 22.9 and 47.5).

Benzyl 6-deoxy-6-fluoro-2,3-O-isopropylidene-α-D-mannopyranoside 49

To a solution of compound **48** (278 mg, 0.48 mmol) in MeOH (5 cm^3) was added 4.6 mol dm^{-3} methanolic MeONa (0.22 cm^3) and the mixture was kept at rt for 2 h. The solution was deionized with Dowex 50W-X4 (H^+), the resin was filtered off and washed with methanol, and the filtrate was concentrated. The residue was dissolved in acetone (5 cm^3), 2,2-dimethoxypropane (0.5 cm^3) and TsOH·H_2O (20 mg) were added, and the mixture was stirred for 15 min at rt. After neutralization with a few drops of Et_3N, the mixture was concentrated. FCC (toluene–ethyl acetate, 92 : 8) of the residue afforded the *alcohol derivative* **49** (128 mg, 85%); $[\alpha]_D^{24}$ +60 (*c* 1, $CHCl_3$); mp 52–54 °C (from hexane); R_f 0.34 (solvent *A*) (Found: C, 61.8; H, 6.8. $C_{16}H_{21}FO_5$ requires C, 61.5; H, 6.8%); δ_H 1.38 and 1.55 (6 H, 2 s, Me_2C), 3.48 (1 H, d, $J_{4,OH}$ 4.3, 4-OH), 3.75 (1 H, ddd, $J_{3,4}$ 6.3, 4-H), 3.85 (1 H, dddd, $J_{4,5}$ 9.9, $J_{5,F}$ 24.5, 5-H), 4.22 (2 H, m, 2-H and 3-H), 4.58 and 4.77 (2 H, AB q, J_{gem} 11.7, C*H*$_2$Ph), 4.64 (1 H, ddd, $J_{5,6a}$ 2.2, $J_{6a,6b}$ 10.2, $J_{6a,F}$ 47.5, 6-H[a]), 4.70 (1 H, ddd, $J_{5,6b}$ 4.1, $J_{6b,F}$ 47.5, 6-H[b]), 5.18 (1 H, s, 1-H) and 7.28–7.43 (5 H, m, Ph).

Benzyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-6-deoxy-6-fluoro-2,3-O-isopropylidene-α-D-mannopyranoside 50

The reaction of the derivative **49** (431 mg, 1.38 mmol) and acetobromogalactose **19** (850 mg, 2.07 mmol, 1.5 eq.) in CH_2Cl_2 (18 cm^3) in the presence of silver triflate (610 mg, 2.38 mmol, 1.72 eq.) and 2,4,6-collidine (0.245 cm^3, 1.86 mmol, 1.35 eq.) was performed as described for the preparation of the disaccharide **20**. FCC (toluene–ethyl acetate, 9 : 1) afforded the *β-linked disaccharide* **50** (712 mg, 80%); $[\alpha]_D^{24}$ +37 (*c* 2, $CHCl_3$); mp 121–123 °C (from ethyl acetate–hexane); R_f 0.57 (solvent *B*) (Found: C, 56.0; H, 6.1. $C_{30}H_{39}FO_{14}$ requires C, 56.1; H, 6.1%); δ_H 1.36 and 1.56 (6 H, 2 s, Me_2C), 2.01, 2.06, 2.08 and 2.17 (12 H, 4 s, 4 × Ac), 3.73 (1 H, dddd, $J_{5,6a}$ 1.5, $J_{5,F}$ 26.2, 5-H), 3.83 (1 H, dd, $J_{4,5}$ 10.1, 4-H), 3.96 (1 H, dt, $J_{5',6'}$ 6.3, 5′-H), 4.18 (1 H, d, $J_{2,3}$ 5.8, 2-H), 4.18 (2 H, d, 6′-H_2), 4.43 (1 H, ddd, $J_{6a,6b}$ 10.2, $J_{6a,F}$ 48.5, 6-H[a]), 4.44 (1 H, dd, $J_{3,4}$ 7.5, 3-H), 4.57 (1 H, ddd, $J_{5,6b}$ 2.7, $J_{6b,F}$ 48.5, 6-H[b]), 4.56 and 4.68 (2 H, AB q, J_{gem} 11.8, C*H*$_2$Ph), 4.75 (1 H, d, $J_{1',2'}$ 8.1, 1′-H), 5.06 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.17 (1 H, s, 1-H), 5.24 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.41 (1 H, dd, $J_{4',5'}$ 1.1, 4′-H) and 7.29–7.40 (5 H, m, Ph).

Benzyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,3-di-O-benzoyl-6-deoxy-6-fluoro-α-D-mannopyranoside 51

A solution of the isopropylidene derivative **50** (800 mg, 1.25 mmol) and pyridinium perchlorate (500 mg) in 90% aq. acetonitrile (15 cm^3) was heated at 75–80 °C for 4 h and then concentrated. The residue was dissolved in chloroform (100 cm^3), and the solution was washed with water, dried (Na_2SO_4), and concentrated. The residue was subjected to benzoylation with benzoyl chloride (1 cm^3) in pyridine (10 cm^3) for 2 h at rt followed by standard aqueous work-up. FCC (toluene–ethyl acetate, 85 : 15) produced the *disaccharide* **51** (910 mg, 90%) as an amorphous solid; $[\alpha]_D^{24}$ −31 (*c* 2, $CHCl_3$); R_f 0.38 (solvent *B*) (Found: C, 60.8; H, 5.3. $C_{41}H_{43}FO_{16}$ requires C, 60.7; H, 5.35%); δ_H 1.85, 1.97, 2.04 and 2.10 (12 H, 4 s, 4 × Ac), 3.34 (1 H, ddd, $J_{5',6a'}$ 5.6, 5′-H), 3.43 (1 H, dd, $J_{6a',6b'}$ 10.9, 6′-H[a]), 3.78 (1 H, dd, $J_{5',6b'}$ 8.2, 6′-H[b]), 3.95 (1 H, dddd, $J_{5,6a}$ 0.9, $J_{5,F}$ 31.6, 5-H), 4.45 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.7, 4-H), 4.55 (1 H, ddd, $J_{6a,6b}$ 10.5, $J_{6a,F}$ 47.9, 6-H[a]), 4.68 and 4.76 (2 H, AB q, J_{gem} 12.0, C*H*$_2$Ph), 4.70 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.71 (1 H, ddd, $J_{5,6b}$ 2.2, $J_{6b,F}$ 47.9, 6-H[b]), 4.91 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.10 (1 H, d, $J_{1,2}$ 1.9, 1-H), 5.16 (1 H, dd, $J_{2',3'}$ 10.3, 2′-H), 5.17 (1 H, dd, $J_{4',5'}$ 1.0, 4′-H), 5.70 (1 H, dd, $J_{2,3}$ 3.6, 2-H), 5.82 (1 H, dd, 3-H) and 7.17–8.05 (15 H, m, 3 × Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,3-di-O-benzoyl-6-deoxy-6-fluoro-α-D-mannopyranose 52

A solution of the benzyl glycoside **51** (600 mg, 0.74 mmol) in a mixture of MeOH (20 cm^3) and ethyl acetate (5 cm^3) containing 20% $Pd(OH)_2$/C (600 mg) was stirred under a slight overpressure of hydrogen at rt for 24 h, filtered through a Celite pad, and concentrated. FCC (toluene–ethyl acetate, 65 : 35) of the residue gave the *hemiacetal* **52** (481 mg, 90%) as an amorphous solid, $[\alpha]_D^{24}$ −78 (*c* 1, $CHCl_3$); R_f 0.16 (solvent *B*) (Found: C, 57.1; H, 5.3. $C_{34}H_{37}FO_{16}$ requires C, 56.7; H, 5.2%); δ_H 1.84, 1.97, 2.05 and 2.10 (12 H, 4 s, 4 × Ac), 3.41 (1 H, ddd, $J_{5',6a'}$ 5.7, 5′-H), 3.46 (1 H, dd, $J_{6a',6b'}$ 10.4, 6′-H[a]), 3.77 (1 H, dd, $J_{5',6b'}$ 7.4, 6′-H[b]), 3.95 (1 H, br d, $J_{1,OH}$ 3.0, 1-OH), 4.26 (1 H, br dd, $J_{5,F}$ 31.4, 5-H), 4.46 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.7, 4-H), 4.67 (1 H, br dd, $J_{5,6a}$ <1, $J_{6a,6b}$ 10.6, $J_{6a,F}$ 48.6, 6-H[a]), 4.71 (1 H, d, $J_{1',2'}$ 8.0, 1′-H), 4.78 (1 H, ddd, $J_{5,6b}$ 2.2, $J_{6b,F}$ 48.6, 6-H[b]), 4.93 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.17 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.18 (1 H, dd, $J_{4',5'}$ 0.9, 4′-H), 5.43 (1 H, br s, 1-H), 5.67 (1 H, dd, $J_{1,2}$ 1.9, $J_{2,3}$ 3.5, 2-H), 5.86 (1 H, dd, 3-H) and 7.17–8.10 (10 H, m, 2 × Ph).

2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,3-di-O-benzoyl-6-deoxy-6-fluoro-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 53

This compound was prepared by the reaction of the hemiacetal **52** (285 mg, 0.40 mmol) with PCl_3 (0.157 cm^3, 1.8 mmol, 4.5 eq.), imidazole (415 mg, 6.1 mmol, 5.1 eq.) and Et_3N (0.89 cm^3,

6.4 mmol, 5.3 eq.) in CH_3CN (16 cm^3) followed by hydrolysis with 1 mol dm^{-3} TEA hydrogen carbonate (5 cm^3) as described for the preparation of the disaccharide H-phosphonate **24**. FCC [CH_2Cl_2–MeOH–Et_3N, (95 : 4.9 : 0.1) ⟶ (85 : 14.9 : 0.1)] afforded the H-phosphonate **53** (300 mg, 86%) as an amorphous solid; $[\alpha]_D^{24}$ −46 (*c* 2, $CHCl_3$); R_f 0.23 (solvent *D*); δ_H 1.37 (9 H, t, *J* 7.1, 3 × CH_3CH$_2$N), 1.79, 1.95, 2.02 and 2.08 (12 H, 4 s, 4 × Ac), 3.10 (6 H, q, 3 × CH$_3$CH_2N), 3.39 (1 H, ddd, $J_{5',6a'}$ 5.7, 5′-H), 3.46 (1 H, dd, $J_{6a',6b'}$ 10.5, 6′-H^a), 3.76 (1 H, dd, $J_{5',6b'}$ 7.6, 6′-H^b), 4.24 (1 H, br dd, $J_{5,F}$ 31.6, 5-H), 4.44 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.8, 4-H), 4.66 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.67 (1 H, br dd, $J_{5,6a}$ <1, $J_{6a,6b}$ 10.4, $J_{6a,F}$ 48.5, 6-H^a), 4.75 (1 H, ddd, $J_{5,6b}$ 2.0, $J_{6b,F}$ 48.5, 6-H^b), 4.89 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.14 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.17 (1 H, dd, $J_{4',5'}$ 1.1, 4′-H), 5.68 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 5.76 (1 H, dd, $J_{1,2}$ 2.1, $J_{1,P}$ 9.2, 1-H), 5.79 (1 H, dd, 3-H), 7.03 (1 H, d, $J_{H,P}$ 636.0, HP) and 7.30–8.05 (10 H, m, 2 × Ph); δ_P 1.48; ESMS(−) data: *m*/*z* 782.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 783.18; $C_{40}H_{53}FNO_{18}P$ requires *M*, 885.30).

Dec-9-enyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1⟶4)-2,3-di-O-benzoyl-6-deoxy-6-fluoro-α-D-mannopyranosyl phosphate, triethylammonium salt 54

This compound was prepared by condensation of the disaccharide H-phosphonate **53** (265 mg, 0.30 mmol) and dec-9-en-1-ol (0.11 cm^3, 0.6 mmol, 2.0 eq.) in pyridine (3 cm^3) in the presence of trimethylacetyl chloride (0.09 cm^3, 0.75 mmol, 2.5 eq.) followed by oxidation with iodine (152 mg, 0.6 mmol, 2.0 eq.) in pyridine–water (95 : 5; 4 cm^3) as described for the synthesis of the phosphodiester **25**. FCC [CH_2Cl_2–MeOH–Et_3N, (95 : 4.9 : 0.1) ⟶ (91 : 8.9 : 0.1)] gave the phosphodiester **54** (230 mg, 74%) as an amorphous solid; $[\alpha]_D^{24}$ −47 (*c* 1, $CHCl_3$); R_f 0.32 (solvent *D*); δ_H (*inter alia*) 1.29 (9 H, t, *J* 7.3, 3 × CH_3CH$_2$N), 1.71, 1.87, 1.94 and 2.00 (12 H, 4 s, 4 × Ac), 3.03 (6 H, q, 3 × CH$_3$CH_2N), 3.31 (1 H, ddd, $J_{5',6a'}$ 5.7, 5′-H), 3.38 (1 H, dd, $J_{6a',6b'}$ 10.8, 6′-H^a), 3.69 (1 H, dd, $J_{5',6b'}$ 7.9, 6′-H^b), 3.88 (2 H, m, CH$_2$CH_2OP), 4.20 (1 H, br dd, $J_{5,F}$ 31.7, 5-H), 4.35 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.7, 4-H), 4.58 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 4.59 (1 H, br dd, $J_{6a,6b}$ 10.4, $J_{6a,F}$ 48.5, 6-H^a), 4.68 (1 H, ddd, $J_{5,6b}$ 2.0, $J_{6b,F}$ 48.5, 6-H^b), 4.82 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.06 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.09 (1 H, dd, $J_{4',5'}$ 1.0, 4′-H), 5.62–5.80 (4 H, m, 1-H, 2-H and 3-H, and CH$_2$=CHCH$_2$) and 7.23–7.97 (10 H, m, 2 × Ph); δ_P −1.54; ESMS(−) data: *m*/*z* 937.0 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 937.31; $C_{50}H_{71}FNO_{19}P$ requires *M*, 1039.43).

1,4-Di-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-α-D-galactopyranose 56

To a solution of methyl 2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactopyranoside[23] **55** (560 mg, 1.39 mmol) in pyridine (5 cm^3) was added acetic anhydride (2.5 cm^3); the mixture was kept at rt overnight and then concentrated. The residue was dissolved in dichloromethane (100 cm^3) and the solution was washed successively with 0.5 mol dm^{-3} aq. HCl and water, and concentrated. To a solution of the residue in acetic anhydride (10 cm^3) was added sulfuric acid (0.08 cm^3) at 0 °C. The solution was kept at 0 °C for 30 min and at rt for 4 h, then poured into ice–water, and the mixture was stirred for 2 h. The precipitate formed was filtered off, then dissolved in dichloromethane (100 cm^3), and the solution was washed successively with saturated aq. $NaHCO_3$ and water, and concentrated. Crystallization of the residue from ethanol gave the *diacetate* **56** (533 mg, 81%); $[\alpha]_D^{24}$ +150 (*c* 2, $CHCl_3$); mp 174–175 °C; R_f 0.47 (solvent *A*) (Found: C, 61.1; H, 4.9. $C_{24}H_{23}FO_9$ requires C, 60.8; H, 4.9%); δ_H 2.19 and 2.21 (6 H, 2 s, 2 × Ac), 4.38–4.66 (3 H, m, 5-H and 6-H$_2$), 5.82–5.85 (3 H, m, 2-H, 3-H and 4-H), 6.65 (1 H, d, $J_{1,2}$ 2.1, 1-H) and 7.36–7.97 (10 H, m, 2 × Ph); δ_C (*inter alia*) 67.6, 68.6 (C-2 and C-3), 68.2 (d, $J_{4,F}$ 5.2, C-4), 70.1 (d, $J_{5,F}$ 23.5, C-5), 81.3 (d, $J_{6,F}$ 172.4, C-6) and 90.2 (C-1).

Benzyl 6-O-benzoyl-2,3-O-isopropylidene-α-D-mannopyranoside 59

*Benzyl 2,3-O-isopropylidene-*α*-*D*-mannopyranoside* **58** (735 mg, 2.37 mmol) {prepared in 72% yield from benzyl α-D-mannopyranoside **46** and 2,2-dimethoxypropane followed by controlled hydrolysis, $[\alpha]_D^{20}$ +63 (*c* 1, $CHCl_3$), mp 81–82 °C (from diethyl ether–hexane) (Found: C, 61.7; H, 7.2. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.15%) as described for the preparation[24] of methyl 2,3-O-isopropylidene-α-D-mannopyranoside} and benzoyl cyanide (315 mg, 2.40 mmol, 1.01 eq.), along with a few drops of Et_3N, were stirred in acetonitrile (20 cm^3) for approximately 30 min. When TLC (ethyl acetate) indicated the reaction was complete, the solution was diluted with methanol (10 cm^3) and stirred for a further 30 min, after which the solution was concentrated. A further portion of methanol (5 cm^3) was evaporated from the residue. FCC of the residue (toluene–ethyl acetate, 80 : 20) gave the *monobenzoate* **59** (805 mg, 82%), which crystallized on drying in vacuum over $CaCl_2$; $[\alpha]_D^{24}$ +14 (*c* 1, $CHCl_3$); mp 57–60 °C; R_f 0.31 (solvent *B*) (Found: C, 66.9; H, 6.3. $C_{23}H_{26}O_7$ requires C, 66.65; H, 6.3%); δ_H 1.32 and 1.46 (6 H, 2 s, Me_2C), 3.65 (1 H, ddd, $J_{3,4}$ 6.5, $J_{4,OH}$ 3.0, 4-H), 3.95 (1 H, ddd, $J_{4,5}$ 9.7, 5-H), 4.20 (2 H, m, 2-H and 3-H), 4.50 (1 H, dd, $J_{5,6a}$ 2.7, $J_{6a,6b}$ 12.0, 6-H^a), 4.53 and 4.75 (2 H, AB q, J_{gem} 11.7, CH_2Ph), 4.68 (1 H, dd, $J_{5,6b}$ 5.4, 6-H^b), 5.12 (1 H, s, 1-H) and 7.20–8.00 (10 H, m, 2 × Ph).

Benzyl 4-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactopyranosyl-(1⟶4)-6-O-benzoyl-2,3-O-isopropylidene-α-D-mannopyranoside 60

To a solution of the diacetate **56** (660 mg, 1.39 mmol) in a mixture of acetic acid (9 cm^3) and acetic anhydride (1 cm^3) was added a 33% solution of HBr in AcOH at 0 °C. The mixture was kept at rt for 4 h, diluted with dichloromethane (100 cm^3), washed successively with ice-cold water, cold saturated aq. $NaHCO_3$ and water, dried by filtration through cotton wool, and concentrated to give the galactosyl bromide **57** (686 mg, quant.) [R_f 0.61 (solvent *A*); δ_H 2.19 (3 H, s, Ac), 4.56 (1 H, ddd, $J_{6a,6b}$ 10.0, $J_{6a,F}$ 46.2, 6-H^a), 4.60 (1 H, ddd, $J_{6b,F}$ 46.2, 6-H^b), 4.74 (1 H, ddt, $J_{5,6a} = J_{5,6b}$ = 5.5, $J_{5,F}$ 15.3, 5-H), 5.62 (1 H, dd, $J_{2,3}$ 10.4, 2-H), 5.84 (1 H, dd, $J_{4,5}$ 1.3, 4-H), 5.91 (1 H, dd, $J_{3,4}$ 3.3, 3-H), 6.90 (1 H, d, $J_{1,2}$ 4.0, 1-H) and 7.30–8.07 (10 H, m, 2 × Ph)].

The reaction of the bromide **57** (664 mg, 1.34 mmol, 1.11 eq.) and the acceptor **59** (500 mg, 1.21 mmol) in CH_2Cl_2 (18 cm^3) in the presence of silver triflate (396 mg, 1.54 mmol, 1.27 eq.) and 2,4,6-collidine (0.16 cm^3, 1.21 mmol, 1.0 eq.) was performed as described for the preparation of the disaccharide **20**. FCC (toluene–ethyl acetate, 93 : 7) afforded the *β-linked disaccharide* **60** (884 mg, 88%) as an amorphous solid; $[\alpha]_D^{24}$ +82 (*c* 2, $CHCl_3$); R_f 0.43 (solvent *A*) (Found: C, 65.2; H, 5.4. $C_{45}H_{45}FO_{14}$ requires C, 65.2; H, 5.5%); δ_H 1.39 and 1.60 (6 H, 2 s, Me_2C), 2.16 (3 H, s, Ac), 3.91–4.02 (2 H, m, 4-H and 5-H), 4.10 (1 H, dddd, $J_{5',6a'}$ 5.3, $J_{5',F}$ 13.6, 5′-H), 4.23 (1 H, d, $J_{2,3}$ 6.1, 2-H), 4.27 (1 H, dd, $J_{5,6a}$ 4.6, $J_{6a,6b}$ 11.9, 6-H^a), 4.49 and 4.69 (2 H, AB q, J_{gem} 11.8, CH_2Ph), 4.51 (1 H, m, 3-H), 4.52 (1 H, ddd, $J_{6a',6b'}$ 9.6, $J_{6a',F}$ 46.3, 6′-H^a), 4.54 (1 H, dd, $J_{5,6b}$ 1.5, 6-H^b), 4.62 (1 H, ddd, $J_{5',6b'}$ 6.4, $J_{6b',F}$ 46.3, 6′-H^b), 4.99 (1 H, d, $J_{1',2'}$ 8.1, 1′-H), 5.10 (1 H, s, 1-H), 5.44 (1 H, dd, $J_{3',4'}$ 3.5, 3′-H), 5.69 (1 H, dd, $J_{4',5'}$ 1.1, 4′-H), 5.76 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H) and 7.20–7.98 (20 H, m, 4 × Ph).

Benzyl 4-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactopyranosyl-(1⟶4)-2,3,6-tri-O-benzoyl-α-D-mannopyranoside 61

This compound was prepared by the reaction of the isopropylidene derivative **60** (802 mg, 0.97 mmol) and pyridinium perchlorate (500 mg) in 90% aq. acetonitrile (15 cm^3) followed by conventional benzoylation with benzoyl chloride (1 cm^3)

in pyridine (10 cm^3) as described for the preparation of the disaccharide **51**. FCC (toluene–ethyl acetate, 95 : 5) gave the *dibenzoate* **61** (938 mg, 97%); $[\alpha]_D^{24}$ +71 (*c* 2, $CHCl_3$); mp 151–153 °C (from ethyl acetate–hexane); R_f 0.50 (solvent *A*) (Found: C, 67.4; H, 4.9. $C_{56}H_{49}FO_{16}$ requires C, 67.5; H, 4.95%); δ_H 1.94 (3 H, s, Ac), 3.67 (1 H, dddd, $J_{5',6a'}$ 6.6, $J_{5',F}$ 11.7, 5′-H), 3.90 (1 H, ddd, $J_{6a',6b'}$ 9.6, $J_{6a',F}$ 46.7, 6′-H[a]), 4.11 (1 H, ddd, $J_{5',6b'}$ 5.4, $J_{6b',F}$ 46.7, 6′-H[b]), 4.15 (1 H, ddd, $J_{5,6a}$ 3.3, 5-H), 4.45 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H[a]), 4.63 and 4.77 (2 H, AB q, J_{gem} 12.0, CH_2Ph), 4.66 (1 H, dd, $J_{5,6b}$ 1.9, 6-H[b]), 4.67 (1 H, t, $J_{3,4} = J_{4,5} = 9.8$, 4-H), 4.92 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.07 (1 H, d, $J_{1,2}$ 1.9, 1-H), 5.26 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.45 (1 H, dd, $J_{4',5'}$ 1.0, 4′-H), 5.65 (1 H, dd, $J_{2',3'}$ 10.5, 2′-H), 5.68 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 5.90 (1 H, dd, 3-H) and 7.18–8.10 (30 H, m, 6 × Ph).

4-O-Acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galacto-pyranosyl-(1⟶4)-2,3,6-tri-O-benzoyl-α-D-mannopyranose 62

A solution of the benzyl glycoside **61** (890 mg, 0.89 mmol) in a mixture of THF and MeOH (1 : 1; 15 cm^3) containing 20% $Pd(OH)_2/C$ (400 mg) was stirred under a slight overpressure of hydrogen at rt for 16 h. More catalyst (400 mg) was added and stirring was continued for another 24 h. The mixture was filtered through a Celite pad and the filtrate was concentrated. FCC (toluene–ethyl acetate, 85 : 15) of the residue gave the *hemiacetal* **62** (652 mg, 81%); $[\alpha]_D^{24}$ +58 (*c* 2, $CHCl_3$); mp 245–247 °C; R_f 0.14 (solvent *A*) (Found: C, 65.0; H, 4.9. $C_{49}H_{43}FO_{16}$ requires C, 64.9; H, 4.8%); δ_H 1.95 (3 H, s, Ac), 3.70 (1 H, dddd, $J_{5',6a'}$ 6.7, $J_{5',F}$ 11.7, 5′-H), 3.92 (1 H, ddd, $J_{6a',6b'}$ 9.6, $J_{6a',F}$ 46.7, 6′-H[a]), 3.98 (1 H, d, $J_{1,OH}$ 4.1, 1-OH), 4.12 (1 H, ddd, $J_{5',6b'}$ 5.3, $J_{6b',F}$ 46.7, 6′-H[b]), 4.36 (1 H, ddd, $J_{5,6a}$ 2.8, 5-H), 4.45 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H[a]), 4.69 (1 H, t, $J_{3,4} = J_{4,5} = 9.7$, 4-H), 4.72 (1 H, dd, $J_{5,6b}$ 1.9, 6-H[b]), 4.94 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.28 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.41 (1 H, dd, $J_{1,2}$ 1.9, 1-H), 5.46 (1 H, dd, 4′-H), 5.65 (1 H, dd, $J_{2',3'}$ 10.1, 2′-H), 5.65 (1 H, dd, $J_{2,3}$ 3.4, 2-H), 5.94 (1 H, dd, 3-H) and 7.20–8.12 (25 H, m, 5 × Ph).

4-O-Acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galacto-pyranosyl-(1⟶4)-2,3,6-tri-O-benzoyl-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 63

This compound was prepared by the reaction of the hemiacetal **62** (357 mg, 0.39 mmol) with PCl_3 (0.157 cm^3, 1.8 mmol, 4.6 eq.), imidazole (415 mg, 6.1 mmol, 5.2 eq.) and Et_3N (0.89 cm^3, 6.4 mmol, 5.5 eq.) in CH_3CN (16 cm^3) followed by hydrolysis with 1 mol dm^{-3} TEA hydrogen carbonate (5 cm^3) as described for the preparation of the disaccharide H-phosphonate **24**. FCC [CH_2Cl_2–MeOH–Et_3N, (95 : 4.9 : 0.1) ⟶ (85 : 14.9 : 0.1)] afforded the H-phosphonate **63** (368 mg, 88%) as an amorphous solid; $[\alpha]_D^{24}$ +48 (*c* 2, $CHCl_3$); R_f 0.28 (solvent *D*); δ_H 1.25 (9 H, t, *J* 7.4, 3 × CH_3CH_2N), 1.84 (3 H, s, Ac), 2.99 (6 H, q, 3 × CH_3CH_2N), 3.69 (1 H, dddd, $J_{5',6a'}$ 6.5, $J_{5',F}$ 11.9, 5′-H), 3.81 (1 H, ddd, $J_{6a',6b'}$ 9.6, $J_{6a',F}$ 46.8, 6′-H[a]), 3.97 (1 H, ddd, $J_{5',6b'}$ 5.4, $J_{6b',F}$ 46.8, 6′-H[b]), 4.29 (1 H, ddd, $J_{5,6a}$ 3.1, 5-H), 4.40 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H[a]), 4.53 (1 H, t, $J_{3,4} = J_{4,5} = 9.4$, 4-H), 4.55 (1 H, dd, $J_{5,6b}$ 1.8, 6-H[b]), 4.80 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.15 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.35 (1 H, dd, $J_{4',5'}$ 1.0, 4′-H), 5.53 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.57 (1 H, dd, $J_{2,3}$ 3.4, 2-H), 5.66 (1 H, dd, $J_{1,2}$ 2.0, $J_{1,P}$ 8.9, 1-H), 5.81 (1 H, dd, 3-H), 6.93 (1 H, d, $J_{H,P}$ 638.0, HP) and 7.12–7.98 (25 H, m 5 × Ph); δ_P 1.51; ESMS(−) data: *m*/*z* 968.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 969.22; $C_{55}H_{59}FNO_{18}P$ requires *M*, 1071.35).

Dec-9-enyl 4-O-acetyl-2,3-di-O-benzoyl-6-deoxy-6-fluoro-β-D-galactopyranosyl-(1⟶4)-2,3,6-tri-O-benzoyl-α-D-manno-pyranosyl phosphate, triethylammonium salt 64

This compound was prepared by condensation of the disaccharide H-phosphonate **63** (338 mg, 0.32 mmol) and dec-9-en-1-ol (0.114 cm^3, 0.64 mmol, 2.0 eq.) in pyridine (2.5 cm^3) in the presence of trimethylacetyl chloride (0.1 cm^3, 0.8 mmol, 2.5 eq.) followed by oxidation with iodine (163 mg, 0.64 mmol, 2.0 eq.) in pyridine–water (95 : 5; 4 cm^3) as described for the synthesis of the phosphodiester **25**. FCC [CH_2Cl_2–MeOH–Et_3N, (97 : 2.9 : 0.1) ⟶ (91 : 8.9 : 0.1)] gave the phosphodiester **64** (285 mg, 74%) as an amorphous solid; $[\alpha]_D^{24}$ +41 (*c* 1, $CHCl_3$); R_f 0.39 (solvent *D*); δ_H (*inter alia*) 1.19 (9 H, t, *J* 7.3, 3 × CH_3CH_2N), 1.84 (3 H, s, Ac), 2.89 (6 H, q, 3 × CH_3CH_2N), 3.56 (1 H, dddd, $J_{5',6a'}$ 6.5, $J_{5',F}$ 11.8, 5′-H), 3.81 (1 H, ddd, $J_{6a',6b'}$ 9.6, $J_{6a',F}$ 47.8, 6′-H[a]), 3.88 (2 H, m, CH_2CH_2OP), 3.97 (1 H, ddd, $J_{5',6b'}$ 5.4, $J_{6b',F}$ 47.8, 6′-H[b]), 4.32 (1 H, ddd, $J_{5,6a}$ 2.9, 5-H), 4.40 (1 H, dd, $J_{6a,6b}$ 12.3, 6-H[a]), 4.54 (1 H, dd, $J_{5,6b}$ 1.9, 6-H[b]), 4.54 (1 H, t, $J_{3,4} = J_{4,5} = 9.7$, 4-H), 4.79 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.14 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.34 (1 H, dd, $J_{4',5'}$ 0.9, 4′-H), 5.53 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.59 (1 H, dd, $J_{1,2}$ 2.1, $J_{1,P}$ 7.9, 1-H), 5.62 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 5.72 [1 H, ddt, *J*(H, CH_2) 6.7, J_{cis} 10.2, J_{trans} 17.0, CH_2=C*H*CH_2], 5.82 (1 H, dd, 3-H) and 7.12–7.96 (25 H, m, 5 × Ph); δ_P −1.42; ESMS(−) data: *m*/*z* 1122.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 1123.35; $C_{65}H_{77}FNO_{19}P$ requires *M*, 1225.48).

2,3,4-Tri-O-benzoyl-β-D-galactopyranosyl-(1⟶4)-1,2,3,6-tetra-O-benzoyl-α-D-mannopyranose 66

A solution of HCl in MeOH [prepared at 0 °C from acetyl chloride (0.6 cm^3) and methanol (14 cm^3)] was added to a solution of disaccharide **65**[4] (1.60 g, 1.73 mmol) in dichloromethane (5 cm^3); the resulting solution was kept at rt for 25 h, concentrated, and pyridine (3 × 10 cm^3) was evaporated off from the residue. The residue was dissolved in pyridine (15 cm^3), *p*,*p*′-dimethoxytriphenylmethyl chloride (820 mg, 2.42 mmol, 1.4 eq.) was added, and the mixture was stirred at rt for 35 h before benzoyl chloride (1.2 cm^3, 7.05 mmol, 1.4 eq.) was also added to the stirred mixture at 0 °C. After 10 h at 20 °C, the reaction mixture was diluted with dichloromethane and washed successively with saturated aq. $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The residue was dissolved in dichloromethane (70 cm^3), and 2% trifluoroacetic acid in dichloromethane (70 cm^3) was added at 0 °C. After 2 min, the solution was washed in turn with saturated aq. $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. FCC [toluene-ethyl acetate, (90 : 10) ⟶ (80 : 20)] of the residue gave the *disaccharide derivative* **66** (1.22 g, 76%) as an amorphous solid; $[\alpha]_D^{24}$ +112 (*c* 1, $CHCl_3$); R_f 0.34 (solvent *B*) (Found : C, 67.8; H, 4.8. $C_{61}H_{50}O_{18}\cdot 1/2H_2O$ requires C, 67.8; H, 4.85%); δ_H 3.07 (1 H, dd, $J_{5',6a'}$ 7.1, $J_{6a',6b'}$ 11.9, 6′-H[a]), 3.19 (1 H, dd, $J_{5',6b'}$ 6.1, 6′-H[b]), 3.64 (1 H, br dd, 5′-H), 4.29 (1 H, dt, $J_{4,5}$ 9.7, 5-H), 4.53 (1 H, dd, $J_{5,6a}$ 2.7, $J_{6a,6b}$ 12.3, 6-H[a]), 4.65 (1 H, dd, $J_{5,6b}$ 2.7, 6-H[b]), 4.69 (1 H, t, $J_{3,4} = J_{4,5} = 11.5$, 4-H), 5.02 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.44 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.62 (1 H, br d, 4′-H), 5.85 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.86 (1 H, dd, $J_{2,3}$ 3.4, 2-H), 6.04 (1 H, dd, 3-H), 6.54 (1 H, d, $J_{1,2}$ 2.3, 1-H) and 7.10–8.20 (35 H, m, 7 × Ph).

6-Azido-2,3,4-tri-O-benzoyl-6-deoxy-β-D-galactopyranosyl-(1⟶4)-1,2,3,6-tetra-O-benzoyl-α-D-mannopyranose 67

To a stirred solution of the alcohol **66** (900 mg, 0.84 mmol), triphenylphosphine (2.62 g, 10 mmol, 12 eq.) and NaN_3 (1.5 g, 23 mmol, 27 eq.) in DMF (20 cm^3) was added tetrachloromethane (4 cm^3). The mixture was stirred at rt for 36 h, diluted with water, and extracted with dichloromethane (3 × 50 cm^3). The combined organic extracts were washed successively with water and brine, dried (Na_2SO_4), and concentrated. FCC (toluene–ethyl acetate, 95 : 5) of the residue gave the *azido derivative* **67** (550 mg, 60%) as an amorphous solid; $[\alpha]_D^{24}$ +85 (*c* 1, $CHCl_3$); R_f 0.80 (solvent *B*) (Found: C, 65.95; H, 4.5; N, 3.9. $C_{61}H_{49}N_3O_{17}\cdot H_2O$ requires C, 65.8; H, 4.6; N, 3.8%); ν_{max} (film)/cm^{-1} (*inter alia*) 1729 (C=O), 2102 (–N_3); δ_H 2.82 (1 H, dd, $J_{5',6a'}$ 7.4, $J_{6a',6b'}$ 12.8, 6′-H[a]), 3.03 (1 H, dd, $J_{5',6b'}$ 5.3, 6′-H[b]), 3.65 (1 H, br dd, 5′-H), 4.28 (1 H, dt, $J_{5,6a} = J_{5,6b} = 2.5$, 5-H), 4.55 (1 H, dd, $J_{6a,6b}$ 12.3, 6-H[a]), 4.69 (1 H, dd, 6-H[b]), 4.81 (1 H, t, $J_{3,4} = J_{4,5} =$ 9.7, 4-H), 5.03 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.35 (1 H, dd, $J_{3',4'}$ 3.4,

3′-H), 5.63 (1 H, br d, 4′-H), 5.76 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.87 (1 H, dd, $J_{2,3}$ 3.3, 2-H), 6.04 (1 H, dd, 3-H), 6.54 (1 H, d, $J_{1,2}$ 2.2, 1-H) and 7.10–8.20 (35 H, m, 7 × Ph).

6-Azido-2,3,4-tri-O-benzoyl-6-deoxy-β-D-galactopyranosyl-(1→4) 2,3,6-tri-O-benzoyl-α-D-mannopyranose 68

To a solution of 1-O-benzoate **67** (500 mg, 0.456 mmol) in MeCN (6 cm^3) was added 2 mol dm^{-3} dimethylamine in THF (2.5 cm^3, 5 mmol, 11 eq.), and the mixture was kept at rt with monitoring by TLC (solvent *B*). After 48 h, the mixture was concentrated and acetonitrile was evaporated off from the residue. FCC [toluene–ethyl acetate, (95 : 5) → (85 : 15)] of the residue gave the *hemiacetal derivative* **68** (357 mg, 79%) as an amorphous solid; $[\alpha]_D^{24}$ +56 (*c* 1, $CHCl_3$); R_f 0.65 (solvent *B*) (Found : C, 65.7; H, 4.7; N, 4.0. $C_{54}H_{45}N_3O_{16}$ requires C, 65.4; H, 4.6; N, 4.2%); ν_{max} (film)/cm^{-1} (*inter alia*) 1731 (C=O), 2111 (–N_3); δ_H 2.73 (1 H, dd, $J_{5',6a'}$ 7.5, $J_{6a',6b'}$ 12.8, 6′-H[a]), 2.95 (1 H, dd, $J_{5',6b'}$ 5.4, 6′-H[b]), 3.42 (1 H, d, $J_{1,OH}$ 4.0, 1-OH), 3.54 (1 H, br dd, 5′-H), 4.25 (1 H, dt, $J_{5,6a} = J_{5,6b}$ = 2.0, 5-H), 4.38 (1 H, dd, $J_{6a,6b}$ 12.3, 6-H[a]), 4.63 (1 H, dd, 6-H[b]), 4.58 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.7, 4-H), 4.89 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.29 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 5.30 (1 H, m, 1-H), 5.53 (1 H, br d, 4′-H), 5.60 (1 H, dd, $J_{1,2}$ 1.9, $J_{2,3}$ 3.3, 2-H), 5.64 (1 H, dd, $J_{2',3'}$ 10.3, 2′-H), 5.86 (1 H, dd, 3-H) and 7.00–8.00 (30 H, m, 6 × Ph).

6-Azido-2,3,4-tri-O-benzoyl-6-deoxy-β-D-galactopyranosyl-(1→4)-2,3,6-tri-O-benzoyl-α-D-mannopyranosyl hydrogenphosphonate, triethylammonium salt 69

This compound was prepared by reaction of the hemiacetal **68** (80 mg, 0.081 mmol) with PCl_3 (0.04 cm^3, 0.458 mmol, 5.7 eq.), imidazole (107 mg, 1.57 mmol, 6.5 eq.) and Et_3N (0.225 cm^3, 1.57 mmol, 6.5 eq.) in CH_3CN (8 cm^3) followed by hydrolysis with 1 mol dm^{-3} TEA hydrogen carbonate (5 cm^3) as described for the preparation of the disaccharide H-phosphonate **24**. FCC [CH_2Cl_2–MeOH–Et_3N, (98.8 : 0.2 : 1) → (91 : 8 : 1)] gave the H-phosphonate **69** (93 mg, quant.) as an amorphous solid; $[\alpha]_D^{24}$ +53 (*c* 1, $CHCl_3$); R_f 0.10 (solvent *D*); ν_{max} (film)/cm^{-1} (*inter alia*) 1733 (C=O), 2107 (–N_3); δ_H 1.35 (9 H, t, *J* 7.3, 3 × C$H_3$$CH_2$N), 2.86 (1 H, dd, $J_{5',6a'}$ 7.3, $J_{6a',6b'}$ 12.8, 6′-H[a]), 3.01 (1 H, dd, $J_{5',6b'}$ 5.4, 6′-H[b]), 3.10 (6 H, q, 3 × CH_3CH_2N), 3.61 (1 H, br dd, 5′-H), 4.41 (1 H, dt, $J_{5,6a} = J_{5,6b}$ = 2.0, 5-H), 4.52 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H[a]), 4.65 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.8, 4-H), 4.67 (1 H, dd, 6-H[b]), 4.95 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.36 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.60 (1 H, br d, 4′-H), 5.70 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.73 (1 H, m, 2-H), 5.76 (1 H, dd, $J_{1,2}$ 2.1, $J_{1,P}$ 8.8, 1-H), 5.94 (1 H, dd, 3-H), 7.05 (1 H, d, $J_{H,P}$ 637.3, HP) and 7.10–8.20 (30 H, m, 6 × Ph); δ_P 0.05; ESMS(−) data: *m*/*z* 1053.7 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 1054.25; $C_{60}H_{61}N_4O_{18}P$ requires *M*, 1156.37).

Decyl 6-azido-2,3,4-tri-O-benzoyl-6-deoxy-β-D-galacto-pyranosyl-(1→4)-2,3,6-tri-O-benzoyl-α-D-mannopyranosyl phosphate, triethylammonium salt 70

This compound was prepared by condensation of the disaccharide H-phosphonate **69** (93 mg, 0.081 mmol) and decan-1-ol (0.03 cm^3, 0.16 mmol, 2.0 eq.) in pyridine (1 cm^3) in the presence of trimethylacetyl chloride (0.025 cm^3, 0.203 mmol, 2.5 eq.) followed by oxidation with iodine (40 mg, 0.158 mmol, 2.0 eq.) in pyridine–water (95 : 5; 1.15 cm^3) as described for the synthesis of the phosphodiester **35**. FCC [CH_2Cl_2–MeOH–Et_3N, (98.9 : 0.1 : 1) → (91 : 8 : 1)] gave the phosphodiester **70** (95 mg, 90%) as an amorphous solid; $[\alpha]_D^{24}$ +51 (*c* 1, $CHCl_3$); R_f 0.32 (solvent *D*); ν_{max} (film)/cm^{-1} (*inter alia*) 1729 (C=O), 2102 (–N_3); δ_H 0.80 (3 H, t, *J* 6.5, C$H_3$$CH_2$$CH_2$), 1.10–1.30 (14 H, m, 7 × CH_2), 1.13 (9 H, t, *J* 7.3, 3 × C$H_3$$CH_2$N), 1.52 (2 H, quintet, *J* 6.9, OCH_2C$H_2$$CH_2$), 2.76 (7 H, m, 3 × CH_3CH_2N and 6′-H[a]), 2.92 (1 H, dd, $J_{6a',6b'}$ 12.8, 6′-H[b]), 3.48 (1 H, br t, $J_{5',6a'} = J_{5',6b'}$ = 6.3, 5′-H), 3.83 (2 H, m, POC$H_2$$CH_2$), 4.34 (1 H, ddd, $J_{5,6a}$ 2.5, 5-H), 4.42 (1 H, dd, $J_{6a,6b}$ 12.2, 6-H[a]), 4.56 (1 H, t, $J_{3,4} = J_{4,5}$ = 9.7, 4-H), 4.57 (1 H, dd, $J_{5,6b}$ 1.5, 6-H[b]), 4.84 (1 H, d, $J_{1',2'}$ 7.9, 1′-H), 5.26 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 5.51 (1 H, br d, 4′-H), 5.58 (1 H, dd, $J_{1,2}$ 2.2, $J_{1,P}$ 8.0, 1-H), 5.61 (1 H, dd, $J_{2',3'}$ 10.4, 2′-H), 5.68 (1 H, dd, $J_{2,3}$ 3.0, 2-H), 5.85 (1 H, dd, 3-H) and 7.10–8.00 (30 H, m, 6 × Ph); δ_P −2.68; ESMS(−) data: *m*/*z* 1209.9 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 1210.40; $C_{70}H_{81}N_4O_{19}P$ requires *M*, 1312.52).

Decyl 6-azido-6-deoxy-β-D-galactopyranosyl-(1→4)-α-D-mannopyranosyl phosphate, triethylammonium salt 71

To a solution of compound **70** (62 mg, 0.047 mmol) in MeOH (20 cm^3) was added 4.6 mol dm^{-3} methanolic NaOMe (0.2 cm^3). The mixture was kept at rt for 14 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 (for removing methyl benzoate) to give the phosphodiester **71** (32 mg, quant.) as an amorphous solid; $[\alpha]_D^{24}$ +26 (*c* 1, MeOH); R_f 0.75 (solvent *E*); ν_{max} (film)/cm^{-1} (*inter alia*) 2105 (–N_3), 3416 (OH); δ_C (D_2O) 8.6 (*C*$H_3$$CH_2$N), 14.1, 22.7, 25.7, 29.3 (2 C), 29.6 (2 C), 31.9 (*C*H_3*C*H_2*C*H_2*C*H_2*C*H_2*C*H_2*C*H_2*C*H_2*C*H_2*C*H_2O), 30.6 (d, $J_{C,P}$ 5.1, *C*$H_2$$CH_2$OP), 47.0 ($CH_3$*C*$H_2$N), 51.5 (C-6′), 60.6 (C-6), 66.9 (d, $J_{C,P}$ 3.7, CH_2*C*H_2OP), 69.2 (2 C, C-3 and C-4′), 70.5 (d, $J_{C,P}$ 9.5, C-2), 70.8 (C-2′), 72.5 (C-5), 72.8 (C-3′), 73.8 (C-5′), 76.3 (C-4), 96.1 (d, $J_{C,P}$ 4.4, C-1), 103.3 (C-1′); δ_P −1.86; ESMS(−) data: *m*/*z* 586.05 (100%, [M − Et_3N − H]$^-$) (expected *m*/*z*, 586.25; $C_{28}H_{57}N_4O_{13}P$ requires *M*, 688.36).

Dec-9-enyl β-D-galactopyranosyl-(1→4)-3-deoxy-α-D-*arabino*-hexopyranosyl phosphate, triethylammonium salt 10

To a solution of compound **25** (65 mg, 0.064 mmol) in MeOH (20 cm^3) was added 4.6 mol dm^{-3} methanolic NaOMe (0.2 cm^3). The mixture was kept at rt for 3 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 (for removing methyl benzoate) to give the phosphodiester **10** (41 mg, quant.) as an amorphous solid; $[\alpha]_D^{24}$ +37 (*c* 1, MeOH); R_f 0.58 (solvent *E*); δ_H (D_2O) (*inter alia*) 1.12 (9 H, t, *J* 7.3, 3 × C$H_3$$CH_2$N), 1.91 (2 H, q, *J* 6.7, CH_2CH_2CH=), 3.03 (6 H, q, 3 × CH_3CH_2N), 4.26 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 5.21 (1 H, br d $J_{1,P}$ 7.4, 1-H) and 5.72 [1 H, ddt, *J*(H, CH_2) 6.7, J_{cis} 10.2, J_{trans} 17.0, CH_2=C*H*CH_2]; δ_C, δ_P and ESMS(−) data: see Table 1.

Dec-9-enyl β-D-galactopyranosyl-(1→4)-3-deoxy-3-fluoro-α-D-mannopyranosyl phosphate, triethylammonium salt 11

De-O-acylation of compound **45** (230 mg) with 0.05 mol dm^{-3} MeONa in methanol (4 h at rt) followed by work-up, as described in the preparation of the phosphodiester **10**, gave the phosphodiester **11** (151 mg, 97%) as an amorphous solid; $[\alpha]_D^{24}$ +24 (*c* 1, MeOH); R_f 0.69 (solvent *E*); δ_H (D_2O) (*inter alia*) 1.14 (9 H, t, *J* 7.4, 3 × C$H_3$$CH_2$N), 1.93 (2 H, q, *J* 6.8, CH_2CH_2CH=), 3.06 (6 H, q, 3 × CH_3CH_2N), 3.42 (1 H, dd, $J_{2',3'}$ 9.9, 2′-H), 4.36 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 5.31 (1 H, ddd, $J_{1,2}$ 2.0, $J_{1,P}$ 7.4, $J_{1,F}$ 5.0, 1-H) and 5.78 [1 H, ddt, *J*(H, CH_2) 6.8, J_{cis} 10.2, J_{trans} 17.0, CH_2=C*H*CH_2]; δ_C, δ_P and ESMS(−) data: see Table 1.

Dec-9-enyl β-D-galactopyranosyl-(1→4)-6-deoxy-6-fluoro-α-D-mannopyranosyl phosphate, triethylammonium salt 12

De-O-acylation of compound **54** (202 mg) with 0.05 mol dm^{-3} MeONa in methanol (6 h at rt) followed by work-up, as described in the preparation of the phosphodiester **10**, gave the phosphodiester **12** (128 mg, 99%) as an amorphous solid; $[\alpha]_D^{24}$ +24 (*c* 1, MeOH); R_f 0.67 (solvent *E*); δ_H (*inter alia*) 1.17 (9 H, t, *J* 7.3, 3 × C$H_3$$CH_2$N), 1.94 (2 H, q, *J* 6.7, CH_2CH_2CH=), 3.08 (6 H, q, 3 × CH_3CH_2N), 3.44 (1 H, $J_{2',3'}$ 10.0, 2′-H), 3.55 (1 H, dd, $J_{3',4'}$ 3.3, 3′-H), 4.32 (1 H, d, $J_{1',2'}$ 7.6, 1′-H), 4.58 (1 H, br dd,

$J_{6a,6b}$ 10.5, $J_{6a,F}$ 48.5, 6-H^a), 4.75 (1 H, br dd, $J_{6b,F}$ 48.5, 6-H^b), 5.28 (1 H, dd, $J_{1,2}$ 1.9, $J_{1,P}$ 7.9, 1-H) and 5.77 [1 H, ddt, J(H, CH_2) 6.7, J_{cis} 10.2, J_{trans} 17.0, CH_2=C*H*CH_2]; δ_C, δ_P and ESMS(−) data: see Table 1.

Dec-9-enyl 6-deoxy-6-fluoro-β-D-galactopyranosyl-(1→4)-α-D-mannopyranosyl phosphate, triethylammonium salt 13

De-O-acylation of compound **64** (212 mg, 0.173 mmol) with 0.05 mol dm^{-3} MeONa in methanol (40 h at rt) followed by work-up, as described in the preparation of the phosphodiester **10**, gave the phosphodiester **13** (112 mg, 97%) as an amorphous solid; $[a]_D^{24}$ +26 (*c* 1, MeOH); R_f 0.55 (solvent *E*); δ_H (D_2O) (*inter alia*) 1.16 (9 H, t, *J* 7.4, 3 × C*H*$_3$CH$_2$N), 1.95 (2 H, q, *J* 6.6, CH_2C*H*$_2$CH=), 3.07 (6 H, q, 3 × CH_3C*H*$_2$N), 3.47 (1 H, dd, $J_{2',3'}$ 9.9, 2′-H), 3.58 (1 H, dd, $J_{3',4'}$ 3.4, 3′-H), 4.38 (1 H, d, $J_{1',2'}$ 7.8, 1′-H), 4.53 (1 H, ddd, $J_{5',6a'}$ 7.5, $J_{6a',6b'}$ 10.1, $J_{6a',F}$ 48.1, 6′-H^a), 4.58 (1 H, ddd, $J_{5',6b'}$ 4.4, $J_{6b',F}$ 48.1, 6′-H^b), 5.29 (1 H, dd, $J_{1,2}$ 1.6, $J_{1,P}$ 7.8, 1-H) and 5.69 [1 H, ddt, J(H, CH_2) 6.6, J_{cis} 10.2, J_{trans} 17.0, CH_2=C*H*CH_2]; δ_C, δ_P and ESMS(−) data: see Table 1.

Decyl β-D-galactopyranosyl-(1→4)-2-amino-2-deoxy-α-D-mannopyranosyl phosphate, sodium salt 14

A solution of compound **36** (33 mg, 0.054 mmol) in MeOH (5.0 cm^3) containing 20% $Pd(OH)_2$/C (20 mg) was stirred under a slight overpressure of hydrogen at rt for 1 h, filtered, and concentrated to produce the phosphodiester **14** (30 mg, 95%) as an amorphous solid; $[a]_D^{24}$ +27 (*c* 1, MeOH); R_f 0.75 (solvent *E*); δ_H (D_2O) (*inter alia*) 0.75 (3 H, t, *J* 6.6, C*H*$_3$CH$_2$CH$_2$), 1.48 (2 H, m, OCH$_2$C*H*$_2$CH$_2$), 4.30 (1 H, d, $J_{1',2'}$ 7.7, 1′-H) and 5.25 (1 H, br d, $J_{1,P}$ 7.5, 1-H); δ_C, δ_P and ESMS(−) data: see Table 1.

Decyl β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-α-D-mannopyranosyl phosphate, triethylammonium salt 15

To a solution of compound **14** (14 mg, 0.025 mmol) in MeOH (2 cm^3) was added a solution (0.1 cm^3) of acetic anhydride in MeOH [prepared from acetic anhydride (0.05 cm^3) and MeOH (0.5 cm^3)]. The mixture was kept at rt for 30 min and concentrated. The aqueous solution of the residue was washed with diethyl ether, then deionized with Dowex 50W-X4 (H^+) resin, filtered and immediately neutralized with Et_3N. The solution was concentrated to produce the phosphodiester **15** (16 mg, 91%) as an amorphous solid; $[a]_D^{24}$ +25 (*c* 1, MeOH); R_f 0.75 (solvent *E*); δ_H (D_2O) (*inter alia*) 0.72 (3 H, t, *J* 6.6, C*H*$_3$CH$_2$CH$_2$), 1.12 (9 H, t, *J* 7.2, 3 × C*H*$_3$CH$_2$N), 1.48 (2 H, m, OCH$_2$C*H*$_2$CH$_2$), 1.90 (3 H, s, Ac), 3.04 (6 H, q, 3 × CH_3C*H*$_2$N), 4.32 (1 H, d, $J_{1',2'}$ 7.6, 1′-H) and 5.20 (1 H, br d, $J_{1,P}$ 7.2, 1-H); δ_C, δ_P and ESMS(−) data: see Table 1.

Decyl 6-amino-6-deoxy-β-D-galactopyranosyl-(1→4)-α-D-mannopyranosyl phosphate, ammonium salt 16

A solution of phosphodiester **71** (33 mg, 0.047 mmol) in water (25 cm^3) treated with Dowex 50W-X4 (Na^+) resin at rt for 4 h. The resin was filtered off and the filtrate was concentrated. A solution of the residue in MeOH (5 cm^3) containing 20% $Pd(OH)_2$/C (20 mg) was stirred under a slight overpressure of hydrogen at rt for 40 min, filtered and concentrated to give a crude product (26 mg, 94%), 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 phosphodisaccharide **16** (12 mg, 44%) as an amorphous solid; $[a]_D^{24}$ +16 (*c* 1, MeOH); R_f 0.58 (solvent *E*); δ_H (D_2O) (*inter alia*) 0.75 (3 H, t, *J* 6.5, C*H*$_3$CH$_2$CH$_2$), 1.50 (2 H, m, OCH$_2$C*H*$_2$CH$_2$), 4.55 (1 H, d, $J_{1',2'}$ 7.7, 1′-H) and 5.27 (1 H, br d, $J_{1,P}$ 7.4, 1-H); δ_C, δ_P and ESMS(−) data: see Table 1.

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