Carbohydrate Research, 204 (1990) 65–78
Elsevier Science Publishers B.V., Amsterdam

Application of the hydrogenphosphonate approach in the synthesis of glycosyl phosphosugars linked through secondary hydroxyl groups*

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(Received September 7th, 1989; accepted for publication, January 4th, 1990)

ABSTRACT

The hydrogenphosphonate approach has been used in syntheses of methyl α-D-mannopyranoside 2-, 3-, and 4-(α-D-mannopyranosyl phosphate), benzyl β-D-galactopyranoside 2-(α-D-mannopyranosyl phosphate), and methyl β-D-galactopyranoside 4-(α-D-mannopyranosyl phosphate). Condensation of 2,3,4,6-tetra-*O*-benzyl- or 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl hydrogenphosphonate with suitable, partially acylated monohydroxy derivatives in the presence of Me_3CCOCl, followed by oxidation of the resulting hydrogenphosphonate diesters with iodine, gave the *O*-protected phosphate diesters in yields of 67–87%. Deprotection then gave the glycosyl phosphosugars.

INTRODUCTION

Glycosyl phosphosugars (**3**) are fragments of several glycoproteins[1,2] and yeast phosphoglycans[3]. They are also structural blocks of poly(glycosyl phosphates) which are present in the cell walls and capsules of numerous bacteria[4]. These biopolymers are composed of mono- or oligo-saccharide units linked with phosphate diester bridges through hemiacetal and alcohol hydroxyl groups of the neighbouring units; in many of the bacterial polymers, secondary hydroxyl groups are involved. The first chemical syntheses of glycosyl phosphosugars were achieved by the phosphate diester and phosphite triester methods[5]. The hydrogenphosphonate approach, initially suggested for the preparation of oligo- and poly-nucleotides[6,7], has been used for the synthesis of (1→6)-linked glycosyl phosphosugars[8–11] and (1→6)-linked oligo(mannosyl phosphates)[12,13]. We now report the application of the hydrogenphosphonate method in the synthesis of glycosyl phosphosugars linked through secondary hydroxyl groups, which are not accessible readily by other methods[5,14].

* Presented at EUROCARB V, the Vth European Carbohydrate Symposium, Prague, Czechoslovakia, August 21–25, 1989.

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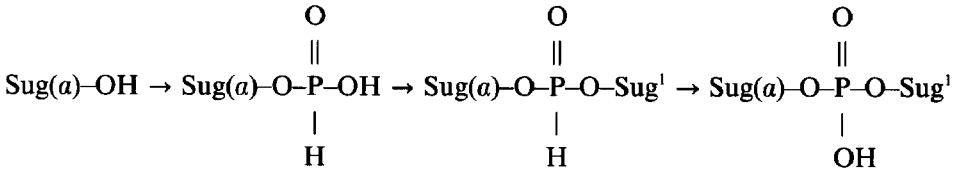
0008-6215/90/$ 03.50

RESULTS AND DISCUSSION

The hydrogenphosphonate approach is based on the interaction of a glycosyl hydrogenphosphonate (**1**) with a partially protected monosaccharide (→**2**) followed by oxidation of the hydrogenphosphonate diesters (**2**) to give **3**.



1 **2** **3**

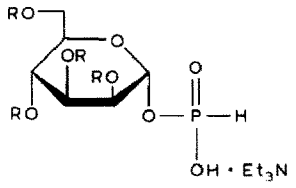
The (1→2)-, (1→3)-, and (1→4)-linked glycosyl phosphosugars **33–37** were synthesized *via* condensation of the *α*-D-mannopyranosyl hydrogenphosphonate derivatives **4** and **5** with partially acylated derivatives of *α*-D-mannopyranose (**9–11**) and *β*-D-galactopyranose (**12** and **13**) followed by oxidation and deprotection. The series of hydroxy derivatives chosen allowed a comparison of the reactivity of most of the possible types of secondary hydroxyl groups in hexopyranoses.

The glycosyl hydrogenphosphonates were prepared from the 2,3,4,6-tetra-*O*-substituted derivatives **6** (ref. 15) and **7**. The latter was obtained (60%) by selective *O*-1-debenzoylation[8] of the perbenzoate **8** with dimethylamine in acetonitrile. The reaction of **6** or **7** with tri-imidazolylphosphine (prepared[6] from PCl_3, imidazole, and Et_3N and used *in situ*) in MeCN followed by hydrolysis at pH 8 gave **4** and **5**, in almost quantitative yields, which were converted into the phosphate diesters without purification.

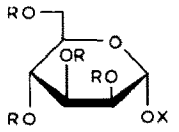
The n.m.r. data for **4** [^{31}P, δ 1.56; ^1H, δ 7.40 (d, $^1J_{H,P}$ 640 Hz)] were typical for hydrogenphosphonate derivatives[16]. Similar data were obtained for **5** [^{31}P, δ 0.82; ^1H, δ 7.13 (d, $^1J_{H,P}$ 638.6 Hz)]. Splitting of the signals for H-1, C-1, and C-2 due to coupling with P was also observed (see Experimental). The *α* configuration at C-1 followed from the characteristic chemical shifts of the signals for C-3 and C-5 (taking into account the effects of the benzyl and benzoyl groups) and was confirmed for **4** by the value (171 Hz) of $J_{C-1,H-1}$ which is typical for *α* derivatives.

The hydroxy compounds **9**, **10**, and **12** were synthesized from the 4,6-*O*-benzylidene derivatives **14** (ref. 17) **15** (ref. 18), and **22** (ref. 19). Each compound was acetylated and then treated with aqueous 70% acetic acid to give the diols **18**, **19**, and **24**, respectively, benzoylation of which yielded the corresponding tribenzoates **20**, **21**, and **25**. Selective *O*-deacetylation[20] by acidic methanolysis at 20° then gave the alcohols **9**, **10**, and **12**, respectively, in overall yields of 53, 63, and 58%, respectively. The hydroxy derivatives **11** and **13** were obtained by selective benzoylation of methyl *α*-D-mannopyranoside[21] and methyl *β*-D-galactopyranoside[22], respectively.

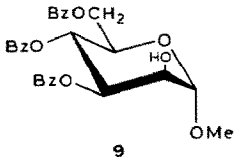
Condensation of the hydrogenphosphonates **4** and **5** severally with **9–13** was



4 R = Bn
5 R = Bz



6 R = Bn, X = H
7 R = Bz, X = H
8 R = X = Bz



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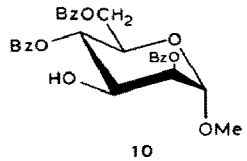

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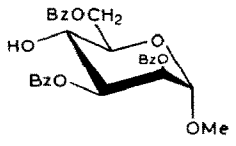

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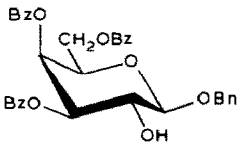

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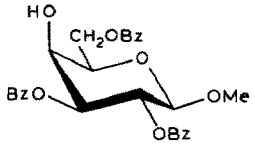

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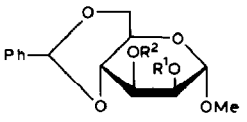
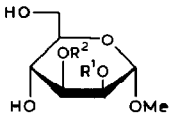
accomplished in pyridine in the presence of trimethylacetyl chloride (2.5 equiv.). The resulting hydrogenphosphonate diesters were oxidized *in situ* with iodine (2 equiv.) in aqueous 98% pyridine in the presence of Et_3N (5 equiv.) to give the *O*-protected glycosyl phosphosugars which were isolated by column chromatography on silica gel. The reaction of **4** and **11** was monitored by ^{31}P-n.m.r. spectroscopy. Immediately after mixing the reactants with Me_3CCOCl, the signal (δ 0.28) of **4** was absent and major signals of hydrogenphosphonate diesters were observed at δ 8.03 and 8.21 ($^1J_{P,H}$ 730 Hz) in the ratio 2.3:1. Several minor signals (δ 5.26, 5.63, 8.85, and 10.58, $^1J_{P,H}$ 730 Hz) were also present, the total integrated intensity of which was ~20% of that of the major peaks. Treatment of the mixture with iodine caused a rapid change in the spectrum, with a new main signal of the phosphate diester **29** at δ −1.98 and a few minor signals (δ 1.02 −7.78, −9.85, and −10.14). The ratio of the integrated intensities of the major signal and the sum of the minor signals was ~3.4:1, and 70% of **29** was isolated.

The (1→2)- and (1→3)-linked mannosyl phosphomannose derivatives **26** (87%) and **28** (77%) were synthesized from **4** and the alcohols **9** and **10**, respectively, by the above procedure. Likewise, reaction of **5** with the galactose derivatives **12** and **13** gave the phosphate diesters **30** (67%) and **31** (69%), respectively. To check whether different type of *O*-protecting groups in the hydrogenphosphonate derivative may influence the efficiency of the condensation, the reaction of **4** and **13** was performed. Since the reaction gave 72% of the diester **32**, the reactivities of the hydrogenphosphonates **4** and **5** in the synthesis of glycosyl phosphosugars are similar.

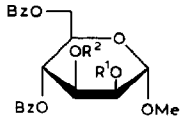
Deprotection of the phosphate diesters **26**, **28**, and **29** was accomplished by hydrogenolysis (Pd–C) followed by deacylation (methanolic sodium methoxide). The



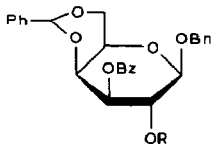
14 $R^1 = H, R^2 = Bz$
15 $R^1 = Bz, R^2 = H$
16 $R^1 = Ac, R^2 = Bz$
17 $R^1 = Bz, R^2 = Ac$



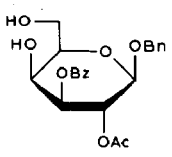
18 $R^1 = Ac, R^2 = Bz$
19 $R^1 = Bz, R^2 = Ac$



20 $R^1 = Ac, R^2 = Bz$
21 $R^1 = Bz, R^2 = Ac$



22 R = H
23 R = Ac



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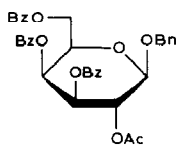

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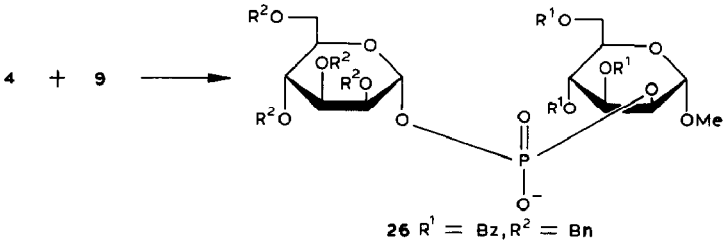
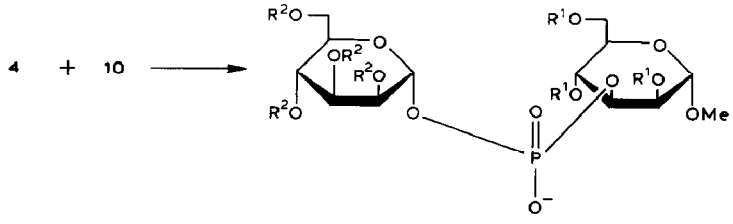
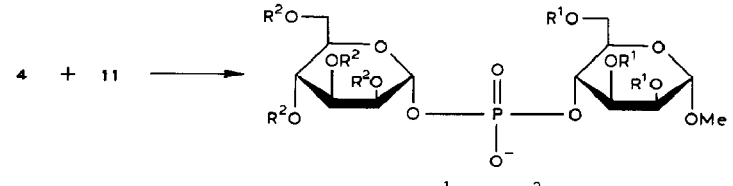


26 $R^1 = Bz, R^2 = Bn$
27 $R^1 = Bz, R^2 = H$
33 $R^1 = R^2 = H$



28 $R^1 = Bz, R^2 = Bn$
34 $R^1 = R^2 = H$



29 $R^1 = Bz, R^2 = Bn$
35 $R^1 = R^2 = H$

TABLE I

^{31}P- and ^{13}C-n.m.r. data (D_2O, δ in p.p.m., J in Hz) for glycosyl phosphosugars **33–37** ($J_{C,P}$ values in brackets)

Atom	**33**[a]	**34**[a]	**35**[a]	**36**[b]	**37**
P	−1.92	−1.85	−1.41	−1.61	−0.90
C-1	100.6	102.0	101.8	102.0d (8.7)	105.2
C-2	75.9d (6.0)	70.6	71.1	77.6d (5.1)	72.2
C-3	71.1d (6.5)	77.7d (5.8)	71.1	74.2br	73.6br
C-4	67.7	67.2d (6.2)	72.7d (5.5)	70.0	75.4d (5.9)
C-5	74.0	73.9	73.6d (7.4)	76.5	75.9br
C-6	62.1	62.3	62.0	62.2	62.1
C-1′	97.6d (5.4)	97.6d (6.0)	97.6d (5.5)	97.7d (5.5)	97.7d (5.5)
C-2′	71.7d (8.1)	71.9d (9.2)	71.6d (7.4)	71.8d (9.5)	71.7d (9.7)
C-3′	71.2	71.3	71.2	71.4	71.3
C-4′	67.9	67.9	67.7	67.9	67.7
C-5′	75.1	75.2	75.0	75.1	75.1
C-6′	62.1	62.3	62.0	62.3	62.1
OCH_3	56.2	56.2	56.0		58.6

[a] Additional ^{13}C signals of Et_3NH^+ were present at δ 47.9–48.1 (CH_2) and 9.4–9.6 (CH_3). [b] Additional ^{13}C signals for the benzyl group were present at δ 72.6 (CH_2), 129.7, 129.8, 130.1, 138.7 (Ph).

use of sodium salts of the diesters was essential for complete hydrogenolysis. The glycosyl phosphosugars **33–35** were isolated by ion-exchange chromatography on Fractogel TSK DEAE (HCO_3^- form) in yields of 58, 77, and 83%, respectively.

The use of dilute solutions of sodium methoxide, limited time of reaction, and lowered temperature of the *O*-debenzoylation procedure were necessary in order to avoid cleavage of the glycosyl phosphate linkage. Similar degradation was observed under conditions of alkaline hydrolysis[14]. Such cleavage was observed only during saponification of the (1→2)-linked derivative **27** and 15% of methyl α-D-mannopyranoside 2-phosphate was isolated in addition to **33**.

The benzoylated phosphate diesters **30** and **31** were deprotected with 0.05M sodium methoxide in methanol–1,4-dioxane (1°) to give **36** (88%) and **37** (75%), respectively.

The n.m.r. data confirmed the structures of the glycosyl phosphosugars **33–37** and the *O*-protected phosphate diesters **26** and **28–32**. The ^{31}P-n.m.r. data (Tables I and III) are characteristic for phosphate diesters of this type[8–13]. The positions of the phosphate diester linkages were indicated by the signals of C-1′ and C-X (X = 2 for **33** and **36**, 3 for **34**, and 4 for **35** and **37**) in the ^{13}C-n.m.r. spectra of **33–37** (Table I). These

TABLE II

^{1}H-n.m.r. data (D_2O, δ in p.p.m., J in Hz) for the glycosyl phosphosugars **33–37**

Atom	**33**[a]	**34**[a]	**35**[a]	**36**[b,c]	**37**[b]
H-1	4.89d ($J_{1,2}$ 1.6)	4.74d ($J_{1,2}$ 1.7)	4.79d ($J_{1,2}$ 1.7)	4.64d ($J_{1,2}$ 7.6)	4.34d ($J_{1,2}$ 8.1)
H-2	4.31ddd ($J_{2,P}$ 8.0)	4.10dd ($J_{2,3}$ 3.2)	3.98dd ($J_{2,3}$ 3.3)	4.18dt ($J_{2,3}$ = $J_{2,P}$ = 9.1)	3.53dd($J_{2,3}$ 10.0)
H-3	3.80dd ($J_{2,3}$ 3.1)	4.25ddd ($J_{3,P}$ 8.0)	3.94dd ($J_{3,4}$ 9.0)	3.85dd ($J_{3,4}$ 3.4)	3.70ddd ($J_{3,4}$ 3.1, $J_{3,P}$ 1.5)
H-4	3.65t ($J_{3,4}$ = $J_{4,5}$ = 9.5)	3.76t ($J_{3,4}$ = $J_{4,5}$ = 9.2)	4.22q ($J_{4,5}$ = $J_{4,P}$ = 9.0)	4.01d	4.46dd ($J_{4,P}$ 9.6)
H-5	3.57ddd ($J_{5,6a}$ 5.0)	3.63ddd ($J_{5,6a}$ 4.9)	3.72ddd ($J_{5,6a}$ 5.6, $J_{5,6b}$ 2.2)		
H-6a	3.73dd ($J_{6a,6b}$ 11.0)	3.82dd ($J_{6a,6b}$ 12)	3.76–3.94m	3.70–3.94m	3.70–3.90m
H-6b	3.86dd ($J_{5,6b}$ 2.2)	3.87dd ($J_{5,6b}$ 2.1)			
H-1′	5.43dd ($J_{1',P}$ 7.5)	5.45dd ($J_{1',P}$ 7.6)	5.51dd ($J_{1',P}$ 7.3)	5.55dd ($J_{1',P}$ 7.1)	5.46dd ($J_{1',P}$ 7.4)
H-2′	3.98dd ($J_{1',2'}$ 2.0)	3.97dd ($J_{1',2'}$ 1.9)	4.04dd($J_{1',2'}$ 2.0)	4.06dd ($J_{1',2'}$ 2.0)	4.01dd ($J_{1',2'}$ 1.9)
H-3′	3.85dd ($J_{2',3'}$ 3.3)	3.87dd($J_{2',3'}$ 3.1)	3.92dd($J_{2',3'}$ 3.2)	3.91dd($J_{2',3'}$ 3.2)	3.88dd ($J_{2',3'}$ 3.2)
H-4′	3.65t ($J_{3',4'}$ = $J_{4',5'}$ = 9.5)	3.66t ($J_{3',4'}$ = $J_{4',5'}$ = 9.5)	3.73t ($J_{3',4'}$ = $J_{4',5'}$ = 9.5)	3.73t ($J_{3',4'}$ = $J_{4',5'}$ = 9.5)	3.68t ($J_{3',4'}$ = $J_{4',5'}$ = 9.6)
H-5′,6a′, 6b′	3.69–3.82m	3.66–3.84m	3.76–3.94m	3.70–3.94m	3.70–3.90m
OCH_3	3.38s	3.38s	3.43s	–	3.57s

[a] Sodium salts. [b] Ammonium salts. [c] Additional signals of benzyl group at δ 4.87 and 5.02 (2 d, 2 H, J 11.5 Hz, CH_2), 7.41–7.62 (m, 5 H, Ph).

TABLE III

^{31}P- and ^{1}H-n.m.r. data ($CDCl_3$, δ in p.p.m., J in Hz) for *O*-protected phosphate diesters **26**[a] and **28–32**[a]

Atom	**26**	**28**	**29**	**30**	**31**	**32**
P	−2.51	−2.88	−2.85	−3.18	−3.03	−2.15
H-1	5.24d ($J_{1,2}$ 1.7)	4.92d ($J_{1,2}$ 1.8)	4.89d ($J_{1,2}$ 1.7)	4.80d ($J_{1,2}$ 7.9)	4.66d ($J_{1,2}$ 7.8)	4.55d ($J_{1,2}$ 7.7)
H-2	4.83ddd ($J_{2,3}$ 3.2, $J_{2,P}$ 8.4)	5.76dd ($J_{2,3}$ 3.1)	5.61dd ($J_{2,3}$ 3.5)	4.98dt ($J_{2,3}$ = $J_{2,P}$ = 9.9)	5.78dd ($J_{2,3}$ 10.1)	5.68dd ($J_{2,3}$ 10.5)
H-3	5.69ddd ($J_{3,P}$ 2.3)	5.13ddd ($J_{3,P}$ 8.5)	5.71dd ($J_{3,4}$ 9.8)	5.43dd ($J_{3,4}$ 3.6)	5.40dd ($J_{3,4}$ 2.9)	5.42ddd ($J_{3,4}$ 3.0, $J_{3,P}$ 0.9)
H-4	5.83t ($J_{3,4}$ = $J_{4,5}$ = 10.0)	5.89t ($J_{3,4}$ = $J_{4,5}$ = 10.0)	5.10q ($J_{4,5}$ = $J_{4,P}$ = 9.8)	5.88dd ($J_{4,5}$ 1.0)	5.20dd ($J_{4,P}$ 10.3)	5.09dd ($J_{4,P}$ 10.6)
H-5	4.33ddd ($J_{5,6a}$ 3.5, $J_{5,6b}$ 5.8)	4.22ddd ($J_{5,6a}$ 4.8, $J_{5,6b}$ 2.5)	4.17ddd ($J_{5,6a}$ 5.6, $J_{5,6b}$ 2.0)	4.11dt ($J_{5,6a}$ 6.1, $J_{5,6b}$ 6.1)	4.17dd ($J_{5,6a}$ 4.7, $J_{5,6b}$ 7.6)	4.05m ($J_{5,6a}$ 4.8, $J_{5,6b}$ 7.5)
H-6a,6b	4.44–4.56m	4.42dd, 4.58dd ($J_{6a,6b}$ 12.0)	4.67dd, 4.98dd ($J_{6a,6b}$ 12.0)	4.38dd, 4.64dd ($J_{6a,6b}$ 11.2)	4.85dd, 4.98dd ($J_{6a,6b}$ 11.6)	4.66dd, 4.83dd ($J_{6a,6b}$ 11.5)
H-1′	5.77dd ($J_{1',P}$ 7.6)	5.65dd ($J_{1',P}$ 7.6)	5.64dd ($J_{1',P}$ 7.4)	5.66dd ($J_{1',P}$ 7.8)	5.85dd ($J_{1',P}$ 7.5)	5.82dd ($J_{1',P}$ 7.8)
H-2′	4.02dd ($J_{1',2'}$ 1.9, $J_{2',3'}$ 2.5)	3.98t ($J_{1',2'}$ = $J_{2',3'}$ = 1.7)	3.86–3.98m ($J_{1',2'}$ 1.5)	5.79dd ($J_{1',2'}$ 2.0)	5.82dd ($J_{1',2'}$ 1.8)	4.12t ($J_{1',2'}$ = $J_{2',3'}$ = 2.1)

TABLE III (continued)

Atom	**26**	**28**	**29**	**30**	**31**	**32**
H-3′	3.88–4.00m	3.95–4.07m	3.86–3.98m	5.90dd ($J_{2',3'}$ 3.1 ($J_{3',4'} = J_{4',5'}$ 6.10t = 10.0)	5.98 dd ($J_{2',3'}$ 3.1) 6.18t ($J_{3',4'} = J_{4',5'}$ = 10.0	3.89–4.00m
H-4′						
H-5′				4.63m	4.73–4.84m	
H-6a′	3.63dd ($J_{5',6a'}$ 1.5, $J_{6a',6b'}$ 11.0)	3.67d ($J_{6a',6b'}$ 11.0)	3.62dd ($J_{5',6a'}$ 1.1, $J_{6a',6b'}$ 11.0)	4.31dd ($J_{5',6a'}$ 3.3, ($J_{6a',6b'}$ 12.5)	4.44dd ($J_{5',6a'}$ 2.5, $J_{6a',6b'}$ 12.5)	3.71dd ($J_{5',6a'}$ 2.1, $J_{6a',6b'}$ 11.0)
H-6b′	3.72dd ($J_{5',6b'}$ 3.9)	3.78dd ($J_{5',6b'}$ 2.4)	3.71dd ($J_{5',6b'}$ 3.2)	4.55dd ($J_{5',6b'}$ 2.4)	4.73–4.84m	3.77dd ($J_{5',6b'}$ 4.3)
OCH_3	3.45s	3.42s	3.45s		3.50s	3.46s
CH_2Ph	4.41d, 4.56d (*J* 12.0)	4.44d, 4.62d (*J* 12.0)	4.41d, 4.56d (*J* 12.0)	4.90d, 5.07d (*J* 12.0)		4.42d, 4.62d (*J* 11.5)
	4.43d, 4.49d (*J* 11.8)	4.55d, 4.64d (*J* 12.0)	4.42d, 4.49d (*J* 12.1)			4.45d, 4.57d (*J* 11.5)
	4.50d, 4.87d (*J* 11.0)	4.56d, 4.92d (*J* 11.0)	4.49d, 4.84d (*J* 11.1)			4.53d, 4.89d (*J* 11.2)
	4.71s (2 H)	4.58s (2 H)	4.57d, 4.63d (*J* 12.5)			4.71s (2 H)

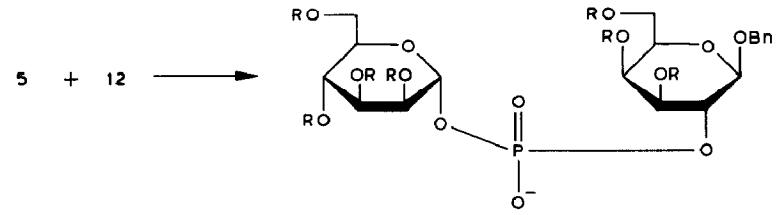
[a] Additional signals of Et_3NH^+ (δ 1.00–1.35t and 2.66–3.06q) and of Ph (7.00–7.60 and 7.85–8.20).

signals were doublets due to coupling with P and were shifted downfield. Signals of some neighbouring atoms (namely, C-2′ for **33**–**37**, C-3 for **33**, C-4 for **34**, C-5 for **35**, and C-1 for **36**) also appeared as doublets with $^3J_{C,P} > {}^2J_{C,P}$. In the ^{1}H-n.m.r. spectra of the phosphate diesters **26** and **28**–**37**, H-1′ and H-X were also coupled to P and the signals were shifted downfield (Tables II and III). The *a* configurations of the glycosyl phosphate linkages in **33**–**37** were elucidated by the chemical shifts of the signals for C-3′ and C-5′ which were typical for *a*-D-mannopyranosyl phosphate[23].

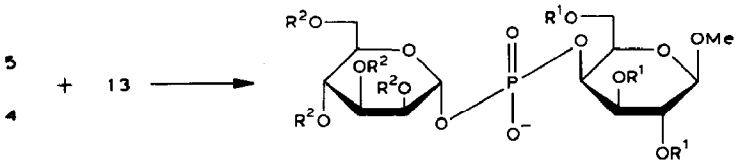
The above results illustrate the high efficiency of the hydrogenphosphonate approach for the synthesis of glycosyl phosphosugars. Both equatorial and axial secondary hydroxyl groups of monosaccharides react smoothly under standard conditions, and *O*-benzylated (**4**) and *O*-benzoylated (**5**) mannosyl hydrogenphosphonate derivatives show similar reactivities. The glycosyl phosphosugars synthesized contained (1→2)-, (1→3)-, and (1→4)-phosphate diester linkages and may be regarded as models for fragments of natural poly(glycosyl phosphates).

EXPERIMENTAL

Optical rotations were measured with a JASCO DIP-360 polarimeter. Melting points were determined with a Kofler apparatus and are uncorrected. N.m.r. spectra



30 R = Bz
36 R = H



31 $R^1 = R^2 =$ Bz
32 R^1 = Bz, R^2 = Bn
37 $R^1 = R^2 =$ H

(^{1}H, ^{13}C, and ^{31}P at 250, 75, and 121.5 MHz, respectively) were recorded with Bruker WM-250 and AM-300 spectrometers for solutions in $CDCl_3$ or D_2O. Chemical shifts (δ in p.p.m.) are given relative to those for Me_4Si (for ^{1}H and ^{13}C) and external aqueous 85% H_3PO_4 (for ^{31}P). T.l.c. was performed on Kieselgel 60 F_{254} (Merck). using *A*, benzene–acetone (95:5); *B*, chloroform–methanol (8:2); *C*, chloroform–methanol (95:5); *D*, dichloromethane–methanol (95:5); *E*, dichloromethane–methanol (9:1); *F*, dichloromethane–methanol (3:1); and *G*, 2-propanol–water (5:1); with detection under u.v. light or by charring with sulfuric acid. Column chromatography was performed on Silicagel L 40/100 (Chemapol, C.S.S.R.) and Silpearl (Sklarny Kavalier, C.S.S.R.). Ion-exchange chromatography was accomplished on a column (18 × 1 cm) of Fractogel TSK DEAE-650 (S) (HCO_3^- form (Merck) by elution at 1 mL. min^{-1} with a linear gradient of water → 0.5M Et_3NHHCO_3 (TEAB) for **33–35** and of water → 0.5M NH_4HCO_3 for **36** and **37**. Solutions were concentrated *in vacuo* at <40°. Acetonitrile was distilled twice from CaH_2 and stored over molecular sieves 4 Å. Pyridine was distilled in sequence from NaOH, P_2O_5. CaH_2, and 1-naphthyl isocyanate and stored over molecular sieves 4 Å.

*2,3,4,6-Tetra-*O*-benzoyl-α-*D*-mannopyranose* (**7**). — Dimethylamine (0.67 mL, 10.12 mmol) was added to a solution of the pentabenzoate **8** (ref. 24) (1 g) in MeCN (8 mL) at −20°, and the mixture was kept at 20°. The reaction was monitored by t.l.c. (solvent *A*). After 5 h, the mixture was concentrated to dryness and acetonitrile was evaporated from the residue. Column chromatography (solvent *A*) of the residue followed by crystallization (ether–hexane) gave **7** (0.52 g, 60%), m.p. 181–182°, $[\alpha]_D^{26}$ −86° (*c* 1.28, chloroform); R_F 0.20 (solvent *A*); lit.[25] m.p. 181°, $[\alpha]_D$ −81°.

Triethylammonium 2,3,4,6-tetra-O-benzyl-α-D-mannopyranosyl hydrogenphosphonate (**4**). — To a stirred solution of imidazole (194 mg, 2.86 mmol) in MeCN (5 mL) at 0° was added PCl_3 (0.076 mL, 0.866 mmol) followed by triethylamine (0.42 mL, 3.02 mmol). Stirring was continued for 15 min, and a solution of **6** (ref. 15) (108 mg, 0.2 mmol) in MeCN (5 mL) was added dropwise during 30 min at 0°. The mixture was stirred at 20° for 5–10 min then quenched with M TEAB (pH 8, 1.4 mL), and the clear solution was stirred for 15 min, and evaporated. Pyridine–triethylamine (4:1) was evaporated from the residue, a solution of which in chloroform (70 mL) was washed with ice-cold water (2 × 30 mL) and M TEAB (2 × 30 mL), dried by filtration through cotton, and concentrated. The residue was dried *in vacuo*, to yield the syrupy homogeneous **4** (140 mg, 100%), $[\alpha]_D^{20}$ + 14° (*c* 2, chloroform); R_F 0 (solvent *A*), 0.35 (solvent *B*). N.m.r. data: ^{1}H (C_6D_6), δ 0.73 (t, 9 H, *J* 7.2 Hz, 3 CH_3CH$_2$), 2.27 (q, 6 H, 3 CH$_3$CH_2), 3.68 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 11.1 Hz, H-6a), 3.78 (dd, 1 H, $J_{5,6b}$ 4.1 Hz, H-6b), 4.04 (dd, 1 H, $J_{2,3}$ 2.5 Hz, H-2), 4.18–4.32 (m, 3 H, H-3,4,5), 4.35 and 4.50 (2 d, 2 H, *J* 12.0 Hz, CH_2Ph), 4.41 (s, 2 H, CH_2Ph), 4.51 and 4.92 (2 d, 2 H, *J* 11.2 Hz, CH_2Ph), 4.63 and 4.69 (2 d, 2 H, *J* 12.2 Hz, CH_2Ph), 6.15 (dd, 1 H, $J_{1,2}$ 1.85, $J_{1,P}$ 8.1 Hz, H-1), 6.92–7.38 (m, 20 H, 4 Ph), 7.40 (d, 1 H, $^1J_{H,P}$ 640 Hz, HP); ^{13}C ($CDCl_3$), δ 8.6 (*C*H$_3$CH$_2$), 45.6 (CH$_3$*C*H$_2$), 69.6 (C-6), 72.1 (*C*H$_2$Ph), 72.7 (*C*H$_2$Ph), 73.3 (C-5), 73.5 (*C*H$_2$Ph), 74.9 (C-4), 75.0 (*C*H$_2$Ph), 75.5 (d, $^3J_{C,P}$ ~7 Hz, C-2), 79.7 (C-3), 93.7 (d, $^2J_{C,P}$ ~5, $J_{C\text{-}1,H\text{-}1}$ 171 Hz, C-1), 127.5–128.4, 138.9 (C_6H_5); ^{31}P, δ 1.56 (in $CDCl_3$); 0.28 (in C_5H_5N).

Triethylammonium 2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyl hydrogenphosphonate (**5**). — Obtained from **7** (66 mg, 0.11 mmol), as described for **4**, **5** was obtained as a chromatographically homogeneous syrup (83 mg, 100%), $[\alpha]_D^{27}$ −49° (*c* 1, chloroform); R_F 0 (solvent *A*), 0.45 (solvent *B*). N.m.r. data ($CDCl_3$): ^{1}H, δ 1.35 (t, 9 H, *J* 8.2 Hz, 3 CH_3CH$_2$), 3.10 (q, 6 H, 3 CH$_3$CH_2), 4.45 (dd, 1 H, $J_{5,6a}$ 2.0 Hz, H-6a), 4.71 (dd, 1 H, $J_{6a,6b}$ 12.3 Hz, H-6b), 4.76 (ddd, 1 H, $J_{5,6b}$ 3.3 Hz, H-5), 5.77 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 5.86 (dd, 1 H, $J_{1,2}$ 1.9, $J_{1,P}$ 8.7 Hz, H-1), 6.01 (dd, 1 H, H-3), 6.16 (t, 1 H, $J_{3,4} = J_{4,5}$ = 10.2 Hz, H-4), 7.13 (d, 1 H, $^1J_{H,P}$ 638.6 Hz, HP), 7.20–7.60 and 7.75–8.15 (m, 20 H, 4 Ph); ^{13}C, δ 8.6 (*C*H$_3$CH$_2$), 45.7 (CH$_3$*C*H$_2$), 62.7 (C-6), 66.8 (C-4), 69.7 (C-3), 70.2 (C-5), 70.9 (d, $^3J_{C,P}$ 6.3 Hz, C-2), 92.9 (d, $^2J_{C,P}$ 3.9 Hz, C-1), 128.2–128.5 and 132.9–133.3 (C_6H_5), 165.3, 165.4, and 166.1 (CO); ^{31}P, δ 0.82.

Methyl 2-O-acetyl-3-O-benzoyl-α-D-mannopyranoside (**18**). — A solution of **14** (ref. 17) (1.33 g) in pyridine (10 mL) and acetic anhydride (5 mL) was kept for 16 h at 20°, then concentrated, and toluene (3 × 10 mL) was evaporated from the residue to yield **16** as a syrup. ^{1}H-N.m.r. data ($CDCl_3$): δ 2.17 (s, 3 H, Ac), 3.46 (s, 3 H, MeO), 3.91 (t, 1 H, $J_{5,6a} = J_{6a,6b}$ = 10.0 Hz, H-6a), 4.04 (ddd, 1 H, $J_{4,5}$ 9.2 Hz, H-5), 4.23 (dd, 1 H, $J_{3,4}$ 10.3 Hz, H-4), 4.35 (dd, 1 H, $J_{5,6b}$ 4.3 Hz, H-6b), 4.75 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.49 (dd, 1 H, $J_{2,3}$ 3.6, H-2), 5.64 (s, 1 H, C*H*Ph), 5.68 (dd, 1 H, H-3), 7.25–7.60 and 7.95–8.05 (m, 10 H, 2 Ph).

A solution of the syrup in aqueous 70% AcOH (30 mL) was kept at 70° for 3 h and then concentrated, and toluene (3 × 10 mL) was evaporated from the residue. Column chromatography (chloroform–methanol, 0→5% of MeOH) gave **18** (1.01 g, 90%), as a solid, $[\alpha]_D^{28}$ +47° (*c* 1, chloroform), R_F 0.26 (solvent *C*). ^{1}H-N.m.r. data ($CDCl_3$): δ 2.16

(s, 3 H, Ac), 3.43 (s, 3 H, MeO), 3.79 (dt, 1 H, $J_{5,6a} = J_{5,6b} = 3.9$ Hz, H-5), 3.92 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 3.97 (dd, 1 H, H-6b), 4.16 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 4.75 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.37 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 5.44 (dd, 1 H, H-3), 7.40–7.65 and 7.95–8.05 (m, 5 H, Ph).

Anal. Calc. for $C_{16}H_{20}O_8$: C, 56.46; H, 5.92. Found: C, 56.44; H, 5.90.

Methyl 2-O-*acetyl-3,4,6-tri*-O-*benzoyl-α*-D-*mannopyranoside* (**20**). — Benzoyl chloride (0.76 mL) was added to a solution of **18** (1 g) in pyridine (10 mL), the mixture was kept at 20° for 16 h, then concentrated. A solution of the residue in chloroform (150 mL) was washed successively with saturated aqueous sodium hydrogencarbonate (2 × 50 mL) and water (2 × 50 mL), dried, and concentrated *in vacuo*. Column chromatography (benzene–acetone, 0→10% of acetone) of the residue gave **20** (1.38 g, 78%), as a solid, $[\alpha]_D^{28}$ +9° (*c* 1, chloroform), R_F 0.50 (solvent *A*). ^{1}H-N.m.r. data ($CDCl_3$): δ 2.15 (s, 3 H, Ac), 3.51 (s, 3 H, MeO), 4.37 (ddd, 1 H, $J_{5,6a}$ 5.3 Hz, H-5), 4.50 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.63 (dd, 1 H, $J_{5,6b}$ 3.0 Hz, H-6b), 4.86 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.47 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 5.79 (d, 1 H, H-3), 5.91 (t, 1 H, $J_{3,4} = J_{4,5} = 10.1$ Hz, H-4), 7.30–8.20 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{30}H_{28}O_{10}$: C, 65.69; H, 5.14. Found: C, 66.12; H, 4.86.

Methyl 3,4,6-tri-O-*benzoyl-α*-D-*mannopyranoside* (**9**). — Acetyl chloride (1.2 mL) was added dropwise to methanol (30 mL) at 0°, **20** (1.3 g) was dissolved in the mixture, which was kept for 16 h at 20° and then concentrated, and toluene (3 × 5 mL) was evaporated from the residue. Column chromatography (as described for **20**) then gave **9** (0.89 g, 75%), as a solid, $[\alpha]_D^{27}$ +21° (*c* 1, chloroform), R_F 0.30 (solvent *A*); lit.[26] $[\alpha]_D^{23}$ +32° (chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 2.30 (bs, 1 H, OH), 3.53 (s, 3 H, MeO), 4.33 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 4.35 (ddd, 1 H, $J_{5,6a}$ 5.4 Hz, H-5), 4.50 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.61 (dd, 1 H, $J_{5,6b}$ 3.0 Hz, H-6b), 4.90 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.68 (dd, 1 H, H-3), 5.94 (t, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4), 7.30–7.60 and 7.90–8.10 (m, 15 H, 3 Ph).

Methyl 3-O-*acetyl-2*-O-*benzoyl-α*-D-*mannopyranoside* (**19**). — This compound was obtained from **15** (ref. 18) (1.6 g) by acetylation [→**17**; ^{1}H-n.m.r. data ($CDCl_3$): δ 2.00 (s, 3 H, Ac), 3.47 (s, 3 H, MeO), 3.92 (t, 1 H, $J_{6a,6a} = J_{5,6b} = 10.0$ Hz, H-6a), 4.04 (dt, 1 H, $J_{4,5}$ 10.0 Hz, H-5), 4.17 (dd, 1 H, $J_{3,4}$ 11.0 Hz, H-4), 4.36 (dd, 1 H, $J_{5,6b}$ 4.0 Hz, H-6b), 4.84 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 5.51 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-3), 5.61 (dd, 1 H, H-2), 5.64 (s, 1 H, C*H*Ph), 7.30–7.70 and 8.08–8.16 (m, 10 H, 2 Ph)] and then acid hydrolysis as described for **18**. Compound **19** (1.08 g, 79%) was isolated as a solid, $[\alpha]_D^{30}$ −65° (*c* 0.2, chloroform), R_F 0.26 (solvent *C*). ^{1}H-N.m.r. data ($CDCl_3$): δ 2.05 (s, 3 H, Ac), 2.17 (t, 1 H, $J_{6,OH}$ 6.4 Hz, HO-6), 2.57 (d, 1 H, $J_{4,OH}$ 5.0, HO-4), 3.45 (s, 3 H, MeO), 3.78 (dt, 1 H, $J_{5,6}$ 3.6 Hz, H-5), 3.95 (dd, 2 H, H-6a,6b), 4.19 (dt, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4), 4.83 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.30 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-3), 5.48 (dd, 1 H, H-2), 7.40–7.65 and 8.02–8.10 (m, 5 H, Ph).

Methyl 2,4,6-tri-O-*benzoyl-α*-D-*mannopyranoside* (**10**). — The diol **19** (1.08 g) was benzoylated under standard conditions to give **21** as a solid, $[\alpha]_D^{29}$ −9.5° (*c* 1.8, chloroform), R_F 0.52 (solvent *A*).^{1}H-N.m.r. data ($CDCl_3$): δ 1.90 (s, 3 H, Ac), 3.52 (s, 3 H, MeO), 4.34 (ddd, 1 H, $J_{5,6a}$ 4.5 Hz, H-5), 4.45 (dd, 1 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.70 (dd, 1 H, $J_{5,6b}$ 2.6 Hz, H-6b), 4.94 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.58 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 5.72 (dd,

1 H, H-3), 5.92 (t, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4), 7.35–7.70 and 7.95–8.27 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{30}H_{28}O_{10}$: C, 65.69; H, 5.14. Found: C, 65.95; H, 5.30.

Treatment of **21** with HCl–MeOH (from 3 mL of AcCl and 75 mL of MeOH), as described for **9**, gave **10** (1.43 g, 80%), as a solid, $[\alpha]_D^{29}$ +4.9° (*c* 0.96, chloroform), R_F 0.30 (solvent *A*). ^{1}H-N.m.r. data ($CDCl_3$): δ 3.50 (s, 3 H, MeO), 4.31 (ddd, 1 H, $J_{5,6a}$ 4.7 Hz, H-5), 4.42 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-3), 4.48 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 4.70 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 4.97 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.44 (dd, 1 H, H-2), 5.71 (t, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4), 7.35–7.67 and 8.02–8.12 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{28}H_{26}O_9$: C, 66.39; H, 5.17. Found: C, 66.36; H, 4.95.

*Methyl 2,3,6-tri-*O*-benzoyl-α-*D*-mannopyranoside* (**11**). — Obtained as described earlier [21]. ^{1}H-N.m.r. data ($CDCl_3$): δ 3.07 (bs, 1 H, OH), 3.50 (s, 3 H, MeO), 4.11 (ddd, 1 H, $J_{5,6a}$ 2.1 Hz, H-5), 4.29 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 4.66 (dd, 1 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.91 (dd, 1 H, $J_{5,6b}$ 3.9 Hz, H-6b), 4.94 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 5.62 (dd, 1 H, H-2), 5.64 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-3), 7.27–7.67 and 7.90–8.20 (m, 15 H, 3 Ph).

*Benzyl 2-*O*-acetyl-3-*O*-benzoyl-4,6-*O*-benzylidene-β-*D*-galactopyranoside* (**23**). — Compound **22** (ref. 19) (0.96 g) was acetylated under standard conditions to give **23** (0.83 g, 81%), m.p. 204–205° (from heptane), $[\alpha]_D^{29}$ +36° (*c* 1, chloroform), R_F 0.54 (solvent *A*). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.99 (s, 3 H, Ac), 3.61 (b, 1 H, H-5), 4.13 (dd, 1 H, $J_{5,6a}$ 1.8, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.43 (dd, 1 H, $J_{5,6b}$ 1.5 Hz, H-6b), 4.55 (d, 1 H, $J_{3,4}$ 3.6 Hz, H-4), 4.66 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.71 (d, 1 H, *J* 12.3 Hz, C*H*$_2$Ph), 4.99 (d, 1 H, C*H*$_2$Ph), 5.16 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-3), 5.54 (s, 1 H, C*H*Ph), 5.70 (dd, 1 H, H-2), 7.30–7.70 and 8.10 (m and d, 15 H, 3 Ph).

Anal. Calc. for $C_{29}H_{28}O_8$: C, 69.04; H, 5.59. Found: C, 68.99; H, 5.68.

*Benzyl 2-*O*-acetyl-3-*O*-benzoyl-β-*D*-galactopyranoside* (**24**). — A solution of **23** (0.83 g) in aqueous 70% AcOH (100 mL) was kept at 70°, then concentrated, and toluene (3 × 10 mL) was evaporated from the residue. Column chromatography (solvent *C*) then gave **24** (0.64 g, 92%), as a syrup, $[\alpha]_D^{29}$ +38° (*c* 0.56, chloroform), R_F 0.15 (solvent *C*). ^{1}H-N.m.r. data ($CDCl_3$ + CD_3OD): δ 1.86 (s, 3 H, Ac), 3.56 (t, 1 H, $J_{5,6a} = J_{5,6b} = 5.8$ Hz, H-5), 3.74 (dd, 1 H, $J_{6a,6b}$ 11.9 Hz, H-6a), 3.80 (dd, 1 H, H-6b), 4.19 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4), 4.53 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.60 (d, 1 H, *J* 12.3, CH_2Ph), 4.84 (d, 1 H, CH_2Ph), 4.95 (dd, 1 H, $J_{2,3}$ 10.6 Hz, H-3), 5.45 (dd, 1 H, H-2), 7.20–7.55 and 7.94 (m and d, 10 H, 2 Ph).

*Benzyl 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**25**). — Obtained from **24** (0.6 g) by the standard benzoylation followed by column chromatography (benzene–acetone, 99:1), **25** (0.88 g, 97%) was isolated as a solid, $[\alpha]_D^{29}$ +34.5° (*c* 1.5, chloroform), R_F 0.60 (solvent *A*). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.97 (s, 3 H, Ac), 4.24 (t, 1 H, $J_{5,6a} = J_{5,6b} = 6.6$ Hz, H-5), 4.42 (dd, 1 H, $J_{6a,6b}$ 11.6 Hz, H-6a), 4.70 (dd, 1 H, H-6b), 4.72 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.74 (d, 1 H, *J* 12.2 Hz, CH_2Ph), 5.00 (d, 1 H, CH_2Ph), 5.39 (dd, 1 H, $J_{3,4}$ 3.7 Hz, H-3), 5.61 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 5.94 (d, 1 H, H-4), 7.25–7.65 and 7.83–8.09 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{36}H_{32}O_{10}$: C, 69.22; H, 5.16. Found: C, 69.32; H, 5.26.

*Benzyl 3,4,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**12**). — Compound **25** (0.82 g)

was treated with HCl–MeOH (obtained from 2 mL of AcCl and 50 mL of MeOH), as described for **9**, to give **12** (0.65 g, 85%), as a solid, $[\alpha]_D^{26}$ −13° (*c* 0.8 chloroform), R_F 0.35 (solvent *A*). ^{1}H-N.m.r data ($CDCl_3$): δ 4.19 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-2), 4.24 (t, 1 H, $J_{5,6a} = J_{5,6b} = 6.6$ Hz, H-5), 4.41 (dd, 1 H, $J_{6a,6b}$ 11.2 Hz, H-6a), 4.63 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.69 (dd, 1 H, H-6b), 4.75 (d, 1 H, *J* 11.5 Hz, CH_2Ph), 5.04 (d, 1 H, CH_2Ph), 5.39 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 5.91 (d, 1 H, H-4), 7.25–7.70 and 7.84–8.09 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{34}H_{30}O_9$: C, 70.09; H, 5.19. Found: C, 70.08; H, 5.37.

*Methyl 2,3,6-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**13**). — Obtained as described earlier[22]. ^{1}H-N.m.r. data ($CDCl_3$): δ 3.56 (s, 3 H, MeO), 4.09 (t, 1 H, $J_{5,6a} = J_{5,6b} = 6.7$ Hz, H-5), 4.36 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 4.62 (dd, 1 H, $J_{6a,6b}$ 11.2 Hz, H-6a), 4.67 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.72 (dd, 1 H, H-6b), 5.37 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-3), 5.78 (dd, 1 H, H-2), 7.27–7.65 and 7.95–8.10 (m, 15 H, 3 Ph).

Synthesis of the O*-protected phosphate diesters* (**26**, **28**–**32**). — A mixture of the glycosyl hydrogenphosphonate derivative (0.11 mmol) and hydroxylic component (0.10 mmol) was dried by evaporation of pyridine (3 × 1 mL) therefrom. The residue was dissolved in the same solvent (0.5 mL), trimethylacetyl chloride (0.25 mmol) was added, the mixture was stirred for 10 min at 20°, and then triethylamine (0.50 mmol) and a freshly prepared solution of iodine (0.20 mmol) in pyridine–water (98:2, 1 mL) were added. After 15 min. chloroform (50 mL) was added, the organic layer was successively washed with cold M aqueous $Na_2S_2O_3$ (2 × 25 mL) and cold M TEAB (2 × 25 mL), dried by filtration through cotton, and concentrated. Column chromatography (dichloromethane–methanol, 1.6→16% of MeOH) of the residue gave the protected phosphate diester derivative. For the ^{1}H- and ^{31}P-n.m.r. data, see Table III. The following compounds were prepared in this manner.

Methyl 3,4,6-tri-*O*-benzoyl-*α*-D-mannopyranoside 2-(2,3,4,6-tetra-*O*-benzyl-*α*-D-mannopyranosyl phosphate), triethylammonium salt (**26**), obtained from **4** (112 mg, 0.16 mmol) and **9** (76 mg, 0.15 mmol), was a solid (160 mg, 87%), $[\alpha]_D^{20}$ −5.8° (*c* 1, chloroform), R_F 0.45 (solvent *D*).

Methyl 2,4,6-tri-O-benzoyl-*α*-D-mannopyranoside 3-(2,3,4,6-tetra-*O*-benzyl-*α*-D-mannopyranosyl phosphate) triethylammonium salt (**28**), obtained from **4** (112 mg, 0.16 mmol) and **10** (76 mg, 0.15 mmol), was a solid (139 mg, 77%), $[\alpha]_D^{21}$ −3° (*c* 1.1, chloroform), R_F 0.45 (solvent *D*).

Methyl 2,3,6-tri-*O*-benzoyl-*α*-D-mannopyranoside 4-(2,3,4,6-tetra-*O*-benzyl-*α*-D-mannopyranosyl phosphate), triethylammonium salt (**29**), obtained from **4** (80 mg), 0.11 mmol) and **11** (50 mg, 0.10 mmol), was a solid (84 mg, 70%), $[\alpha]_D^{29}$ −11.3° (*c* 1, chloroform), R_F 0.45 (solvent *D*).

Benzyl 3,4,6-tri-*O*-benzoyl-*β*-D-galactopyranoside 2-(2,3,4,6-tetra-*O*-benzoyl-*α*-D-mannopyranosyl phosphate), triethylammonium salt (**30**), obtained from **5** (83 mg, 0.11 mmol) and **12** (58 mg, 0.10 mmol), was a solid (90 mg, 67%), $[\alpha]_D^{25}$ +9° (*c* 1, chloroform), R_F 0.55 (solvent *E*).

Methyl 2,3,6-tri-*O*-benzoyl-*β*-D-galactopyranoside 4-(2,3,4,6-tetra-*O*-benzoyl-*α*-D-mannopyranosyl phosphate) triethylammonium salt (**31**), obtained from **5** (83 mg, 0.11 mmol) and **13** (51 mg, 0.10 mmol), was a solid (88 mg, 69%), $[\alpha]_D^{23}$ +11.5° (*c* 1, chloroform), R_F 0.40 (solvent *E*).

Methyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside 4-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl phosphate), triethylammonium salt (**32**), obtained from **4** (112 mg, 0.16 mmol) and **13** (76 mg, 0.15 mmol), was a solid (130 mg, 72%), $[\alpha]_D^{27}$ +28° (*c* 1, chloroform), R_F 0.50 (solvent *E*).

Methyl α-D-mannopyranoside 2-(α-D-mannopyranosyl phosphate), triethylammonium salt (**33**). — A solution of **26** (160 mg) in methanol – 1,4-dioxane (2:1) was treated with Dowex 50W-X4 (Na^+) resin for 2 h at 20°, then filtered, and concentrated *in vacuo*. A solution of the residue in methanol–tetrahydrofuran (2:1) was hydrogenolysed over 10% Pd–C for 5–10 h at 20°. The reaction was monitored by t.l.c. (solvent *F*, R_F 0.15 for **27**). The mixture was filtered and concentrated to dryness, and the residue was treated with 0.1M MeONa in MeOH (6 mL) at 1°. The reaction was monitored by t.l.c. (solvent *G*). After 2.5 h, the mixture was deionized with KU-2 (H^+) resin, filtered, immediately neutralized with triethylamine, and concentrated to dryness. Ion-exchange chromatography of the residue (see general part of Experimental) gave **33** (40 mg, 58%) as a solid, $[\alpha]_D^{27}$ +35.5° (*c* 1, water), R_F 0.30 (solvent *G*). For the ^{13}C-, ^{31}P-, and ^1H-n.m.r. data, see Tables I and II. Also obtained was methyl α-D-mannopyranoside 2-phosphate triethylammonium salt (7.5 mg, 15%), $[\alpha]_D^{27}$ +23.4° (*c* 0.7, methanol), R_F 0.15 (solvent *G*). N.m.r. data (D_2O): ^1H, δ 1.25 (t, 9 H, 3 CH_3CH_2), 3.12 (q, 6 H, 3 CH_3CH_2), 3.40 (s, 3 H, MeO), 3.62 (ddd, 1 H, $J_{5,6a}$ 5.0 Hz, H-5), 3.70 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.0 Hz, H-4), 3.77 (dd, 1 H, $J_{6a,6b}$ 12.0 Hz, H-6a), 3.82 (dd, 1 H, H-3), 3.89 (dd, 1 H, $J_{5,6b}$ 2.1 Hz, H-6b), 4.33 (ddd, 1 H, $J_{2,3}$ 3.1, $J_{2,P}$ 8.6 Hz, H-2), 4.94 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1); ^{31}P, δ 0.88 (at pD 6, for mono-anion), 4.87 (at pD 9, for di-anion).

Methyl α-D-mannopyranoside 3-(α-D-mannopyranosyl phosphate), triethylammonium salt (**34**). — The phosphate diester **28** (70 mg) was deprotected and isolated as described for the synthesis of **33** (but with saponification for 22 h, at 1°), to give **34** (23 mg, 77%), as a solid, $[\alpha]_D^{27}$ +52° (*c* 1.15, water), R_F 0.30 (solvent *G*). For the ^{13}C-, ^{31}P-, and ^1H-N.m.r. data, see Tables I and II.

Methyl α-D-mannopyranoside 4-(α-D-mannopyranosyl phosphate), triethylammonium salt (**35**). — The phosphate diester **29** (70 mg) was deprotected and isolated as described for the synthesis of **33** (saponification with 0.05M MeONa in MeOH for 1.5 h at 20°), to give **35** (25 mg, 83%) as a solid, $[\alpha]_D^{20}$ +72° (*c* 0.96, methanol), R_F 0.30 (solvent *G*); lit.[14] $[\alpha]_D^{20}$ + 75.7° for the cyclohexylammonium salt. For the ^{13}C-, ^{31}P-, and ^1H-n.m.r. data, see Tables I and II.

Benzyl β-D-galactopyranoside 2-(α-D-mannopyranosyl phosphate), ammonium salt (**36**). — A mixture of **30** (90 mg) in 1,4-dioxane (3 mL) and 0.1M MeONa in MeOH (3 mL) was kept for 4 h at 1°. The reaction was monitored by t.l.c. (solvent *G*). The mixture was deionized as described for **33**, to give **36** (31 mg, 88%), isolated by ion-exchange chromatography (see general part of Experimental) as a solid, $[\alpha]_D^{28}$ +14° (*c* 1, water), R_F 0.40 ((solvent *G*). For the ^{13}C-, ^{31}P-, and ^1H-n.m.r. data, see Tables I and II.

Methyl β-D-galactopyranoside 4-(α-D-mannopyranosyl phosphate), ammonium salt (**37**). — A solution of **31** (70 mg) in 0.05M MeONa in MeOH – 1,4-dioxane (3:1, 4 mL) was kept for 30 h at 1°. The reaction was monitored by t.l.c. (solvent *G*). The

mixture was deionized, as described for **33**, to give **37** (19 mg, 75%) isolated by ion-exchange chromatography as a solid, $[\alpha]_D^{28}$ +31.4° (*c* 1, water), R_F 0.30 (solvent *G*). For the ^{13}C-, ^{31}P-, and ^1H-n.m.r. data, see Tables I and II.

ACKNOWLEDGEMENTS

We thank Dr. A. S. Shashkov and Mr. A. V. Ignatenko for recording the n.m.r. spectra.

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