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Synthesis and ^{13}C NMR spectra of 2,3-di-*O*-glycosyl derivatives of methyl α-L-rhamnopyranoside and methyl α-D-mannopyranoside *

Nikolay E. Nifant'ev, Alexander S. Shashkov, Grigory M. Lipkind and Nikolay K. Kochetkov

N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow (Russian Federation)

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ABSTRACT

The syntheses are described of 2,3-di-*O*-glycosyl derivatives of methyl α-L-rhamnopyranoside (**1–5**) and α-D-mannopyranoside (**6–9**).

X-(1 → 2)
Y-(1 → 3) > α-L-Rha*p*-OMe

	X	Y
1	α-L-Rha*p*	α-D-Glc*p*
2	α-D-Glc*p*	α-L-Rha*p*
3	α-L-Rha*p*	β-D-Glc*p*
4	α-L-Rha*p*	β-L-Fuc*p*
5	β-D-Glc*p*	β-D-Gal*p*

X-(1 → 2)
Y-(1 → 3) > α-D-Man*p*-OMe

	X	Y
6	α-L-Rha*p*	α-D-Glc*p*
7	α-D-Man*p*	α-D-Glc*p*
8	β-L-Fuc*p*	β-L-Fuc*p*
9	α-L-Fuc*p*	β-L-Fuc*p*

The deviation from additivity in ^{13}C NMR spectra calculated for **1–9** were similar for stereochemically related trisaccharides.

INTRODUCTION

As part of the development of a computerised approach to the elucidation of the structure of polysaccharides[2], sixteen 2,3-di-*O*-glycosyl derivatives of methyl α-L-rhamnopyranoside that had monosaccharide substituents with the α-D, β-D, α-L, and β-L configurations were synthesised[3–5] and the deviations from additivity ($\Delta\Delta$) in their ^{13}C NMR spectra were calculated[6,7]. The values of the deviations for

Correspondence to: Dr. N.E. Nifant'ev, N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow, Russian Federation.

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the resonances of C-1/6 of the disubstituted rhamnose residue and for C-1′ and C-1″ of the 2- and 3-substituents, respectively, were included in a computer program for the analysis of ^{13}C NMR spectra of regular branched polysaccharides containing 2,3-di-*O*-glycosyl-α-L-rhamnose units[7]. This program was validated[8] on the basis of the ^{13}C NMR spectra of polysaccharides whose structures had been elucidated by traditional methods.

Although the $\Delta\Delta$ values in the computer program were related to the absolute and anomeric configurations of substituents, the most essential parameters for determining the spectral and conformational properties of oligo- and poly-saccharides[7,9], namely, the effects of the stereochemistry at C-2,3,4, were not considered. Therefore, for the correct use of the computer program for the elucidation of the structure of unknown polysaccharides, it was necessary to assess the dependence of the $\Delta\Delta$ values on the configuration of C-2,3,4 in the monosaccharide substituents.

Moreover, in order to broaden the use of the program, it was necessary to prove experimentally the proposal[7] about the applicability of the compiled $\Delta\Delta$ matrix also for the analysis of polysaccharides with 2,3-di-*O*-glycosyl-α-D-mannopyranose moieties.

In order to answer these questions, the model trisaccharide methyl glycosides **1–9** were synthesised and their ^{13}C NMR spectra examined.

X-(1 → 2)
Y-(1 → 3)> α-L-Rha*p*-OMe

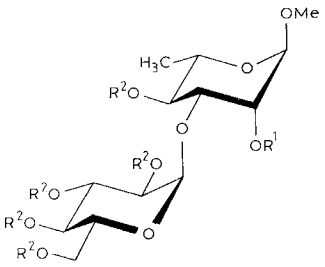
	X	Y
1	α-L-Rha*p*	α-D-Glc*p*
2	α-D-Glc*p*	α-L-Rha*p*
3	α-L-Rha*p*	β-D-Glc*p*
4	α-L-Rha*p*	β-L-Fuc*p*
5	β-D-Glc*p*	β-D-Gal*p*

X-(1 → 2)
Y-(1 → 3)> α-D-Man*p*-OMe

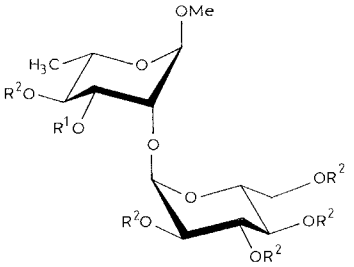
	X	Y
6	α-L-Rha*p*	α-D-Glc*p*
7	α-D-Man*p*	α-D-Glc*p*
8	β-L-Fuc*p*	β-L-Fuc*p*
9	α-L-Fuc*p*	β-L-Fuc*p*

RESULTS AND DISCUSSION

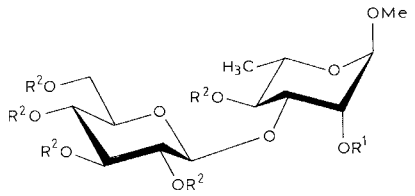
Synthesis of **1–9**.—The trisaccharide methyl glycosides **1**, **2**, **6**, and **7** were synthesised using the corresponding selectively substituted disaccharide precursors **18**, **25**, and **32**, each of which contained a 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl residue. Thus, **18** was prepared by the reaction[10] of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide (**12**) with methyl 2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside[4,5] (**10**) in dichloromethane in the presence of mercuric cyanide. When this reaction was carried out at −50°C, and not at room temperature[10], there was an increase in the α-stereoselectivity. The resulting mixture of disaccharide deriva-



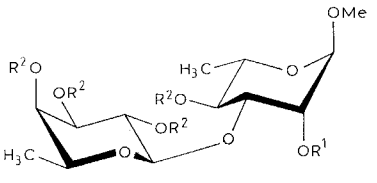
1 R^1 = α-L-Rhap, R^2 = H
17 R^1 = Ac, R^2 = Bn
18 R^1 = H, R^2 = Bn
19 R^1 = RHA, R^2 = Bn



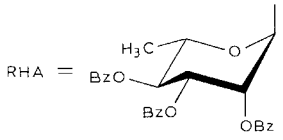
2 R^1 = α-L-Rhap, R^2 = H
24 R^1 = 4-MeOBn, R^2 = Bn
25 R^1 = H, R^2 = Bn
26 R^1 = RHA, R^2 = Bn

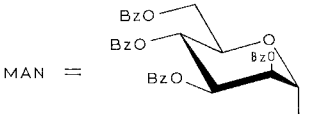


3 R^1 = α-L-Rhap, R^2 = H
20 R^1 = Ac, R^2 = Bn
21 R^1 = H, R^2 = Bn
22 R^1 = H, R^2 = Bz
23 R^1 = RHA, R^2 = Bz



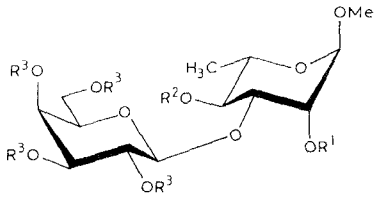
4 R^1 = α-L-Rhap, R^2 = H
35 R^1 = H, R^2 = Bz
36 R^1 = RHA, R^2 = Bz



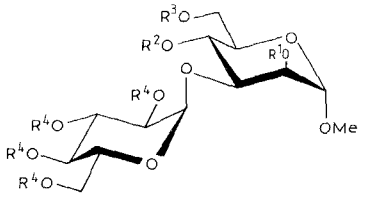


tives (**17** and **20**) was *O*-deacetylated to give **18** (73%) and **21** (16.5%) with HO-2 unsubstituted. The α,β-ratio was 4.5 : 1 (cf. 2.3 : 1 in ref. 10).

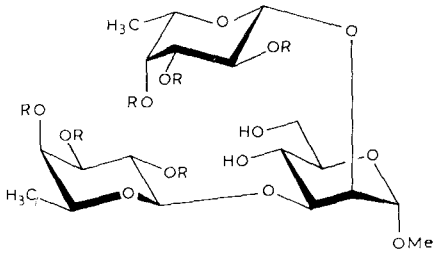
Compound **25** was obtained by the reaction of methyl 4-*O*-benzyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranoside[4,5] (**11**) with **12** at room temperature, which gave almost equal proportions of the α (**24**) and β derivative (**27**). Selective removal of the 4-methoxybenzyl groups then gave **25** (48%) and its β isomer **28** (42%), respectively, with HO-3 unsubstituted. The glycosylation of **11** with **12** at −50°C was more α-stereoselective and gave **25** and **28** in yields of 62 and 27%, respectively. The α-stereoselectivity was not increased by reaction at −78°C and the efficiency of the glycosylation was reduced.



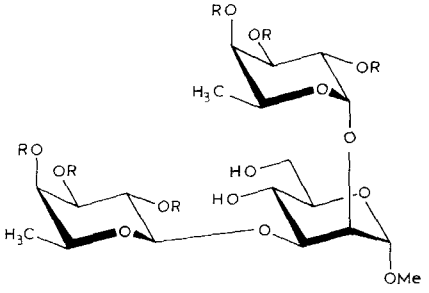
5 R^1 = β-D-Glcp, R^2 = R^3 = H



6 R^1 = α-L-Rhap, R^2 = R^3 = R^4 = H
7 R^1 = α-D-Manp, R^2 = R^3 = R^4 = H
31 R^1 = Bz, R^2, R^3 = PhCH, R^4 = Bn
32 R^1 = H, R^2, R^3 = PhCH, R^4 = Bn
33 R^1 = RHA, R^2 = R^3 = H, R^4 = Bn
34 R^1 = MAN, R^2 = R^3 = H, R^4 = Bn



8 R = H
48 R = Bz

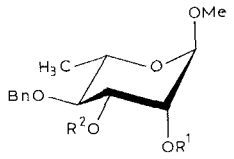


9 R = H
49 R = Bz

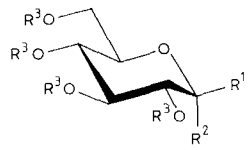
Attempts to synthesise **25** by the reaction of **11** with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl trichloroacetimidate[11] (**13**) under catalysis with trimethylsilyl triflate or with (2-pyridyl) 2,3,4,6-tetra-*O*-benzyl-1-thio-D-glucopyranoside[12] (**14**) in the presence of methyl iodide were unsuccessful, probably because of the instability of the 4-methoxybenzyl group in **11** in the presence of trimethylsilyl triflate (cf. ref. 13) and the low reactivity of **11** in the second reaction. The reaction of **11** with **14** in the presence of 0.3 mol[12] of methyl iodide proceeded slowly and increase in the amount of the promoter caused decomposition of **14**. In contrast to the reported[12] stereospecific α-glucosylation with **14**, the reaction of **11** with **14** gave both the α (**24**) and the β derivative (**27**), and the α,β-ratio was ~ 2–3 : 1 (TLC).

Compound **32** was prepared by the reaction of methyl 3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-mannopyranoside[14] (**29**) with **12** with subsequent *O*-debenzoylation. Even at room temperature, mainly α-glucosylation of **12** occurred and ~ 80% of **32** was obtained.

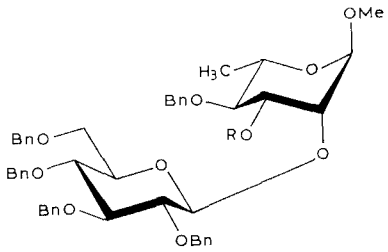
The structures of Glc residues in the disaccharide derivatives **25**, **28**, and **32** were proved by ^{1}H NMR spectroscopy (Table I), in particular, $J_{1',2'}$ values (3.5 Hz for α-Glc in **25** and **32**, and 7.5 Hz for β-Glc in **28**).



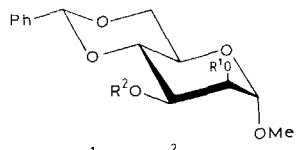
10 R^1 = Ac, R^2 = Bn
11 R^1 = H, R^2 = 4-MeOBn



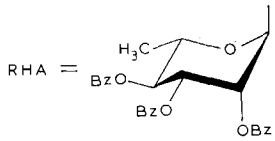
12 R^1 = H, R^2 = Br, R^3 = Bn
13 R^1 = $CCl_3C(=NH)O$, R^2 = H, R^3 = Bn
14 R^1, R^2 = H, (2-pyridyl)thio, R^3 = Bn
15 R^1 = H, R^2 = Br, R^3 = Bz
16 R^1, R^2 = H, 4-NO_2Bz, R^3 = Bn



27 R = 4-MeOBn
28 R = H



29 R^1 = Bz, R^2 = H
30 R^1 = H, R^2 = Bz



The reaction of **18**, **22**[4,5], **25**, **32**, and **35**[4,5] severally with 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide (**37**) under Helferich conditions gave the trisaccharide derivatives **19**, **23**, **26**, **33**, and **36**, respectively, in yields of 82–94%, which were converted by the usual methods into the respective target trisaccharide methyl glycosides **1**, **3**, **2**, **6**, and **4**, the structures of which were established, as previously[1,3–5], after removal of protecting groups, by ^1H and ^{13}C NMR spectroscopy (Tables II and III). The ^1H NMR spectra were assigned using a combination of ^1H–^1H COSY and RCT 2D experiments, and the ^{13}C NMR spectra by 2D ^1H–^{13}C correlated spectroscopy. In the analysis of NMR spectra, the anomeric configurations of the D-Gal*p*, D-Glc*p*, and L-Fuc*p* units were determined on the basis of the $J_{1',2'}$ values. The α configuration of the D-Man*p* and L-Rha*p* residues was proved by the characteristic chemical shifts of their C-5 resonances.

The reaction of **32** with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl bromide (**38**) under Helferich conditions and *O*-debenzoylation of the resulting trisaccharide derivative gave the diol **34** (82%). Removal of remaining protective groups from **34** gave the target trisaccharide methyl glycoside **7**.

Attempted syntheses of **5** by the reaction of **28** with ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**39**) in the presence of nitrosyl tetrafluoro-

TABLE I

^{1}H NMR data [a] (δ in ppm, J in Hz) for **25, 28, 32, 43, 45**, and **64**

Compound	Residue	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
25	Glc	5.04	3.72	4.13	3.69	4.18			3.5	9.4	9.4	9.4			
	Rha	4.87	3.91	4.07	3.40	3.81	1.47		1.6	3.2	9.5	9.5	6.2		
28	Glc	4.62			3.64	3.51			7.5		9.2	9.2			
	Rha	4.60	3.92	3.93	3.15	3.65	1.35		1.6		9.0	9.0	6.2		
32	Glc	5.56	3.63	4.10	3.66	4.02	3.77	3.82	3.5	9.4	9.4	9.4	3.9	2.0	10.5
	Man	4.78	4.17	4.30——4.40					1.2	3.5	5.1				
43	Gal	4.64	5.21	5.01	5.36	3.92	4.03	4.10	7.8	10.2	3.4	1.1	6.5	6.5	10.7
	Rha	4.61	5.08	3.86	3.60——3.72		1.32		1.6	3.5	9.0		5.8		
45	Gal	5.13	5.88	5.60	5.96	4.38	4.50	4.61	7.8	10.6	3.5	1.0	4.5	7.5	11.0
	Rha	4.43	4.07	4.03	3.45	3.60	1.16		1.7	3.5	9.0	9.0	6.3		
64	Rha	5.12	5.66	5.83	5.57	4.23	0.87		1.7	3.5	10.0	10.0	6.2		
	Man	4.88	4.38	5.47	4.42	3.78	3.99	3.99	1.7	3.5	10.0	10.0	3.8	3.8	0

[a] Other signals: aromatic, δ 6.90–8.15; OMe, 3.18–3.47; AcO, 1.95–2.16 (for **43**); PhC*H*, 5.63 (for **32**); PhCH_2, 4.20–5.10.

TABLE II

^{1}H NMR data [a] (δ in ppm, J in Hz) for trisaccharides **1–9** and disaccharides **57** and **59–63**

Compound	Residue	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{6,6a}$	$J_{5,6b}$	$J_{6a,6b}$
1	α-L-Rha-(1 → 2)	5.10	4.05	3.81	3.45	3.74	1.28		1.7	3.4	9.6	9.6	6.4		
	α-D-Glc-(1 → 3)	5.06	3.60	3.77	3.46	3.91	3.70——3.82		3.6	10.0	10.0	9.0	4.8	2.5	
	α-L-Rha-OMe	4.80	4.14	3.88	3.60	3.71	1.33		1.8	3.0	9.4	9.4	6.0		
2	α-D-Glc-(1 → 2)	5.05	3.53	3.77	3.48	3.86	3.75——3.90		3.6	10.0	9.0	9.0	5.0	2.0	
	α-L-Rha-(1 → 3)	5.15	4.06	3.74	3.46	3.76	1.30		1.6	3.4	9.6	9.6	6.2		
	α-L-Rha-OMe	4.86	4.01	3.93	3.68	3.75	1.32		1.7	3.1	9.5	9.5	5.6		
3	α-L-Rha-(1 → 2)	5.14	4.05	3.79	3.43	3.72	1.27		1.6	3.4	9.6	9.6	6.1		
	β-D-Glc-(1 → 3)	4.62	3.33	3.49	3.38——3.45		3.74	3.90	7.6	9.1	9.1		5.0	2.0	12.0
	α-L-Rha-OMe	4.73	4.21	3.91	3.61	3.73	1.32		1.8	3.2	9.5	9.5	6.1		
4	α-L-Rha-(1 → 2)	5.07	4.05	3.79	3.44	3.73	1.28		1.8	3.1	9.7	9.7	6.0		
	β-L-Fuc-(1 → 3)	4.46	3.51	3.65	3.76	3.78	1.25		7.8	9.8	3.3	<1	6.3		
	α-L-Rha-OMe	4.79	4.11	3.99	3.57	3.71	1.33		1.8	3.3	9.6	9.6	6.1		

5	β-D-Glc-(1 → 2)	4.78	3.35	3.52	3.40—3.56				7.5	8.8	9.0					
	β-D-Gal-(1 → 3)	4.62	3.60	3.69	3.95	3.73			7.2	9.5	3.1	< 1				
	α-L-Rha-OMe	4.93	4.32	3.97	3.69	3.76	1.34		1.7	3.1	9.1	9.1	5.6			
6	α-L-Rha-(1 → 2)	4.93	3.97	3.88	3.45	3.97	1.32		1.8	3.2	9.5	9.5	6.2			
	α-D-Glc-(1 → 3)	5.32	3.54	3.70	3.45	3.73	3.77	3.89	3.8	9.7	9.5	9.5	5.5	2.5	12.2	
	α-D-Man-OMe	4.88	4.03	3.97	3.95	3.64	3.77	3.89	1.5	3.5	9.4	9.4	5.5	2.5	12.2	
7	α-D-Man-(1 → 2)	5.13	4.04	3.86	3.62	3.75			1.6	3.3	9.6	9.6				
	α-D-Glc-(1 → 3)	5.22	3.56	3.68	3.43	3.71			3.6	9.8	9.1	9.1				
	α-D-Man-OMe	4.98	4.11	3.99	3.91	3.65			1.6	2.7	9.2	9.2				
8	β-L-Fuc-(1 → 2)	4.73	3.49	3.66	3.73	3.76	1.26		7.8	10.0	3.4	1.1	5.0			
	β-L-Fuc-(1 → 3)	4.54	3.52	3.65	3.72	3.78	1.24		7.6	9.9	3.5	1.1	4.9			
	α-D-Man-OMe	4.90	4.31	3.95	3.90	3.67	3.79	3.89	1.7	3.5	9.6	9.6	5.5	2.5	12.0	
9	α-L-Fuc-(1 → 2)	4.97	3.76	3.95	3.85	4.45	1.23		3.8	10.0	3.0	< 1	5.0			
	β-L-Fuc-(1 → 3)	4.63	3.53	3.65	3.74	3.76	1.26		7.5	9.9	2.7	< 1	5.1			
	α-D-Man-OMe	4.85	4.08	4.00	3.97	3.65	3.78—3.91		1.6	2.9	9.4	9.4				
57	β-D-Gal-(1 → 3)	4.60	3.59	3.66	3.93	3.67—3.81			7.1	9.2	3.0	< 1				
	α-L-Rha-OMe	4.71	4.18	3.87	3.60	3.74	1.33		1.7	3.1	9.0	9.0	6.1			
59	α-L-Rha-(1 → 2)	4.90	3.99	3.84	3.45	4.01	1.27		1.7	3.2	9.7	9.7	6.1			
	α-D-Man-OMe	4.89	3.95	3.87	3.68	3.63	3.76	3.91	1.6	3.4	9.5	9.5	5.8	2.2	12.5	
60	α-L-Fuc-(1 → 2)	4.97	3.78	3.90	3.83	4.36	1.21		3.8	10.4	6.0	< 1	6.4			
	α-D-Man-OMe	4.87	3.92	3.93	3.75	3.63			1.5	6.8	9.2	9.2	4.6	2.5		
61	β-L-Fuc-(1 → 2)	4.55	3.55	3.66	3.75	3.79	1.26		7.5	9.6	3.2	< 1	6.4			
	α-D-Man-OMe	5.02	4.04	3.86	3.73	3.61			1.6	3.2	9.4	9.4				
62	α-D-Glc-(1 → 3)	5.23	3.56	3.79	3.42	3.80			3.6	9.7	9.7					
	α-D-Man-OMe	4.76	4.10	3.90	3.85	3.66		3.91	1.6	2.7	9.6	9.6	5.5	2.5	11.8	
63	β-L-Fuc-(1 → 3)	4.59	3.56	3.67	3.75	3.78	1.26		7.5	9.7	3.2	< 1	6.4			
	α-D-Man-OMe	4.78	4.20	3.88	3.82	3.67	3.78	3.92	1.7	3.0	9.3	9.3	6.0	2.1	12.0	

[a] Signals for OMe at δ 3.40–3.43.

TABLE III

^{13}C NMR data for trisaccharides **1–9**, disaccharides **50–63**, and methyl α-L-rhamnopyranoside (**68**) and methyl α-D-mannopyranoside (**69**) (D_2O; δ in ppm)

Compound	Residue	C-1	C-2	C-3	C-4	C-5	C-6	OMe
1	α-L-Rha-(1 → 2)	102.9	71.5	71.5	73.4	70.3	18.1	
	α-D-Glc-(1 → 3)	96.4	72.5	74.2	70.9	73.1	61.9	
	α-L-Rha-OMe	101.0	75.3	76.8	72.0	69.9	17.9	56.1
2	α-D-Glc-(1 → 2)	98.6	72.5	73.7	70.7	73.4	61.7	
	α-L-Rha-(1 → 3)	102.9	71.2	71.4	73.3	70.3	17.8	
	α-L-Rha-OMe	99.1	76.4	76.2	73.4	70.3	17.6	56.1
3	α-L-Rha-(1 → 3)	102.7	71.4	71.5	73.4	69.8	18.0	
	β-D-Glc-(1 → 3)	105.1	74.9	77.1	70.9	77.1	62.2	
	α-L-Rha-OMe	101.1	78.0	81.3	72.5	70.3	17.9	56.1
4	α-L-Rha-(1 → 2)	103.2	71.4	71.4	73.4	70.5	18.1	
	β-L-Fuc-(1 → 3)	102.0	71.8	74.5	72.7	72.3	16.7	
	α-L-Rha-OMe	101.0	76.5	78.8	72.0	70.0	18.0	56.2
5	β-D-Glc-(1 → 2)	104.6	74.8	77.1	71.0	77.1	62.2 [a]	
	β-D-Gal-(1 → 3)	105.8	72.5	74.0	70.0	76.4	61.7 [a]	
	α-L-Rha-OMe	101.4	79.5	80.9	72.5	70.5	17.9	56.1
6	α-L-Rha-(1 → 2)	99.4	71.7	71.1	73.6	70.3	18.7	
	α-D-Glc-(1 → 3)	101.6	72.9	74.1	70.8	73.6	61.8	
	α-D-Man-OMe	99.1	76.3	77.0	68.2	74.4	61.9	56.2
7	α-D-Man-(1 → 2)	102.5	71.2	71.5	67.9	74.3	62.1	
	α-D-Glc-(1 → 3)	101.7	72.7	74.0	70.7	73.8	61.9	
	α-D-Man-OMe	100.5	78.4	79.3	67.7	73.9	61.7	55.9
8	β-L-Fuc-(1 → 2)	104.6	72.3	74.2	72.6	72.0	16.7	
	β-L-Fuc-(1 → 3)	105.8	72.3	74.2	72.6	72.0	16.6	
	α-D-Man-OMe	101.4	78.4	81.5	67.1	73.8	62.1	56.2
9	α-L-Fuc-(1 → 2)	99.3	69.4	70.5	73.2	68.3	16.7	
	β-L-Fuc-(1 → 3)	105.6	72.4	74.3	72.6	72.1	16.6	
	α-D-Man-OMe	99.9	77.5	79.1	67.6	74.0	61.5	56.1
50	α-L-Rha-(1 → 2)	103.4	71.4	71.4	73.4	70.3	18.1	
	α-L-Rha-OMe	100.9	79.6	71.4	73.6	69.8	17.8	56.2
51	β-D-Glc-(1 → 2)	105.5	74.8	77.0	70.7	77.2	62.1	
	α-L-Rha-OMe	101.2	81.0	71.6	73.7	69.7	17.9	56.1
52	α-D-Glc-(1 → 2)	98.9	72.7	74.1	70.9	73.3	61.8	
	α-L-Rha-OMe	99.6	77.4	71.1	73.4	70.0	17.9	56.1
53	α-D-Glc-(1 → 3)	97.0	72.7	74.3	70.9	73.1	61.8	
	α-L-Rha-OMe	101.8	68.0	77.2	71.7	69.8	18.0	56.0
54	β-D-Glc-(1 → 3)	105.0	74.9	77.3	71.1	77.2	62.2	
	α-L-Rha-OMe	102.0	71.2	81.5	72.5	69.7	18.2	56.1
55	α-L-Rha-(1 → 3)	103.3	71.1	71.1	73.0	70.0	17.6	
	α-L-Rha-OMe	101.8	70.8	79.0	72.4	69.6	17.6	56.1
56	β-L-Fuc-(1 → 3)	102.35	71.9	74.2	72.7	72.4	16.8	
	α-L-Rha-OMe	101.95	69.2	79.7	71.9	69.65	18.15	56.15
57	β-D-Gal-(1 → 3)	105.5	72.3	73.8	69.8	76.3	62.2	
	α-L-Rha-OMe	101.8	71.1	81.2	72.3	69.5	17.8	55.9
58	α-D-Man-(1 → 2)	103.0	71.7	71.7	67.8	74.1 [a]	61.8 [b]	
	α-D-Man-OMe	100.1	79.3	70.8	67.8	73.4 [a]	61.9 [b]	55.7
59	α-L-Rha-(1 → 2)	99.7	70.2	71.5	73.4	71.8	17.8	
	α-D-Man-OMe	99.3	76.2	71.2	68.3	74.3	62.3	56.2
60	α-L-Fuc-(1 → 2)	99.2	69.4	71.4	73.2	68.3	16.4	
	α-D-Man-OMe	99.9	77.4	70.8	68.1	74.1	62.0	56.1

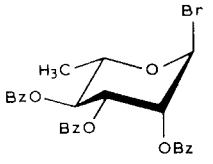
TABLE III (continued)

Compound	Residue	C-1	C-2	C-3	C-4	C-5	C-6	OMe
61	β-L-Fuc-(1 → 2)	105.9	72.2 [a]	74.3	72.4 [a]	72.6	16.7	
	α-D-Man-OMe	101.4	80.6	72.0	68.5	73.9	62.2	56.2
62	α-D-Glc-(1 → 3)	102.0	73.0	74.2	71.0	73.6	62.0	
	α-D-Man-OMe	101.6	71.0	79.9	67.4	73.9	62.2	55.9
63	β-L-Fuc(1 → 3)	105.4	72.3	74.2	72.6	72.0	16.7	
	α-D-Man-OMe	101.9	71.0	81.6	67.2	73.7	62.3	56.0
68	α-L-Rha-OMe	102.1	71.3	71.6	73.3	69.6	17.8	55.9
69	α-D-Man-OMe	102.1	71.2	71.9	68.1	73.6	62.3	55.9

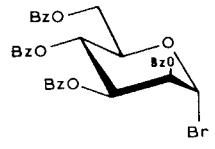
[a,b] Assignments may be interchanged.

borate[1,15–17] or with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (**40**) under catalysis with trimethylsilyl triflate[1,18] were unsuccessful, probably due to the low reactivity of **28**. In contrast, the reaction of **39** with the rhamnoside **10** gave 83% of the disaccharide **42**.

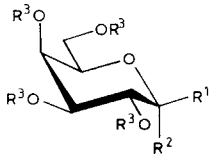
A successful route to **5** involved the following reactions. Glycosylation of **10** with ethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside[1] (**41**) in the presence of nitrosyl tetrafluoroborate gave the β-linked disaccharide derivative **44** (83%),



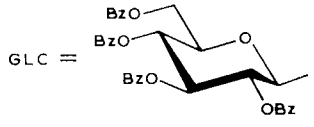
37

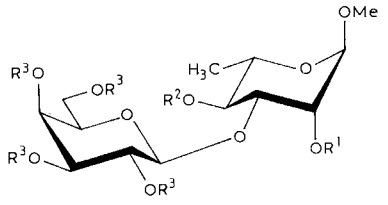


38



39 R^1 = SEt, R^2 = H, R^3 = Ac
40 R^1 = H, R^2 = $CCl_3C(=NH)O$, R^3 = Ac
41 R^1 = SEt, R^2 = H, R^3 = Bz





42 R^1 = R^3 = Ac, R^2 = Bn
43 R^1 = R^3 = Ac, R^2 = H
44 R^1 = Ac, R^2 = Bn, R^3 = Bz
45 R^1 = H, R^2 = Bn, R^3 = Bz
46 R^1 = GLC, R^2 = Bn, R^3 = Bz
47 R^1 = GLC, R^2 = H, R^3 = Bz
57 R^1 = R^2 = R^3 = H

TABLE IV

Deviations from additivity ($\Delta\Delta$ values in ppm) in the ^{13}C NMR spectra of trisaccharides **1–9** and **68–74**

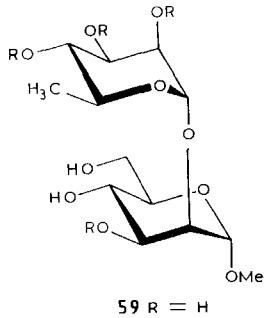
Compound	Stereochemical code [a]	Deviations from additivity							
		C-1	C-2	C-3	C-4	C-5	C-6	C-1′ [b]	C-1″ [b]
α-L-Rha-(1 → 2) α-D-Glc-(1 → 3)-α-L-Rha-OMe **1**	LDL,αα	0.2	−1.0	−0.2	0	−0.1	0	−0.5	0
α-L-Fuc-(1 → 2) α-D-Man-(1 → 3)-α-L-Rha-OMe **68**	LDL,αα	0.5	−0.6	0.4	−0.2	0	0	−0.2	0.4
α-D-Glc-(1 → 2) α-L-Rha-(1 → 3)-α-L-Rha-OMe **2**	DLL,αα	−0.2	−0.2	−2.3	0.9	0.3	−0.1	−0.3	−0.4
α-L-Rha-(1 → 2) α-D-Glc-(1 → 3)-α-D-Man-OMe **6**	LDD,αα	0.2	0.6	−1.9	1.0	0.3	0.3	−0.5	−0.3
α-D-Man-(1 → 2) α-L-Rha-(1 → 3)-α-L-Rha-OMe **69**	DLL,αα	0.3	0.3	−2.0	1.2	0.2	0.3	−0.5	−0.3
α-L-Rha-(1 → 2) β-D-Glc-(1 → 3)-α-L-Rha-OMe **3**	LDL,αβ	0.3	−1.5	0	−0.3	0.4	−0.2	−0.7	0.1
α-L-Fuc-(1 → 2) β-D-Glc(1 → 3)-α-L-Rha-OMe **70**	LDL,αβ	0.5	−1.7	−0.1	−0.5	0	−0.2	−1.0	0.3
α-L-Rha-(1 → 2) β-L-Fuc-(1 → 3)-α-L-Rha-OMe **4**	LLL,αβ	0.6	−0.9	−0.5	−0.2	−0.1	−0.2	−0.3	−0.4
α-L-Fuc-(1 → 2) β-L-Fuc-(1 → 3)-α-L-Rha-OMe **71**	LLL,αβ	0.6	−1.1	−0.4	−0.3	0.1	0.1	−0.7	−0.2
β-D-Glc-(1 → 2) β-D-Gal-(1 → 3)-α-L-Rha-OMe **5**	DDL,ββ	−0.5	−1.3	−0.4	−0.3	0.3	0	−0.9	0
β-L-Fuc-(1 → 2) β-L-Fuc-(1 → 3)-α-D-Man-OMe **8**	LLD,ββ	0.2	−1.9	−0.1	−0.5	−0.2	−0.2	−1.2	0.6
β-D-Glc-(1 → 2) β-D-Glc-(1 → 3)-α-L-Rha-OMe **72**	DDL,ββ	0.6	−0.5	−0.2	−0.4	0.1	0	−0.2	0.1
α-D-Man-(1 → 2) α-D-Glc-(1 → 3)-α-D-Man-OMe **7**	DDD,αα	0.5	−0.7	0.5	0.6	0.2	0.3	−0.5	0.1
α-L-Rha-(1 → 2) α-L-Rha-(1 → 3)-α-L-Rha-OMe **73**	LLD,αα	0.6	−0.2	0.2	0.6	0.3	0.6	−0.5	0.3

TABLE IV (continued)

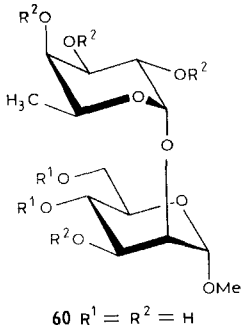
Compound	Stereochemical code [a]	Deviations from additivity							
		C-1	C-2	C-3	C-4	C-5	C-6	C-1′ [b]	C-1″ [b]
α-L-Fuc-(1 → 2) β-L-Fuc-(1 → 3)>α-D-Man-OMe **9**	LLD,αβ	−0.6	0.3	−1.4	0.4	−0.2	−0.5	0.1	0.2
α-D-Man-(1 → 2) β-D-Glc-(1 → 3)>α-L-Rha-OMe **74**	DDL,αβ	0.6	0.5	−1.3	0.2	−0.1	0.1	−0.1	0.4

[a] Absolute configurations of the substituents at O-2 and O-3 and of the bis-glycosylated unit, and the anomeric configurations of the substituents at O-2 and O-3, respectively. [b] C-1′ and C-1″ refer to the (1 → 2)- and (1 → 3)-linked residues, respectively.

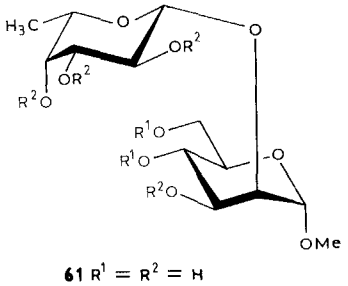
methanolysis of which yielded **45** (88%). Reaction of **45** with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (**15**), under promotion with silver triflate in nitromethane[4,5], gave the trisaccharide derivative **46** (92%). Hydrogenolysis of **46** and then *O*-debenzoylation gave the target trisaccharide methyl glycoside **5**.



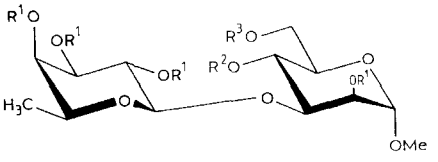
59 R = H
64 R = Bz



60 $R^1 = R^2 = H$
65 R^1 = Ac, R^2 = Bz



61 $R^1 = R^2 = H$
66 R^1 = Ac, R^2 = Bz



63 $R^1 = R^2 = R^3 = H$
67 R^1 = Bz, R^2, R^3 = PhCH

The isomeric di-*O*-fucosylmannosides **8** and **9** were prepared by *O*-debenzoylation of the trisaccharide derivatives **48** and **49**, respectively, the syntheses of which will be described elsewhere.

In addition to the trisaccharide methyl glycosides **1–9**, the disaccharide methyl glycosides **57** and **59–63** were also synthesised, since their ^{13}C NMR data were necessary for the calculation of the $\Delta\Delta$ values for **1–9**. Other fragments of **1–9**, namely, the disaccharide methyl glycosides **50–56** and **58**, have been described[7,20].

R-(1 → 2)-α-L-Rha*p*-OMe

50 R = α-L-Rha*p*
51 R = β-D-Glc*p*
52 R = α-D-Glc*p*

R-(1 → 3)-α-L-Rha*p*-OMe

53 R = α-D-Glc*p*
54 R = β-D-Glc*p*
55 R = α-L-Rha*p*
56 R = β-L-Fuc*p*
57 R = β-D-Gal*p*

R-(1 → 2)-α-D-Man*p*-OMe

58 R = α-D-Man*p*
59 R = α-L-Rha*p*
60 R = α-L-Fuc*p*
61 R = β-L-Fuc*p*

R-(1 → 3)-α-D-Man*p*-OMe

62 R = α-D-Glc*p*
63 R = β-L-Fuc*p*

Compounds **57** and **59–63** were prepared by the usual methods from substituted derivatives **43, 64–66, 32**, and **67**, respectively. The rhamnosyl-mannoside **64** was obtained by glycosylation of **30** with **37** and subsequent acidic hydrolysis. The syntheses of the di- (**65–67**) and tri-saccharide (**48** and **49**) derivatives will be described elsewhere.

The deviations from additivity (ΔΔ values) in ^{13}C NMR spectra of **1–9**.—The $\Delta\Delta$ values for **1–9** are listed in Table IV, which also contains data for the trisaccharide methyl glycosides **68–74** studied previously[6,7].

X-(1 → 2)\
Y-(1 → 3)/ α-L-Rha*p*-OMe

	X	Y
68	α-L-Fuc*p*	α-D-Man*p*
69	α-D-Man*p*	α-L-Rha*p*
70	α-L-Fuc*p*	β-D-Glc*p*
71	α-L-Fuc*p*	β-L-Fuc*p*
72	β-D-Glc*p*	β-D-Glc*p*
73	α-L-Rha*p*	α-L-Rha*p*
74	α-D-Man*p*	β-D-Glc*p*

The $\Delta\Delta$ value for the resonance of each carbon atom (Ci) in the methyl α-L-rhamnoryranoside fragment was calculated[6,7] using equation *1*, and for those of C-1′ and C-1″ using equations *2* and *3*, respectively.

$$\Delta\Delta\text{Ci} = \delta\text{Ci}_{TS} - \delta\text{Ci}_{(1\rightarrow 2)} - \delta\text{Ci}_{(1\rightarrow 3)} + \delta\text{Ci}_{\alpha\text{-L-Rha}p\text{-OMe}} \quad (1)$$

$$\Delta\Delta\text{C-1}' = \delta\text{C-1}'_{TS} - \delta\text{C-1}'_{(1\rightarrow 2)} \quad (2)$$

$$\Delta\Delta\text{C-1}'' = \delta\text{C-1}''_{TS} - \delta\text{C-1}'_{(1\rightarrow 3)} \quad (3)$$

In equation *1*, δCi_{TS}, $\delta\text{Ci}_{(1\rightarrow 2)}$, $\delta\text{Ci}_{(1\rightarrow 3)}$, and $\delta\text{Ci}_{\alpha\text{-L-Rha}p\text{-OMe}}$ are the chemical shifts of the resonances of Ci in the trisaccharide, the corresponding (1 → 2)- and (1 → 3)-linked disaccharides, and methyl α-L-rhamnopyranoside, respectively.

In the following discussion, the five-component code used for the branched trisaccharide methyl glycosides is made up of the absolute configurations of the 2- and 3-*O*-glycosyl substituents and the 2,3-di-*O*-glycosylated residue, and the anomeric configurations of the former two substituents.

It was found[6,7] for the 2,3-di-*O*-glycosylated methyl α-L-rhamnopyranosides that the $\Delta\Delta$ values varied within the range −2 to +1.5 ppm. As can be seen from the data in Table IV, the $\Delta\Delta$ values for **1**–**4** were not greatly different from those of the stereochemically similar[9] trisaccharides **68**–**71**. For example, for **1** and **68**, the deviations from additivity are small and even the larger ones for C-2 differ by only 0.4 ppm (−0.6 and −1.0 ppm) in spite of the difference in configurations of C-2′, C-2″, and C-4′.

Likewise, there are similarities in the $\Delta\Delta$ values for the pairs **2** and **69** (DLL,αα) and for **3** and **70** (LDL,αα), for which large values were found, namely, $\Delta\Delta$C-3 (−2.3 and −2.0 ppm) for **2** and **69** and $\Delta\Delta$C-2 (−1.5 and −1.7 ppm) for **3** and **70**. For **3** and **70**, the $\Delta\Delta$ values for C-1′ were also substantial (−0.7 and −1.0 ppm).

Comparison of the data for **4** and **71** also demonstrates the similarity of the $\Delta\Delta$ values for the stereochemically related trisaccharides. The components of the pairs **2** and **69**, **3** and **70**, and **4** and **71** differ in the configurations of C-2′ and C-4′, and the data in Table IV indicate that the $\Delta\Delta$ values depend to a smaller extent on the configuration of C-2,3,4 in the substituent residues than the respective chemical shifts taken into account in equations *1*–*3*. For example, the chemical shifts of the C-2 resonances for **2** and **69** on one hand, and those for their disaccharide fragments α-D-Glc*p*-(1 → 2)-α-L-Rha*p*-OMe (**52**) and α-D-Man*p*-(1 → 2)-α-L-Rha*p*-OMe[6,7] on the other, differ by 0.9 and 1.4 ppm, respectively, but, the $\Delta\Delta$C-2 values for **2** and **69** are approximately equal (−0.2 and 0.3 ppm).

Similar $\Delta\Delta$ values were found for the 2,3-di-*O*-glycosyl-α-D-mannopyranosides **6**, **7**, and **9** on one hand, and **2** and **69** (both refer to **6**), **73**, and **74**, respectively, on the other. The trisaccharides in the pairs **7** and **73**, **9** and **74**, **2** and **6**, and **6** and **69** are distinguished from each other not only by the absolute configurations of the monosaccharide constituents but also by the configurations of C-2′ and C-2″ (**2** and **6**) or C-2′, C-4′, and C-4″ (**9** and **74**).

Another situation was observed for **8** (LLD,$\beta\beta$) and **72** (DDL,$\beta\beta$). In the earlier work[6,7], no noticeable $\Delta\Delta$ values were found for 2,3-di-*O*-glucosyl-α-L-rhamnoside (**72**), whereas, for 2,3-di-*O*-β-L-fucosyl-α-D-mannoside (**8**), they were -1.9 and -1.2 ppm for the C-2 and C-1′ resonances, respectively. The lack of similarity in the $\Delta\Delta$ values for **8** and **72** may be due to the different orientations of HO-4″. Indeed, molecular models of **8** and **72** show that the inversion of configuration at C-4″ may alter the non-bonded interactions of the monosaccharide substituents, which could be reflected in ^{13}C NMR spectra.

In order to assess this proposal, the trisaccharide methyl glycoside **5**, which differs from **72** only in the configuration of C-4″, was studied. Compound **5**, like **8** and unlike **72**, had the predicted $\Delta\Delta$ values for the C-2 and C-1′ signals (-1.3 and -0.9 ppm).

Thus, for oligosaccharides branched at vicinal positions and in which non-bonded monosaccharide residues are in close proximity, inversion of configuration in the region C-2,3,4 of the substituent residues may affect the chemical shifts of the ^{13}C resonances of other monosaccharide residues. The possibility of such effects should be taken into account in considerations of the results of computer-based calculations of the spectra of branched polysaccharides, in particular, in the choice of the admissible value of the deviation between experimental and calculated spectra.

It is concluded that, in the ^{13}C NMR spectra of branched oligosaccharides with 2,3-di-*O*-glycosylated α-L-rhamnopyranose residues, the $\Delta\Delta$ values for stereochemically similar compounds are usually similar. In general, the $\Delta\Delta$ values for 2,3-di-*O*-glycosyl-α-L-rhamnopyranosides can be used to calculate the spectra of corresponding α-D-mannopyranose derivatives, provided the absolute configurations are inverted. These facts allow the reliable application of the $\Delta\Delta$ values reported here and earlier[7] for the analysis of the structure of unknown polysaccharides with 2,3-di-*O*-glycosylated residues of α-rhamnopyranose and α-mannopyranose.

EXPERIMENTAL

General.—The reagents, solvents, and NMR instruments used in this work have been described elsewhere[3,5,7]. Optical rotations for substituted compounds were determined on solutions in $CHCl_3$ and for oligosaccharides **1–9**, **57**, and **59–63** on solutions in water with a JASCO DIP-360 digital polarimeter at 26–30°C.

TLC was performed on Kieselgel-60 (Merck) with EtOAc–toluene (*A*, 1:7; *B*, 1:2) and detection by charring with sulphuric acid. Column chromatography was performed on Silica Gel L 40/100 μm (C.S.F.R.) by gradient elution with benzene–EtOAc.

Methyl 4-O-benzyl-3-O-(2,3,4,6-tetra-O-benzyl-α- (**18**) *and- β-D-glucopyranosyl)-α-L-rhamnopyranoside* (**21**).—A mixture of methyl 2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside[4,5] (**10**; 310 mg, 1.0 mmol), $Hg(CN)_2$ (380 mg, 1.5 mmol), and

molecular sieves 4A in CH_2Cl_2 (10 mL) was stirred for 1 h under Ar. A solution of the glucosyl bromide **12** [prepared[10] from the nitrobenzoate **16** (1.03 g, 1.5 mmol)] in CH_2Cl_2 (10 mL) was added dropwise during 30 min at −50°C. The mixture was stirred for 30 min at −50°C, then diluted with $CHCl_3$ (50 mL), filtered through Celite, washed with satd aq KBr and water, filtered through cotton, and concentrated. Column chromatography of the residue gave a fraction (~ 1 g) with R_F 0.40–0.50 (solvent *A*) that contained **17** and **20**. A solution of **17** and **20** in dry CH_2Cl_2 (5 mL) was treated with 0.1 M MeONa in MeOH (10 mL) for 20 min at room temperature and then concentrated. A solution of the residue in $CHCl_3$ (50 mL) was washed with water (2 × 50 mL) and concentrated. Column chromatography of the residue gave **18** (580 mg, 73%) and **21** (130 mg, 16.5%).

Compound **18** was amorphous and had $[\alpha]_D$ +33° (*c* 2), R_F 0.25 (solvent *A*); lit.[10] $[\alpha]_D$ +33° (*c* 1.2, $CHCl_3$).

Compound **21** was amorphous and had $[\alpha]_D$ −7° (*c* 2), R_F 0.16 (solvent *A*); lit.[10] $[\alpha]_D$ −11.1° (*c* 1.1, $CHCl_3$).

The ^1H NMR data for **18** and **21** are listed in Table I.

*Methyl 4-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl)-α-*L*-rhamnopyranoside* (**19**).—A mixture of **18** (158 mg, 0.2 mmol), $Hg(CN)_2$ (100 mg, 0.4 mmol), $HgBr_2$ (30 mg), and molecular sieves 4A in MeCN (3 mL) was stirred for 45 min at 20°C under Ar, and a solution of **37** [prepared[2] from tetra-*O*-benzoyl-L-rhamnopyranose (230 mg, 0.4 mmol)] in 3:2 MeCN–CH_2Cl_2 (5 mL) was added dropwise during 1 h. The mixture was stirred for 1 h, then diluted with $CHCl_3$ (50 mL) and satd aq KBr, filtered through Celite, washed with aq KBr and water, and concentrated. Column chromatography of the residue gave amorphous **19** (210 mg, 84%), $[\alpha]_D$ +130.5° (*c* 2), R_F 0.70 (solvent *A*).

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl)-α-*L*-rhamnopyranoside* (**23**).—Glycosylation of **22**[4,5] (187 mg, 0.22 mmol) with **37** [prepared[2] from tetra-*O*-benzoyl-L-rhamnopyranose (232 mg, 0.4 mmol)], as for the synthesis of **19**, gave amorphous **23** (270 mg, 94%), $[\alpha]_D$ +56° (*c* 2), R_F 0.51 (solvent *A*).

*Methyl 4-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-* (**25**) *and -β-*D*-glucopyranosyl)-α-*L*-rhamnopyranoside* (**28**).— (*a*) Glycosylation of **11**[4,5] (97 mg, 0.25 mmol) with **12** [prepared[10] from **16** (340 mg, 0.5 mmol)], as for the synthesis of **17** and **20**, but at room temperature, gave a mixture (205 mg, 90%) of **24** and **27**, R_F 0.52 and 0.46 (solvent *A*). To a solution of the mixture in 9:1 MeCN–water (10 mL) was added $(NH_4)_2Ce(NO_3)_6$ (275 mg, 0.5 mmol). The mixture was stirred for 20 min at 20°C, then diluted with $CHCl_3$ (50 mL), washed with water, aq $NaHCO_3$, and water, and concentrated. Column chromatography of the residue gave **25** (85 mg, 48%) and **28** (75 mg, 42%).

Compound **25** was amorphous and had $[\alpha]_D$ +37° (*c* 2), R_F 0.27 (solvent *A*).

Compound **28** was amorphous and had $[\alpha]_D$ −5° (*c* 2), R_F 0.18 (solvent *A*).

The ^1H NMR data for **25** and **28** are listed in Table I.

(*b*) Glycosylation of **11** (388 mg, 1.0 mmol) with **12** [prepared[10] from **16** (340 mg, 0.5 mmol)], as described above, but at −50°C (as in the synthesis of **17** and **20**), and subsequent treatment with $(NH_4)_2Ce(NO_3)_6$ gave **25** (490 mg, 62%) and **28** (210 mg, 27%).

Methyl 4-O-benzoyl-2-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**26**).—Glycosylation of **25** (158 mg, 0.2 mmol) with **37** [prepared[2] from tetra-*O*-benzoyl-L-rhamnopyranose (232 mg, 0.4 mmol)], as for the synthesis of **19**, gave amorphous **26** (206 mg, 82%), $[\alpha]_D$ +74° (*c* 2), R_F 0.70 (solvent *A*).

Methyl 4,6-O-benzylidene-3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-α-D-mannopyranoside (**32**).—Glycosylation of **29**[18] (386 mg, 1.0 mmol) with **12** [prepared[10] from **16** (1.03 g, 1.5 mmol)], as for the synthesis of **17** and **20**, but at room temperature, gave, after column chromatography, methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-α-D-mannopyranoside [**31**; 680 mg, 75%; R_F 0.70 (solvent *A*)] and 105 mg of a mixture (~1:1) that contained **31** and an impurity with R_F 0.53 (solvent *A*), probably the product of β-glucosylation. *O*-Debenzoylation of **31** (680 mg), as for the synthesis of **18** and **21**, gave amorphous **32** (524 mg 87%), $[\alpha]_D$ +64° (*c* 1), R_F 0.10 (solvent *A*).

The ^{1}H NMR data are listed in Table I.

Methyl 3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-2-O-(2,3,4-tri-O-benzyl-α-L-rhamnopyranosyl)-α-D-mannopyranoside (**33**).—Glycosylation of **32** (120 mg, 0.15 mmol) with **37** [prepared[2] from tetra-*O*-benzoyl-L-rhamnopyranose (174 mg, 0.3 mmol)] was performed as for the synthesis of **19**. The reaction mixture was filtered, washed with aq KBr and water, and concentrated as described above. To a solution of the residue in $CHCl_3$ (3 mL) was added aq 90% trifluoroacetic acid (1 mL). The mixture was stirred for 40 min, diluted with $CHCl_3$ (20 mL), washed with water, aq $NaHCO_3$, and water, filtered through cotton, and concentrated. Column chromatography of the residue gave amorphous **33** (154 mg, 89%), $[\alpha]_D$ +73° (*c* 1), R_F 0.30 (solvent *B*).

Methyl 3-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-2-O-(2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**34**).—Glycosylation of **32** (200 mg, 0.25 mmol) with **38** [prepared[2] from penta-*O*-benzoyl-D-mannopyranose (420 mg, 0.6 mmol)] as for the synthesis of **33**, with subsequent acid hydrolysis, gave amorphous **34** (265 mg, 82%), $[\alpha]_D$ −20° (*c* 1), R_F 0.32 (solvent *B*).

Methyl 4-O-benzoyl-3-O-(2,3,4-tri-O-benzoyl-β-L-fucopyranosyl)-2-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**36**).—Glycosylation of **35**[4,5] (300 mg, 0.41 mmol) with **37** [prepared[2] from tetra-*O*-benzoyl-L-rhamnopyranose (490 mg, 0.85 mmol)], as for the synthesis of **19**, gave amorphous **36** (430 mg, 87%), R_F 0.37 (solvent *A*), $[\alpha]_D$ −38° (*c* 2).

Methyl 2-O-acetyl-3-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-α-L-rhamnopyranoside (**43**).—A mixture of **10**[4,5] (174 mg, 0.56 mmol), **39**[1] (285 mg, 0.73 mmol), and molecular sieves 4A in CH_2Cl_2 (2 mL) was stirred for 30 min at 20°C under Ar, and $NOBF_4$ (85 mg, 0.73 mmol) was added. The mixture was stirred for 40 min

at 20°C, then diluted with $CHCl_3$ (30 mL), filtered through Celite, and washed with aq $NaHCO_3$ and water, and the solvent was evaporated. Column chromatography of the residue gave methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-rhamnopyranoside (**42**; 298 mg, 83%), R_F 0.80 (solvent *B*). A solution of **42** in EtOAc (10 mL) and EtOH (5 mL) was shaken with 10% Pd/C at 40–42°C under H_2 (1 atm) for 2 h, then filtered, and the solvent was evaporated in vacuo. Column chromatography of the residue gave amorphous **43** (234 mg, 91%), $[\alpha]_D$ +11.5° (*c* 2), R_F 0.10 (solvent *B*).

The ^1H NMR data are listed in Table I.

Methyl 4-O-benzyl-3-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-α-L-rhamnopyranoside (**45**).—Glycosylation of **10**[4,5] (140 mg, 0.45 mmol) with **41**[1] (375 mg, 0.59 mmol), as for the synthesis of **42**, gave methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-L-rhamnopyranoside (**44**; 332 mg, 83%) R_F 0.34 (solvent *A*). A solution of **44** (230 mg, 0.26 mmol) in $CHCl_3$ (2 mL) was treated with methanolic HCl (prepared at 0°C from AcCl (0.2 mL) and MeOH (5 mL)]. The mixture was kept for 4 h at 20°C, diluted with $CHCl_3$ (30 mL), washed with aq $NaHCO_3$ and water, and concentrated. Column chromatography of the residue gave amorphous **45** (193 mg, 88%), $[\alpha]_D$ +73° (*c* 2), R_F 0.21 (solvent *A*).

The ^1H NMR data are listed in Table I.

Methyl 3-O-(2,3,4,6-tetra-O-benzyl-β-D-galactopyranosyl)-2-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**47**).—A mixture of **45** (175 mg, 0.21 mmol), **15** [prepared from penta-*O*-benzoyl-D-glucopyranose (280 mg, 0.4 mmol)], and molecular sieves 4A in $MeNO_2$ (6 mL) was stirred for 45 min at 20°C under Ar. Using a syringe, a solution of silver triflate (103 mg, 0.4 mmol) in $MeNO_2$ (2.6 mL) was introduced portionwise during 30 min at −20 to −30°C. The cooling bath was removed, $CHCl_3$ (30 mL) and satd aq $Na_2S_2O_3$ (5 mL) were added, and the mixture was stirred for 20 min, filtered through Celite, washed with aq $Na_2S_2O_3$ and water, and concentrated. The residue was treated with Ac_2O (3 mL) in pyridine (5 mL) for 16 h at 20°C, then concentrated. Column chromatography of the residue yielded amorphous **46** [272 mg, 92%; R_F 0.35 (solvent *A*)] which was then subjected to catalytic hydrogenolysis, as for the preparation of **43**, to give amorphous **47** (244 mg, 96%), $[\alpha]_D$ +90° (*c* 2), R_F 0.15 (solvent *A*).

Methyl 3-O-benzoyl-2-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-D-mannopyranoside (**64**).—Glycosylation of **30**[18] (77 mg, 0.2 mmol) with **37** [prepared[2] from tetra-*O*-benzoyl-L-rhamnopyranose (290 mg, 0.5 mmol)] as for the synthesis of **33**, with subsequent acid hydrolysis, gave amorphous **64** (113 mg, 75%), $[\alpha]_D$ +49° (*c* 2), R_F 0.27 (solvent *B*).

The ^1H NMR data are listed in Table I.

Preparation of di- and tri-saccharide glycosides **1–9**, **57**, *and* **59–63**.—(*a*) *Procedure A*. The acylated precursor (100–300 mg) was treated with 0.1 M MeONa in MeOH (10 mL) for 16–20 h at 20°C. The solution was neutralised with KU-2 (H^+) resin, filtered, and concentrated. The residue was partitioned between water (10

mL) and $CHCl_3$ (10 mL). The aqueous layer was washed with $CHCl_3$ (4 × 10 mL), then concentrated, and the residue was subjected to gel filtration on fracto-gel TSK HW-40(S) (25–40 μm, V_o 50 mL) in deionised water to give the product as an amorphous powder.

(*b*) *Procedure B.* The substituted compound was subjected to catalytic hydrogenolysis over Pd/C, as for the preparation of **43**, and then treated with MeONa and purified as in procedure A.

The ^1H and ^{13}C NMR data for **1–9**, **57**, and **59–63** are listed in Tables II and III.

Methyl 3-O-α-D-glucopyranosyl-2-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**1**).—Removal of protecting groups from **19** (210 mg) (procedure B) gave **1** (73 mg, 89%), $[\alpha]_D$ +57° (*c* 1.6); lit.[10] $[\alpha]_D$ +21.8° (*c* 1.6). The ^{13}C NMR spectrum of **1** is identical to that in ref. 10.

Methyl 2-O-α-D-glucopyranosyl-3-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**2**).—Removal of protecting groups from **26** (206 mg) (procedure B) gave **2** (70 mg, 87%), $[\alpha]_D$ +28° (*c* 2).

Methyl 3-O-β-D-glucopyranosyl-2-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**3**).—Debenzoylation of **23** (270 mg) (procedure A) gave **3** (92 mg, 92%), $[\alpha]_D$ −41° (*c* 1.8).

Methyl 3-O-β-L-fucopyranosyl-2-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**4**).—Debenzoylation of **36** (370 mg) (procedure A) gave **4** (123 mg, 85%), $[\alpha]_D$ −19° (*c* 2).

Methyl 3-O-β-D-galactopyranosyl-2-O-β-D-glucopyranosyl-α-L-rhamnopyranoside (**5**).—Debenzoylation of **51** (244 mg) (procedure A) gave **5** (79 mg, 86%), $[\alpha]_D$ −5° (*c* 1).

Methyl 3-O-α-D-glucopyranosyl-2-O-α-L-rhamnopyranosyl-α-D-mannopyranoside (**6**).—Removal of protecting groups from **33** (154 mg) (procedure B) gave **6** (55 mg, 83%), $[\alpha]_D$ +48° (*c* 1).

Methyl 3-O-α-D-glucopyranosyl-2-O-α-D-mannopyranosyl-α-D-mannopyranoside (**7**).—Removal of protecting groups from **34** (265 mg) (procedure B) gave **7** (98 mg, 92%), $[\alpha]_D$ +101° (*c* 2).

Methyl 2,3-di-O-β-L-fucopyranosyl-α-D-mannopyranoside (**8**).—Debenzoylation of **48** (313 mg) (procedure A) gave **8** (115 mg, 84%), $[\alpha]_D$ +12° (*c* 2).

Methyl 2-O-α-L-fucopyranosyl-3-O-β-L-fucopyranosyl-α-D-mannopyranoside (**9**).—Debenzoylation of **49** (239 mg) (procedure A) gave **9** (87 mg, 83%), $[\alpha]_D$ −47° (*c* 2).

Methyl 3-O-β-D-galactopyranosyl-α-L-rhamnopyranoside (**57**).—Removal of protecting groups from **43** (230 mg) (procedure A) gave **57** (116 mg, 82%), $[\alpha]_D$ −28° (*c* 2.3).

Methyl 2-O-α-L-rhamnopyranosyl-α-D-mannopyranoside (**59**).—Debenzoylation of **64** (100 mg) (procedure A) gave **59** (38 mg, 85%), $[\alpha]_D$ −34° (*c* 1).

Methyl 2-O-α-L-fucopyranosyl-α-D-mannopyranoside (**60**).—Debenzoylation of **65** (175 mg) (procedure A) gave **60** (62 mg, 87%), $[\alpha]_D$ −96° (*c* 1).

Methyl 2-O-β-L-fucopyranosyl-α-D-mannopyranoside (**61**).—Debenzoylation of **66** (38 mg) (procedure A) gave **61** (13 mg, 82%), $[\alpha]_D$ +2° (*c* 2).

Methyl 3-O-α-D-glucopyranosyl-α-D-mannopyranoside (**62**).—Removal of protecting groups from **32** (50 mg) (procedure B, but without the *O*-deacylation step) gave **62** (18 mg, 84%), $[\alpha]_D$ +148° (*c* 1).

Methyl 3-O-β-L-fucopyranosyl-α-D-mannopyranoside (**63**).—Removal of the benzylidene group in **67** (150 mg) by acidic hydrolysis (as for the preparation of **33** and **34**), with subsequent debenzoylation (procedure A), gave **63** (55 mg, 91%), $[\alpha]_D$ +48° (*c* 1).

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