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Synthesis of di-*O*-glycosyl derivatives of methyl α-L-rhamnopyranoside*

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ABSTRACT

The syntheses are described of 2,3-di-*O*-glycosyl derivatives (**1**–**12**) of methyl α-L-rhamnopyranoside where the glycosyl moieties are variously α-L-fucopyranose, β-L-fucopyranose, β-D-glucopyranose, α-D-mannopyranose, and α-L-rhamnopyranose. The syntheses involve stereoselective glycosylation of methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**21**), methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**25**), methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**29**), methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**35**), and methyl 4-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**59**). In the syntheses of compounds **7**–**9**, the α-L-fucopyranosyl residues are introduced stereoselectively, using 2,3,4-tri-*O*-benzoyl-α-L-fucopyranosyl bromide (**17**) and ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside (**47**) as glycosyl donors.

INTRODUCTION

As part of the development of a computerised approach to the elucidation of the structure of polysaccharides[2], sixteen model 2,3-di-*O*-glycosyl derivatives of α-L-rhamnopyranose that have monosaccharide substituents with the α-D, β-D, α-L, and β-L configurations were required. Four members of this series, namely, methyl α-L-rhamnopyranosides with two α-D-manno-, β-D-gluco-, α-L-rhamno-, and β-L-fuco-pyranosyl substituents have been synthesised[3] and studied[4]. The syntheses of the other members of this series (**1**–**12**), in which the substituents differ in absolute and/or anomeric configurations, are now described.

RESULTS AND DISCUSSION

Since **1**–**12** contain different substituents at O-2 and O-3, and since the next stage of our programme involves the study of 3,4-di-*O*-glycosylated derivatives of α-L-rhamnopyranose, syntheses that started from (1→3)-linked disaccharide derivatives were developed. These precursors had substituents at positions 2 and 4, which could be removed selectively depending on the desired position (2 or 4) of attachment of the third

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X-(1→2)
\
α-L-Rha*p*-OMe
/
Y-(1→3)

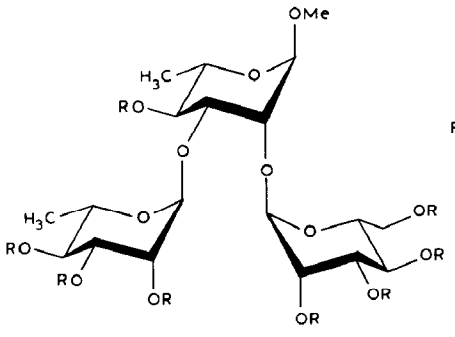
	X	Y
1	α-D-Man*p*	α-L-Rha*p*
2	α-D-Man*p*	β-D-Glc*p*
3	α-D-Man*p*	β-L-Fuc*p*
4	β-D-Glc*p*	α-D-Man*p*
5	β-D-Glc*p*	α-L-Rha*p*
6	β-D-Glc*p*	β-L-Fuc*p*
7	α-L-Fuc*p*	β-L-Fuc*p*
8	α-L-Fuc*p*	α-D-Man*p*
9	α-L-Fuc*p*	β-D-Glc*p*
10	β-L-Fuc*p*	α-L-Rha*p*
11	β-L-Fuc*p*	α-D-Man*p*
12	β-L-Fuc*p*	β-D-Glc*p*

monosaccharide unit. Taking into account these considerations, the availability of the starting monosaccharides, and the fact that 1,2-*trans*-glycosidic linkages are usually synthesised more easily than 1,2-*cis* linkages, the derivatives methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**18**), methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**22**), methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**26**), and methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**32**) were chosen as the precursors. The "non-reducing" moiety of each precursor is benzoylated and positions 2 and 4 carry acetyl and benzyl groups, respectively. These protecting groups were chosen since (*a*) 1,2-*trans* linkages are obtained when the glycosyl donor has an acyl group at position 2, and (*b*) benzyl groups can be removed easily by catalytic hydrogenolysis and acetyl groups by methanolysis under conditions which do not affect benzoyl groups[5]. Moreover, methyl 2-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranoside (**13**), necessary for the synthesis of the precursors, is much more readily available than its 4-*O*-acetyl-2-*O*-benzyl isomer.

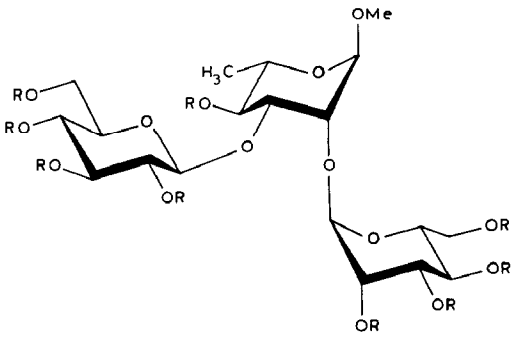
The precursors **18**, **22**, **26**, and **32** were synthesised by glycosylation of **13** with the glycosyl bromides **14**–**17** (2 equiv.) under Helferich conditions [acetonitrile–mercuric cyanide (2 equiv.)–mercuric bromide (catalytic amount)] at room temperature, except for **16** when heating at 60–70° was necessary[3]. Rhamnosylation and mannosylation of **13** were effective and stereospecific, and gave **18** and **22** in yields of 91 and 97%, respectively. The reactions of **16** and **17** gave the desired 1,2-*trans*-linked products **26** and **32**, together with small proportions of the 1,2-*cis*-linked products **30** and **36**, respectively. The fucosyl-rhamnosides **32** and **36** were isolated by chromatography in yields of 81 and 15%, respectively. Debenzylation of the mixture of glycosyl-rhamnosides **26** and **30** yielded **27** and **31** in yields of 67 and 5%, respectively. That the glucosyl and fucosyl units in **26** and **32** were β followed from the ^{1}H-n.m.r. data in Table I ($J_{1,2}$ 7.5 and 7.8 Hz, respectively). Likewise, the $J_{1,2}$ values (3.5 Hz) indicated the glucosyl and fucosyl residues in **31** and **36** to be α.

Catalytic hydrogenolysis of **18**, **22**, and **32** gave monohydroxy derivatives **19**, **23**, and **33**, respectively, which, together with **27**, were suitable for the preparation of 3,4-di-*O*-glycosylated α-L-rhamnopyranosides. For the synthesis of **1**–**12**, compounds **19**, **23**, **27**, and **33** were each benzoylated and then *O*-deacetylated to give **21**, **25**, **29**, and **35**, respectively, in yields of 82–91%. The location of the hydroxyl group at position 4 in **19**, **23**, **27**, and **33**, and at position 2 in **21**, **25**, **29**, and **35**, followed from the upfield chemical shifts of the resonances for H-4 and H-2, respectively, in their ^{1}H-n.m.r. spectra (Table I), and was confirmed by deuterium exchange which simplified the signals.

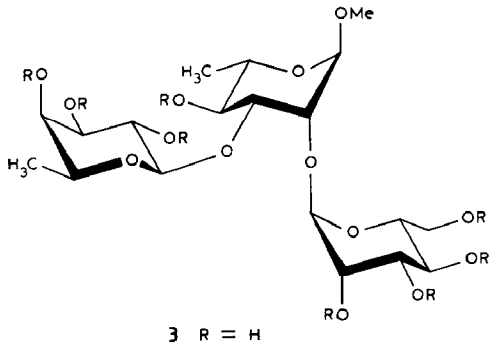
The syntheses of **1**–**3**, which contained 2-*O*-α-D-mannopyranosyl residues, were achieved by glycosylation of **21**, **29**, and **35** with the glycosyl bromide **15** (2 equiv.) under Helferich conditions, which afforded **37**–**39** in yields of 71, 83, and 77%, respectively. Glycosylation of **35** occurred rapidly, but those of **29** and **21** required reaction for 1.5 and 3 h, respectively.



1 R = H
37 R = Bz



2 R = H
38 R = Bz



3 R = H
39 R = Bz

O-Debenzoylation of **37**–**39** then gave the respective target trisaccharide methyl glycosides **1**–**3**.

As described previously[3], the structures of **1**–**3** were established on the basis of ^{1}H- and ^{13}C-n.m.r. data. The full data will be included in a subsequent paper[6]. The mannnopyranosyl units in **1**–**3** were indicated to be α by the characteristic chemical shifts (73.6–74.5) of their C-5 signals.

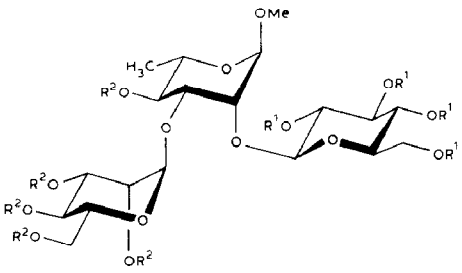
TABLE I

^{1}H-N.m.r. data (δ in p.p.m., J in Hz) for substituted derivatives **18**–**25**, **27**–**29**, **31**–**36**, **48**, **49**, **55**, and **59**[a]

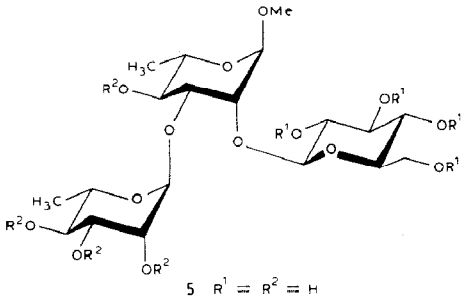
Compound	*Residue*[b]	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a*	*H-6b*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
18	R	4.57	5.21	4.16	3.53	3.68	1.30		1.7	3.5	9.3	9.3	6.0		
	N	5.26	5.69	5.72	5.58	4.19	1.28		1.5	3.1	9.4	9.4	6.2		
19	R	4.67	5.28	4.07	3.76	3.73	1.39		1.7	3.5	9.2	9.2	5.7		
	N	5.36	5.71	5.74	5.66	4.23	1.34		1.1	3.2	9.7	9.7	6.0		
20	R	4.74	5.38	4.42	5.48	3.97	1.34		1.8	3.6	9.8	9.8	6.2		
	N	5.16	5.32	5.67	5.56	4.26	1.32		1.8	3.1	9.5	9.5	6.2		
21	R	4.82	4.16	4.29	5.48	4.31	1.36		1.6	3.0	9.5	9.5	6.1		
	N	5.22	5.40	5.77	5.59	3.96	1.32		1.6	3.2	9.8	9.8	6.2		
22	R	4.67	5.38	4.37	3.59	3.83	1.44		1.5	3.0	9.6	9.6	6.1		
	N	5.31	5.66	5.92	6.11	4.60	4.22	4.58	1.6	3.2	10.0	10.0	9.0	2.2	12.1
23	R	4.66	5.33	4.11	3.69	3.66	1.38		1.5	3.4	9.0	9.0	5.8		
	N	5.28	5.60	5.93	6.04	4.80	4.48	4.74	1.6	3.0	9.7	9.7	8.7	2.3	12.6
24	R	4.76	5.47	4.50	5.51	4.04	1.36		1.6	3.3	9.7	9.7	6.1		
	N	5.27	5.57–5.62		5.97	4.18	3.92	4.42	1.6		10.0	10.0	4.0	2.3	12.2
25	R	4.84	4.21	4.38	5.56	4.00	1.33		1.6	3.0	9.6	9.6	6.0		
	N	5.28	5.71	5.66	6.00	4.23	3.97	4.42	1.6	3.1	9.8	9.8	3.9	2.4	12.2
27	R	4.58	5.25	3.93	3.55–3.66		1.27		1.5	3.3	9.4		7.2		
	N	5.04	5.52	5.92	5.69	4.15	4.44	4.62	7.5	9.6	9.6	9.6	4.5	3.0	12.3

28	R	4.61	5.37	4.27	5.28	3.82	1.13		1.7	3.5	9.4	9.4	6.4		
	N	4.95	5.43	5.73	5.56	4.10	4.44	4.57	7.5	9.5	9.5	9.5	5.2	3.2	12.1
29	R	4.60	4.17	4.12	5.36	3.85	1.15		1.6	3.1	9.1	9.1	6.0		
	N	5.00	5.52	5.84	5.57	4.20	4.47	4.72	8.0	9.8	9.8	9.8	6.6	2.6	12.1
31	R	4.55	5.16	4.05	3.70	3.55	1.32		1.6	3.3	9.2	9.2	6.0		
	N	5.54	5.38	6.23	5.61	4.87	4.46	4.65	3.5	10.0	10.0	10.0	6.0	2.5	11.9
32	R	4.58	5.17	4.46	3.47	3.75	1.35		1.6	3.4	9.0	9.0	6.3		
	N	4.95	5.81	5.57	5.74	4.12	1.36		7.8	10.3	3.3	1.0	6.3		
33	R	4.54	4.97	3.93	3.62	3.69	1.38		1.6	3.5	8.8	8.8	5.6		
	N	4.82	5.75	5.56	5.74	4.18	1.37		7.9	10.5	3.2	1.0	6.2		
34	R	4.64	5.14	4.41	5.28	3.96	1.30		1.7	3.5	9.6	9.6	6.3		
	N	4.84	5.56	5.40	5.58	3.94	1.03		7.8	10.5	3.1	1.1	6.5		
35	R	4.68	3.86	4.20	5.38	3.91	1.28		1.7	3.5	9.5	9.5	6.2		
	N	4.86	5.62	5.46	5.44	3.78	0.80		7.6	10.3	3.2	1.0	6.2		
36	R	4.71	5.84	4.27	3.56	3.77	1.28		1.6	3.3	9.2	9.2	6.0		
	N	5.68	5.82	6.09	5.34	4.60	1.32		3.5	11.0	3.1	1.2	6.3		
48[c]		4.70	4.17	5.38	5.47	4.07	1.25		1.8	2.8	10.0	9.5	6.1		
49[c]		4.58	3.96	3.62	3.38	3.57	1.24		1.7	3.0	9.2	9.2	6.0		
55	R	4.69	3.81–3.89		3.27	3.60	1.31		1.0		9.0	9.0	6.0		
	N	5.58	5.65	5.96	5.75	4.52	1.24		3.2	10.5	3.2	1.0	6.5		
59	R	4.46	3.99	3.89	3.22	3.49	1.03		1.7	3.2	9.0	9.0	6.1		
	N	4.84	5.75	5.57	5.72	4.14	1.35		7.8	10.3	3.1	1.0	6.5		

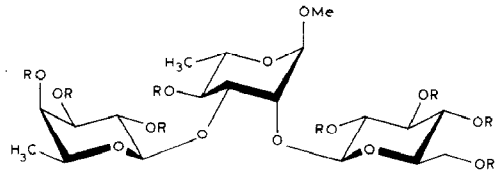
[a] For solutions in $CDCl_3$, unless stated otherwise. [b] R, "reducing" unit; N, "non-reducing" unit. [c] For solutions in CD_3CN.



4 $R^1 = R^2 = H$
42 R^1 = Ac, R^2 = Bz



5 $R^1 = R^2 = H$
43 R^1 = Ac, R^2 = Bz



6 R = H
44 R = Bz

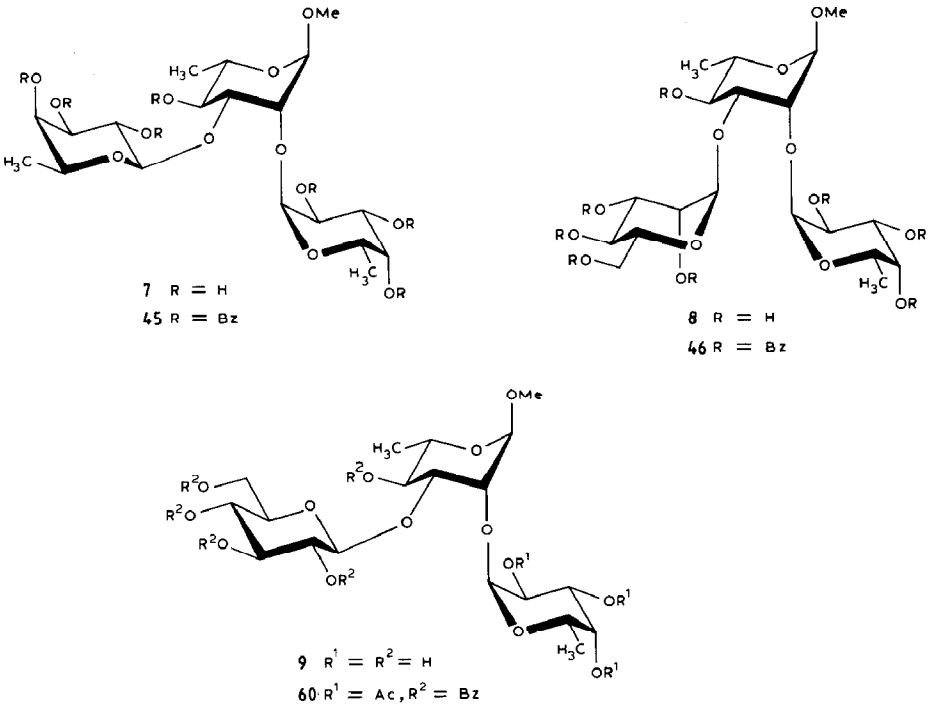
The target trisaccharide glycosides **4**–**6**, which each contain a 2-*O*-β-D-glucopyranosyl unit, were synthesised by glycosylation of methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**21**), methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**25**), and methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**35**) with ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside[7] (**40**) in the presence of nitrosyl tetrafluoroborate[8]. The reaction of **25** with **40** (1.5 equiv.) afforded 56% of the desired trisaccharide derivative **42** together with the 2-acetate **24** (29%). The glucosylation of **21**, like mannosylation (see above), was less effective than that of **25** and required 2.8 equiv. of **40**, and yielded **43** (48%) and the 2-acetate **20** (32%).

Since the efficiency of glucosylation of **21** and **25** with **40** was low, **35** was glycosylated with the glycosyl bromide **16** in the presence of silver triflate in nitromethane[9,10], which gave the desired trisaccharide derivative **44** in a yield of 83%.

For the synthesis of **4**–**6**, the possibility of using 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**41**) as the glycosyl donor in the presence of trimethylsilyl triflate[10–16] was investigated. However, **41** was a less effective glucosyl donor than **16** and **40**. Thus, the reaction of **25** and **41** (2 equiv.) yielded mainly the 2-acetate **24** (61%) and only 19% of the trisaccharide derivative **42**. The acetylation of glycosyl acceptors during glycosylation with glycosyl acetates is well documented[13–15].

Compounds **42**–**44** were *O*-debenzoylated to give the target trisaccharide glycosides **4**–**6**, respectively. That the glucosyl units in **4**–**6** were β was indicated by the ^{1}H-n.m.r. spectra ($J_{1,2}$ 7.5 Hz) and the low-field location of the C-1 signals (δ 105.0–105.5) in the ^{13}C-n.m.r. spectra.

The planned 2-*O*-α-L-rhamnosylation of methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**25**), methyl 4-*O*-ben-



zoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**29**), and methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**35**) was abandoned, since examination of the oligosaccharides which contained the 2,3-di-*O*-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside fragment[4] indicated that, in order to simplify analysis of ^{1}H-n.m.r. spectra and the results of n.O.e. experiments, the 2-*O*-α-L-fucopyranosyl derivatives **7**–**9** would be more suitable.

The precursor of **7**, the heptabenzoate **45**, was obtained[3] as a single product of di-*O*-fucosylation of methyl 4-*O*-benzoyl-α-L-rhamnopyranoside with the glycosyl bromide **17** under Helferich conditions[3]. The derivative **45** was also obtained as a major product of the glycosylation of **35** with **17** in the presence of silver triflate[3]. Removal of protecting groups from **45** gave **7**.

Taking into account the high stereoselectivity of 2-*O*-α-L-fucosylation in the syntheses of **45**, the route selected to **8** involved glycosylation of the acceptor **25** with **17**, and not with one of the 2-*O*-benzylated fucosyl donors traditionally used for α-L-fucosylation. The coupling of **25** and **17** under Helferich conditions afforded the desired trisaccharide derivative **46** (87%). Removal of the protecting groups from **46** gave **8**.

For the synthesis of **9**, the ethyl 1-thiofucoside **47**[17] was used as the glycosyl donor. In a model glycosylation, the dibenzoate **48**[18] was reacted with **47** in the presence of nitrosyl tetrafluoroborate, and the isomeric disaccharide derivatives **51** and **56** were obtained in the ratio 1:1.2 (run 1 in Table II) and isolated as the known[3] pentabenzoates **52** and **57**, respectively. Taking into account the result of this experiment, we performed a glycosylation of **29** with **47**, aimed at the synthesis of two trisaccharides of interest in

TABLE II

Fucosylation of rhamnosides **48** and **49** with the glycosyl bromide **17** and the 1-thiofucoside **47**

Run	*Glycosyl donor*	*Glycosyl acceptor*	*Promoter*	*1,2-cis-linked*		*1,2-trans-linked*	
				Product	*Yield (%)*	*Product*	*Yield (%)*
1	**47**	**48**	$NOBF_4$	**52**[a]	31	**57**[a]	38
2	**17**	**48**	$Hg(CN)_2$–$HgBr_2$	**52**	58	**57**	traces
3	**17**	**49**	$Hg(CN)_2$–$HgBr_2$	**55**[b]	50	**59**[b]	39
4[c]	**17**	**49**	CF_3SO_3Ag	**55**[b]	33	**59**[b]	39
5[d]	**17**	**49**	CF_3SO_3Ag	**55**[b]	28	**59**[b]	59

[a] This compound was obtained after deacylation and subsequent benzoylation of the products. [b] Obtained after removal of the 4-methoxybenzyl group. [c] The bromide **17** was added to the mixture of **49** and silver triflate. [d] Silver triflate was added to the mixture of **17** and **49**.

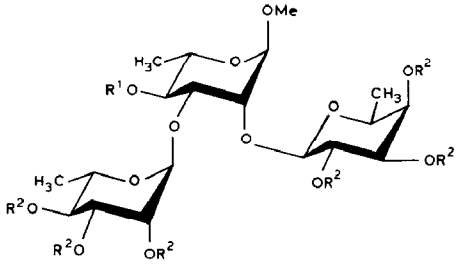
our programme: namely, product **60** with a 2-*O*-α-L-fucopyranosyl unit and its 2-*O*-β-L-fucosylated isomer. However, the glycosylation was more stereoselective than in the reaction of **48**, and gave the 2-*O*-α-L-fucosylated derivative **60** (64%) together with 25–30% of the 2-acetate (**28**) of **29**. In glycosylations with the 1-thioglucoside **40** and the 1-thiofucoside **47**, acetylation of the glycosyl acceptors also occurred. Apparently, this side reaction has not been observed previously and may limit the use of this method, especially with glycosyl acceptors of low reactivity (see ref. 19).

Removal of the protecting groups from **60** gave **9**. That the 2-*O*-fucosyl residues in **7**–**9** were α was indicated by the ^{1}H-n.m.r. data ($J_{1,2}$ 3.8 Hz).

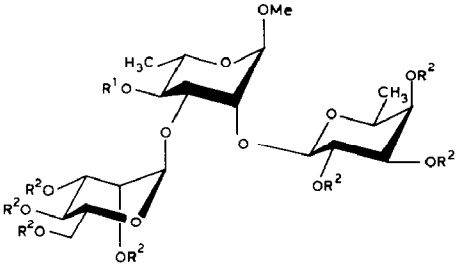
O-Debenzoylation of **52** gave the disaccharide derivative **53**, which was necessary for n.m.r. and conformational studies of **7**–**9**. Other (1→2)- and (1→3)-linked disaccharides were synthesised as described previously[3,20,21].

The synthesis of the trisaccharide glycosides **10**–**12**, each of which contains a 2-*O*-β-L-fucopyranosyl group, was planned initially by fucosylation of **21**, **25**, and **29** with the glycosyl bromide **17** or the 1-thiofucoside **47**. However, in this way, the formation of α-L-fucosylated products preponderated. Therefore, an alternative route was used which involved 3-*O*-glycosylation of the methyl 2-O-(β-L-fucopyranosyl)-α-L-rhamnopyranoside precursor with the glycosyl bromides **14**–**16**.

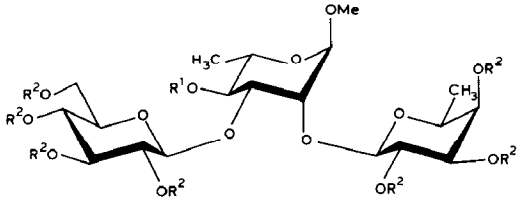
This route required β-L-fucosylation of a suitably substituted methyl α-L-rhamnopyranoside derivative, with HO-2 free and position 3 protected temporarily. The stereochemical outcome of the fucosylation of the 3-benzoate **48** with **17** and **47** (runs 1 and 2 in Table II) indicated that a 3-*O*-acyl group should not be used. Methyl 4-



10 $R^1 = R^2 = H$
62 $R^1 = Bn$, $R^2 = Bz$
63 $R^1 = H$, $R^2 = Bz$



11 $R^1 = R^2 = H$
64 $R^1 = Bn$, $R^2 = Bz$
65 $R^1 = H$, $R^2 = Bz$

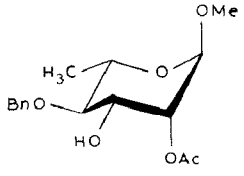


12 $R^1 = R^2 = H$
66 $R^1 = Bn$, $R^2 = Bz$
67 $R^1 = H$, $R^2 = Bz$

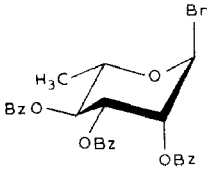
O-benzyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranoside (**49**) was therefore selected as the β-L-fucopyranosyl acceptor, since the 4-methoxybenzyl group can be removed selectively in the presence of benzyl and acyl groups by treatment with ammonium cerium(IV) nitrate in aqueous medium. Compound **49** was prepared from the diol **50**[22] by regioselective 4-methoxybenzylation *via* the 2,3-*O*-dibutylstannylidene intermediate[14].

Fucosylation of **49** with **17** (2 equiv.) under Helferich conditions (run 3 in Table II) afforded a mixture of the isomeric disaccharide derivatives **54** and **58** in a combined yield of 94%. Removal of the 4-methoxybenzyl groups from **54** and **58** gave **55** and **59**, which were isolated and their structures established on the basis of ^{1}H-n.m.r. data (Table I).

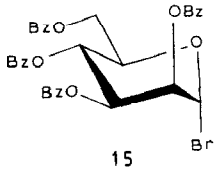
The data in Table II show that the fucosylation of the 3-*O*-(4-methoxybenzyl) derivative **49** proceeded more readily than that of the 3-benzoate **48**. The difference in the reactivity of the acceptors **48** and **49** is probably due to the weaker nucleophilicity of O-2 in **49** and not to differences in conformation, because the ^{1}H-n.m.r. spectra



13



14



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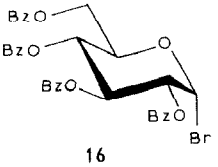

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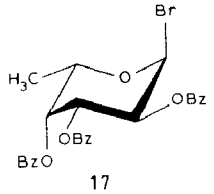
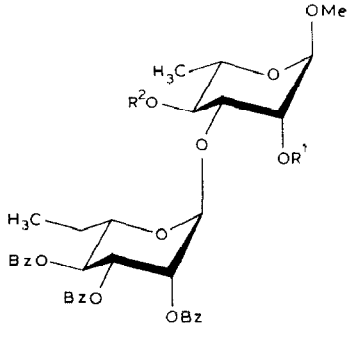
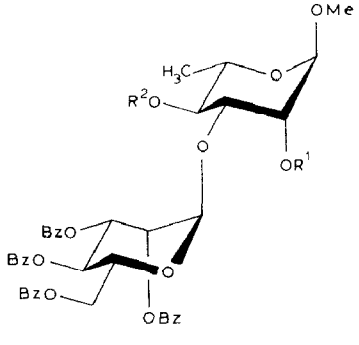


17



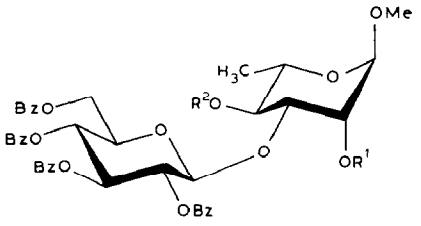
18 R^1 = Ac, R^2 = Bn
19 R^1 = Ac, R^2 = H
20 R^1 = Ac, R^2 = Bz
21 R^1 = H, R^2 = Bz



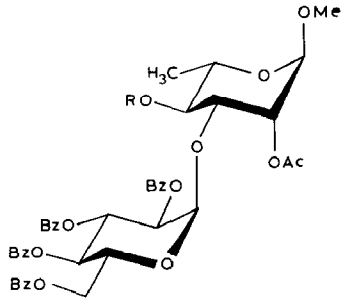
22 R^1 = Ac, R^2 = Bn
23 R^1 = Ac, R^2 = H
24 R^1 = Ac, R^2 = Bz
25 R^1 = H, R^2 = Bz

(CD_3CN, since MeCN was the solvent used for the glycosylation reactions) in Table I indicated similar conformations of **48** and **49**.

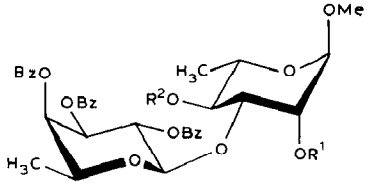
In the previous study[3] of the glycosylation of **35** and **48** with **17**, it was proposed that the low efficiency of β-fucosylation was due to the low reactivity of the glycosyl acceptor. Whereas the results of the fucosylation of **13** and/or **49** compared with that of **48** support this view, the results of the fucosylation of **13** and **49** do not, because the total yields of 1,2-*cis*- and 1,2-*trans*-linked disaccharides in these reactions were similar (96 and 94%, respectively), although the ratios were markedly different (1:5.5 and 1.3:1). However, for the fucosylation of **13** and **49**, a 100% excess of **17** was used; under these conditions, the similarity of total yields of disaccharide products in both reactions does not exclude a difference of fucosyl acceptor activity of **13** and **49**. In order to compare their reactivities, a mixture of **13** and **49** was glycosylated with **17** (molar ratios **13**:**49**:**17** of 1:1:1). Under these conditions, the fucosylation of **13** markedly preponderated (the yield of **32** was 62.5%, see Experimental): hence, **13** was more reactive than **49**. Therefore, the presence of electron-withdrawing substituents in positions vicinal to the hydroxyl group to be glycosylated favours α-fucosylation, even with glycosyl donors that contain participating groups at O-2 usually employed to control the β-stereoselectivity. This observation, which is important for the design of oligosaccharide syntheses, can be illustrated by the syntheses of the trisaccharide derivatives **45**, **46**, and **60**, in which stereoselective α-fucosylation was achieved with the glycosyl bromide **17** and the 1-thiofucoside **47**.



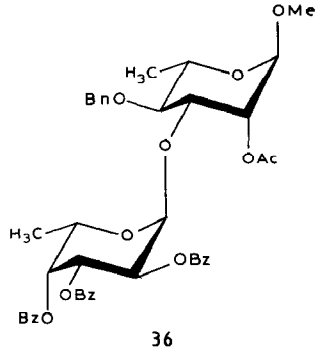
26 R^1 = Ac, R^2 = Bn
27 R^1 = Ac, R^2 = H
28 R^1 = Ac, R^2 = Bz
29 R^1 = H, R^2 = Bz



30 R = Bn
31 R = H

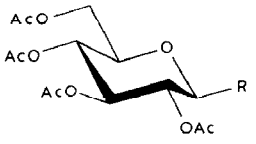


32 R^1 = Ac, R^2 = Bn
33 R^1 = Ac, R^2 = H
34 R^1 = Ac, R^2 = Bz
35 R^1 = H, R^2 = Bz

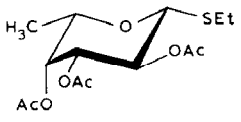


36

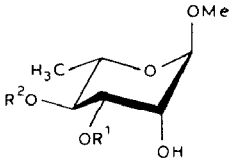
Fucosylation with **17** in the presence of silver triflate proceeds with higher β-stereoselectivity than under Helferich conditions[3]. In seeking to improve the synthesis of the disaccharide derivative **58**, the fucosylation of **49** with **17** in the presence of silver triflate was also studied. In two experiments, the order of mixing of the reagents was changed (runs 4 and 5 in Table II). It was found that the fucosylation of **49** was more effective in the presence of silver triflate than in the presence of mercuric salts (run 3, Table II). Reaction was more rapid in run 5, than in run 4, and some decomposition



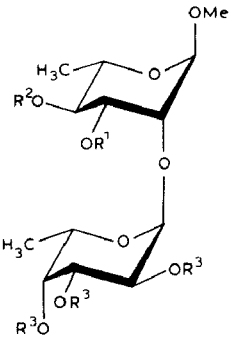
40 R = SEt
41 R = OAc

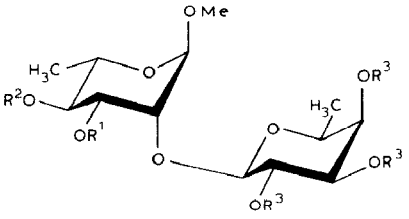


47



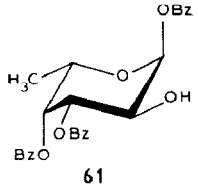
48 $R^1 = R^2 = Bz$
49 $R^1 = MBn, R^2 = Bn$
50 $R^1 = H, R^2 = Bn$
(MBn = 4-$MeOC_6H_4CH_2$)





51 $R^1 = R^2 = Bz, R^3 = Ac$
52 $R^1 = R^2 = R^3 = Bz$
53 $R^1 = R^2 = R^3 = H$
54 $R^1 = MBn, R^2 = Bn, R^3 = Bz$
55 $R^1 = H, R^2 = Bn, R^3 = Bz$

56 $R^1 = R^2 = Bz, R^3 = Ac$
57 $R^1 = R^2 = R^3 = Bz$
58 $R^1 = MBn, R^2 = Bn, R^3 = Bz$
59 $R^1 = H, R^2 = Bn, R^3 = Bz$



61

occurred in the latter run. In the reactions promoted by silver triflate, 1,3,4-tri-*O*-benzoyl-α-L-fucopyranose (**61**) was formed as a by-product (22% in run 4). The structure of **61** was indicated by the ^{1}H-n.m.r. data (Table I). Apparently, the formation of products analogous to **61** has not been observed previously in glycosylations with acylglycosyl halides.

Glycosylation of methyl 4-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**59**) with **14** and **15** under Helferich conditions, and with **16** in the presence of silver triflate, gave the trisaccharide derivatives **62** (83%), **64** (96%), and **66** (82%), respectively, which were converted into **63**, **65**, and **67** by catalytic hydrogenolysis and then into the target glycosides **10**–**12** by saponification. The structures of **10**–**12** were confirmed by the ^{1}H- and ^{13}C-n.m.r. data (see Tables VII and VIII in ref. 6).

The details of the n.m.r. and conformational studies of trisaccharide glycosides **1**–**12** will be considered in a subsequent paper[6].

EXPERIMENTAL

General. — The reagents and solvents, as well as n.m.r. instruments, used in this work have been described elsewhere[3,4,10]. Melting points were determined with a Kofler apparatus and are uncorrected. Optical rotations for substituted compounds were determined on solutions in chloroform, and for **1**–**12** and **53** on solutions in water, with a JASCO DIP-360 digital polarimeter at 26–30°.

T.l.c. was performed on Kieselgel 60 (Merck) with EtOAc–toluene (*A*, 1:7; *B*, 1:4; *C*, 1:2; *D*, 1:1) and EtOAc–heptane (*E*, 1:1), and with 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.

The glycosyl bromides **14**–**17** were prepared from the benzoylated sugars as described[3].

Methyl 2-O-acetyl-4-O-benzyl-α-L-rhamnopyranoside (**13**). — A solution of methyl 4-*O*-benzyl-α-L-rhamnopyranoside[22] [**50**, 5.36 g, 20 mmol; R_F 0.19 (solvent *D*)], trimethyl orthoacetate (7 mL, 56 mmol), and TsOH·H_2O (20 mg) in MeCN (10 mL) was kept for 20 min at 20° to give the 2,3-orthoacetate (R_F 0.80). Aqueous 80% AcOH (10 mL) was added, and the mixture was stirred for 30 min, then poured into water (100 mL), and extracted with $CHCl_3$ (2 × 50 mL). The combined extracts were washed with aqueous $NaHCO_3$ and water, filtered through cotton, concentrated, and dried *in vacuo*, to give **13** (5.95 g, 96%), syrup, $[\alpha]_D$ −39° (*c* 1), R_F 0.39 (solvent *D*); lit.[23] $[\alpha]_D$ −35.3° (*c* 2.2, chloroform).

Methyl 2-O-acetyl-4-O-benzyl-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**18**). — To a stirred solution of **13** (1.24 g, 4.0 mmol), $Hg(CN)_2$ (2.02 g, 8.0 mmol), and $HgBr_2$ (100 mg) in MeCN (13 mL) was added a solution of **14** [prepared from tetra-*O*-benzoyl-L-rhamnopyranose (4.64 g, 8.0 mmol)] in 4:1 MeCN–benzene (100 mL) dropwise during 1 h. The mixture was stirred for 20 min, then concentrated, and partitioned between $CHCl_3$ (150 mL) and saturated aqueous KBr

(150 mL). The organic layer was washed again with aqueous KBr and water, and concentrated. Column chromatography of the residue gave amorphous **18** (2.80 g, 91%), $[\alpha]_D$ +115.5° (*c* 1), R_F 0.42 (solvent *A*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 2-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-benzoyl-*α*-*L*-rhamnopyranosyl)-*α*-*L*-rhamnopyranoside* (**19**). — A solution of **18** (2.5 g, 3.7 mmol) in MeOH (20 mL) and EtOAc (20 mL) was shaken with 10% Pd/C at 37° under hydrogen (1 atm.) for 5 h, then filtered, and the solvent was evaporated *in vacuo*. Column chromatography of the residue gave amorphous **19** (1.94 g, 88%), $[\alpha]_D$ +113° (*c* 1), R_F 0.15 (solvent *A*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-*α*-*L*-rhamnopyranosyl)-*α*-*L*-rhamnopyranoside* (**21**). — A solution of **19** (1.4 g, 2.1 mmol) in CH_2Cl_2 (10 mL) was treated with BzCl (0.5 mL), pyridine (0.5 mL), and 4-dimethylaminopyridine (10 mg) for 16 h at 40°. Water (5 mL) was added, and the mixture was diluted with $CHCl_3$ (60 mL), washed with aqueous $NaHCO_3$ and water, then concentrated. A solution of the residue in $CHCl_3$ (5 mL) was put on a column (2 × 10 cm) of silica gel, and eluted with 9:1 benzene–EtOAc (100 mL). Concentration of the eluate gave **20** (1.6 g), R_F 0.46 (solvent *D*). A solution of **20** in $CHCl_3$ (4 mL) was treated with methanolic HCl [prepared at 0° from AcCl (0.4 mL) and MeOH (10 mL)]. The mixture was kept for 17 h at 20°, diluted with $CHCl_3$ (70 mL), washed with aqueous $NaHCO_3$ and water, and concentrated. Column chromatography of the residue (EtOAc–heptane, 1:2) gave amorphous **21** (1.35 g, 89%), $[\alpha]_D$ + 124.5° (*c* 1), R_F 0.46 (solvent *D*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-*α*-*D*-mannopyranosyl)-*α*-*L*-rhamnopyranoside* (**22**). — Glycosylation of **13** (1.24 g, 4.0 mmol) with **15** [prepared from penta-*O*-benzoyl-D-mannopyranose (5.60 g, 8.0 mmol)], as for the synthesis of **18**, gave amorphous **22** (3.40 g, 97%), $[\alpha]_D$ −11° (*c* 1), R_F 0.35 (solvent *A*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 2-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-*α*-*D*-mannopyranosyl)-*α*-*L*-rhamnopyranoside* (**23**). — Catalytic hydrogenolysis of **22** (2.5 g, 2.82 mmol), as for the preparation of **19**, gave amorphous **23** (2.10 g, 94%), $[\alpha]_D$ −59° (*c* 1), R_F 0.12 (solvent *A*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-*α*-*D*-mannopyranosyl)-*α*-*L*-rhamnopyranoside* (**25**). — Benzoylation of **23** (1.25 g, 1.57 mmol) followed by deacetylation, as for the synthesis of **21**, gave amorphous **25** (1.13 g, 84%), $[\alpha]_D$ +24° (*c* 1), R_F 0.35 (solvent *D*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 2-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-* (**31**) *and -β-*D*-glucopyranosyl)-α-*L*-rhamnopyranoside* (**27**). — Glycosylation of **13** (1.24 g, 4.0 mmol) with **16** [prepared from penta-*O*-benzoyl-D-glucopyranose (5.6 g, 8.0 mmol)], as for the synthesis of **18** and at 60–70°, gave a mixture [2.5 g, R_F 0.36–0.40 (solvent *A*)] of **26** and **30** and an unknown by-product. Catalytic hydrogenolysis of the mixture, as for the preparation of **19**, gave **27** (2.15 g, 67%) and **31** (0.16 g, 5%).

Compound **27** was amorphous and had $[\alpha]_D$ +32° (*c* 1), R_F 0.24 (solvent *B*) and 0.33 (solvent *D*).

Compound **31** was amorphous and had $[\alpha]_D$ +57° (*c* 1), R_F 0.26 (solvent *B*).

The ^{1}H-n.m.r. data for **27** and **31** are listed in Table I.

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-α-*L*-rhamnopyranoside* (**29**). — Benzoylation of **27** (1.0 g, 1.26 mmol) followed by methanolysis, as for the preparation of **21**, gave amorphous **29** (0.98 g, 91%), $[\alpha]_D$ −5° (*c* 0.5), R_F 0.35 (solvent *C*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 2-*O*-acetyl-4-*O*-benzyl-3-*O*-(2,3,4-tri-*O*-benzoyl-α-* (**36**) *and -β-*L*-fucopyranosyl)-α-*L*-rhamnopyranoside* (**32**). — Glycosylation of **13** (1.24 g, 4.0 mmol) with **17** [prepared from penta-*O*-benzoyl-L-fucopyranose (4.64 g, 8.0 mmol)], as for the synthesis of **18**, gave **32** (2.50 g, 82%) and **36** (0.45 g, 15%).

Compound **32** was amorphous and had $[\alpha]_D$ −75° (*c* 1), R_F 0.22 (solvent *A*) and 0.50 (solvent *D*).

Compound **36** was amorphous and had $[\alpha]_D$ −202° (*c* 1.1), R_F 0.35 (solvent *A*).

The ^{1}H-n.m.r. data for **32** and **36** are listed in Table I.

*Methyl 2-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-*L*-fucopyranosyl)-α-*L*-rhamnopyranoside* (**33**). —Catalytic hydrogenolysis of **32** (3.5 g, 4.56 mmol), as for the preparation of **19**, gave amorphous **33** (2.90 g, 94%), $[\alpha]_D$ −173° (*c* 1), R_F 0.33 (solvent *D*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-*L*-fucopyranosyl)-α-*L*-rhamnopyranoside* (**35**). — Benzoylation of **33** (1.74 g, 2.57 mmol) followed by deacetylation, as for the synthesis of **21**, gave amorphous **35** (1.56 g, 82%), $[\alpha]_D$ −128° (*c* 0.7), R_F 0.20 (solvent *A*) and 0.36 (solvent *D*).

The ^{1}H-n.m.r. data are listed in Table I.

*Methyl 4-*O*-benzoyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-*D*-mannopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl)-α-*L*-rhamnopyranoside* (**37**). — Glycosylation of **21** (222 mg, 0.3 mmol) with **15** [prepared from penta-*O*-benzoyl-D-mannopyranose (420 mg, 0.6 mmol)], as for the synthesis of **18**, gave amorphous **37** (280 mg, 71%), $[\alpha]_D$ +67° (*c* 2), R_F 0.53 (solvent *A*).

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-*D*-mannopyranosyl)-α-*L*-rhamnopyranoside* (**38**). — Glycosylation of **29** (258 mg, 0.3 mmol) with **15** [prepared from penta-*O*-benzoyl-D-mannopyranose (420 mg, 0.6 mmol)], as for the synthesis of **18**, gave amorphous **38** (360 mg, 83%), $[\alpha]_D$ −51° (*c* 2), R_F 0.45 (solvent *A*).

*Methyl 4-*O*-benzoyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-*D*-mannopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzoyl-β-*L*-fucopyranosyl)-α-*L*-rhamnopyranoside* (**39**). — Glycosylation of **35** (222 mg, 0.3 mmol) with **15** [prepared from penta-*O*-benzoyl-D-mannopyranose (420 mg, 0.6 mmol)], as for the synthesis of **18**, gave amorphous **39** (350 mg, 77%), $[\alpha]_D$ −46° (*c* 2), R_F 0.42 (solvent *A*).

Glycosylation of **25**. — (*a*) *With ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-*D*-glucopyranoside* (**40**). A mixture of **25** (172 mg, 0.2 mmol), **40**[6] (118 mg, 0.3 mmol), and molecular

sieves type 4A in CH_2Cl_2 (7 mL) was stirred for 45 min at 20° under Ar, and $NOBF_4$ (35 mg, 0.3 mmol) was added. The mixture was stirred for 1 h at 20°, then diluted with $CHCl_3$ (30 mL), filtered through Celite, and washed with aqueous $NaHCO_3$ and water, and the solvent was evaporated. Column chromatography of the residue gave methyl 4-*O*-benzoyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-L-rhamnopyranoside (**42**; 133 mg, 56%) and the 2-acetate **24** (52 mg, 29%).

Compound **24** was amorphous and had $[\alpha]_D$ +42° (*c* 0.4), R_F 0.80 (solvent *C*). The ^{1}H-n.m.r. data are listed in Table I.

Compound **42** was amorphous and had $[\alpha]_D$ +28° (*c* 1), R_F 0.56 (solvent *C*).

(*b*) *With β-D-glucopyranose penta-acetate* (**41**). A mixture of **25** (172 mg, 0.2 mmol), **41** (156 mg, 0.4 mmol), and molecular sieves type 4A in CH_2Cl_2 (10 mL) was stirred for 45 min at 20° under Ar, and trimethylsilyl triflate (80 μL, 0.4 mmol) was added. The mixture was stirred for 17 h at 20°, then processed as in (*a*) to give **24** (110 mg, 61%) and **42** (45 mg, 19%).

Glycosylation of **21** *with* **40**. — Glycosylation of **21** (444 mg, 0.6 mmol) with **40**[6] (353 mg, 0.9 mmol) in the presence of $NOBF_4$ (111 mg, 0.95 mmol) was performed as for the reaction of **40** with **25**. The mixture was stirred for 1 h when t.l.c. revealed **43** and **20**, much **21** but no **40**. More **40** (196 mg, 0.5 mmol) was added followed by $NOBF_4$ (58 mg, 0.5 mmol). Stirring was continued for 1 h, and more **40** (100 mg, 0.26 mmol) and $NOBF_4$ (30 mg, 0.26 mmol) were added. Stirring was continued for 1 h, then the mixture was processed as described above, to give methyl 4-*O*-benzoyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**43**; 310 mg, 48%) and the 2-acetate **20** (141 mg, 32%).

Compound **20** had m.p. 174–176° (from EtOAc–hexane), $[\alpha]_D$ +149° (*c* 0.5); R_F 0.52 (solvent *C*). The ^{1}H-n.m.r. data are listed in Table I.

Anal. Calc. for $C_{43}H_{42}O_{14}$: C, 65.70; H, 5.81. Found: C, 65.60; H, 5.61.

Compound **43** was amorphous and had $[\alpha]_D$ +131° (*c* 1), R_F 0.42 (solvent *C*).

Methyl 4-O-benzoyl-2-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-3-O-(2,3,4-tri-O-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**44**). — A mixture of **35** (148 mg, 0.2 mmol), **16** [prepared from penta-*O*-benzoyl-D-glucopyranose (280 mg, 0.4 mmol)], and molecular sieves type 4A in $MeNO_2$ (6 mL) was stirred for 45 min at 20° under Ar. Using a syringe, a solution of silver triflate (103 mg, 0.4 mmol) in $MeNO_2$ (3 mL) was introduced portionwise during 30 min at −20° to −30°. The mixture was stirred for 1 h at −20° to −30° when t.l.c. revealed some unreacted **35**. A solution of **16** [prepared from penta-*O*-benzoyl-D-glucopyranose (70 mg, 0.1 mmol)] in $MeNO_2$ (2 mL) was added, and stirring was continued for 1 h at −20° to −30°. A solution of silver triflate (26 mg, 0.1 mmol) in $MeNO_2$ (1 mL) was introduced portionwise during 30 min at −20° to −30°, and stirring was continued for 1 h at −20° to −30°. The cooling bath was removed, and $CHCl_3$ (10 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL) were added. The mixture was stirred for 20 min, filtered through Celite, washed with aqueous $Na_2S_2O_3$ and water, then concentrated. The residue was treated with Ac_2O (3 mL) in pyridine (5 mL) for 16 h at 20°, then concentrated. Column chromatography of the residue yielded amorphous **44** (220 mg, 83%), $[\alpha]_D$ −22° (*c* 1.5), R_F 0.46 (solvent *A*).

*Methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzoyl-α-L-fucopyranosyl)-α-L-rhamnopyranoside* (**46**). — Glycosylation of **25** (218 mg, 0.25 mmol) with **17** [prepared from tetra-*O*-benzoyl-L-fucopyranose (348 mg, 0.6 mmol)], performed as for the synthesis of **18**, gave amorphous **46** (264 mg, 81%), $[\alpha]_D$ −41.5° (*c* 1.5), R_F 0.34 (solvent *A*).

*Glycosylation of methyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside* (**48**) *with ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside* (**47**) *(run 1 in Table II).* — Compound **48**[16] (193 mg, 0.5 mmol) was reacted with **47**[15] (300 mg, 0.9 mmol) in the presence of $NOBF_4$ (105 mg, 0.9 mmol), as for the glycosylation of **21** with **40**. The mixture was processed as described above, and the product was treated with 0.1M MeONa in MeOH (10 mL) for 17 h at 20°. M AcOH in MeOH (2 mL) was added, the solvent was evaporated *in vacuo*, and the residue was treated with BzCl (3 mL) in pyridine (6 mL) for 17 h at 20°. After conventional work-up and column chromatography, methyl 3,4-di-*O*-benzoyl-2-*O*-(2,3,4-tri-*O*-benzoyl-α-L-fucopyranosyl)-α-L-rhamnopyranoside (**52**; 130 mg, 31%) and methyl 3,4-di-*O*-benzoyl-2-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**57**; 160 mg, 38%) were obtained. Their ^{1}H-n.m.r. spectra were identical with those published[3].

Glycosylation of **29** *with ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside* (**47**). — The reaction of **29** (430 mg, 0.5 mmol) with **47**[15] (500 mg, 1.5 mmol) in the presence of $NOBF_4$ (176 mg, 1.5 mmol) was performed as for the glycosylation of **21** and **25** with **40**, to give amorphous methyl 4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-α-L-rhamnopyranoside (**60**; 360 mg, 64%), $[\alpha]_D$ −52° (*c* 2), R_F 0.28 (solvent *B*), and a mixture of side products with $R_F \sim 0.5$ (solvent *B*), in which methyl 2-*O*-acetyl-4-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (**28**) preponderated and was identified by ^{1}H-n.m.r. spectroscopy (see Table I).

*Methyl 4-*O*-benzyl-3-*O*-(4-methoxybenzyl)-α-L-rhamnopyranoside* (**49**). — A mixture of methyl 4-*O*-benzyl-α-L-rhamnopyranoside[22] (**50**; 5.0 g, 18.7 mmol) and Bu_2SnO (4.75 g, 19.1 mmol) in benzene (80 mL) was boiled under reflux for 7 h with azeotropic removal of water. The temperature was reduced to 50–60°, and Bu_4NBr (6.0 g, 18.6 mmol) and 4-methoxybenzyl chloride (2.9 mL, 21.4 mmol) were added. The mixture was stirred for 1.5 h at 50–60° and the solvent was evaporated. A solution of the residue in 1:2 $CHCl_3$–hexane (200 mL) was washed with water (5 × 200 mL) and concentrated. A solution of the residue in $CHCl_3$ (5 mL) was put on a column (2 × 10 cm) of silica gel and eluted with 1:2 $CHCl_3$–hexane (150 mL). Concentration of the eluate and column chromatography of the residue gave **49** (5.0 g, 81.5%), and a fraction (1.0 g) that contained **49** and an impurity with R_F 0.51 (solvent *C*), probably the product of 3-*O*-(4-methoxybenzylation).

Compound **49** was syrup and had $[\alpha]_D$ −40° (*c* 2), R_F 0.48 (solvent *C*); lit.[14] $[\alpha]_D$ −42.1° (*c* 1.6).

The ^{1}H-n.m.r. data are listed in Table I.

Glycosylation **49** *with* **17** *(runs 3–5 in Table II).* — (*a*) *Run 3.* Glycosylation of **49** (291 mg, 0.75 mmol) with **17** [prepared from tetra-*O*-benzoyl-L-fucopyranose (870 mg,

1.5 mmol)] was performed as for the synthesis of **18**, and gave a mixture (600 mg, 95%) of **54** and **58**, R_F 0.45 and 0.40 (solvent *A*). To a solution of the mixture in 9:1 MeCN–water (10 mL) was added $(NH_4)_2Ce(NO_3)_6$ (770 mg, 1.4 mmol). The mixture was stirred for 20 min at 20°, then diluted with $CHCl_3$ (50 mL), washed with water, aqueous $NaHCO_3$, and water, and concentrated. Column chromatography of the residue gave methyl 4-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzoyl-α-L-fucopyranosyl)-α-L-rhamnopyranoside (**55**; 270 mg, 50%) and methyl 4-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**59**; 210 mg, 39%).

Compound **55** was amorphous and had $[\alpha]_D$ −219° (*c* 1), R_F 0.25 (solvent *A*).

Compound **59** was amorphous and had $[\alpha]_D$ −130° (*c* 0.5), R_F 0.11 (solvent *A*).

The ^{1}H-n.m.r. data for **55** and **59** are listed in Table I.

(*b*) *Run 4.* A mixture of **49** (582 mg, 1.5 mmol), silver triflate (370 mg, 1.5 mmol), $(Me_2N)_2CO$ (0.27 mL, 3.0 mmol), and molecular sieves type 4A in $MeNO_2$ (10 mL) was stirred for 45 min under Ar. A solution of **17** [prepared from tetra-*O*-benzoyl-L-fucopyranose (1.74 g, 3.0 mmol)] in $MeNO_2$ (10 mL) was added dropwise during 1 h at −25° to −30°. The mixture was stirred for 2.5 h at that temperature and then processed as for the synthesis of **44**, but without acetylation. The resulting mixture of **54**, **58**, and **61** (1.2 g) was treated with $(NH_4)_2Ce(NO_3)_6$ (1.41 g, 2.57 mmol) as described above, to give **55** (355 mg, 33%), **59** (420 mg, 39%), and 1,3,4-tri-*O*-benzoyl-α-L-fucopyranose (**61**; 300 mg, 22%).

Compound **61** had m.p. 145–147° (from EtOAc–hexane) and $[\alpha]_D$ −216° (*c* 0.4), R_F 0.45 (solvent *A*). The ^{1}H-n.m.r. data are listed in Table I.

Anal. Calc. for $C_{27}H_{24}O_8$: C, 68.06; H, 5.08. Found: C, 68.24; H, 5.13.

(*c*) *Run 5.* A mixture of **49** (194 mg, 0.5 mmol), **17** [prepared from tetra-*O*-benzoyl-L-fucopyranose (580 mg, 1.0 mmol)], $(Me_2N)_2CO$ (90 μL, 1.0 mmol), and molecular sieves type 4A in $MeNO_2$ (5 mL) was stirred for 45 min under Ar. To this mixture was added a solution of silver triflate (257 mg, 1.0 mmol) in $MeNO_2$ (6 mL), portionwise with a syringe during 20 min at −25° to −30°. The mixture was stirred for 20 min at that temperature, and then processed as for the synthesis of **44**, including acetylation, to give **54** and **58** which were treated with $(NH_4)_2Ce(NO_3)_6$ (275 mg, 0.5 mmol), as described above, to give **55** (102 mg, 28%) and **59** (214 mg, 59%).

Competitive glycosylation of **13** *and* **49** *with* **17**. — A mixture of **13** (193 mg, 0.5 mmol) and **49** (194 mg, 0.5 mmol) was reacted with **17** [prepared from tetra-*O*-benzoyl-L-fucopyranose (290 mg, 0.5 mmol)] in the presence of $Hg(CN)_2$ (142 mg, 0.5 mmol), $HgBr_2$ (50 mg), and molecular sieves type 4A, as for the synthesis of **18**. The mixture contained (t.l.c.) **32** and **49** as major components, **13** and **36** as minor components, and traces of the disaccharide derivatives **54** and **58**. The products were conventionally acetylated with Ac_2O (3 mL) in pyridine (5 mL) for 16 h at 20°. Column chromatography of the products gave **32** (240 mg, 62.5%). Compound **36** was eluted together with the products of acetylation of **13** and **49**, and was not isolated pure.

Methyl 2-O-(2,3,4-tri-O-benzoyl-β-L-fucopyranosyl)-3-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**63**). — Glycosylation of **59** (180 mg, 0.25 mmol) with **14** [prepared from tetra-*O*-benzoyl-L-rhamnopyranose (290 mg, 0.5

mmol)], as for the synthesis of **18**, gave **62** (245 mg, 83%), R_F 0.40 (solvent *A*). Catalytic hydrogenolysis of **62** in EtOAc (4 mL) and EtOH (13 mL), in the presence of 10% Pd/C at 40°, gave amorphous **63** (206 mg, 91%), $[\alpha]_D$ +13° (*c* 2), R_F 0.22 (solvent *A*).

Methyl 3-O-(2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyl)-2-O-(2,3,4-tri-O-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**65**). — Glycosylation of **59** (180 mg, 0.25 mmol) with **15** [prepared from penta-*O*-benzoyl-D-mannopyranose (350 mg, 0.5 mmol)], as for the synthesis of **18**, gave **64** (311 mg, 96%), R_F 0.40 (solvent *A*). Catalytic hydrogenolysis of **64**, as for the preparation of **63**, gave amorphous **65** (280 mg, 97%), $[\alpha]_D$ −82° (*c* 2), R_F 0.21 (solvent *A*).

Methyl 3-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2-O-(2,3,4-tri-O-benzoyl-β-L-fucopyranosyl)-α-L-rhamnopyranoside (**67**). — Glycosylation of **59** (220 mg, 0.3 mmol) with **16** [prepared from penta-*O*-benzoyl-D-glucopyranose (420 mg, 0.6 mmol)], as for the synthesis of **44**, gave **66** (320 mg, 82%), R_F 0.48 (solvent *A*). Catalytic hydrogenolysis of **66**, as for the preparation of **63**, gave amorphous **67** (275 mg, 92%), $[\alpha]_D$ −77° (*c* 2), R_F 0.20 (solvent *A*).

Preparation of trisaccharide glycosides **1**–**12** *and* **53**. — The acylated precursor (100–300 mg) was treated with 0.1M MeONa in MeOH (10 mL) for 16–20 h at 20°. 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 dried *in vacuo*, to give the product as an amorphous powder.

The n.m.r. data for **1**–**12** and **53** are listed in Tables VII and VIII in ref. 6.

Methyl 2-O-(α-D-mannopyranosyl)-3-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**1**). — Debenzoylation of **37** (210 mg) gave **1** (66 mg, 85%), $[\alpha]_D$ −2° (*c* 1).

Methyl 3-O-(β-D-glucopyranosyl)-2-O-(α-D-mannopyranosyl)-α-L-rhamnopyranoside (**2**). — Debenzoylation of **38** (290 mg) gave **2** (90 mg, 85%), $[\alpha]_D$ +28° (*c* 1).

Methyl 3-O-(β-L-fucopyranosyl)-2-O-(α-D-mannopyranosyl)-α-L-rhamnopyranoside (**3**). — Debenzoylation of **39** (220 mg) gave **3** (76 mg, 92%), $[\alpha]_D$ +42° (*c* 1).

Methyl 2-O-(β-D-glucopyranosyl)-3-O-(α-D-mannopyranosyl)-α-L-rhamnopyranoside (**4**). — Debenzoylation of **42** (125 mg) gave **4** (46 mg, 87%), $[\alpha]_D$ +38.5° (*c* 1).

Methyl 2-O-(β-D-glucopyranosyl)-3-O-(α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**5**). — Deacylation of **43** (300 mg) gave **5** (112 mg, 82%), $[\alpha]_D$ −42° (*c* 1.3).

Methyl 2-O-(β-D-glucopyranosyl)-3-O-(β-L-fucopyranosyl)-α-L-rhamnopyranoside (**6**). — Debenzoylation of **44** (205 mg) gave **6** (69 mg, 91%), $[\alpha]_D$ +7° (*c* 1.5).

Methyl 2-O-(α-L-fucopyranosyl)-3-O-(β-L-fucopyranosyl)-α-L-rhamnopyranoside (**7**). — Deacylation of **45** (250 mg) gave **7** (90 mg, 92%), $[\alpha]_D$ −40° (*c* 0.7).

Methyl 2-O-(α-L-fucopyranosyl)-3-O-(α-D-mannopyranosyl)-α-L-rhamnopyranoside (**8**). — Debenzoylation of **46** (264 mg) gave **8** (81 mg, 83%), $[\alpha]_D$ −26° (*c* 2).

Methyl 2-O-(α-L-fucopyranosyl)-3-O-(β-D-glucopyranosyl)-α-L-rhamnopyranoside (**9**). — Deacylation of **50** (280 mg) gave **9** (105 mg, 87%), $[\alpha]_D$ −83° (*c* 1).

Methyl 2-O-(β-L-fucopyranosyl)-3-O-(β-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**10**). — Debenzoylation of **63** (200 mg) gave **10** (80 mg, 95%), $[\alpha]_D$ −30.5° (*c* 1.6).

Methyl 2-O-(β-L-fucopyranosyl)-3-O-(α-D-mannopyranosyl)-α-L-rhamnopyranoside (**11**). — Debenzoylation of **65** (280 mg) gave **11** (102 mg, 91%), $[\alpha]_D$ +48° (*c* 2).

Methyl 2-O-(β-L-fucopyranosyl)-3-O-(α-D-glucopyranosyl)-α-L-rhamnopyranoside (**12**). — Debenzoylation of **67** (240 mg) gave **12** (87 mg, 91%), $[\alpha]_D$ −9° (*c* 2).

Methyl 2-O-(α-L-fucopyranosyl)-α-L-rhamnopyranoside (**53**). — Debenzoylation of **52** (330 mg) gave **53** (113 mg, 89%), $[\alpha]_D$ −121° (*c* 2).

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