Carbohydrate Research, 84 (1980) 225–235
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

SYNTHESIS AND ^{13}C-N.M.R. SPECTRA OF β-L-RHAMNOPYRANOSIDES

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(Received October 29th, 1979; accepted for publication, January 11th, 1980)

ABSTRACT

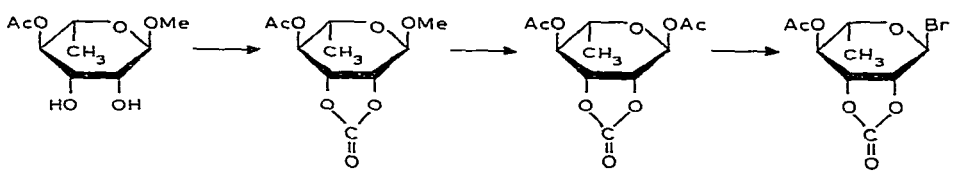
Syntheses of methyl β-L-rhamnopyranoside, 6-*O*-β-L-rhamnopyranosyl-D-glucose and -D-galactose, and 4-*O*-β-L-rhamnopyranosyl-L-rhamnose, based on the use of 4-*O*-acetyl-2,3-*O*-carbonyl-α-L-rhamnopyranosyl bromide as glycosylating agent, are described. The ^{13}C-n.m.r. spectra of β-L-rhamnosides are compared with those of the respective α anomers.

INTRODUCTION

In a study of the glycosylation of trityl ethers of monosaccharides by 1,2-(ortho thioesters) of sugars, in particular of L-rhamnose[1], α- and β-linked rhamnose disaccharides were required for quantification of the stereoselectivity of the glycosylation reaction. To the best of our knowledge, the directed synthesis of β-L-rhamnosides has not been reported; methyl β-L-rhamnopyranoside is a minor product of the Fischer synthesis of methyl α-L-rhamnopyranoside[2–4]. We now describe the synthesis of methyl β-L-rhamnopyranoside (**6**) and three disaccharides containing a β-L-rhamnopyranosidic bond.

RESULTS AND DISCUSSION

The syntheses of β-L-rhamnopyranosides involved the same approach that had been used for preparation of β-D-mannopyranosides[5,6]. The glycosylating agent, 4-*O*-acetyl-2,3-*O*-carbonyl-α-L-rhamnopyranosyl bromide (**4**), was obtained as follows.



1 2 3 4

The crystalline diol **1** was treated with methyl chloroformate in a mixture of benzene and 1,4-dioxane in the presence of triethylamine, as in ref. 6, to give the

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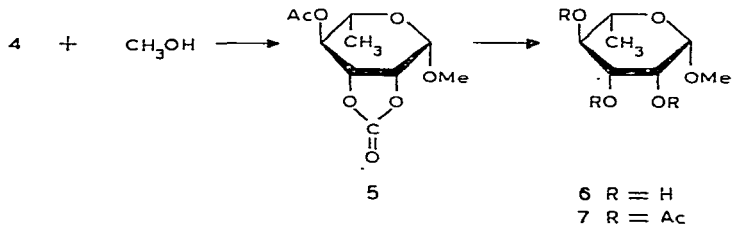
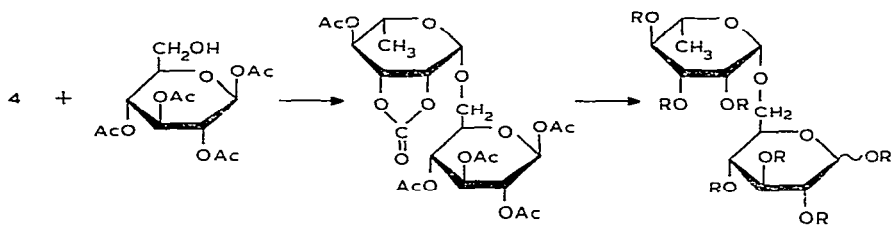
cyclic carbonate **2** in 87% yield; the structure of **2** was supported by i.r. and ^{1}H-n.m.r. data and by elemental analysis. Acetolysis of **2** afforded 1,4-di-*O*-acetyl-2,3-*O*-carbonyl-α,β-L-rhamnopyranose in 90% yield, with an $\alpha:\beta$ ratio of 4:1 according to the ^{1}H-n.m.r. spectrum. The α anomer **3** was isolated in 60% yield by crystallisation. Conventional treatment of **3** with 40% hydrogen bromide in glacial acetic acid (1 h, 20°) quantitatively converted it into the crystalline bromide **4**. Elemental analysis of **4** and the presence of a characteristic n.m.r. signal at δ 6.64 for H-1 confirmed its structure.

Condensation of **4** with dry methanol (200 molar equiv.) in acetonitrile in the presence of mercuric cyanide gave methyl 4-*O*-acetyl-2,3-*O*-carbonyl-β-L-rhamnopyranoside (**5**) in 66% yield. The ^{1}H-n.m.r. spectrum of **5** differed from that of the α anomer **2**. De-esterification of **5** afforded methyl β-L-rhamnopyranoside (**6**); the properties of **6** and of its triacetate **7** coincided with the literature data.



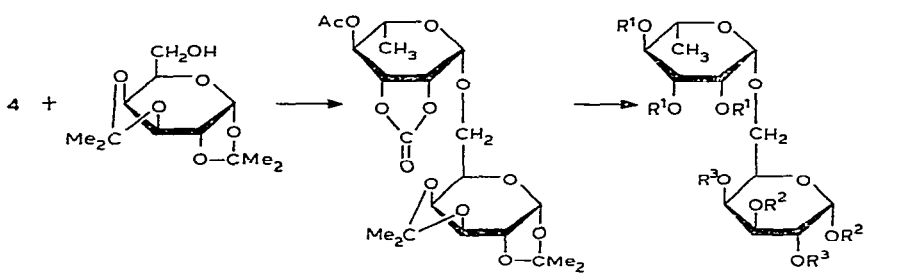
5

6 R = H
7 R = Ac



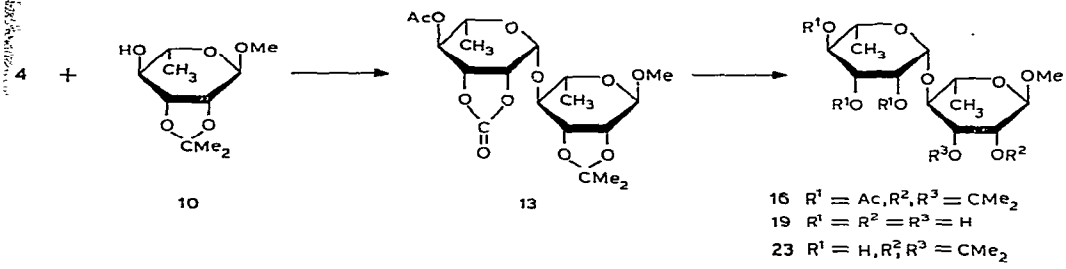
8 11

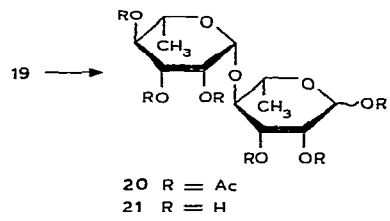
14 R = Ac
17 R = H



9 12

15 R^1 = Ac, R^2,R^3 = CMe_2
18 R^1 = R^2 = R^3 = H
22 R^1 = H, R^2,R^3 = CMe_2





Synthesis of disaccharide derivatives containing a β-L-rhamnosidic bond was performed under Koenigs–Knorr conditions, namely, in dry dichloromethane in the presence of silver oxide and molecular sieves (4 Å) for 2.5 h at room temperature.

Compounds **11**, **12**, and **13** were isolated by column chromatography in yields of 77, 82, and 65%, respectively. Deacylation of **11**–**13** followed by acetylation afforded **14**–**16**, which differed from the respective α anomers in R_F (t.l.c.) and $[\alpha]_D$ values as well as by ^{1}H-n.m.r. spectra. Condensation of **4** with **10** in acetonitrile in the presence of mercuric cyanide followed by deacylation and acetylation gave a mixture of **16** and its α anomer (major component) identified by t.l.c. The preponderant formation of α-glycosides from a related bromide, 4,6-di-*O*-acetyl-2,3-*O*-carbonyl-α-D-mannopyranosyl bromide, under Helferich conditions, has been reported[6,7].

Saponification of **14** gave 6-*O*-β-L-rhamnopyranosyl-D-glucose (**17**). Mild hydrolysis of **15** with 99% trifluoroacetic acid in chloroform followed by deacetylation afforded 6-*O*-β-L-rhamnopyranosyl-D-galactose (**18**). Removal of the *O*-isopropylidene group from **16** and subsequent de-esterification gave methyl 4-*O*-β-L-rhamnopyranosyl-α-L-rhamnopyranoside (**19**). Acetolysis of **19** followed by deacetylation of the resulting 4-*O*-β-L-rhamnopyranosyl-L-rhamnopyranose hexa-acetate (**20**) yielded the disaccharide **21**.

The structures of **17**–**19** were confirmed by methylation analysis. The absence of acetyl migration during glycosylation of **8** by **4** was proved by periodate oxidation of the methylated alditols derived from **17**. The formation of 2,3,4-tri-*O*-methylxylitol from 2,3,4-tri-*O*-methylglucitol, and the absence of 2,3-di-*O*-methylthreitol which could have arisen from 2,3,6-tri-*O*-methylglucitol, unequivocally confirmed the absence of any (1→4)-linked disaccharide.

The chromatographic mobilities (p.c.) of **17** and **18** were less than those of the respective α anomers. All three disaccharides (**17**, **18**, and **21**) were homogeneous

in ion-exchange chromatography in borate buffer and possessed lower retention times (T 44, 38, and 24 min) than the respective α anomers (T 58, 50, and 35 min).

The peracetylated β-rhamnosylalditols derived from **17**, **18**, and **21** were completely oxidised with chromium trioxide[8] (45 min, 40°), whereas the peracetates of α-L-rhamnopyranosyl-D-glucitol, -D-galactitol, and -L-rhamnitol were oxidised under these conditions to a lesser extent (degree of oxidation, 15, 35, and 10%, respectively).

TABLE I

^{13}C-N.M.R. DATA FOR PROTECTED SUGARS

Compound	*Anomer*[a]	*Chemical shifts (p.p.m.)*						
		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OCH$_3$*
25	α	98.7	69.9	69.3	71.2	66.4	17.5	55.1
7	β	99.6	69.0	70.9	71.2	70.6	17.4	57.3
26	α′	98.6	69.9	69.0	71.2	66.9	17.5	
	β	91.9	70.6	73.0	68.9	74.1	67.3	
14	β′	98.6	69.0	70.9	71.1	70.7	17.4	
		98.7						
	β	92.0	70.7	73.0	68.8	73.5	68.0	
	α	89.2	69.5	70.1	68.8	70.9	67.6	
28	α′	97.5	70.0	69.4	71.0	66.5	17.3	
	α	96.4	70.9	70.9	71.3	65.6	66.5	
15	β′	99.0	69.2	70.9	71.2	70.7	17.5	
	α	96.4	70.7	70.7	70.8	66.1	68.3	
9	α	96.5	70.9	71.0	71.6	68.6	62.1	
29	α′	100.2	71.0	71.8	72.8	68.5	17.6	
	α	96.4	70.7	70.7	71.2	66.0	67.2	
22	β′	100.5	71.0	74.2	72.6	72.6	17.7	
	α	96.4	70.7	70.7	71.0	66.1	67.8	
31	α′	96.0	70.0	69.3	71.0	67.0	17.5	
	α	98.2	76.2	77.6	78.3	63.7	18.2	54.8
16	β′	98.2	68.7	70.9	71.3	70.9	17.4	
	α	98.2	76.0	76.9	82.3	63.9	17.4	54.7
10	α	98.4	76.0	78.9	74.6	65.8	17.5	54.8
32	α′	98.8	71.6	71.6	72.7	69.0	17.6	
	α	98.2	76.3	77.4	78.7	64.2	18.2	54.8
23	β′	100.2	71.4	74.8	72.7	72.7	17.9	
	α	98.5	76.3	76.7	81.2	64.8	17.6	54.9

[a]Anomers marked with a prime refer to non-reducing residues; the others refer to "reducing" residues.

The ^{13}C-n.m.r. data of the foregoing β-L-rhamnopyranosides were compared with those of the respective α anomers, namely, methyl α-L-rhamnopyranoside (**24**), the triacetate (**25**) of **24**, 6-*O*-α-L-rhamnopyranosyl-D-glucose hepta-acetate[1] (**26**), 6-*O*-α-L-rhamnopyranosyl-D-glucose (rutinose, **27**; obtained by Zemplén deacetylation of **26**), 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-D-galactopyranose[1] (**28**), 1,2:3,4-di-*O*-isopropylidene-6-*O*-α-L-rhamnopyranosyl-α-D-galactopyranose (**29**, obtained by deacetylation of **28**), 6-*O*-α-L-rhamnopyranosyl-D-galactose (robinobiose, **30**; obtained by hydrolysis of **28** followed by deacetylation), methyl 2,3-*O*-isopropylidene-4-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside[1] (**31**), methyl 2,3-*O*-isopropylidene-4-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**32**, obtained by deacetylation of **31**), and methyl 4-*O*-L-rhamnopyranosyl-α-L-rhamnopyranoside (**33**, obtained by mild hydrolysis of **31** with acid followed by deacetylation). The chemical shifts of the carbon atoms in the derivatives under discussion are listed in Tables I and II.

The assignments of signals in **6**, **7**, **9**, **10**, **24**, and **25** were made by the use of selective decoupling experiments, and the resulting data were used for the inter-

TABLE II

^{13}C-N.M.R. DATA FOR UNPROTECTED SUGARS

Compound	*Anomer*[a]	*Chemical shifts (p.p.m.)*						
		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OCH$_3$*
24	α	102.3	71.4	71.7	73.4	69.6	18.0	55.8
6	β	102.4	71.8	74.1	73.4	73.4	17.9	58.0
27	α′	102.1	71.4	71.7	73.5	69.9	17.9	
		101.9						
	β	97.4	75.5	77.2	71.2	76.1	68.3	
	α	93.4	72.9	74.1	71.2	71.8	68.5	
17	β′	101.3	71.9	74.0	73.4	73.5	18.0	
	β	97.4	75.5	76.9	71.5	76.0	69.0	
	α	93.5	72.9	74.0	70.7	71.9	69.0	
30	α′	101.7	71.3	71.5	73.3	69.9	17.9	
	β	97.8	73.2	74.1	70.0	74.7	68.2	
	α	93.6	70.2	69.6	70.7	70.3	68.7	
18	β′	101.2	71.8	73.9	73.4	73.4	17.9	
	β	97.8	73.1	74.2	70.0	76.3	69.5	
	α	93.6	70.4	69.5	71.2	70.4	69.3	
33	α′	103.0	71.7	71.8	73.2	70.6	18.0	
	α	102.1	71.9	72.4	81.1	68.2	18.7	55.9
19	β′	101.8	70.7	74.1	73.2	73.5	18.0	
	α	102.0	71.9	70.5	83.9	68.1	17.8	56.0

[a]Anomers marked with a prime refer to non-reducing residues; the others refer to "reducing" residues.

pretation of spectra of other compounds. The spectra of **24–27** and **30** were in close agreement with those recently reported[9]. The systematic deviation of chemical-shift values determined in this work as compared with the literature data[9] (downfield shift of 0.5–0.7 p.p.m.) may be due to the different conditions under which the spectra were recorded.

As can be seen from the data in the Tables, α- and β-rhamnosides differ mainly in the chemical shifts for C-3 and C-5. Signals for C-3 exhibit downfield shifts of 2.3–2.4 and 1.5–1.9 p.p.m. for unprotected and protected β-rhamnosides, respectively. For the C-5 resonances, the corresponding downfield shifts are 2.9–3.8 and 3.9–4.2 p.p.m. The C-1 resonances cannot be regarded as characteristic; for **6**, **7**, **15**, **16**, and **23**, they occur 0.1–2.2 p.p.m. downfield, and, for **17–19**, 0.5–1.2 p.p.m. upfield, in comparison with the corresponding signals for the α anomers.

The configuration of the rhamnosidic bond has some influence on the chemical shifts of the *O*-glycosylated, aglyconic carbon atoms, the respective resonances for β anomers being shifted downfield. Such a change for the OMe signals of methyl rhamnosides (**6**/**24** and **7**/**25**) is 2.2 p.p.m. The resonances of C-4 in the "reducing" L-rhamnopyranose moieties in **16** and **19** are shifted downfield by 4.0 and 2.8 p.p.m. in comparison with those in **31** and **33**. The C-6 resonances of the galactose moiety in the 6-*O*-β-L-rhamnopyranosyl-D-galactose derivatives **15** and **18** are shifted by 0.6–1.8 p.p.m. in comparison with those in the α anomers **28** and **30**; even smaller differences (0.5–0.7 p.p.m.) are observed for the positions of the C-6 signals in 6-*O*-rhamnopyranosyl-D-glucose derivatives.

The data presented here indicate that the bromide **4** is an effective β-L-rhamnosylating agent and that ^{13}C-n.m.r. spectroscopy is useful for determining the configuration of L-rhamnosidic bonds.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter at 20 ±2°. Analytical ion-exchange chromatography (i.e.c.) of unprotected sugars was performed on a Technicon SC-II System with a glass column (25 × 0.6 cm) packed with DA X4 resin (Durrum, U.S.A.) and elution with 0.5M sodium borate buffer (pH 8.95) at 55° and a rate of 1 ml/min. The orcinol–sulphuric acid reagent was used to monitor separations. G.l.c. was conducted with a dual, heated, hydrogen flame-ionisation detector. Separations were carried out on a steel column (150 × 0.6 cm) packed with 3% of SE-30 on Diatomite CQ (100–120 mesh) at 270°. G.l.c.–m.s. was performed on a Varian MAT-111 GNOM apparatus with a column packed with 5% of SE-30 on Chromaton N. I.r. spectra were recorded on a UR-20 instrument, for potassium bromide pellets. ^{1}H-N.m.r. spectra were recorded on Varian DA-60-IL and Tesla BS-497 (100 MHz, C.S.S.R.) instruments with tetramethylsilane as internal standard. The ^{13}C-n.m.r. spectra were measured at ambient temperature with a Bruker WP-60 instrument in the deuterio-lock mode (internal

tetramethylsilane and methanol for solutions in deuteriochloroform and deuterium oxide, respectively). The shift of methanol *vs.* tetramethylsilane (50.15 p.p.m.) was confirmed separately. Proton-decoupled f.t.-spectra were measured with a repetition time of 1.1 sec, a pulse width of 3 sec (30°), 3750-Hz sweep-width, and 4K real data-points. Selective decoupling ($^{13}C^{i}$–H^{i}) experiments were made after the determination of proton chemical-shifts by ^{1}H-n.m.r. spectroscopy.

1,4-Dioxane was dried and distilled from potassium hydroxide. Chloroform was washed with conc. sulphuric acid and water, dried with calcium chloride, and distilled from potassium carbonate. Dichloromethane was washed with conc. sulphuric acid and water, dried with calcium chloride, and distilled from calcium hydride. Acetonitrile was distilled from calcium chloride and calcium hydride. Molecular sieves (4 Å) were powdered and heated at 350° for 4 h. T.l.c. was performed on Silica Gel L 5/50 μm (C.S.S.R.) with *A*, 1:1 ether–benzene; and *B*, 1:1 ethyl acetate–benzene. Components were detected by spraying with 25% sulphuric acid and heating at ~150°. Column chromatography was performed on Silica Gel L 100/250 μm (C.S.S.R.) with a gradient of benzene→ether. P.c. was conducted on Filtrak FN-11 paper with solvent system *C*, 4:3:1 1-butanol–pyridine–water, and detection with the potassium periodate–silver nitrate–potassium hydroxide reagent[10].

De-esterification was performed with sodium methoxide (0.1M) in methanol (1 h, 20°), sodium ions were removed with KU-2 (H^{+}) resin, and methanolic solutions were then evaporated. Methylation analysis was performed as follows: a sample of disaccharide (10 mg) was subjected to Hakomori methylation[11], the product was hydrolysed with M hydrochloric acid (4 h, 100°), the solution was evaporated to dryness, and traces of acid were removed by addition and evaporation of water (2 × 2 ml). The resulting products were reduced with sodium borohydride (2–5 mg) for 4 h, followed by neutralisation with KU-2(H^{+}) resin, evaporation to dryness, successive additions and evaporations of methanol (5 × 5 ml), and acetylation with 1:1 acetic anhydride–pyridine (2 ml) (15 min, 100°). The resulting mixture was treated with methanol (1 ml) for 0.5 h and then evaporated with water and toluene to dryness; the residue was dissolved in chloroform (0.5 ml) and subjected to g.l.c.–m.s. examination.

Solutions were concentrated *in vacuo* at 40°.

Methyl 4-O-acetyl-2,3-O-carbonyl-α-L-rhamnopyranoside (**2**). — Compound **1** (13.2 g, 60 mmol)[1] in 1,4-dioxane (10 ml) was treated with a solution of triethylamine (20 ml) in benzene (300 ml), and the mixture was then cooled in an ice–water bath. While the mixture was shaken manually, methyl chloroformate (53 ml) was added dropwise during ~40 min. The mixture was diluted with benzene (200 ml) and washed successively with water (300 ml), 10% hydrochloric acid (300 ml), and water (2 × 300 ml). Evaporation of the solvents, followed by evaporation of 40% aqueous ethanol from the solid residue, gave **2** (13 g, 87%), m.p. 137–138°, $[\alpha]_D$ −22.1° (*c* 1.60, chloroform), R_F 0.58 (*A*), ν_{max}^{KBr} 1755 (OAc) and 1830 cm^{-1} (cyclic carbonate). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.15 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 2.05 (s, 3 H, OAc), and 3.36 (s, 3 H, OMe).

Anal. Calc. for $C_{10}H_{14}O_7$: C, 48.78; H, 5.73. Found: C, 48.30; H, 5.66.

1,4-Di-O-acetyl-2,3-O-carbonyl-α-L-rhamnopyranose (**3**). — To a solution of **2** (12.3 g, 50 mmol) in acetic anhydride (50 ml) was added 1% (v/v) sulphuric acid in acetic anhydride (50 ml). After 1 h at room temperature, the mixture showed one component (R_F 0.48) in t.l.c. (*A*). The solution was stirred with water (1000 ml) for 2 h and then extracted with chloroform (3 × 150 ml). The combined extracts were washed successively with water (2 × 200 ml), saturated, aqueous sodium hydrogencarbonate (100 ml), and water (200 ml), and evaporated to a syrup (12.3 g, 90%), $[\alpha]_D$ −21.0° (*c* 1.26, chloroform), ν_{max}^{KBr} 1765 (OAc) and 1820 cm^{-1} (cyclic carbonate). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.15 (d, 2.4 H, $J_{5,6}$ 7 Hz, CMe), 1.20 (d, 0.6 H, $J_{5,6}$ 7 Hz, CMe), 2.05 (s, 6 H, 2 OAc), 3.80 (m, 1 H, H-5), 6.05 (s, 0.2 H, H-1), and 6.15 (s, 0.8 H, H-1).

Crystallisation of this syrup from ethanol gave **3** (8.2 g, 60%), m.p. 91–92°, $[\alpha]_D$ −26.5° (*c* 2.44, chloroform).

Anal. Calc. for $C_{11}H_{14}O_8$: C, 48.18; H, 5.15. Found: C, 48.33; H, 5.26.

4-O-Acetyl-2,3-O-carbonyl-α-L-rhamnopyranosyl bromide (**4**). — Compound **3** (2 g, 7.3 mmol) in chloroform (80 ml) was treated with 40% hydrogen bromide in glacial acetic acid (20 ml) for 1 h at room temperature. The solution was then quickly washed, successively, with ice–water (2 × 50 ml), saturated, aqueous sodium hydrogencarbonate (50 ml), and ice–water (50 ml), filtered through cotton, and evaporated, to give a solid residue (2.1 g, 98%), R_F 0.68 (dry ether–benzene, 1:1), $[\alpha]_D$ −117.5° (*c* 1.48, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.30 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 2.16 (s, 3 H, OAc), 4.10 (m, 1 H, H-5), and 6.64 (s, 1 H, H-1). The analytical sample of bromide **4**, obtained by crystallisation from dry ether–pentane, had m.p. 118–119°, $[\alpha]_D$ −131.0° (*c* 1.40, chloroform).

Anal. Calc. for $C_9H_{11}BrO_6$: C, 36.63; H, 3.76; Br, 27.08. Found: C, 36.48; H, 3.65; Br, 26.85.

Methyl 4-O-acetyl-2,3-O-carbonyl-β-L-rhamnopyranoside (**5**). — A solution of compound **4** (340 mg, 1.16 mmol) in acetonitrile (5 ml) was stirred with anhydrous methanol (10 ml) and mercuric cyanide (370 mg, 1.47 mmol) for 4 h. The solvents were evaporated, the residue was dissolved in chloroform (40 ml), and the solution was washed successively with M potassium bromide (2 × 40 ml), saturated, aqueous sodium hydrogencarbonate (40 ml), and water (40 ml), and evaporated. Column chromatography then afforded **5** as a syrup (200 mg, 66%), R_F 0.45 (*A*), $[\alpha]_D$ +81.5° (*c* 1.50, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.30 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 2.13 (s, 3 H, OAc), and 3.55 (s, 3 H, OMe).

Methyl β-L-rhamnopyranoside (**6**). — Compound **5** (150 mg, 0.61 mmol) was de-esterified with sodium methoxide. Crystallisation of the product from ethanol gave **6** (80 mg, 74%), m.p. 140–141°, $[\alpha]_D$ +95.1° (*c* 2.1, water); lit.[2] m.p. 140–141°, $[\alpha]_D$ +95.4° (water).

Methyl 2,3,4-tri-O-acetyl-β-L-rhamnopyranoside (**7**). — Compound **6** (50 mg, 0.28 mmol) was treated with pyridine (1 ml) and acetic anhydride (1 ml) for 16 h at room temperature. The excess of reagents was removed by successive evaporation

with ethanol and then with water. Crystallisation of the residue from ethanol gave **7** (55 mg, 63%), m.p. 151–153°, $[\alpha]_D$ +42.5° (*c* 1.8, chloroform); lit.[2] m.p. 151–152°, $[\alpha]_D$ +45.7° (chloroform).

1,2,3,4-Tetra-O-*acetyl-6*-O-(*4*-O-*acetyl-2,3*-O-*carbonyl*-β-L-*rhamnopyranosyl*)-β-D-*glucopyranose* (**11**). — A solution of **8** (400 mg, 1.15 mmol) in dichloromethane (10 ml) was stirred magnetically for 1 h with silver oxide (500 mg) and molecular sieves (4 Å; 3 g). A solution of **4** (500 mg, 1.7 mmol) in dichloromethane (10 ml) was added dropwise during 2 h, and stirring was continued for an additional 0.5 h. The mixture was filtered, and the filtrate was evaporated to a syrup (800 mg) that showed a major component (R_F 0.30) in t.l.c. (*B*). This syrup was treated with pyridine (1 ml) and acetic anhydride (1 ml) for 16 h at room temperature, and the mixture was worked-up as described above. Column chromatography of the product gave amorphous **11** (500 mg, 77%), $[\alpha]_D$ +26.1° (*c* 1.1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.28 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 1.98–2.13 (15 H, 5 OAc), and 5.72 (d, 1 H, $J_{1,2}$ 8 Hz, H-1).

6-*O*-(*4*-O-*Acetyl-2,3*-O-*carbonyl*-β-L-*rhamnopyranosyl*)-*1,2*:*3,4-di*-O-*isopropylidene*-α-D-*galactopyranose* (**12**). — Compound **9** (300 mg, 1.15 mmol) in dichloromethane (10 ml) was treated with **4** (500 mg, 1.7 mmol) in the presence of silver oxide and molecular sieves (4 Å) as described above. The product (without acetylation) was chromatographed, and amorphous **12** (445 mg, 82%) was obtained, R_F 0.43 (*B*), $[\alpha]_D$ −10.2° (*c* 0.75, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.26 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 1.28, 1.30, 1.38, 1.50 (4 s, 12 H, 2 CMe_2), and 2.08 (s, 3 H, OAc).

Methyl 4-O-(*4*-O-*acetyl-2,3*-O-*carbonyl*-β-L-*rhamnopyranosyl*)-*2,3*-O-*isopropylidene*-α-L-*rhamnopyranoside* (**13**). — Compound **10** (220 mg, 1.0 mmol) was glycosylated with bromide **4** (500 mg, 1.7 mmol), as described for the synthesis of **11**. The product was chromatographed (without prior acetylation) and yielded amorphous **13** (280 mg, 65%), R_F 0.63 (*B*), $[\alpha]_D$ +27.6° (*c* 2.4, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.30 (d, 3 H, $J_{5,6}$ 6 Hz, CMe), 1.33 (d, 3 H, $J_{5,6}$ 6 Hz, CMe), 1.35, 1.50 (2 s, 6 H, CMe_2), 2.10 (s, 3 H, OAc), and 3.35 (s, 3 H, OMe).

1,2,3,4-Tetra-O-*acetyl-6*-O-(*2,3,4-tri*-O-*acetyl*-β-L-*rhamnopyranosyl*)-D-*glucopyranose* (**14**). — Compound **11** (400 mg, 0.71 mmol) was de-esterified, and the product was acetylated with pyridine (1 ml) and acetic anhydride (1 ml) for 16 h. The excess of reagents was removed by evaporation with ethanol, the residue was dissolved in chloroform (20 ml), and the solution was washed with water (3 × 20 ml) and evaporated, to give amorphous **14** (410 mg, 93%), $[\alpha]_D$ +65.0° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.21 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 1.99–2.15 (21 H, 7 OAc), 5.61 (d, 0.5 H, $J_{1,2}$ 7 Hz, H-1), and 6.13 (d, 0.5 H, $J_{1,2}$ 3 Hz, H-1).

Anal. Calc. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.88. Found: C, 50.34; H, 5.96.

1,2:*3,4-Di*-O-*isopropylidene-6*-O-(*2,3,4-tri*-O-*acetyl*-β-L-*rhamnopyranosyl*)-α-D-*galactopyranose* (**15**). — Compound **12** (350 mg, 0.74 mmol) was de-esterified to yield 1,2:3,4-di-*O*-isopropylidene-6-*O*-β-L-rhamnopyranosyl-α-D-galactopyranose (**22**). This product was acetylated as described in the synthesis of **14**, to give amorphous **15** (380 mg, 96%), $[\alpha]_D$ −5.5° (*c* 1.05, chloroform). ^{1}H-N.m.r. data (CCl_4):

δ 1.23 (d, 3 H, $J_{5,6}$ 7 Hz, CMe), 1.27, 1.31, 1.39, 1.48 (4 s, 12 H, 2 CMe_2), 1.93, 1.97, and 2.15 (3 s, 9 H, 3 OAc).

Anal. Calc. for $C_{24}H_{36}O_{13}$: C, 54.13; H, 6.81. Found: C, 54.35; H, 7.02.

Methyl 2,3-O-isopropylidene-4-O-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**16**). — Compound **13** (250 mg, 0.58 mmol) was deacylated to yield methyl 2,3-*O*-isopropylidene-4-*O*-β-L-rhamnopyranosyl-α-L-rhamnopyranoside (**23**). This product was acetylated, as described in the synthesis of **14**, to give amorphous **16** (270 mg, 95%), $[\alpha]_D$ +56.2° (*c* 1.05, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.18 (d, 3 H, $J_{5,6}$ 6 Hz, CMe), 1.24 (d, 3 H, $J_{5,6}$ 6 Hz, CMe), 1.27, 1.47 (2 s, 6 H, CMe_2), 1.91, 1.96, 2.15 (3 s, 9 H, 3 OAc), and 3.27 (s, 3 H, OMe).

Anal. Calc. for $C_{22}H_{34}O_{12}$: C, 53.87; H, 6.99. Found: C, 53.77; H, 7.06.

6-O-β-L-Rhamnopyranosyl-D-glucose (**17**). — Compound **14** (300 mg, 0.48 mmol) was deacetylated to yield **17** (150 mg, 96%), $[\alpha]_D$ +63.7° (*c* 0.8, water); R_{Glc} 0.70 (*C*), $R_{Rutinose}$ 0.74 (*C*); retention time in i.e.c., 44 min.

Compound **17** was subjected to methylation analysis, and 1,5-di-*O*-acetyl-2,3,4-tri-*O*-methylrhamnitol and 1,5,6-tri-*O*-acetyl-2,3,4-tri-*O*-methylglucitol (1 : 1) were identified by g.l.c.–m.s. Periodate oxidation[12] of the methylated alditols, followed by reduction with sodium borohydride and acetylation, resulted (g.l.c.–m.s.) in disappearance of the glucitol derivative and formation of 1,5-di-*O*-acetyl-2,3,4-tri-*O*-methylxylitol; 1,4-di-*O*-acetyl-2,3-di-*O*-methylthreitol was absent.

6-O-β-L-Rhamnopyranosyl-D-galactopyranose (**18**). — A solution of compound **15** (100 mg, 0.19 mmol) in chloroform (5 ml) was treated with trifluoroacetic acid containing 1% of water (5 ml) for 1 h at room temperature. The mixture was then concentrated, and remaining trifluoroacetic acid was removed by several additions and evaporations of toluene–heptane–ethanol (3 : 1 : 1). The resulting syrup was deacetylated to yield **18** (60 mg, 100%,) $[\alpha]_D$ +60.8° (*c* 2.4, water); R_{Glc} 0.60 (*C*), $R_{Robinobiose}$ 0.71 (*C*); retention time in i.e.c., 38 min.

When **18** was subjected to methylation analysis, 1,5-di-*O*-acetyl-2,3,4-tri-*O*-methylrhamnitol and 1,5,6-tri-*O*-acetyl-2,3,4-tri-*O*-methylgalactitol were identified in the ratio 1 : 1.

Methyl 4-O-β-L-rhamnopyranosyl-α-L-rhamnopyranoside (**19**). — A solution of **16** (240 mg, 0.56 mmol) in chloroform (5 ml) was treated with trifluoroacetic acid containing 1% of water (5 ml), as described in the synthesis of **18**, and the product was deacetylated to yield **19** (170 mg, 94%), $[\alpha]_D$ −16.5° (*c* 2.45, water).

Compound **19** was subjected to methylation analysis, and 1,5-di-*O*-acetyl-2,3,4-tri-*O*-methylrhamnitol and 1,4,5-tri-*O*-acetyl-2,3-di-*O*-methylrhamnitol were identified in the ratio 1 : 1.

1,2,3-Tri-O-acetyl-4-O-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)-L-rhamnopyranose (**20**). — Compound **19** (100 mg, 0.31 mmol) in acetic anhydride (2 ml) was treated for 2 h at room temperature with 1% (v/v) conc. sulphuric acid in acetic anhydride (2 ml). The mixture was then diluted with chloroform (10 ml), shaken for 1 h with ice–water (5 ml), and washed successively with water (2 × 10 ml), saturated, aqueous sodium hydrogencarbonate (10 ml), and water (2 × 10 ml).

Column chromatography of the product afforded **20** (140 mg, 80%), R_F 0.5 (*A*), $[\alpha]_D$ −14.5° (*c* 2.5, chloroform). ^{1}H-N.m.r. data (CCl_4): δ 1.19 (d, 3 H, $J_{5,6}$ 6 Hz, CMe), 1.25 (d, 3 H, $J_{5,6}$ 6 Hz, CMe), 1.80–2.15 (18 H, 6 OAc), and 5.80 (d, 1 H, $J_{1,2}$ 3 Hz, H-1).

Deacetylation of **20** (56 mg, 0.1 mmol) gave 30 mg of amorphous 4-*O*-β-L-rhamnopyranosyl-L-rhamnopyranose (**21**), $[\alpha]_D$ +4.3° (*c* 2, water), R_{Glc} 1.62 (*C*); retention time in i.e.c., 24 min.

Oxidation of rhamnopyranosyl-alditols peracetates with chromium trioxide in acetic acid. — Samples (10 mg) of disaccharides **17**, **18**, **21**, **27**, **30**, and 4-*O*-α-L-rhamnopyranosyl-L-rhamnopyranose[1] were severally dissolved in water (1 ml) and treated with sodium borohydride (2–5 mg) for 3 h at 20°. Each mixture was then neutralised with KU-2(H^+) resin, followed by evaporation to dryness, successive additions and evaporations of methanol (5 × 5 ml), and acetylation with acetic anhydride (1 ml) and pyridine (1 ml) for 16 h at room temperature. The excess of reagents was removed by the addition and evaporation of ethanol and then of toluene. The residue was mixed with glucitol hexa-acetate (5 mg), and the ratio of rhamnosyl-alditol acetate to glucitol acetate in the resulting mixture was established by g.l.c. Half of this mixture was dissolved in glacial acetic acid (0.5 ml), acetic anhydride (0.1 ml) and chromium trioxide (50 mg) were added, and the resulting mixture was stirred at 40° for 45 min. The mixture was then diluted with chloroform (5 ml) and washed with water until a colourless organic layer was obtained. The solvent was then evaporated, the residue was dissolved in chloroform (0.5 ml), and aliquots of this solution were analysed by g.l.c. to determine the ratio of rhamnosyl-alditol acetate to glucitol acetate.

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