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CARBOHYDRATE COMPONENTS OF FLAVONOL TRIAOSIDES: A CONVENIENT SYNTHESIS OF *O*-α-L-RHAMNOPYRANOSYL-(1→3)-*O*-α-L-RHAMNOPYRANOSYL-(1→6)-D-GALACTOSE AND *O*-α-L-RHAMNOPYRANOSYL-(1→2)-*O*-α-L-RHAMNOPYRANOSYL-(1→6)-D-GALACTOSE

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ABSTRACT

Condensation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**1**) with 2,4-di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl bromide (**2**), followed by subsequent removal of the isopropylidene and acetyl groups from the product, afforded the first of the title trisaccharides. The reaction of **1** with 3,4-di-*O*-benzyl-2-*O*-*p*-nitrobenzoyl-α-L-rhamnopyranosyl bromide and deacylation of the product gave a disaccharide derivative that was treated with 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide. Removal of the protecting groups from the product gave the second (**15**) of the title trisaccharides. The reaction of **1** with the acetobromo derivative of 2-*O*-α-L-rhamnopyranosyl-L-rhamnose, with subsequent removal of protecting groups from the product, also gave trisaccharide **15**.

INTRODUCTION

Flavonol glycosides isolated from different Rhamnus species contain trisaccharide moieties, consisting of one D-galactose and two L-rhamnose residues, which are always attached to the flavonol skeletons through the D-galactosyl residue. Thus, for xanthorhamnine A and C and for catharticine, isolated from *Rhamnus saxatilis* Jacq., *ssp. saxatilis* (inc. *Rhamnus infectorius* L.)[1], *Rh. saxatilis*, *ssp. tinct.* (Waldst. et Kit) Neyman (= *Rhamnus tinctorius* Waldst. et Kit.), *Rh. catharticus* L.[2–4], and *Rh. petiolaris* Bois.[6], *O*-α-L-rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose[7,8] was proposed as the carbohydrate component. For the synthesis of this trisaccharide, two procedures were elaborated[9,10]. Recently, using *O*-α-L-rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose

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nona-acetate as starting material, it was shown by synthesis and ^{13}C-n.m.r. spectroscopy[11] that none of the structures proposed was correct and that the foregoing natural flavonol glycosides contain *O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose. For this reason, the name "isorhamninose" was proposed[11] for *O*-α-L-rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose, and "rhamninose" for *O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactopyranose.

Rhamninose proved to be the carbohydrate component of alaternine, isolated from *Rh. alaternus* L.[5,7], and it was found as free trisaccharide in different Rhamnus species[12]. A synthesis was recently published[13]. The structure of alaternine had not been verified hitherto by synthesis.

The trisaccharide of the so-called F_2-component isolated from *Rh. petiolaris* Bois[6] should be *O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose, which is attached to rhamnetine (7-*O*-methylquercetine).

The carbohydrate component of a kaempferol-triaoside isolated[14] from *Astragalus caucasicus* is a branched trisaccharide, the structure of which has been reported to be 3,4-di-*O*-α-L-rhamnopyranosyl-D-galactose.

We now report an unequivocal synthesis of the title compounds, with the purpose of providing reference compounds for the structural elucidation of alaternine and F_2-component, the structures of which were postulated on the basis of spectroscopic studies. Recently, the first trisaccharide originating from a natural source was used for immunochemical studies[15].

RESULTS AND DISCUSSION

The method elaborated[16,17] in our laboratory for the preparation of *O*-α-L-rhamnopyranosyl-(1→3)-L-rhamnose made possible a convenient synthesis of rhamninose (**5**), which is very similar to that described by Lafitte *et al.*[13]. The coupling product (**3**) of the acetobromo-dirhamnose derivative **2** and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[18] (**1**) could be isolated pure and proved to be suitable for ^{13}C-n.m.r. spectroscopy. The proton-coupled spectrum of **3** showed clearly that the postulated anomeric configurations were correct for all three anomeric centers ($J_{C\text{-}1,H\text{-}1}$ 178.8, $J_{C\text{-}1',H\text{-}1'}$ 171.9, and $J_{C\text{-}1'',H\text{-}1''}$ 171.3 Hz). The assignment was based on the spectral data for **1**, methyl 2,4-di-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside[17], and 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-D-galactopyranose[9]. A glycosylation shift of +4.1 p.p.m. was observed for C-6 and assigned to the interglycosidic linkage. Acid hydrolysis of the isopropylidene groups of **3**, followed by acetylation, gave the crystalline nona-acetate **4**, which melted ~70° above the published[13] value. Deacetylation of **4** gave the trisaccharide **5**. The ^{13}C-n.m.r. spectra of **5** (see Table I) and robinobiose were very similar to those reported[13].

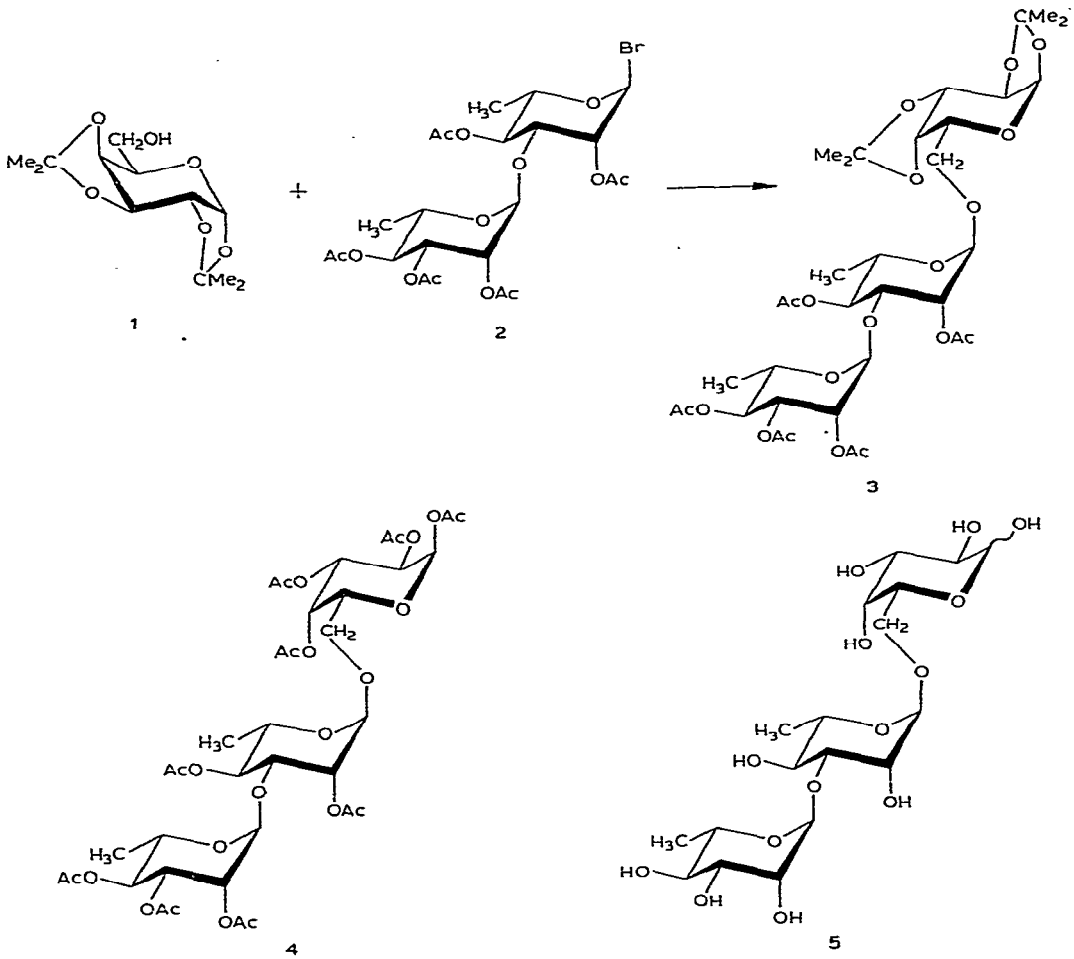
For the synthesis of *O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose (**15**), **1** was again used as "aglycon". In the first version of the

TABLE I

CHEMICAL SHIFTS AND COUPLING CONSTANTS (Hz)

Atom	**1**[a]	[a,b]	**3**[a]	**13**[a]	**8**[a]	**10**[a]	**5**		[c]		**15**		[d]	
C-1	96.4	96.3	96.3	96.3		96.4	93.1	97.4	93.1	97.4	93.1	97.3	93.1	97.3
($^1J_{C,H}$)		(179)	(179)	(178.8)									(170)	(160.5)
C-2	71.4	70.8	70.7	70.9		70.7	69.2	72.8	69.2	72.8	69.0	72.6	69.1	72.7
C-3	71.0	71.0	71.0	71.0		71.1	69.6	73.7	69.8	73.7	69.8	73.7	69.8	73.6
C-4	71.0	70.8	70.7	70.9		70.8	70.2	70.0	70.3	69.7	70.2	69.6	70.2	69.6
C-5	68.9	66.6	66.7	66.5		67.0	69.6	74.2	69.8	74.3	69.8	74.2	69.9	74.2
C-6	61.7	65.7	65.8	65.0		66.2	67.9	67.6	68.0	67.8	68.3	67.8	68.1	67.7
C-1′			97.4	98.7	92.6	97.7		101.1		101.0	99.9	99.8		
($^1J_{C,H}$)			(171)	(171.9)										
C-2′			71.0	76.9	69.7	70.7		70.7		71.4		79.2		
C-3′			75.0	70.9	77.5	78.3		78.8		71.3		70.8		
C-4′			72.6	71.8	79.5	80.1		73.0		80.4		72.8		
C-5′			67.2	67.2	71.0	69.7		69.6		67.9		69.6		
C-6′			17.2	17.4	18.2	18.1		17.5		18.1		17.4		
C-1″		97.5	98.8	99.3				102.8		102.2		102.9	101.3	101.2
($^1J_{C,H}$)		(171.9)	(172)	(171.3)										(169.7)
C-2″		69.4	68.6	68.9				71.0		71.8		70.8		70.8
C-3″		70.0	70.4	70.3				71.1		71.3		70.8		71.1
C-4″		71.3	71.2	71.5				73.0		72.8		72.8		72.9
C-5″		66.5	66.4	67.2				69.6		70.0		69.8		69.4
C-6″		17.2	17.2	17.3				17.5		17.3		17.4		17.4

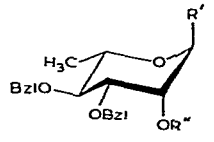
[a]Measured in $CDCl_3$; all other compounds were measured in D_2O. [b]1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-D-galactopyranose[9]. [c]*O*-α-L-Rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→6)-D-galactose. [d]*O*-α-L-Rhamnopyranosyl-(1→6)-D-galactose (Robinobiose).



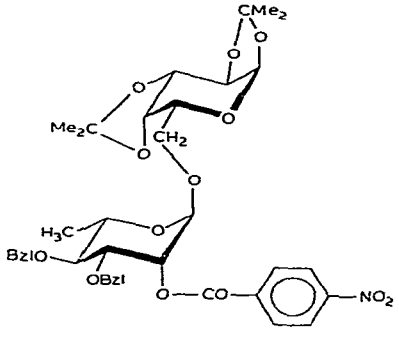
synthesis, the route used for **5** was not followed, because the presence of the non-participating 2-*O*-rhamnosyl moiety of the acetobromo derivative of 2-*O*-α-L-rhamnosyl-L-rhamnose meant that exclusive formation of an α-glycosidic linkage between the rhamnose and galactose residues would not have been ensured. The non-participating character of 2-glycosyl groups in glycoside synthesis has been demonstrated in many syntheses[19–21]. Therefore, an alternative route was used.

Acid hydrolysis of methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside[16,17] gave crystalline 3,4-di-*O*-benzyl-L-rhamnose (**6**), which was converted into the crystalline 1,2-diacetate (**7**) and 1,2-bis(*p*-nitrobenzoate) (**8**). Treatment of **8** with hydrogen bromide in dichloromethane furnished the glycosyl bromide **9** (90% yield), and the Koenigs–Knorr reaction of **9** with **1** and subsequent chromatography gave the disaccharide derivative **10** in 40% yield. The structure of **10** was confirmed by i.r. (1720 cm^{-1}, strong carbonyl absorption), ^{1}H-n.m.r. (the presence of the isopropylidene and benzyl groups), and ^{13}C-n.m.r. spectroscopy; the chemical shift of C-1′

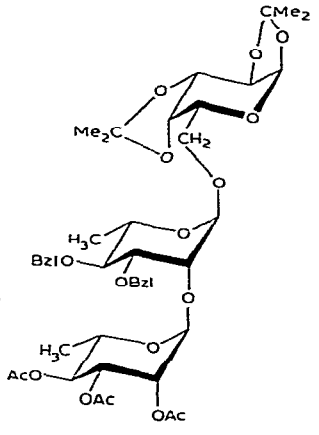
was 97.7 p.p.m., characteristic for α-L($^1C_4$)-rhamnopyranosides. Saponification of **10** gave a disaccharide derivative containing HO-2′ unsubstituted, which was a suitable "aglycon" for the synthesis of **15**. The reaction of the deacylated product of **10** with 2,3,4-tri-*O*-acetyl-α-L-rhamnosyl bromide gave the trisaccharide derivative **11** (53% yield after chromatography). The structure of **11**, with the exception of the anomeric configuration, was established by ^{1}H-n.m.r. spectroscopy.



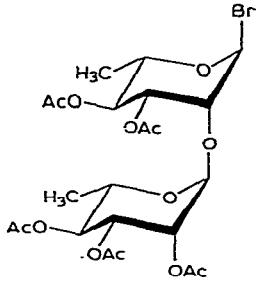
6 R′ = OH, R″ = H
7 R′ = OAc, R″ = Ac
8 R′ = O-4-Nitrobenzoyl, R″ = 4-Nitrobenzoyl
9 R′ = Br, R″ = 4-Nitrobenzoyl



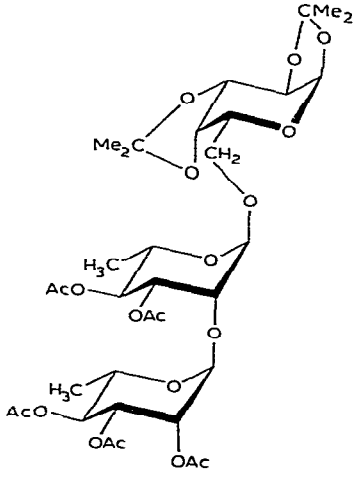
10



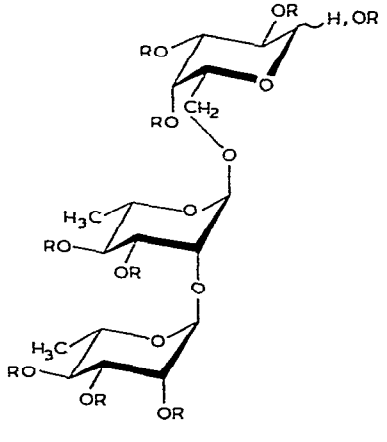
11



12



13



14 R = Ac
15 R = H

Catalytic hydrogenation of **11** and then acetylation yielded **13**. Analysis of the ^{13}C-n.m.r. spectrum of **13** was based on data for methyl 3,4-di-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside[17] and **1**. The α-anomeric configurations were deduced from the proton-coupled ^{13}C-spectrum, the values of

the $^1J_{C,H}$ coupling constants being 178.8 Hz for C-1–H-1, 171.9 Hz for C-1′–H-1′, and 171.3 Hz for C-1″–H-1″.

As mentioned above, use of the acetylhalogeno derivative of 2-*O*-α-L-rhamnopyranosyl-L-rhamnopyranose was avoided in the synthesis of **13**. Fréchet and Baer[22] have shown that methanolysis of 2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl bromide gave an αβ-mixture, in which the α anomer preponderated. The reaction without stereoselectivity may be due to the increased anomeric effect which is especially strong in the case of an axial C-2 substituent[22,28]. Nevertheless, the outcome of glycosylation reactions is still unpredictable in the case of rhamnosyl halides bearing a non-participating group at C-2.

1,3,4-Tri-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranose[17] was converted into the glycosyl bromide **12**, which with **1** gave only one trisaccharide derivative (**13**). Clearly, the other anomer, which remained undetected under the conditions used, could only be present in minor quantity. Acid hydrolysis removed the isopropylidene groups from **13** and acetylation then gave compound **14**. Deacetylation of **14** gave the trisaccharide **15**.

The signal for C-1′ in the ^{13}C-n.m.r. spectrum of **15** is a doublet with intensity corresponding to the ratio of the α and β anomers of the reducing galactopyranose residue. This effect was first observed by Usui *et al.*[23] for 2-*O*-glycosyl-glucoses, and subsequently by others[24,25]. The splitting of C-1′ of **15** illustrates the high conformational sensitivity of ^{13}C-n.m.r. spectroscopy. Similar shift-effects have been observed in the ^{1}H-n.m.r. spectra of some oligosaccharides[26,27].

EXPERIMENTAL

Melting points were determined with a Kofler apparatus and are uncorrected. A Perkin–Elmer 241 polarimeter was used for measurement of optical rotations at 22°. ^{13}C-N.m.r. spectra were recorded with a Varian XL-100-FT-15 or a Bruker WP-200 spectrometer at room temperature. ^{1}H-N.m.r. spectra were recorded with a Jeol MH-100 spectrometer. T.l.c. was performed on precoated plates of Silica Gel F_{254} (Merck).

2,4-Di-O-*acetyl-3*-O-(*2,3,4-tri*-O-*acetyl*-α-L-*rhamnopyranosyl*)-α-L-*rhamnopyranosyl bromide* (**2**). — A saturated solution of hydrogen bromide in glacial acetic acid (3 ml) was added to a solution of 1,2,4-tri-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranose[16,17] (700 mg) in dichloromethane (1 ml). After the mixture had been kept at room temperature for 2 h, it was diluted with dichloromethane (50 ml), washed with ice–water, dried, filtered, and concentrated, to yield **2** (710 mg, 98%), m.p. 108–110° (from ether–hexane), $[\alpha]_D$ −101° (*c* 0.78, chloroform), R_F 0.58 (toluene–ether, 1:1).

Anal. Found: C, 46.02; H, 5.41; Br, 13.95. Calc. for $C_{22}H_{31}BrO_{13}$: C, 45.29; H, 5.35; Br, 13.69.

6-O-[*2,4-Di*-O-*acetyl-3*-O-(*2,3,4-tri*-O-*acetyl*-α-L-*rhamnopyranosyl*)-α-L-*rhamnopyranosyl*]-*1,2*:*3,4-di*-O-*isopropylidene*-α-D-*galactopyranose* (**3**). — A solution of **1**

(0.80 g) in dry benzene (20 ml) and nitromethane (20 ml) was concentrated at atmospheric pressure to half its volume, cooled to 45°, treated with $Hg(CN)_2$ (0.39 g) and **2** (0.875 g). The mixture was stirred for 16 h under anhydrous conditions, diluted with dichloromethane (50 ml), filtered, and concentrated. The residue was treated with dichloromethane (50 ml), the mixture was filtered, and the filtrate was washed with 5% aqueous KI (2 × 20 ml) and water (3 × 20 ml), dried (Na_2SO_4), and concentrated. The syrupy residue was chromatographed on a column of Kieselgel G (60 g) with 3:1 dichloromethane–ethyl acetate, to give amorphous **3** (750 mg, 65.5%), $[\alpha]_D$ −57.4° (*c* 3.26, chloroform), R_F 0.62 (dichloromethane–ethyl acetate, 3:1). ^{1}H-n.m.r. data ($CDCl_3$): δ 5.60–3.40 (m, 17 H, skeleton protons), 2.30–1.90 (m, 15 H, 5 OAc), and 1.60–1.10 (m, 18 H, CH_3 protons).

Anal. Found: C, 54.03; H, 6.72. Calc. for $C_{34}H_{50}O_{19}$: C, 53.53; H, 6.60.

1,2,3,4-Tetra-O-*acetyl-6*-O-[*2,4-di*-O-*acetyl-3*-O-(*2,3,4-tri*-O-*acetyl*-α-L-*rhamnopyranosyl*)-α-L-*rhamnopyranosyl*]-D-*galactopyranose* (**4**). — A solution of **3** (750 mg) in dichloromethane (35 ml) was treated for 1 h at room temperature with trifluoroacetic acid (3 ml) containing 1% of water. The mixture was then concentrated, and remaining trifluoroacetic acid was removed by co-distillation with toluene. The resulting syrup was treated with pyridine (5 ml) and acetic anhydride (5 ml) for 16 h at room temperature. The excess of reagent was removed by evaporation, and the residue was treated with ice–water. The resulting, crude product (700 mg, 84%) was crystallised twice from ethanol, to yield **5**, m.p. 218°, $[\alpha]_D$ +0.8° (*c* 0.64, chloroform), R_F 0.80 (hexane–ethyl acetate, 3:7); lit.[13] m.p. 152°.

Anal. Found: C, 51.01; H, 5.95. Calc. for $C_{36}H_{50}O_{23}$: C, 50.82; H, 5.88.

O-α-L-*Rhamnopyranosyl*-(*1*→*3*)-O-α-L-*rhamnopyranosyl*-(*1*→*6*)-D-*galactose* (**5**). — The peracetate **4** (0.60 g) was deacetylated with methanolic sodium methoxide (0.1M, 1 ml) in methanol (30 ml) for 14 h at room temperature. After work-up in the usual manner, the syrupy product was dissolved in D_2O (2 ml). The solution was freeze-dried, to give a foam (235 mg; 70.5%), m.p. 215°, $[\alpha]_D$ −46.1° (*c* 0.56, water); lit.[13] foam, $[\alpha]_D^{25}$ −43° (*c* 0.4, water).

3,4-Di-O-*benzyl*-α-L-*rhamnopyranose* (**6**). — A solution of methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside[17] (8.0 g) in 1,4-dioxane (200 ml) and M sulfuric acid (67 ml) was boiled under reflux for 4 days. The hot solution was neutralised with barium carbonate, filtered, and evaporated, to give a syrup that was dissolved in dichloromethane (150 ml). The solution was washed with water (3 × 30 ml), dried (Na_2SO_4), and evaporated. The residue was crystallised from ethyl acetate–cyclohexane (1:10, 130 ml), to give **6** (4.60 g, 59.9%), m.p. 111–112°, $[\alpha]_D$ −19.1° (*c* 0.60, chloroform), R_F 0.21 (dichloromethane–acetone, 9:1).

Anal. Found: C, 70.03; H, 7.09. Calc. for $C_{20}H_{24}O_5$: C, 69.74; H, 7.02.

1,2-Di-O-*acetyl-3,4-di*-O-*benzyl*-α-L-*rhamnopyranose* (**7**). — Compound **6** (1.0 g) was treated with pyridine (15 ml) and acetic anhydride (15 ml) for 12 h at room temperature. After work-up in the usual manner, the solid product was crystallised from ethanol (12 ml), to give **7** (1.18 g, 95.1%), m.p. 106–108°, $[\alpha]_D$ −22.3° (*c* 0.64, chloroform).

Anal. Found: C, 67.49; H, 6.68. Calc. for $C_{24}H_{28}O_7$: C, 67.27; H, 6.58.

3,4-Di-O-benzyl-1,2-di-O-p-nitrobenzoyl-α-L-rhamnopyranose (**8**). — To compound **6** (0.80 g) in dry pyridine (15 ml) was added *p*-nitrobenzoyl chloride (1.30 g) at 0°. The mixture was stirred overnight at ambient temperature and processed with ice–water (100 ml) in the usual manner. The solid product was washed thoroughly with water and with saturated, aqueous sodium hydrogencarbonate, and then crystallised from dichloromethane–ethanol (1:4, 50 ml), to give **8** (1.02 g, 91.9%), m.p. 170–171°, $[\alpha]_D$ −22.1° (*c* 1.36, chloroform), R_F 0.38 (benzene–ether, 99:1).

Anal. Found: C, 63.76; H, 4.81; N, 4.42. Calc. for $C_{34}H_{30}N_2O_{11}$: C, 63.54; H, 4.70; N, 4.38.

6-O-(3,4-Di-O-benzyl-2-O-p-nitrobenzoyl-α-L-rhamnopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**10**). — Compound **8** (1.0 g) was dissolved in dry dichloromethane (30 ml) saturated with hydrogen bromide at room temperature. *p*-Nitrobenzoic acid started to precipitate after 4 min and, after 10 min, it was collected by filtration (265 mg, 94.3%). The filtrate was evaporated *in vacuo*, to give syrupy 3,4-di-*O*-benzyl-2-*O*-*p*-nitrobenzoyl-α-L-rhamnopyranosyl bromide (**9**), $[\alpha]_D$ −16° (*c* 0.68, chloroform), R_F 0.54 (benzene–ether, 99:1).

Compound **1** (390 mg) was treated with **9** (600 mg) for 4 h in (1:1) benzene–nitromethane (50 ml) in the presence of $Hg(CN)_2$ (397 mg), as described for **3**. The syrupy product was chromatographed on a column of Kieselgel G (60 g), using dichloromethane–acetone (96:4), to yield **10** (318 mg, 40.1%), $[\alpha]_D$ −6.2° (*c* 1.2, chloroform), R_F 0.62 (dichloromethane–acetone, 96:4). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.21 (s, 4 H, *p*-NO_2-Ph), 7.35–7.15 (m, 10 H, 2 Ph), 5.66 (q, 1 H, H-2'), 5.52 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.00–3.25 (m, 14 H, skeleton protons and CH_2-Ph), and 1.60–1.18 (m, 15 H, 5 CH_3).

Anal. Found: C, 64.00; H, 6.19; N, 1.98. Calc. for $C_{39}H_{45}NO_{13}$: C, 63.66; H, 6.16; N, 1.90.

6-O-[3,4-Di-O-benzyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**11**). — Compound **10** (238 mg) was treated with methanolic sodium methoxide (0.01M, 10 ml) for 12 h at room temperature. T.l.c. then showed the disappearance of **10** (R_F 0.62; dichloromethane–acetone, 96:4) and the presence of one product (R_F 0.16). The solution was evaporated, and the residue was extracted with cyclohexane (20 ml) to remove the *p*-nitrobenzoic acid. The extract was concentrated and the residue (181 mg) was treated with 2,3,4-tri-*O*-acetyl-α-L-rhamnosyl bromide (165 mg) for 6 h in dry benzene–nitromethane (1:1, 15 ml) in the presence of $Hg(CN)_2$ (116 mg), as described for **3**. The crude product was chromatographed on a column of Kieselgel G (20 g), using dichloromethane–ethyl acetate (9:1), to yield **11** (146 mg, 52.7%), $[\alpha]_D$ −63.3° (*c* 0.47, chloroform), R_F 0.56 (dichloromethane–ethyl acetate, 9:1). ^{13}C-N.m.r. data ($CDCl_3$): δ 99.25 (C-1''), 99.14 (C-1'), and 96.40 (C-1).

Anal. Found: C, 61.40; H, 6.71. Calc. for $C_{44}H_{58}O_{17}$: C, 61.52; H, 6.80.

3,4-Di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl bromide (**12**). — 1,3,4-Tri-*O*-acetyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyrano-

syl)-α-L-rhamnopyranose[16,17] (580 mg) was stirred with dichloromethane (2 ml) and 40% hydrogen bromide in acetic acid (4 ml) for 2 h at 0°. The mixture was diluted with dichloromethane (50 ml), washed with ice–water (2 × 20 ml), saturated, aqueous sodium hydrogencarbonate (30 ml), and ice–water (2 × 20 ml), dried, and evaporated, to give **12** as a syrup (570 mg, 95%), $[\alpha]_D$ −88.2° (*c* 0.76, chloroform), R_F 0.46 (toluene–ether, 1:1).

6-O-[3,4-Di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**13**). — (*a*) A solution of **11** in ethanol (30 ml) was hydrogenated over Pd/C (10%, 50 mg) for 3 h, the mixture was filtered, the filtrate was evaporated, and the residue was acetylated in pyridine (2 ml) with acetic anhydride (2 ml). The product **13** was a syrup (95 mg; 89%), $[\alpha]_D$ −52.6° (*c* 1.05, chloroform), R_F 0.59 (dichloromethane–ethyl acetate, 3:1).

(*b*) Compound **1** (520 mg) was treated with **12** (583 mg) for 2 h in dry benzene–nitromethane (1:1, 30 ml) in the presence of $Hg(CN)_2$ (252 mg), as described for **3**. After 2 h, t.l.c. showed the complete disappearance of **12**, and the formation of only one trisaccharide derivative. The reaction mixture was purified on a column of Kieselgel G (50 g) with dichloromethane–ethyl acetate (3:1). The product (360 mg, 47.2%) was indistinguishable from **13** prepared in (*a*), and had $[\alpha]_D$ −53.5° (*c* 0.60, chloroform), R_F 0.60 (dichloromethane–ethyl acetate, 3:1). The ^{13}C-n.m.r. spectrum showed three anomeric carbon signals: 96.3 (178.8 Hz), 98.7 (171.9 Hz), and 99.3 p.p.m. (171.3 Hz); the high values of the coupling constants proved the α configuration in each case.

1,2,3,4-Tetra-O-acetyl-6-O-[3,4-di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl]-α,β-D-galactopyranose (**14**). — A solution of **13** (240 mg) in dichloromethane (15 ml) was treated for 5 h at room temperature with trifluoroacetic acid (2 ml) containing 1% of water. Work-up as described for **4**, followed by acetylation, gave **14** (210 mg, 75%), $[\alpha]_D$ −135.2° (*c* 0.60, chloroform), R_F 0.52 (hexane–ethyl acetate, 3:7). The ^{1}H- and ^{13}C-n.m.r. spectra showed the presence of the α and β anomers at the reducing end; their ratio was 1:1 (C-1α, 89.9; C-1β, 92.5; C-1′, 99.6 and 99.2; C-1″, 99.4 p.p.m.).

O-α-L-rhamnopyranosyl-(1→2)-O-α-L-rhamnopyranosyl-(1→6)-D-galactose (**15**). — Treatment of the peracetate **14** (0.11 g) with 0.1M methanolic sodium methoxide (0.5 ml) in methanol (10 ml) for 12 h at room temperature gave, after work-up in the usual manner, a foam that was dissolved in D_2O (1 ml) and freeze-dried, to give amorphous **15** (53 mg, 86%), $[\alpha]_D$ −53° (*c* 0.49, water), R_F 0.53 (1-butanol–methanol–water, 3:1:1).

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