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UNAMBIGUOUS SYNTHESIS OF (1→2)- AND (1→3)-RHAMNOPYRANOSYL-RHAMNOPYRANOSE DERIVATIVES AND THEIR ^{13}C-NMR STUDY

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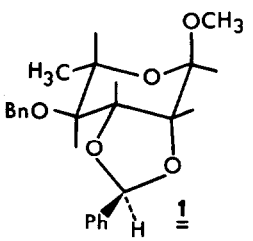
Rhamnobioses are widely distributed in nature and are commonly found as structural units in glycolipids[1,2] and bacterial polysaccharides[3,4] and as constituents of glycosides[5]. In order to study the immunological properties of these oligosaccharides and for synthesizing naturally occurring flavonol-glycosides, we have prepared a series of oligosaccharides containing L-rhamnose[6-9], including all three O-α-L-rhamnopyranosyl-L-rhamnoses. Up to now from the rhamnobioses only two unambiguous syntheses[6,10] of the 4-O-α-L-rhamnopyranosyl-L-rhamnopyranose have been published.

Recently, also, the synthesis of the 2-O-α-L-rhamnopyranosyl-L-rhamnopyranose[11] and 3-O-α-L-rhamnopyranosyl-L-rhamnopyranose[12] has been reported by different authors. They used modified versions of the "open chain oligosaccharide synthesis", introduced by King and Bishop[13]. Since this method always results in a mixture of different structural isomers, which have to be separated by column chromatography, the above two syntheses cannot be accepted as a proof of structure. Furthermore it is necessary to point out that the main routes of the two syntheses were opposite; i.e. in the case of benzyl 4-O-benzyl-β-L-rhamnopyranoside the main product of the reaction with α-acetobromo-L-rhamnose was the 2-O-α-L-rhamnopyranosyl-L-rhamnose[11] deriva-

Table. Assignment of the ^{13}C chemical shifts and $^{1}J_{CH}$ data

Carbon	Compound									
	1	2	3	4	6	7	8	9	10	11
1	92.8	98.0	100.5	98.3	100.0	98.5	99.8	98.7	100.5	101.6
$^{1}J_{CH}$						(167)	(164)	(171)	(170)	(170.2)
2	75.7	78.3	68.6	78.9	76.0	78.1	76.9	71.2	79.0	70.8
3	79.7	78.3	80.2	71.7	79.9	78.5	70.8	75.1	70.9	78.8
4	78.0	81.2	80.2	82.2	80.3	80.9	71.5	72.8	73.1	72.2
5	64.2	64.3	67.4	67.3	68.2	68.3	67.2	64.7	69.2	69.4
6	17.9	17.8	18.0	18.1	18.0	18.1	17.6	17.5	17.7	17.8
1'					99.3	99.4	99.4	99.0	102.9	102.9
$^{1}J_{CH}$						(174)	(172)	(173)	(170.6)	(170.3)
2'					69.3	69.3	68.9	68.8	71.1	71.0
3'					69.9	70.1	70.2	70.6	70.9	71.1
4'					71.3	71.3	71.3	71.4	72.9	73.0
5'					66.9	67.0	66.5	66.7	69.7	69.6
6'					17.4	17.5	17.3	17.3	17.8	17.8

$^{1}J_{CH}$ coupling constants are given in brakets (Hz). All chemical shifts are refered to TMS (i). For D_2O solutions the dioxane (i) line was used (67.3 ppm).



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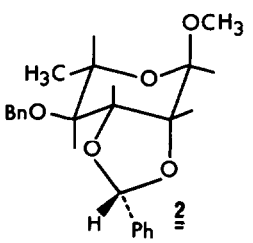

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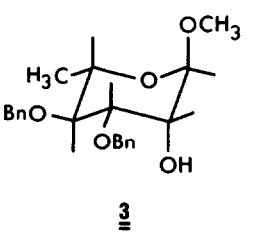

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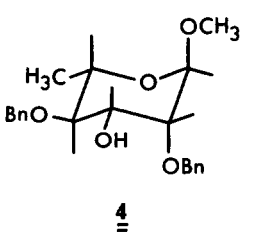

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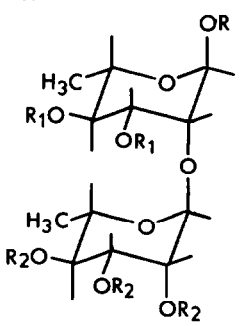

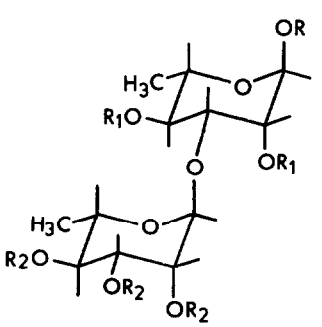

6 R = CH_3; R_1 = Bn; R_2 = Ac
8 R = CH_3; R_1 = R_2 = Ac
10 R = CH_3; R_1 = R_2 = H
12 R = R_1 = R_2 = Ac

7
9
11
13

tive, while the methyl α-L-rhamnopyranoside reacted with α-acetobromo-L-rhamnose to a 3-O-α-L-rhamnopyranosyl-L-rhamnose[12] derivative.

Here we describe the unambiguous synthesis of 2-O- and 3-O-α-L-rhamnopyranosyl-L-rhamnopyranose starting from methyl 3,4-di-O-benzyl-α-L-rhamnopyranoside (3) and methyl 2,4-di-O-benzyl-α-L-rhamnopyranoside (4) respectively. 3 was prepared by the hydrogenolysis of methyl 4-O-benzyl-exo-2,3-O-benzylidene-α-L-rhamnopyranoside (1)[14] with $LiAlH_4$-$AlCl_3$ reagent[15] with the following data (3, 98%, syrup, $[\alpha]_D$ -46.4° ($CHCl_3$). The hydrogenolysis of methyl 4-O-benzyl-endo-2,3-O-benzylidene-α-L-rhamnopyranoside (2)[14] under the same reaction conditions gave 4 (96%, syrup, $[\alpha]_D$ -15.4° ($CHCl_3$). Compound 3 and 4 were coupled with α-acetobromo-L-rhamnose (5) in benzene-nitromethane (1:1) as solvent and in the presence of $Hg(CN)_2$ to obtain after purification 6 (62.5%, m.p. 96-98°C, $[\alpha]_D$ -38.4° ($CHCl_3$) and 7 (78.8%, syrup, $[\alpha]_D$ -46.1° ($CHCl_3$), respectively. Catalytic debenzylation of 6 and 7 over Pd/C and subsequent acetylation resulted in methyl 3,4-di-O-acetyl-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (8) (92.7%, m.p. 149-150°C, $[\alpha]_D$ -44.8° ($CHCl_3$), and methyl 2,4-di-O-acetyl-3-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (9) (95%, m.p. 135-136°C, $[\alpha]_D$ -43.6° ($CHCl_3$), lit.[12] m.p. 125°C, $[\alpha]_D$ -48° ($CHCl_3$), respectively. Deacetylation of 8 and 9 gave methyl 2-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (10, 96%, syrup, $[\alpha]_D$ -92° (H_2O), and methyl 3-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (11, 95%, syrup, $[\alpha]_D$ -78° (H_2O), respectively. Acetolysis of compounds 8 and 9 yielded the hexa-O-acetyl-dirhamnoses (12 and 13) as anomeric mixtures at the reducing rhamnopyranose ring. The predominating anomers were identified as α-anomers (12: 62%, m.p. 118-120°C, $[\alpha]_D$ -48° ($CHCl_3$); 13: 65%, m.p. 75-76°C, $[\alpha]_D$ -38° ($CHCl_3$), lit.[12] syrup, $[\alpha]_D$ -32° ($CHCl_3$). The structures of compounds 1 - 4, and 6 -11 were verified by ^1H- and ^{13}C-NMR spectroscopy. The $^1J_{CH}$ coupling constants were measured for 8 - 11 to determine the anomeric configuration of the interglycosidic bonds. They were all found to be α-L (1C), (see Table).

The hydrogenolysis of dioxane- and dioxolane-type benzylidene derivatives opens a general method for preparing selectively blocked sugar derivatives as starting material for the synthesis of complex oligosaccharides. Further

investigations are in progress.

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16) Values of $[\alpha]_D$ were measured with a Perkin-Elmer 241 automatic polarimeter. ^{1}H-NMR spectra were measured with a Jeol MH-100 spectrometer, and ^{13}C-NMR spectra with a Varian XL-100-FT-15 spectrometer in 10-25% (w/v) $CDCl_3$ or D_2O solutions at 50°C. $^1J_{CH}$ coupling constants were determined from natural-abundance proton coupled spectra by gated decoupling technique.

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