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SYNTHESIS OF POLYSACCHARIDES. GLUCORHAMNAN →6-D-Glcp 1$\overset{\beta}{\rightarrow}$4-L-Rhap1$\overset{\alpha}{\rightarrow}$

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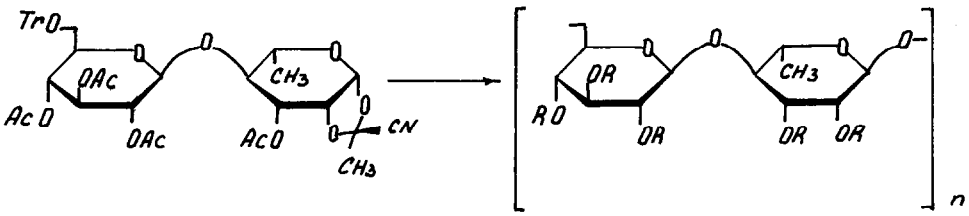
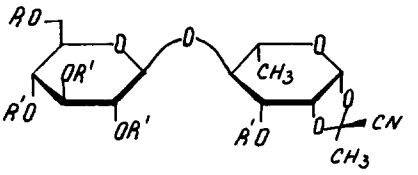
Summary: The regular heteropolysaccharide glucorhamnan →6-D-Glcp 1$\overset{\beta}{\rightarrow}$4-L-Rhap 1→ was obtained by polycondensation of 3-O-acetyl-4-O-(2,3,4-tri-O-acetyl-6-O-trityl-β-D-glucopyranosyl)-1,2-O-(1-exo-cyanoethylidene)-β-L-rhamnopyranose catalysed with triphenylmethylium perchlorate.

As has been shown recently[1] the polycondensation of 1,2-O-cyanoethylidene derivatives of mono- and oligosaccharides containing O-trityl grouping proceeds with absolute stereospecificity thus opening a general route to the synthesis of polysaccharides with regular structure including heteropolysaccharides with repeating oligosaccharide units, many of which are biologicaly important. Here we report the first synthesis of regular heteropolysaccharide →6)-β-D-Glcp(1→4)-α-L-Rhap(1→6)-β-D-Glcp(1→4)-α-L-Rhap(1→ by polycondensation of appropriate derivative of 4-O- -D-glycopyranosyl-L-rhamnose.



The starting monomer for polycondensation, 3-O-acetyl-4-O-(2,3,4-tri-O-acetyl-6-O-trityl-β-D-glucopyranosyl)-1,2-O-(1-exo-cyanoethylidene)-β-L-rhamnopyranose (I) was obtained as follows. Pentaacetate of 1,2-O-(1-exo-cyanoethylidene)-4-O-(β-D-glucopyranosyl)-L-rhamnopyranose (II)[2] was deace-

tylated with 0.005 M CH_3ONa in CH_3OH (20°, 0.5 h)[3] and the product obtained (III) without purification was treated with trityl cloride in pyridine (20°, 72 h) and then acetylatet with Ac_2O in pyridine (20°, 15 h). Monomer I was isolated by column chromatography (SiO_2, elution C_6H_6 → ether) in 49% yield (calculated on II), m.p. 256° (from ethanol), $[\alpha]_D^{20}$ +15.4° (c 2.2, $CHCl_3$). Its structure was proved by PMR spectrum (δ, ppm): 1.43 (d, CH_3 of rhamnose), 1.7 (s, CH_3 of cyanoethylidene), 1.86, 1.96, 2.00, 2.22 (12 H, AcO); 5.38 (d, H1 of rhamnose, $J_{1,2}$ 2 Hz), 7.2 - 7.7 (aromatic protons).



I R = $(C_6H_5)_3C$, R' = Ac

II R = R' = Ac

III R = R' = H

Polycondensation of I (330 mg, 420 umol) was performed as described earlier[1] in the presence of triphenylmethylium perchlorate (14.4 mg, 42 μmol) in CH_2Cl_2 (3 ml) using vacuum technique. After 50 hours dry methanol (1 ml) and then pyridine (1 ml) were added in order to stop the reaction. The reaction mixture was diluted with $CHCl_3$ (15 ml), washed with water (5 x 15 ml) and organic solution was then evaporated to dryness. Treatment of a residue of acetylated polymer with 0.15 M CH_3ONa in CH_3OH (20°, 72 h) gave rise to free polysaccharide. After column chromatography on Biogel P-10 (90 x 1.4cm, V_t 95 ml, V_o 34 ml, elution with 0.1 M AcOH, 1.5 ml/min) two fractions were obtained: 1 - 53 mg (38.9%, eluted within 34-54 ml) and 2 - 65 mg (47.8%, eluted within 54-78 ml), which proved to be structurally identical and differed only by molecular weight.

The structure of synthetic glucorhamnan was established as follows. The samples of polysaccharides from both fractions after formolysis (85% HCOOH, 100°, 2 h), hydrolysis (0.1 M HCl, 100°, 15 h), $NaBH_4$ reduction and acetylation with Ac_2O in pyridine (20°, 15 h) gave only acetates of D-glucitol and L-rhamnitol in the ratio 0.93 : 1. Methylation of both samples with subsequent standard procedure[4] gave rise only to 1,5-di-O-acetyl-2,3,4,6-tetra-O-methyl-D-glucitol (IV), 1,5,6-tri-O-acetyl-2,3,4-tri-O-methyl-D-glucitol (V) and 1,4,5-tri-O-acetyl-2,3-di-O-methyl-L-rhamnitol (VI). The absence of other partially methylated glucitols and rhamnitols unambigously proved the regiospecificity of polycondensation process, regularity of synthetic polysaccharide and absence of branching in its linear chain. The IV : V ratio (1 : 29 for fraction 1 and 1 : 22 for fraction 2) indicates on the degree of polymerization (and molecular weight) of polymer which is ca. 30 (9000) and 23 (7000) respectively.

The full absence of 1,5-di-O-acetyl-2,3,4-tri-O-methyl-L-rhamnitol in products of methylation is especially significant. It means that nonreducing terminal of polysaccharide contains exclusively glucose unit. This is a good evidence for absence of any cleavage of glycosidic linkages in the new formed polysaccharide molecule during the polycondensation process. Quite clear that such cleavages could disturb the strong regularity of polysaccharide.

The complete stereoregularity of synthetic glucorhamnan followed from ^{13}C NMR data of both fractions 1 and 2, (^{13}C NMR spectra were measured on a Bruker WP-60 apparatus, working frequency 15.08 MHz in D_2O, CH_3OH as internal standard, 50°).

Table summerizes ^{13}C NMR data for polysaccharide and some reference substances. As can be seen, in anomeric (C1) region of polysaccharide only two signals at δ 101.45 (C1 of L-rhamnose) and 104.7 ppm (C1 of β-D-glucose) were present that demonstrates regularity and rather high molecular weight of polymer. The absence of signals at ca. 74 ppm (C3) and 73 ppm (C5) which is diagnostic for β-rhamnosidic linkages[7,8] proved the complete absence of β-rhamnosidic linkages in synthetic glucorhamnan. The optical rotation of polysaccharide $[\alpha]_D^{20}$ -52.5° (c 1.1, water), which is comparable with $[\alpha]_D^{20}$ -57.5° (CH_3OH)[5] for β-D-Glcp (1→4)-α-L-Rhap-OMe is also in agreement with this conclusion.

Table

^{13}C NMR data of polysaccharide and model compounds (δ-scale, D_2O, internal standard CH_3OH, 50.15 relative to Me_4Si, 50°).

		Compound			
		Glucorhamnan	VII	VIII	IX
Chemical shifs of	rhamnose moiety				
	C-1	101.45	101.9	102.5	102.4
	C-2	71.1	71.4	71.4	71.8
	C-3	71.1	71.7	71.8	74.1
	C-4	82.75	73.5	82.5	73.4
	C-5	68.3	69.9	68.25	73.4
	C-6	18.3	17.9	18.1	17.9
	glucose moiety				
	C-1	104.7	97.4	104.7	
	C-2	75.2	75.5	75.2	
	C-3	77.05	77.2	77.3	
	C-4	71.1	71.2	71.0	
	C-5	76.0	76.1	77.3	
	C-6	68.3	68.3	62.1	

VII Rhap $1\xrightarrow{\alpha}6$ Glcp[7]

VIII Glcp $1\xrightarrow{\beta}4$ Rhap $\xrightarrow{\alpha}$ OMe[8]

IX Rhap $\xrightarrow{\beta}$ OMe[7]

The synthetic glucorhamnan has high molecular weight and its degree of polymerization is comparable with α-(1→3)-rhamnan which is described in preceeding paper[6]. The synthetic glucans which were obtained earlier[1] have lower degree of polymerization. This difference is probably due to different reactivity of 1,2-O-cyanoethylidene grouping for different sugars, this question is now under investigation.

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