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**Preliminary communication**

# Synthesis of homopolysaccharides and block-heteropolysaccharides carrying a spacer arm

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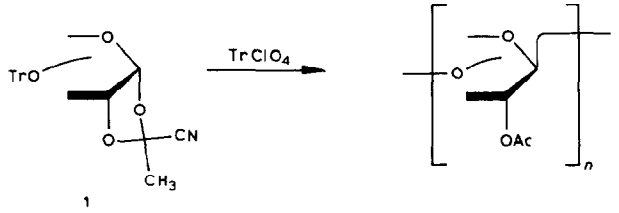
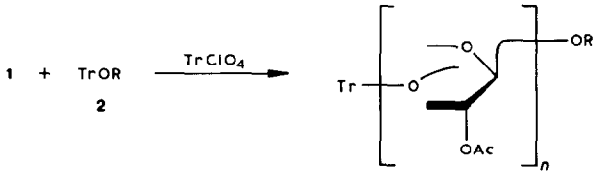
Polycondensation of tritylated 1,2-*O*-(1-cyanoethylidene) derivatives of mono- and oligo-saccharides **1** is an effective method for the synthesis of regular, including some bacterial, polysaccharides[1].




**1**

Recently, we suggested an approach to synthetic polysaccharides of type **3** by polycondensation of **1** in the presence of a trityl ether **2** which becomes the "reducing" terminus of the polysaccharide chain.




**3**

A model, triphenylmethylium perchlorate-catalysed polycondensation of the mannose cyanoethylidene derivative **4** in the presence of the trityl ether **5** (0.1 equiv.) afforded **6** which, on deprotection and fractionation, gave the (1→6)-α-D-mannan **7** ($n$ = 10–11), the terminal residue of which was a 6-aminohexyl glucoside moiety[2] which served as the "internal standard" in the determination of d.p. This approach can be applied in the synthesis of determinants for the preparation of artificial antigens.

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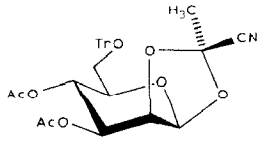
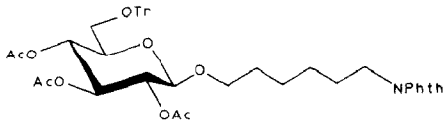
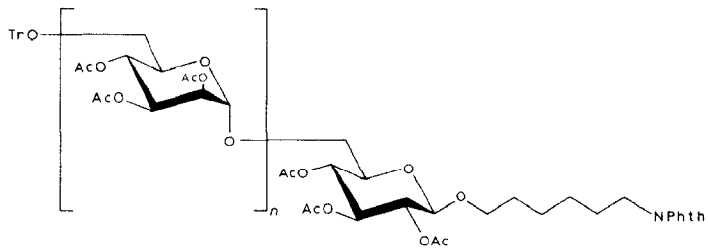
An important feature of the polycondensation of **4** in the presence of **5** is the presence of trityl groups in the polycondensation products **6**, which is shown by a yellow colour upon spraying with $H_2SO_4$ after t.l.c.[2], whereas polycondensation of **4** alone yields only detritylated products[3]. The presence of trityl groups at non-reducing termini of **6** enables their use as trityl ethers of the type **2**.




**4**




**5**

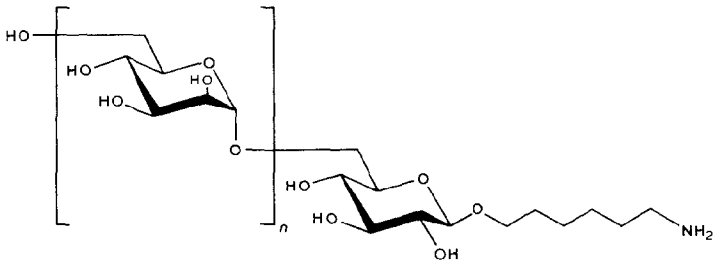



**6**

We now describe the application of this approach to the synthesis of homopolysaccharides and block-heteropolysaccharides. The reaction mixture obtained by polycondensation of **4** in the presence of **5** (0.1 equiv.) and catalyst ($TrClO_4$, 0.1 equiv.) in dichloromethane for 8 h was treated with more **4** or with analogues prepared from other monosaccharides.

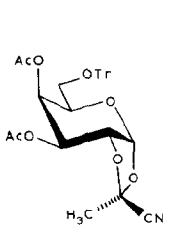
The products were then detritylated with aqueous 90% trifluoroacetic acid (0.5 h, 20°) and the acetylated polymer was isolated by column chromatography on silica gel (gradient elution benzene → acetone). *N,O*-Deacylation was then effected with hydrazine hydrate in boiling ethanol for 8 h and the carbohydrate products were isolated by gel chromatography on TSK HW-40(S) in 0.1M acetic acid. The basic fraction of the type **7** was then isolated by using a cation-exchange resin ($H^+$), and the high-molecular-weight components were separated by gel chromatography on TSK HW-40(S).

Introduction of **4** into the reaction mixture resulted in formation of the (1→6)-α-D-mannan derivative **7** with a d.p. of 17–18. The d.p. of **7** and other polysaccharides synthesised in this manner was calculated from the ratio of monosaccharides formed on hydrolysis. The $^{13}C$-n.m.r. spectrum of **7** differed from that described previously[2] only in the ratio of intensities for terminal and "internal" monosaccharide units. The primary polycondensation products contain trityl groups and the possibility for elongation exists.

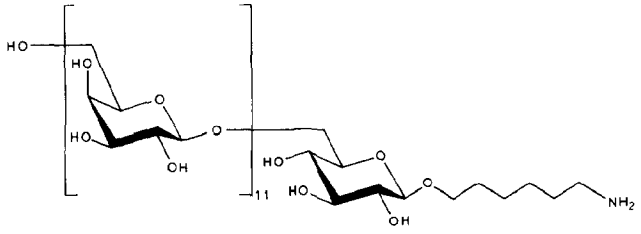


7

The next polysaccharide synthesised comprised blocks of different monosaccharides, *viz.*, mannose and galactose. Polycondensation of the *galacto*-monomer **8**[4] in the presence of **5** (**8**:**5** = 10:1) afforded, after deprotection, the (1→6)-β-D-galactan derivative **9**, $[\alpha]_D$ +3.5° (*c* 0.6, water), which contained 11 galactose residues on average. The $^{13}$C-n.m.r. spectrum ($D_2O$) of **9** contained signals for the 6-aminohexyl glucoside residue at δ 25.67, 26.35, 27.70, 29.64 (4 $-CH_2-$), 40.74 ($CH_2$–N), 71.55 ($CH_2$–O), 103.43 (C-1), 74.35 (C-2), 77.10 (C-3), 70.95 (C-4), and 76.15 (C-5), for the 6-substituted β-D-galactopyranosyl residues at δ 104.56 (C-1), 72.00 (C-2), 73.93 (C-3), 69.92 (C-4), 74.97 (C-5), and 70.48 (C-6), and for an unsubstituted β-D-galactopyranosyl group at δ 74.08 (C-3), 70.27 (C-4), 76.31 (C-5), and 62.22 (C-6).

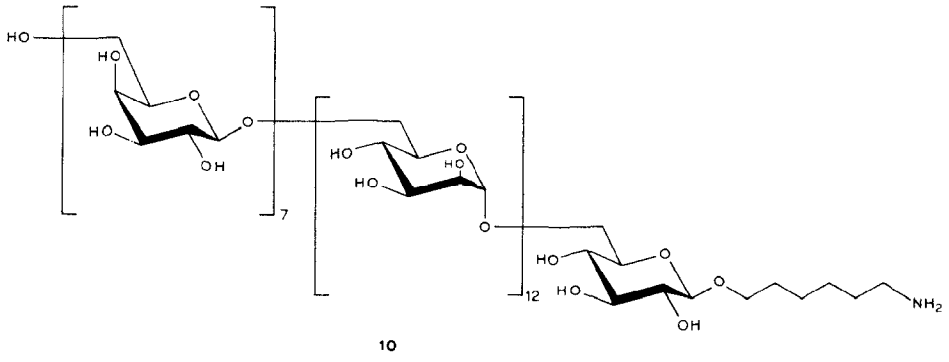


8



9

The sequential introduction in the polycondensation of the monomer **4** and then **8** in the presence of trityl ether **5** (molar ratios of **4**:**8**:**5** = 10:10:1) afforded, after deprotection, the novel polysaccharide derivative **10** {24%, $[\alpha]_D$ +45.5° (*c* 0.8, water)} containing blocks built of different monosaccharides. Monosaccharide analysis of **10** revealed glucose, mannose, and galactose in the ratios 1:12:7. $^{13}$C-N.m.r. data ($D_2O$): 6-aminohexyl glucoside residue, δ 25.70, 26.37, 27.70, 29.67 (4 $-CH_2-$), 40.73 ($CH_2$–N), 71.90 ($CH_2$–O), 103.40 (C-1), 74.32 (C-2), 77.32 (C-3), 71.02 (C-4), 75.25 (C-5); 6-substituted α-D-mannopyranosyl residue, δ 100.59 (C-1), 71.24 (C-2), 72.09 (C-3,5), 68.04 (C-4), 67.02 (C-6); 6-substituted β-D-galactopyranosyl residue, δ 104.52 (C-1), 72.09 (C-2), 73.92 (C-3), 69.89 (C-4), 74.94 (C-5), 70.42 (C-6); unsubstituted β-D-galactopyranosyl group, δ 74.06 (C-3), 70.23 (C-4), 76.27 (C-5), 62.19 (C-6).



10

Methylation analysis of **10** gave acetylated 2,3,4-tri-*O*-methyl-mannitol and -galactitol together with 2,3,4,6-tetra-*O*-methyl-galactitol and -mannitol. The presence of the latter component indicates that the polysaccharide obtained is a mixture of **10** and **7**. The ratio (4:1) of tetra-*O*-methyl-galactitol to -mannitol shows that the degree of substitution of the mannose chains with the galactose chains is ~80%. This situation is due probably to partial detritylation of the products of the type **6** formed initially.

Thus, the foregoing approach enables preparation of homopolysaccharides and block-heteropolysaccharides with a spacer arm, and studies of its scope and limitation are in progress.

## REFERENCES

1 N. K. KOCHETKOV, *Tetrahedron*, 43 (1987) 2389–2436.
2 YU. E. TSVETKOV, L. V. BACKINOWSKY, AND N. K. KOCHETKOV, *Bioorg. Khim.*, 12 (1986) 1144–1146.
3 V. I. BETANELI, M. M. LITVAK, L. V. BACKINOWSKY, AND N. K. KOCHETKOV, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1985) 1172–1177.
4 N. K. KOCHETKOV AND A. YA. OTT, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1984) 2358–2363.