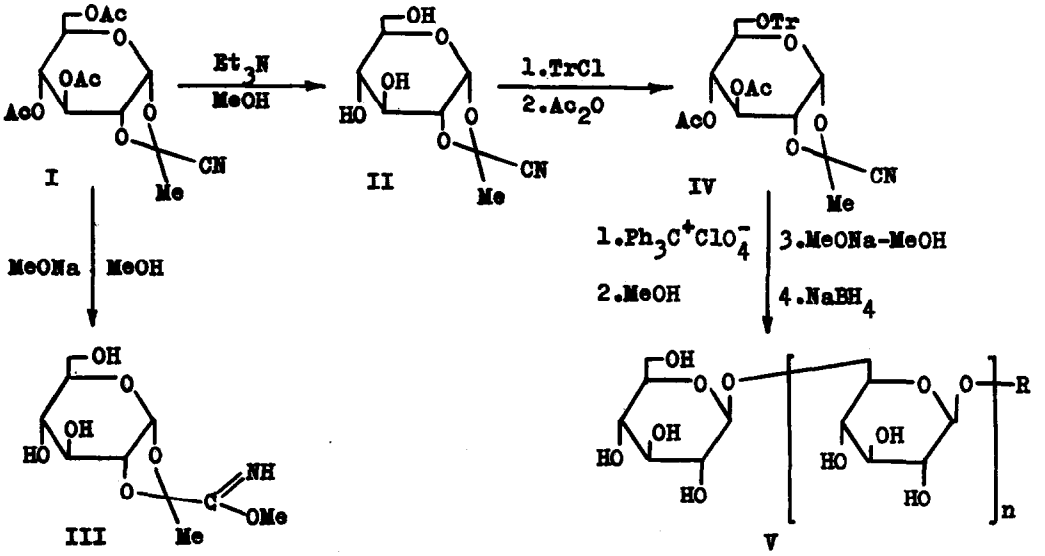
Tetrahedron Letters No. 39, pp 3403 - 3406, 1975. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF β-1→6-D-GLUCAN; A NEW REACTION OF POLYCONDENSATION

A.P.Rochkov, I.V.Obruchnikov, V.M.Kalinevich and N.K.Kochetkov*
N.D.Zelinsky' Institute of Organic Chemistry, USSR Academy of Sciences,
Moscow

(Received in UK 4 August 1975; accepted for publication 18 August 1975)

Recently we reported[1] a new method of 1,2-trans-glycosylation by condensation of cyclic pyruvonitrile ketal I[2] with trityl ethers, catalyzed by triphenylcarbonium salts. This approach could be used for a new synthesis of polysaccharides by polycondensation of a mono- or oligosaccharide derivative containing pyruvonitrile ketal and trityl groups in the same molecule. Here we describe the synthesis of the simplest monomer of this type and its polycondensation into a regular polysaccharide, a β-1→6-D-glucan.



Deacetylation of ketal I with Et_3N in abs. MeOH gave rise to triol II, while iminoester III was obtained after treatment of I with MeONa in abs. MeOH, as described earlier by Helferich and Bettin[3]. After tritylation (TrCl, C_5H_5N, 5°) and subsequent acetylation (Ac_2O, C_5H_5N, 5°) II was converted into

trityl ether IV, m.p. 130-131°, $[\alpha]_D$+33°($CHCl_3$). PMR and analytical data correspond to the structure shown.

Polycondensation of IV in CH_2Cl_2 using 0.2 mole of triphenylcarbonium perchlorate[4] as a catalyst at room temperature for 16 h was performed in a sealed tube with careful protection from nucleophilic impurities (cf.[1]). The reaction mixture was treated with abs. MeOH for detritylation[1] and with MeONa in abs. MeOH for deacetylation, and the reaction products were reduced with $NaBH_4$. Subsequent fractionation of the products on Biogel P-4 and P-10 columns led to isolation of synthetic glucan S-5 (V) with a yield of 10% (for synthetic glucans S-1 to S-4 see[5-7]). The structure of glucan S-5 has been determined as follows.

Acid hydrolysis (3 N H_2SO_4, 100°, 4 h) gave D-glucose as the only product in quantitative yield as revealed by analysis with glucose oxidase. Hakomori methylation[8] followed by formolysis (92% HCOOH, 100°, 2 h), hydrolysis (1 N H_2SO_4, 100°, 6 h), $NaBH_4$ reduction and acetylation gave rise to acetates of 2,3,4,6-tetra-O-methyl-D-glucitol and 2,3,4-tri-O-methyl-D-glucitol in a ratio of 1:14, as revealed by GLC (SE-30) and GLC-MS data. Isomeric tri-O-methyl-D-glucitols were not found. Hence, the polysaccharide contained only D-glucopyranose residues linked by 1→6-glycosidic bonds; the number-average degree of polymerisation was about 15.

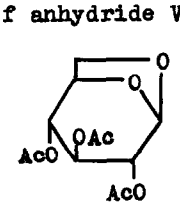
3,4-Di-O-methyl-D-glucitol tetraacetate was also detected in the mixture of partially methylated glucitol derivatives, its content being ca. 40% relative to that of 2,3,4,6-tetra-O-methyl-D-glucitol diacetate. This derivative arises by methylation of a nitrile terminus of the polymer chain, modified under conditions of the polycondensation.

The optical rotation of glucan S-5 ($[\alpha]_D$-24° (H_2O)) is in accordance with a value estimated by extrapolation of the reported data on the optical rotation of gentiodextrins[9] to a polymer with $\overline{DP}_n$ 15. Thus, the polycondensation of monomer IV proceeds stereo- and regio-specifically.

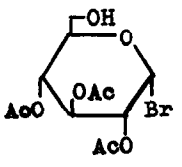
One could expect two complications in the course of polycondensation of ketal IV: 1) Formation of 2,3,4-tri-O-acetyl-1,6-anhydro-β-D-glucopyranose VI due to intramolecular glycosylation. Such a reaction was shown to predominate

with 2,3,4-tri-O-acetyl-α-D-glucopyranosyl bromide VII[10] under conditions of Koenigs-Knorr reaction. Similarly under conditions of the orthoester method of glycosylation[11] 3,4-di-O-acetyl-α-D-glucopyranose 1,2-ethylorthoacetate VIII leads mainly to anhydride VI unstead of polycondensation products. 2) Polymerisation of anhydride VI or its co-polymerisation with monomer IV, initiated by carbonium ions, which can easily take place under similar conditions[12].

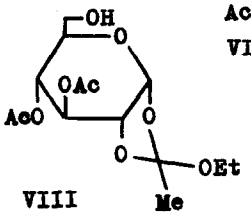
GLC analysis of the reaction mixture after polycondensation showed that anhydride VI was formed to some extent (yield ca. 13%). The possibility of its participation as an intermediate in the formation of polysaccharide material was therefore examined. A mixture of monomer IV and ^{14}C-anhydride VI was treated under the conditions of polycondensation and the products were analyzed by paper chromatography. About 30% of total radioactivity was then found in the zone of poly- and oligosaccharides. However the polysaccharide fraction isolated by gel chromatography as described above (yield ca. 12%) had a specific radioactivity of 0.65% of that of starting anhydride VI. Thus, although the polymerisation of VI under conditions described or its co-polymerisation with nitrile IV takes place to some extent, it leads almost solely to formation of oligosaccharides. Therefore glucan S-5 is formed practically exclusively through polycondensation of monomer IV without noticeable incorporation of anhydride VI.



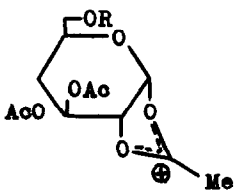
VI



VII

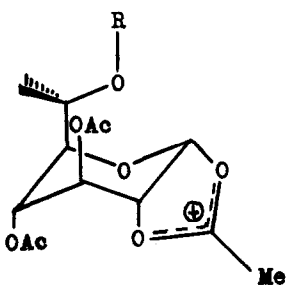


VIII



IX; R= H

X; R=Tr



XI; R= H

XII; R=Tr

The essential difference in behaviour between monomer IV on one hand and bromide VII or orthoester VIII on the other may probably be explained as follows. In spite of differences in the types of reactions, polycondensation of all these compounds probably proceeds via the same type of key intermediate, viz. the

acyloxonium IX or X. Intramolecular reaction leading to VI requires the ions IX or X to adopt a ring conformation close to $^1C_4$ (XI or XII) and in addition, for O-6 in each ion to be suitably situated to attack C-1, which involves a sterically unfavoured rotamer about the C_5-C_6 bond. The overall conformation seems to be energetically less favorable for ion XII than for ion XI, thus preventing the monomer IV from readily cyclizing to a 1,6-anhydro derivative.

REFERENCES

1. A.F.Bochkov and N.K.Kochetkov, Carbohyd. Res., 39, 355 (1975).
2. B.Coxon and H.G.Fletcher, Jr., J.Am.Chem.Soc., 85, 2637 (1963).
3. B.Helferich and K.L.Bettin, Chem.Ber., 104, 1701; 3356 (1971).
4. H.J.Dauben, L.R.Honnen and K.M.Harmon, J.Org.Chem., 25, 1442 (1960).
5. N.K.Kochetkov and A.F.Bochkov, Carbohyd.Res., 9, 61 (1969).
6. A.F.Bochkov, T.A.Sokolovskaya and N.K.Kochetkov, Zh.Obshch.Khim., 41, 2761 (1971).
7. N.K.Kochetkov, A.F.Bochkov and T.A.Sokolovskaya, Carbohyd.Res., 19, 1 (1971).
8. S.Hakomori, J.Biochem., 55, 205 (1964).
9. K.Takiura, S.Honda and K.Kakehi, Chem.Pharm.Bull., 20, 438 (1972).
10. S.Haq and M.J.Whelan, J.Chem.Soc., 4543 (1956).
11. N.K.Kochetkov, A.J.Khorlin and A.F.Bochkov, Tetrahedron, 23, 693 (1967).
12. J.Zachoval and C.Schuerch, J.Am.Chem.Soc., 91, 1165 (1969).