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MACROCYCLIC ORTHOESTER OF GLUCOSE: A NEW TYPE OF SUGAR DERIVATIVE

N.K.Kochetkov* and A.F.Bochkov*

Institute for Chemistry of Natural Products,

USSR Academy of Sciences, Moscow, USSR

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Transesterification resulting in the formation of new orthoesters is one of the two possible reactions of sugar orthoesters with alcohols (1-6). This reaction may proceed either intermolecularly giving bicyclic orthoesters (4,5) or intramolecularly yielding tricyclic orthoesters (1-3,6). A third type of condensation which is intermolecular but results in the formation of macrocyclic orthoesters is described in this paper.

Saponification of 4,6-O-benzylidene-3-O-acetyl-1,2-O-methylorthoacetyl-α-D-glucopyranose (I)(7) and subsequent self-condensation of the resulting product (II) under conditions of either transesterification or glycosylation (4,5)(e.g. under the action of mercuric bromide in nitromethane) results in the elimination of methanol to give a crystalline trimer (III) which is only slightly soluble in many solvents except chloroform and has the following properties: m.p. 281-3°; $[\alpha]_D$ +120° (c, 0.38; $CHCl_3$). Found: C, 61.77; H, 5.80; -OMe 0%. $(C_{15}H_{16}O_5)_n$ requires: C, 61.63; H 5.52%. The structure of this compound follows from the following considerations.

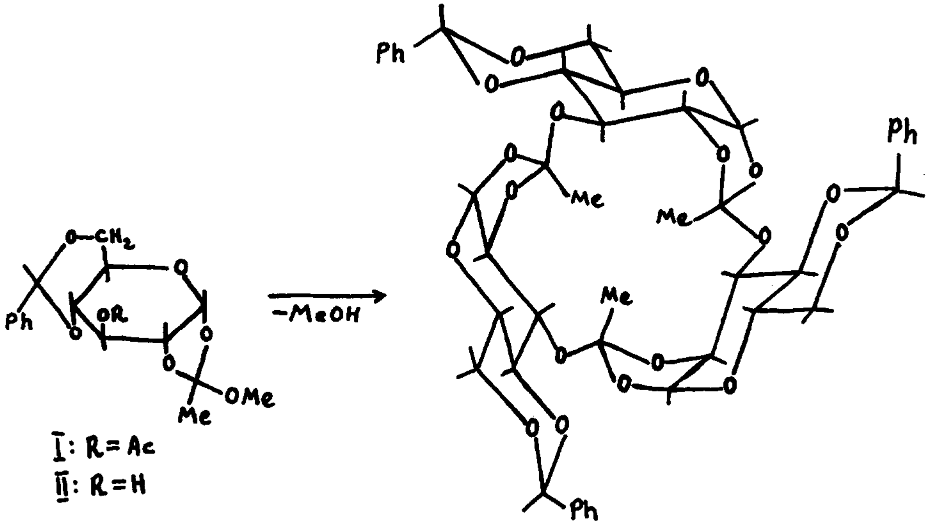
Hydrolysis of III in the mixture of 0.1N H_2SO_4 with 1,2-dichloroethane at 100° during 1 hr. gives glucose as the only product identified by chromatography. III behaves like an orthoester as it is capable of splitting under mild acidic conditions of hydrolysis (5). In the NMR spectrum there is an unsplitted signal τ 8.23 showing a C-methyl group of orthoacetate in the endo-

*Present adress: N.D.Zelinsky Institute of Organic Chemistry, Academy of Sciences of USSR, Moscow, B-334, Leninsky prospect, 47.

position (cf. (8, 9)). Hence compound III should be an orthoacetate of glucose. Further in the NMR spectrum there are singlets at τ 4.52 corresponding to benzylic protons and at τ 2.79 corresponding to five aromatic protons of the benzylidene group; such signals are also present in the starting orthoester I. No bands corresponding to hydroxyl and ester groups could be detected in the IR spectrum. The absence of an hydroxyl group excludes a linear structure, as in this form the end residues of glucose would possess free hydroxyl groups. In conformity with the mechanism of the reaction, the condensation of alcohols with sugar orthoesters may take place via glycosylation (5), but the absence of an ester group in the compound III and the formation of glucose (see earlier) under mild acidic conditions excludes this possibility. Compound III is therefore an oligomeric macrocyclic orthoacetate of 4,6-O-benzylidene-α-D-glucopyranose with orthoester linked in positions 1,2,3'. Spin-spin coupling constant $J_{1,2}$ 5.5 c.p.s. shows in aggreement with Karplus equation (10) that the dihedral angle $H-C_1-C_2-H$ is near 35° corresponding to a distorted conformation C1 for the pyranose ring in the macrocyclic structure. Examination of molecular models shows that for an orthoester with an endo-configuration of the methyl group, the dimeric cyclic structure is not possible. However, a higher degree of polymerisation from three onward is permissible for cyclic oligomers. The molecular weight (or DP) determination by the thermistor method in $CHCl_3$ gives the following values for III (in n units): 2.87; 3.20; 3.55; 3.10. Homogeneity of III by TLC shows that this compound cannot be an oligomer-homologue mixture. In agreement with the data, the orthoester III must have the structure cyclo-tri-(4,6-O-benzylidene-1,2,3'-O-orthoacetyl-α-D-glucopyranose).

The compound III is the first representative of a new type of sugar orthoester viz. macrocyclic oligomer, and its formation is the first example

of a new type of oligocyclisation of sugar derivatives in which monosaccharide residues are connected by orthoester bonds.



I: R=Ac
II: R=H

III

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