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Abstract

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CHEMISTRY

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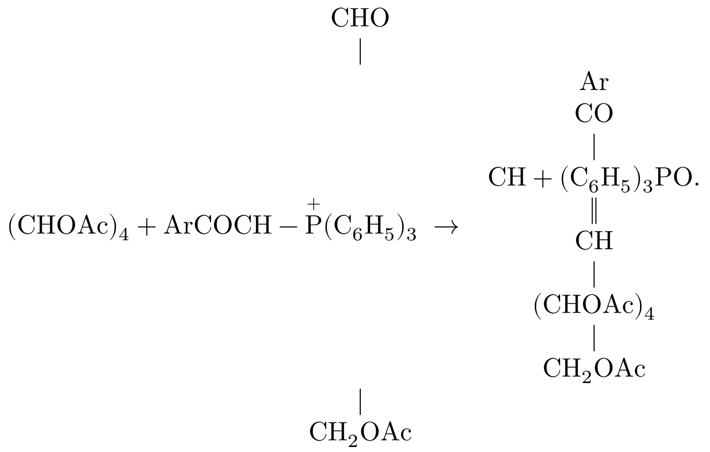
SYNTHESIS OF C-SUBSTITUTED UNSATURATED KETOSES BY MEANS OF THE WITTIG REACTION

(Presented by Academician B. A. Kazanskii, 4 VII 1964)

The methods currently known for the synthesis of C-glycosides are reduced to reactions of organometallic synthesis (1–4) and catalytic alkylation of aromatic compounds with acetohalogenoses (5). The organomagnesium method, which has found the broadest application, has made it possible to synthesize numerous representatives of the class of C-glycosides (6); however, it does not make it possible to obtain compounds containing many functional groups in the aglycone (carbonyl, carboxyl, hydroxyl, etc.).

In the search for new methods for building up the carbon skeleton of carbohydrates and synthesizing C-glycosides, we turned to the Wittig reaction (7,8), which is widely used in the chemistry of natural compounds. Recently Kochetkov and Dmitriev (9,10), and independently of them the authors of the present paper (11,12), showed that, in the interaction of acetylated aldehydo forms of sugars (9,11,12) or unsubstituted monosaccharides (10) with carbethoxymethylenetriphenylphosphorane, elongation of the carbon chain of sugars readily occurs with formation of esters of higher unsaturated aldonic acids.

Continuing the study of the synthetic possibilities of the indicated method, we investigated the condensation reaction of acetylated aldehydo forms of *D*-glucose, *D*-galactose, and *D*-mannose with acetyl- (13), benzoyl-, *p*-nitro-, *p*-methoxy-, and *p*-ethoxybenzoylmethylenetriphenylphosphoranes and synthesized in this way a new type of acyclic C-glycosides having the structure of 1-C-aryl-substituted unsaturated octuloses:



$$\begin{array}{c}\mathrm{CHO}\\ |\\ (\mathrm{CHOAc})_4\\ |\\ \mathrm{CH_2OAc}\end{array} + \mathrm{ArCOCH}-\overset{+}{\mathrm{P}}(\mathrm{C_6H_5})_3 \rightarrow \begin{array}{c}\mathrm{Ar}\\ \mathrm{CO}\\ |\\ \mathrm{CH}\\ \|\\ \mathrm{CH}\\ |\\ (\mathrm{CHOAc})_4\\ |\\ \mathrm{CH_2OAc}\end{array} + (\mathrm{C_6H_5})_3\mathrm{PO}.$$

The condensation proceeds in high yield (70–80%) upon boiling an equimolecular mixture of the components in methanolic or chloroform solution for 4–7 hours. The end of the reaction and the individuality of the compounds obtained were determined by the disappearance of the aldehydo forms upon chromatography of the reaction mixture in a thin layer of aluminum oxide.

Compounds having the *D*-galacto configuration are readily isolated from the reaction mixture in the form of crystalline precipitates and are apparently trans isomers. Substances of the *D*-manno and *D*-gluco configurations were isolated as noncrystallizing syrups, purified from triphenylphosphine oxide by deacetylation with ammonia in methanol. Attempts to obtain, under ordinary conditions, 2,4-dinitrophenylhydrazones and semicarbazones of 1-C-aryl-substituted unsaturated ketoses proved unsuccessful, since the carbonyl group in the condensation products obtained is evidently passivated because of steric factors.

The structure of the synthesized 1-*C*-aryl-substituted unsaturated ketoses was confirmed by elemental analysis and by destructive oxidation with alkaline permanganate to the corresponding arylcarboxylic acids. The substances quantitatively add bromine at the double bond.

The IR spectra of the samples obtained contain frequencies of 1675–1671 cm^{-1}, characteristic of the trans configuration of the double bond.

The absorption spectra in the ultraviolet region of the 1-*C*-aryl-substituted unsaturated ketoses obtained exhibit absorption maxima characteristic of chalcone analogs, *p*-methoxy- and *p*-nitrochalcones ($^{14-16}$).

Experimental Part

The starting arylalkyl ketones were synthesized by the procedure (^{17}); their subsequent bromination was carried out according to the procedures indicated in (^{18}). The individuality of the final condensation products was checked by thin-layer chromatography on alumina.

1-*C*-phenyl-2,3-didehydro-2,3-dideoxy-4,5,6,7,8-penta-*O*-acetyl-*D*-galacto-1-octulose (I).

1.5 g of benzoylmethylenetriphenylphosphorane (^{19}) and 1.5 g of 2,3,4,5,6-penta-*O*-acetyl-aldehydo-*D*-galactose are dissolved in 12 ml of dry chloroform, boiled for four hours, and left at room temperature for two days. Thin-layer chromatography on alumina (chloroform:benzene = 4:1) indicates formation of a product with R_f 0.56 and absence of the starting aldehydo form of galactose. The chloroform is evaporated to dryness and the solid residue is recrystallized from methanol. The product, obtained as colorless crystals, is filtered off and washed with cold methanol; m.p. 134.5–135.5° (from methanol), yield 1.45 g (79%). The substance is described for the first time.

Found %:	C 58.60, 58.39;	H 5.67, 5.61
$C_{24}H_{28}O_{11}$. Calculated %:	C 58.54;	H 5.69

IR spectrum: 1734, 1675, 1632, 1586 cm^{-1}. $\lambda_{\max}$ (in methanol) 226 mμ ($\lg\varepsilon = 3.962$); 260 mμ ($\lg\varepsilon = 4.106$).

1-*C*-phenyl-2,3-didehydro-2,3-dideoxy-4,5,6,7,8-penta-*O*-acetyl-*D*-gluco-1-octulose (II).

2.0 g of benzoylmethylenetriphenylphosphorane and 2.05 g of 2,3,4,5,6-penta-*O*-acetyl-aldehydo-*D*-glucose are dissolved in 25 ml of absolute methanol, boiled for seven hours, and left at room temperature for 2 days. The solvent is evaporated, and the remaining noncrystallizing syrup is dried in a vacuum desiccator over phosphorus anhydride. The syrup is deacetylated with ammonia and 1.1 g (74%) of a dark syrupy substance is obtained. Phosphine oxide is removed by repeated treatment of the product with warm benzene and chloroform. The substance is described for the first time.

Found %:	C 58.48, 58.35;	H 6.65, 6.53
$C_{14}H_{18}O_6$. Calculated %:	C 59.43;	H 6.05

On oxidation of the product with an alkaline solution of potassium permanganate, benzoic acid with m.p. 119–120° is obtained.

Acetylation of the syrup with acetic anhydride in pyridine gave, in the form of a noncrystallizing syrup, 1-*C*-phenyl-2,3-didehydro-2,3-dideoxy-4,5,6,7,8-penta-*O*-acetyl-*D*-gluco-1-octulose. The substance is described for the first time.

Found %:	C 58.77, 58.89;	H 5.11, 5.26
$C_{24}H_{28}O_{11}$. Calculated %:	C 58.54;	H 5.69

IR spectrum: 1743, 1672 cm^{-1}.

1-C-(p-methoxyphenyl)-2,3-didehydro-2,3-dideoxy-4,5,6,7,8-penta-O-acetyl-D-galacto-1-octulose (III). From 0.7 g of *p*-methoxybenzoylmethylenetriphenylphosphorane and 0.7 g of 2,3,4,5,6-pentaacetyl-aldehydo-D-galactose in 10 ml of chloroform, analogously to (I), a substance is obtained with m.p. 140.5–141.5° (from methanol), $R_f = 0.33$ (chloroform : benzene = 4 : 1), yield 0.65 g (70%). The substance is described for the first time.

$$\begin{array}{rll} \text{Found \%:} & \text{C } 57.66,\ 57.46; & \text{H } 5.69,\ 5.68 \\ C_{25}H_{30}O_{12}.\ \text{Calculated \%:} & \text{C } 57.47; & \text{H } 5.74 \end{array}$$

IR spectrum: 1728, 1689, 1672, 1628, 1590 cm^{-1}. $\lambda_{\max}$ (in methanol) 230 mμ (lg $\varepsilon = 4.076$); 300 mμ (lg $\varepsilon = 4.143$).

1-C-(p-methoxyphenyl)-2,3-didehydro-2,3-dideoxy-D-gluco-1-octulose (IV). From 1.5 g of *p*-methoxybenzoylmethylenetriphenylphosphorane and 1.5 g of 2,3,4,5,6-penta-O-acetyl-aldehydo-D-glucose in 10 ml of chloroform, upon heating for 4.5 hours, a product with $R_f = 0.49$ (chloroform : benzene = 3 : 1) is obtained. The chloroform is evaporated; in the residue a noncrystallizing syrupy substance is obtained. After deacetylation with ammonia, a syrup with a tendency to crystallize is isolated (when an attempt is made to recrystallize the mixture of syrup and crystals from absolute isopropyl alcohol, the crystals pass into a syrupy form). The substance is described for the first time.

$$\begin{array}{rll} \text{Found \%:} & \text{C } 56.26,\ 56.11; & \text{H } 6.62,\ 6.79 \\ C_{15}H_{20}O_{7}.\ \text{Calculated \%:} & \text{C } 57.69; & \text{H } 6.41 \end{array}$$

On oxidation of the substance with an alkaline solution of potassium permanganate, anisic acid is isolated, m.p. 181° (from water).

1-C-(p-nitrophenyl)-2,3-didehydro-2,3-dideoxy-4,5,6,7,8-penta-O-acetyl-D-galacto-1-octulose (V). From 0.65 g of *p*-nitrobenzoylmethylenetriphenylphosphorane and 0.6 g of 2,3,4,5,6-penta-O-acetyl-aldehydo-D-galactose in 7 ml of dry chloroform, upon heating for 12 h, analogously to I, 0.65 g (78.3%) of a substance weakly colored yellow is obtained, with m.p. 149.5–150.5° (ethanol : acetone = 1 : 1), $R_f = 0.28$ (chloroform : benzene = 3 : 1). The substance is described for the first time.

$$\begin{array}{rll} \text{Found \%:} & \text{C } 53.83,\ 53.73; & \text{H } 4.85,\ 4.92 \\ C_{24}H_{27}O_{13}N,\ \text{Calculated \%:} & \text{C } 53.63; & \text{H } 5.03 \end{array}$$

By oxidation of the product with an alkaline solution of potassium permanganate, *p*-nitrobenzoic acid is obtained, m.p. 235–236° (from water); according to literature data, m.p. 238° (^{20}).

IR spectrum: 1742, 1747, 1671, 1628, 1604 cm^{-1}. λ_{max} (in methanol) 268 mμ (lg $\varepsilon = 4.287$).

1-C-(p-ethoxyphenyl)-2,3-didehydro-2,3-dideoxy-4,5,6,7,8-penta-O-acetyl-D-galacto-1-octulose (VI). 2.1 g of *p*-ethoxybenzoylmethylenetriphenylphosphorane and 1.85 g of 2,3,4,5,6-penta-O-acetyl-aldehydo-D-galactose are boiled in 15 ml of chloroform for 4.5 h and then treated as indicated for (1). A substance is isolated with m.p. 135–136° (from methanol), yield 54%, R_f 0.41 (chloroform : benzene = 4 : 1). The substance is described for the first time.

Found %: C 58.14; H 6.00
$C_{26}H_{32}O_{12}$. Calculated %: C 58.20; H 5.97

In the reaction of the acetylated aldehydo forms of mannose and glucose with *p*-nitrobenzoylmethylenetriphenylphosphorane, slowly cry-

crystallizing syrups, which are difficult to purify. The deacetylated condensation products have characteristic bands in the IR spectrum at 1670, 1636, and 1600 cm^{-1}.

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