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CONDENSATION OF AL-FORMS OF SUGARS WITH PYRIDINE SALTS CONTAINING AN ACTIVE N-METHYLENE GROUP

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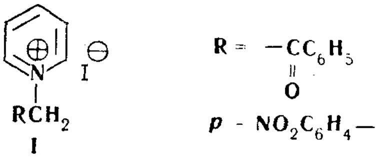
A crotonaldehyde type of condensation takes place in acetic anhydride between phenacylpyridinium iodide and al-D-glucose or al-D-galactose, to give mono-products, while al-D-mannose heptaacetate gives a di-product. If the heating time is increased, al-D-galactose is also found to give a di-product. Condensation of al-D-glucose with p-nitrolylpyridinium iodide in ethanol in the presence of pyridine gives a mono-product. In ethanol, the iodides obtained react with $Ba(ClO_4)_2$ to give perchlorates, deacetylated by perchloric acid in methanol.

We previously showed that fully acetylated hexoses condense with heterocyclic compounds containing active methylene groups (4-hydroxycoumarin, barbituric acid) [1, 2]. In the present work an attempt is made to condense the al-form of sugars with type I piperidinium salts



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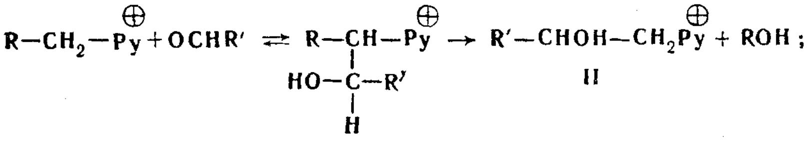
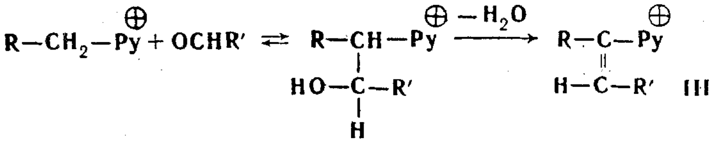
In such salts, the hydrogen atoms of the N-methylene group are activated by the adjacent piridinium ring, so that such compounds can be condensed with carboxylic acids, aldehydes, and α-ketoaldehydes [3].

Depending on the nature of the carbonyl compound and activity of the N-methylene group, of the pyridinium salt, reaction can proceed in two directions: firstly, formation of so-called pyridinium ethanol (II)) [4]:



$$R{-}CH_2{-}\overset{\oplus}{Py}+OCHR' \rightleftarrows \underset{\substack{|\\HO-C-R'\\|\\H}}{R{-}CH{-}\overset{\oplus}{Py}} \rightarrow \underset{II}{R'{-}CHOH{-}CH_2\overset{\oplus}{Py}} + ROH;$$

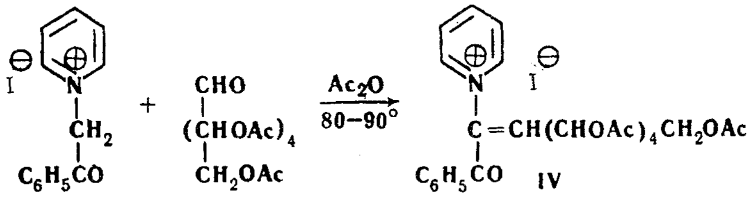
secondly, formation of vinylpyridinium salts (III)

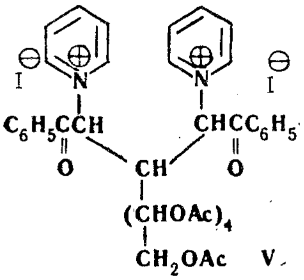


$$R{-}CH_2{-}\overset{\oplus}{Py}+OCHR' \rightleftarrows \underset{\substack{|\\HO-C-R'\\|\\H}}{R{-}CH{-}\overset{\oplus}{Py}} \xrightarrow{-H_2O} \underset{\substack{\|\\H-C-R'}}{R{-}C{-}\overset{\oplus}{Py}} \quad III$$

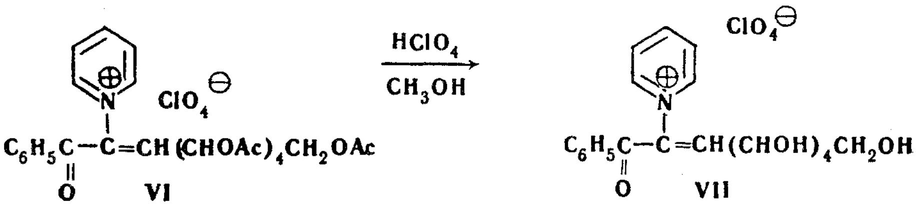
The second mode is effected when the methylene group is connected with particularly effective substituents (COC_6H_5, p-$NO_2C_6H_4$). Then vinylpyridinium salts are formed in hot ethanol in the presence of piridine as a basic catalyst. Crotonaldehyde type of condensation also takes place without a basic catalyst on heating in acetic anhydride, if the carbonyl group of the aldehyde is connected to an electron-donating substituent (e.g., p-dimethylaminobenzaldehyde) [5].

It is now shown that reaction of pyridinium salts I with fully acetylated al-hexoses gives vinylpyridinium salts. The reactivity of the methylene group in these salts is enhanced, since they lie between a pyridine nitrogen atom, and an activating electron-accepting group (COC_6H_5, p-$NO_2C_6H_4$). Consequently, condensation was carried out in ethanol in the presence of catalytic quantities of pyridine, and in acetic anhydride without a catalyst. With phenacylpyridinium iodide, heating for 25 hr in the presence of acetic anhydride gives, in the cases of al-D-glucose and al-D-galactose, monoproducts (IV), while al-D-mannose heptaacetate gives the bis product (V)

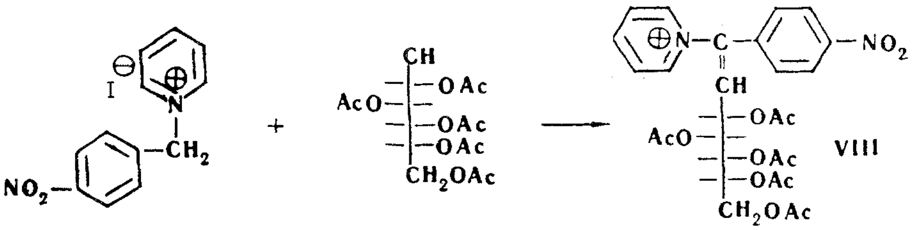




V is also formed when al-D-galactose is heated for longer. The iodides obtained were converted by reacting with $Ba(ClO_4)_2$ to perchlorates VI, deacetylated to VII by perchloric acid in dry methanol:



Heating together p-nitrobenzylpyridine and al-D-glucose together in ethanol in the presence of pyridine gives VIII.



Experimental

1'-α-(D-Gluco-2, 3, 4, 5, 6-penta-acetoxyhexylid-1-ene) phenylpyridinium iodide (IVa). 2.27 g (0.007 mole) phenylpyridinium iodide was dissolved in 70 ml Ac_2O, when much heat was evolved. The solution was cooled to 70–80° C, and 2.75 g (0.007 mole) 2,3,4,5,6-penta-O-acetyl-al-D-glucose added, after which the mixture was heated for 25 hr on a water bath. The acetic anhydride was then distilled off under a water-pump vacuum, at boiling water bath temperature. The residue was dissolved in MeOH, and the solution run through an aluminum oxide column. Removal of the MeOH and drying in a vacuum-desiccator gave IVa as a dark red glassy mass. Yield 0.92 g (19%). The substance was soluble in MeOH, EtOH, $CHCl_3$, and Me_2CO, insoluble in water, ether, and benzene. Found:* N 2.3; I 18.7%. Calculated for $C_{29}H_{32}INO_{11}$: N 2.0; I 18.2%.

1'-α-(D-Galacto-2, 3, 4, 5, 6-penta-acetoxyhexylid-1-ene) phenylpyridinium iodide (IVb). Prepared similarly, yield 15%. Dark red glass substance, soluble in MeOH, CHCl and acetone, insoluble in ether, and water. Found: N 1.5; I 18.4%. Calculated for $C_{29}H_{32}INO_{11}$: N 2.0; I 18.2%.

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* The substances obtained were analyzed for halogen by potentiometric titration [7], and for nitrogen by the Kjeldahl method [8].

1'-α-(D-Gluco-2, 3, 4, 5, 6-pentaacetoxyhexylid-1-ene) phenylpyridinium perchlorate. 0.5 g (0.7 mmole) IVa was dissolved in 15 ml EtOH, and 0.14 g (0.26 mmole) $Ba(ClO_4)_2$ added. The mixture was refluxed on a water bath for 3 hr. The alcohol was evaporated off under a water-pump vacuum, the residue treated with warm acetone, filtered to remove BaI_2, and the acetone vacuum-distilled. The perchlorate formed a syrup, yield 0.22 g (45%). Found: C 51.3; H 4.3%. Calculated for $C_{29}H_{32}ClNO_{15}$: C 51.94; H 4.8%.

1'-α-(D-Gluco-2, 3, 4, 5, 6-pentahydroxyhexylid-1-ene) phenacylpyridinium perchlorate (VII). 0.46 g (0.7 mmole) VIa was dissolved in dry MeOH, 2 drops of 70% $HClO_4$ added, and the mixture heated for 2 hr on a gently boiling water bath. After cooling the $HClO_4$ was neutralized with $NaHCO_3$, the solution treated with active charcoal, filtered, and evaporated on a water bath under a water-pump vacuum. Yield 0.25 g (54%). The substance, obtained as a syrup, was soluble in water, EtOH, and $CHCl_3$. It is here described for the first time. Found: C 48.74; H 4.43%. Calculated for $C_{19}H_{22}ClNO_{10}$: C 49.6; H 4.8%.

1, 1'-α, α'-(D-Manno-1-desoxy-2, 3, 4, 5, 6-pentaacetoxyhexylidene) diphenacylpyridinium iodide. 0.65 g (0.002 mole) phenacylpyridinium iodide was dissolved in 20 ml Ac_2O, when there was marked heating. The solution was cooled to 70–80° C, 0.49 g (0.001 mole) al-D-mannose heptaacetate added, and the reaction mixture heated for 12 hr on a water bath. The Ac_2O was removed under a water-pump vacuum at boiling water bath temperature. The residue was twice recrystallized from hot EtOH, yield 0.38 g (18%), glistening brown plates, mp 130° C. It was soluble in EtOH, MeOH, and acetone, but insoluble in ether and water. Found: N 2.3; I 25.3%. Calculated for $C_{42}H_{44}I_2NO_{12}$: N 2.7; I 24.9%.

1, 1'-α, α'-(D-Manno, 2, 3, 4, 5, 6-pentaacetoxyhexylid-1-ene) phenacylpyridinium perchlorate. Prepared from Va similarly to the perchlorate VIa, yield 50%. Colorless crystals, mp 180–182° C (ex acetone, then ex EtOH). Found: C 52.07; H 4.13; Cl 7.56%. Calculated for $C_{42}H_{44}Cl_2N_2O_{20}$: C 52.12; H 4.58; Cl 7.32%.

1, 1'-α, α-(D-Manno-2, 3, 4, 5, 6-pentahydroxyhexylid-1-ene) bis(phenacylpyridinium) perchlorate. Prepared similarly to derivative VII by deacetylating the above pentaacetyl derivative. Yield 30%, mp 195–200° C. Soluble in EtOH, MeOH, and acetone, insoluble in ether. Found: C 50.25; H 4.20; Cl 9.75. Calculated for $C_{32}H_{34}Cl_2N_2O_{15}$: C 50.73; H 4.52; Cl 9.36%.

1, 1'-α, α'-(D-Galacto-2, 3, 4, 5, 6-pentaacetoxyhexylid-1-ene) bis(phenacylpyridinium) iodide (Vb). A mixture of 2.73 g (0.007 mole) 2, 3, 4, 5, 6-penta-O-acetyl-al-D-galactose, 2.27 g (0.007 mole) phenacylpyridinium iodide, and 70 ml Ac_2O was heated on a water bath for 35 hr. The Ac_2O was distilled off under a water-pump vacuum, at boiling water-bath temperature, the residue treated with EtOH, the precipitate filtered off, washed with EtOH and ether, and dissolved in $CHCl_3$–MeOH. The solution was run through an aluminum oxide column, and the solvent removed. The residue was washed with EtOH and ether, and dried in a vacuum-desiccator. Yield 0.9 g (18%), mp 185° C (decomp). Green powder. Found: N 2.3; I 24.10%. Calculated for $C_{42}H_{44}I_2N_2O_{12}$: N 2.74; I 24.9%.

1'-α-(D-Gluco-2, 3, 4, 5, 6-pentaacetoxyhexylid-1-ene)-p-nitrobenzylpyridinium iodide (VIII). 0.35 g (0.001 mole) p-nitrobenzylpyridinium iodide and 0.39 g (0.01 mole) 2, 3, 4, 5, 6-penta-O-acetyl-al-D-glucose were dissolved in 40 ml EtOH, 1 ml pyridine added, and the mixture heated on a water bath for 30 hr. The EtOH was removed under vacuum. The residue was dissolved in $CHCl_3$, boiled with active charcoal, filtered, and the $CHCl_3$ distilled off. The reaction product was obtained as a light orange powder, mp 245° C (decomp). Yield 0.07 g (10%). Found: N 3.5; I 18.5%. Calculated for $C_{28}H_{31}IN_2O_{12}$: N 3.6; I 18.2%.

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