LONG CARBON CHAIN CARBOHYDRATE POLYMERS

1,3-(BIS-5-ALDOXYLOSYLIDENE-1)-ACETONE AND ITS POLYMER WITH 1,3-DICARBETHOXYACETONE

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ABSTRACT

1,3-Dicarbethoxy-1,3-(bis-(4′,5′-*O*-isopropylidene-D-xylofuranosylidene))-acetone was hydrolyzed and decarboxylated to produce 1,3-(bis-D-xylofuranosylidene-5)-acetone (III) and 1,3-(bis-5-aldoxylosylidene-1)-acetone (IV). Compound IV reacted with 1,3-dicarbethoxyacetone in 75% methanol, with piperidine as catalyst, to give polymers V and VI and some intermediates. The main component of polymer V had a molecular weight between 2 000 and 4 000, and there were six to seven components with molecular weights of less than 2 000. Because the molecular weight of the repeating unit is approximately 500, a polymer with a molecular weight of 2 500 would have 80 carbons in a continuous chain, and one with a molecular weight of 3 500 would have 112 carbons. The work presented in this article may open broad areas of further research.

INTRODUCTION

It has been shown previously that 1 mole of diethylacetonedicarboxylate condenses with 2 moles of an aldose in a 75% methanol solution, with piperidine as catalyst, to give long carbon chain sugars (1). In another method (2), diethylacetonedicarboxylate was condensed with an aldose in the molar proportions of 1:2 in concentrated hydrochloric acid at 0° to form long carbon chain sugars.

On one occasion, 2 moles of 1,2-*O*-isopropylidene-D-xylopentodialdose was condensed with 1 mole of diethylacetonedicarboxylate, with piperidine as catalyst, to give 1,3-dicarbethoxy-bis-(4′,5′-*O*-isopropylidene-D-xylofuranosylidene)-acetone, which is a dialdehydo unsaturated keto sugar with a chain of 13 carbon atoms (I) (1).

It was pointed out then that the hydrolysis of the isopropylidene groups of compound I could give rise to two free aldehyde groups in this compound, and might open the way for chain polymerization with diethylacetonedicarboxylate or other appropriate reagents.

Schaffer and Isbell (3) observed that the hydrogen on carbon 4 in 5-aldo-1,2-*O*-isopropylidene-D-xylopentodialdofuranose is alpha with respect to the aldehyde group, and helps to make the compound susceptible to aldol condensation. They observed the aldol reaction of two molecules of this compound to form a branched-chain 10-carbon sugar.

The present report deals with the hydrolysis of the isopropylidene and the carbethoxy groups of I to give compound II, the decarboxylation of the resulting β-ketonic acids to produce compound III, and the aldol condensation of the dialdehydo form of the resulting 13 carbon atom sugar (IV) with 1,3-dicarbethoxyacetone to give polymer V. An intermediate compound representing the first step of the aldol condensation was isolated and is represented by formula VI. The formulae may represent one of the possible *cis–trans* isomers.

Thus, 1,3-dicarbethoxy-1,3-(bis-(4′,5′-*O*-isopropylidene-D-xylofuranosylidene))-acetone (I) was hydrolyzed with 1% H_2SO_4. Both the isopropylidene and the carbethoxy esters were hydrolyzed. The latter gave rise to carboxylic groups (II), both of which have the keto group in the β-position. It is known that β-ketonic acids lose CO_2 when heated in an acid solution. Under such conditions, compound II was decarboxylated to give III, the alpha and beta forms of which are expected, in aqueous solution, to form an equilibrium with the dialdehydo form (IV).

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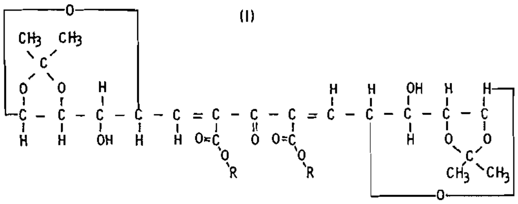
(I)



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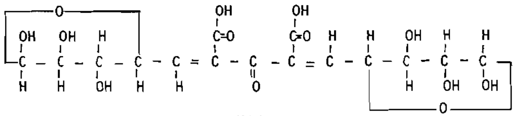

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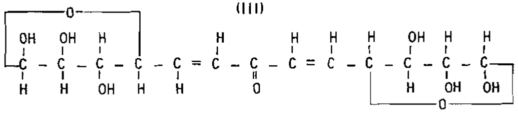

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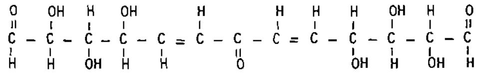
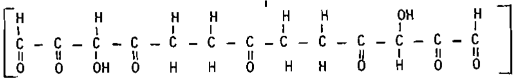


$\mathrm{OHC{-}CH(OH){-}CH(OH){-}CH(OH){-}CH{=}CH{-}CO{-}CH{=}CH{-}CH(OH){-}CH(OH){-}CH(OH){-}CHO}$

(IV)



$\left[\mathrm{OHC{-}CO{-}CH(OH){-}CO{-}CH_2{-}CH_2{-}CO{-}CH_2{-}CH_2{-}CO{-}CH(OH){-}CO{-}CHO}\right]$

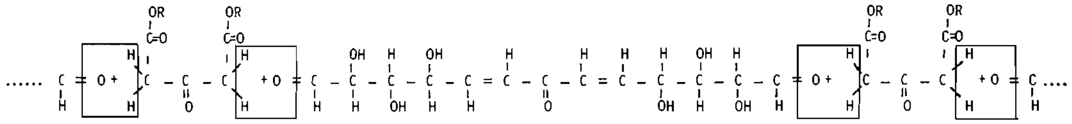
In the next step, compound IV and 1,3-dicarbethoxyacetone, in the molar proportions of 1:1, were condensed in 75% methanol with piperidine as catalyst. After the product was processed, it analyzed as if polymerization had taken place. The polymer unit, taken x times, is shown within the brackets of formula V.

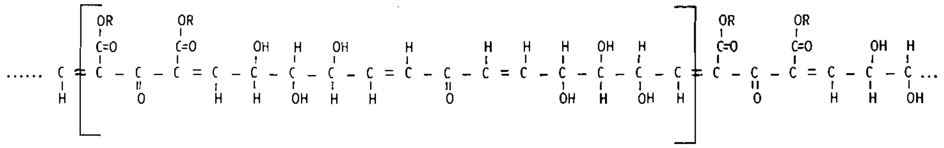
The approximate molecular weights were determined as follows by Dr. Wayne Ryan and James Dworak of the Eugene C. Eppley Institute for Research in Cancer and Allied Diseases. "The polymer was chromatographed on Bio-rad polyacrylamide gels with a 0.9 × 150 cm column and a flow rate of 20 ml/h, which was maintained with a Spinco accuflow pump. The effluent from the column was monitored by a Spinco 135 Spectro-monitor programmed at 220 mμ and at 260 mμ. Polyacrylamide gels with exclusion limits of 2 000, 4 000, and 10 000 were used. The results of this study indicated that the polymer contained one component with a molecular weight between 2 000 and 4 000, and six to seven components with a molecular weight of less than 2 000."

The main product of the polymerization is the compound with a molecular weight between 2 000 and 4 000. On the basis of this information, the molecular weight of this component may have approximately one of the following values: 2 000, 2 500, 3 000, 3 500, or 4 000. With a molecular weight of 2 500 there would be 80 carbon atoms in the long carbon chain. A molecular weight of 3 500 would correspond to a carbohydrate with a chain of 112 carbon atoms.

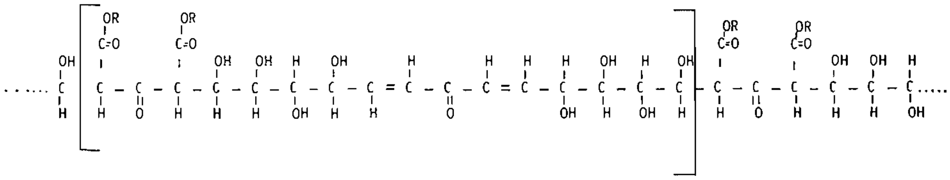
The ultraviolet and infrared spectra were taken and interpreted by Dr. Curtis Leicht, Chemistry Department, Creighton University.

The ultraviolet spectral data tentatively support the structural assignments given for V and VI. These polymers, as well as compound I, exhibited absorption in a region near 240 mμ, the intensity being somewhat greater for the polymers. Unfortunately, both ethylmethyleneacetoacetate, deemed to be an approximate model for compound V, and diethylacetonedicarboxylate, a model for formula VI, also exhibit absorption very near





(V)



(VI)

240 mμ, with very similar intensities (λ_{max} 239 mμ, log ϵ = 3.24 (4), and λ_{max} 237 mμ log ϵ = 3.5, respectively).

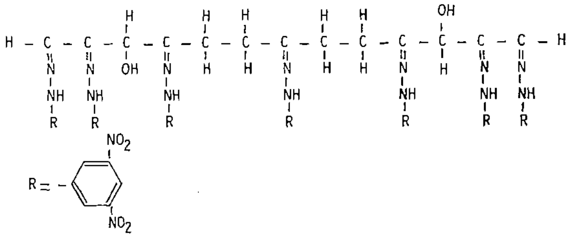
However, diethylacetonedicarboxylate dissolved in approximately 1% ethanolic KOH demonstrated a bathochromic shift of about 35 mμ, with a concomitant 12-fold increase in the absorption intensity (λ_{max} 272 mμ, log ϵ = 4.6). A very similar change in the wavelength and intensity of absorption was shown by compound VI with the same solvent change (λ_{max} 278 mμ, $E^{1\,cm}_{1\%}$ = 8 000). Although compounds I and V also demonstrated similar bathochromic shifts, the changes in intensity were much more modest (λ_{max} 282 mμ, log ϵ = 4.4, and λ_{max} 280 mμ, $E^{1\,cm}_{1\%}$ = 315, respectively). The tenuous nature of these interpretations is demonstrated by the fact that polymer VI and ethylmethyleneacetoacetate both exhibit somewhat similar longer wavelength absorptions (λ_{max} 324 mμ, $E^{1\,cm}_{1\%}$ = 17.5, and λ_{max} 307 mμ, log ϵ = 1.5, respectively). Furthermore, polymer VI and compound I show very similar longer wavelength absorptions in basic solution (λ_{max} 355 mμ, $E^{1\,cm}_{1\%}$ = 406, and λ_{max} 352 mμ, log ϵ = 3.7, respectively).

Since the infrared spectra of compounds V and VI were so similar, no further support for the structural assignments could be obtained by this means.

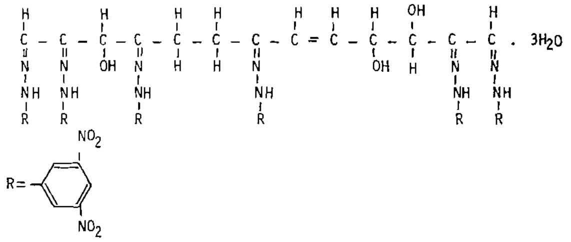
This work opens the way for several investigations. Further research will be carried out on the preparation of other polymers and the synthesis of derivatives analogous to those of the simpler carbohydrates which may have scientific, medicinal, or industrial importance.

During this investigation, the following derivatives (new compounds) were made and analyzed: (*a*) a crystalline 1,2-*O*-isopropylidene-3-*O*-(3,5-dinitrobenzoate)-D-xylopentofuranose; (*b*) a 3,5-dinitrobenzoate ester of I (the product corresponds to 1,2-*O*-isopropylidene-6,8-dicarbethoxy-7-oxo-3,11-di-(*O*-benzoate-3,5-dinitro)-5,8-diene-D-tridecadialdoxyfuranose; an *O*-diisopropylidene derivative was expected; apparently in the process one isopropylidene group was hydrolyzed); and (*c*) a 2,4-dinitrophenylhydrazine derivative of IV, 3,10,11-trihydroxy-hexakis-1,2,4,7,12,13-(2,4-dinitrophenylhydrazone)-tridecaene-8 (VIII) (osazone reaction and tautomerization of the hydrogens in IV and hydrazone reaction of the resulting carbonyl groups in (IV)$_1$ should result in compound VII; because of the inadequate amount of 2,4-dinitrophenylhydrazine used, only six 2,4-dinitrophenylhydrazines reacted, thereby giving compound VIII).

(VII)



(VIII)



EXPERIMENTAL

Ultraviolet spectra were run on a Beckman DU spectrophotometer in 95% ethanol. Infrared spectra were run on a Beckman IR-8 instrument in chloroform solution.

*5-Aldo-1,2-O-isopropylidene-*D*-xylopentofuranose (5–7)*

This was prepared according to the method described by Grosheintz and Fischer.

*1,2-O-Isopropylidene-3-O-(3,5-dinitrobenzoate)-*D*-xylopentodialdose*

1,2-*O*-Isopropylidene-D-xylopentodialdose (1.88 g, 0.01 mole), 3,5-dinitrobenzoyl chloride (2.30 g, 0.01 mole), pyridine (1 ml), and dry ether (30 ml) were mixed at 0° for ½ h, and then allowed to stand at room temperature overnight. The mixture was then refluxed for 1 h, allowed to cool, and poured into ice water. A precipitate was collected and recrystallized from methyl alcohol, m.p. 150°.

Anal. Calcd. for $C_{15}H_{14}O_{10}N_2$: C, 47.12; H, 3.69. Found: C, 47.43; H, 3.32.

*1,2;12,13-O-Diisopropylidene-6,8-dicarbethoxy-7-oxo-3,11-dihydroxy-5,8-diene-*D*-tridecadialdoxylofuranose or 1,3-Dicarbethoxy-1,3-(bis-(4′,5′-O-isopropylidene-*D*-xylofuranosylidene))-acetone (I)*

The title compound was prepared according to the method described by Papadakis (1). The analytical results agreed with the experimental values found previously (1) and with the theoretical values.

Anal. Calcd. for $C_{25}H_{34}O_{13}$: C, 55.35; H, 6.31. Found: C, 55.37; H, 6.34.

Specific rotation: $[\alpha]_D^{18}$ +45.62° (*c*, 3.051 in acetone); after 16 h $[\alpha]_D^{21}$ +22.9°; after 40 h $[\alpha]_D^{21}$ +22.9°. Ultraviolet spectrum: λ_{max} 234 and 247 mμ, log ϵ = 3.7 and 3.8, respectively. Infrared spectrum: absorption at 3 420, 3 020, 2 985, 2 940, 1 725, 1 655, 1 620, 1 370, 1 230, 1 080, and 1 020 cm^{-1}.

3,5-Dinitrobenzoyl Chloride Derivative of I

A mixture of 1.0 g (0.0018 mole) of I, 0.92 g (0.0036 mole) of 3,5-dinitrobenzoyl chloride, and 0.32 ml (0.0036 mole) of pyridine in a dry dioxane medium was kept at 0° for 1 h. After having stood at room temperature overnight, the mixture was heated at 60° under reflux for 1 h. The dioxane was removed under reduced pressure and the product poured over crushed ice. The residue was washed with 10 ml of 2% sodium bicarbonate. Recrystallization from ether – petroleum ether gave a white solid, m.p. 150–152°.

Anal. Calcd. for $C_{36}H_{36}O_{24}N_4$: C, 47.57; H, 3.99; N, 6.16. Found: C, 47.45; H, 4.26; N, 6.06. (In the process one isopropylidene was hydrolyzed.)

1,3-(Bis-5-aldoxylosylidene-1)-acetone (IV)

Hydrolysis of I was accomplished by heating with dilute acid. To a solution of 5 g of I in dioxane, 50 ml of 0.1 *N* sulfuric acid was added. The mixture was heated under reflux on a water bath at 75–80° for 2½ h. The sulfuric acid was neutralized with barium hydroxide, the $BaSO_4$ filtered off, and the filtrate evaporated to dryness. The residue was boiled with distilled water and filtered to remove any unhydrolyzed I, which is insoluble in water. The solution was evaporated again to dryness and the material was pulverized to an amorphous powder which softened at 93° and completely melted at 110°.

Anal. Calcd. for $C_{13}H_{18}O_9 \cdot 1\frac{1}{2}H_2O$: C, 45.21; H, 6.08. Found: C, 44.85; H, 6.31.

The analytical results correspond to a hydrated compound (IV).

3,10,11-Trihydroxy-hexakis-1,2,4,7,12,13-(2,4-dinitrophenylhydrazone)-tridecaene-8 (VIII)

To 1.11 g (0.0056 mole) of 2,4-dinitrophenylhydrazine, 2.5 ml of concentrated sulfuric acid was added. Water was added dropwise, with stirring, until solution was completed. To a solution of 0.3 g (0.0008 mole) of crude IV in ethanol, the 2,4-dinitrophenylhydrazine – sulfuric acid solution was added, and the mixture was allowed to stand overnight. After centrifugation the red precipitate was collected and recrystallized from 95% alcohol. It sintered at 224° and melted at 229–235°.

Anal. Calcd. for $C_{49}H_{44}O_{30}N_{24}$: C, 40.60; H, 3.04; N, 23.20. Found: C, 40.48; H, 2.71; N, 23.76.

Preparation of the Long Carbon Chain Polymers V and VI

A quantity of 1.53 ml (0.008 mole) of diethylacetonedicarboxylate was added to 2.832 g (0.008 mole) of 1,3-(bis-5-aldoxylosylidene-1)-acetone (IV) in a benzene medium. After piperidine (five drops) was added to catalyze the reaction, the mixture was left at room temperature overnight. This was followed by heating under reflux in a water bath at 80° for 1 h. After a second day of standing, it was again heated for 1 h. The solution was then filtered and the filtrate evaporated to dryness. The hardened syrup was purified in the following manner. It was divided into two portions, one soluble in water and the other in 95% ethanol. A residue was precipitated from the former by the addition of 95% ethanol, and from the latter by the addition of water. The residue was removed by filtration (analysis later proved that it was not the polymer). This purification process was repeated several times. The amber solution of the water-soluble and alcohol-soluble materials containing the polymer was treated with Darco in an unsuccessful attempt to remove the color. This was followed by evaporation to dryness. The hardened amber syrups were pulverized.

The material from the first portion (represented by VI) softened at 72° and had completely melted at 85°. The material from the second portion (represented by V) melted at 78–81°.

Compound VI

Anal. Calcd. for $C_{22}H_{32}O_{14}$: C, 50.76; H, 6.15. Found: C, 50.86; H, 6.01.

Ultraviolet spectrum: $\lambda_{\max}$ 238 (4) and 324 mμ, $E^{1\,\mathrm{cm}}_{1\%} = 406$ and 17.5, respectively. Infrared spectrum: absorption at 3 400, 3 010, 2 980, 1 720, 1 580 (broad), 1 440, 1 370, 1 220, 1 090, and 1 030 cm^{-1}.

Compound V

Anal. Calcd. for $C_{22}H_{28}O_{12}$: C, 54.54; H, 5.78. Found: C, 54.77; H, 6.07.

Ultraviolet spectrum: $\lambda_{\max}$ 240 mμ (4), $E^{1\,\mathrm{cm}}_{1\%} = 180$. Infrared spectrum: absorption at 3 400, 3 010, 2 920, 1 720, 1 615 (broad), 1 440, 1 370, 1 220, and 1 020 cm^{-1}.

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