# Isomerization of Tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose

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Acid-catalyzed acetolysis was found to isomerize tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I, "2,3,4,6-tetra-*O*-acetyl-2-hydroxy-D-glucal") to three new unsaturated structures. The structure of the most readily obtained isomer (about 80% yield) was shown, by application of n.m.r. spectroscopy and conversion to compounds of known structure (D-arabinonic acid and 2-deoxy-D-*erythro*-pentose), to be tetra-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranose (III). The structure of a second isomer, which was also obtained by isomerization of tetra-*O*-acetyl-1-deoxy-D-*lyxo*-hex-1-enopyranose (VIII), was assigned, mainly on the basis of n.m.r. spectroscopy, the structure of tetra-*O*-acetyl-(3,4-dideoxy-α-D-*glycero*-hex-3-enosulopyranose 2-hydrate) (VII).

Dehydrobromination of the 2,3,4,6-tetra-*O*-acetylglycosyl bromides derived from α-D-glucose[3,4] and α-D-galactose,[5] normally through the agency of diethylamine,[6] yields the unsaturated compounds first reported as 2,3,4,6-tetra-*O*-acetyl-1,2-D-glycoseens and more recently as 2,3,4,6-tetra-*O*-acetyl-2-hydroxy-D-glycals. This communication is concerned with isomerizations of these unsaturated compounds designated herein as tetra-*O*-acetyl-1-deoxy-D-hex-1-enopyranoses.

The isomerizations and other reactions of acylated aldo-1-enoses have received considerable attention and the subject has recently been reviewed.[7] The facile dissociation of the 3-substituent in these compounds is readily understood as resulting from activation of the 3-position toward carbonium ion formation by the allylic double bond.[8] The activation is especially strong for the 1-enose structures since the ring oxygen can participate in the charge delocalization. It was anticipated that 2-acetoxy-1-enose structures would undergo similar isomerizations.

It was found that treatment of tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I) at room temperature in acetic anhydride containing zinc chloride resulted in a rapid increase in the rotation of the solution. This change was followed by a slower decrease in rotation. When the reaction was interrupted at the point of maximum rotation, a crystalline product isomeric with the starting material was readily isolated in about 80% yield. The same compound (III) was formed on treating I either in acetic anhydride with sulfuric acid or in acetic acid with *p*-toluenesulfonic acid. A small amount of a second isomer (IV or V) was isolated from the mother liquor of the zinc chloride catalyzed reaction. When the reaction was allowed to proceed for 20 hr., a third isomer (VII) was obtained. The latter compound was also obtained by isomerization of the other two isomers. The melting points and rotations of these and other isomeric substances are reported in Table I. The structures indicated for the new compounds described above were established mainly by application of n.m.r. spectroscopy

TABLE I

PROPERTIES OF ISOMERIC TETRA-*O*-ACETYL-DEOXY-D-HEXENOPYRANOSES

| Compd. | M.p., °C. | $[\alpha]^{25}D$ ($CHCl_3$), deg. |
|---|---|---|
| Tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I)[a] | 65–66 | −32 |
| Tetra-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranose (III) | 70–71 | +50 |
| Tetra-*O*-acetyl-1(3)-deoxy-D-hex-1(2)-enopyranose (IV or V) | 83.5–84 | +151 |
| Tetra-*O*-acetyl-(3,4-dideoxy-α-D-*glycero*-hex-3-enosulopyranose 2-hydrate) | 122–123 | −182 |
| Tetra-*O*-acetyl-1-deoxy-D-*lyxo*-hex-1-enopyranose (VIII)[b] | 110–111 | +5.0 |

[a] Reference 6. [b] Reference 5.

at 100 Mc.p.s. with the use of spin decoupling to assign the origins of the signals. The conclusions reached were confirmed by chemical investigations except for the isomer of undetermined structure, probably IV or V. The structure of this isomer is believed to be restricted to IV or V in view of its position in the isomerization scheme. An amount sufficient for n.m.r. investigation was not available.

Spectra, at both 60 and 100 Mc.p.s., of isomer III are shown in Figure 1. The multiplet at about $\tau$ 5.9 (just to highfield and overlapped by the "singlet" at $\tau$ 5.8) must arise from the proton at the 5-position. The "singlet" can be assigned to the two protons on the 6-carbon. This follows from the now extensive experience with the n.m.r. spectra of acetylated hexopyranose structures. Irradiation at $\tau$ 5.90 while observing the rough doublet at 4.47 caused the doublet to collapse to a rough singlet. Therefore, the signal at $\tau$ 4.47 arose from the C-4 proton and $J_{4,5}$ is about 9.0 c.p.s. This magnitude for the coupling constant is in keeping with the diaxial orientation of these protons on neighboring carbons.[9] On irradiating the signal of the C-4 proton and observing individually the doublets at $\tau$ 3.69 and 4.13, these signals both collapsed to singlets. On observing the signal for the C-4 proton while irradiating the doublet at $\tau$ 4.13, a signal in the form of a quartet with spacings of about 1.0 and 9.0 c.p.s. was obtained. In view of the coupling with the C-4 proton, the doublet with the spacing of 2.2 c.p.s. at $\tau$ 4.13 is assigned to an olefinic proton at

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the 3-position. The chemical shift of the C-2 proton of tri-*O*-acetyl-1,2-dideoxy-D-*arabino*-hex-1-enopyranose (D-glucal triacetate) is at $\tau$ 5.15 and the spacing arising from coupling with the C-3 proton is 3.0 c.p.s. The chemical shift of 1.02 p.p.m. between the olefinic C-3 proton of III and the C-2 proton of the glucal triacetate is understandable in view of the acetoxy substituent on the ethylenic group of III. The doublet with a spacing of about 1.0 c.p.s. at $\tau$ 3.69 is assigned to the proton at the anomeric center of an acetylated C-2 enose structure. The splitting of this signal by long-range $^5J_{HH}$ coupling with the C-4 proton suggests that the 1-hydrogen is an equatorial orientation in order that the "rear" portion of the $sp^3$-orbital of the C-1–H bond be directed toward that of the C-4–H bond.[10,11] Long-range coupling interactions which result from $^4J_{HH}$ coupling[12] and which conform with this interpretation have been observed in carbohydrate structures.[13,14] Evidence for this configuration for the anomeric center as well as the presence of an acetoxy group at the anomeric center of III was provided by the n.m.r. spectrum (Figure 2) of the product from the hydrogenation of III in acetic acid using palladium on carbon as catalyst. Although hydrogenolysis with the liberation of acetic acid was extensive, about 30% of the hydrogenation yielded 3-deoxyhexose tetraacetate as indicated by the appearance of signals for anomeric hydrogens at $\tau$ 3.76 and 4.00 with spacings of 3.3 and <2 c.p.s., respectively. No other signals for anomeric protons at acetylated anomeric centers were in evidence (see Figure 2). Since the signals observed agree well in their chemical shifts and spacings with those found for 1,2,3,4,6-penta-*O*-acetyl derivatives $\alpha$-D-glucose and $\alpha$-D-mannose, namely $\tau$ 3.69 (3.3 c.p.s.) and 3.93 (1.0 c.p.s.), respectively, it is clear that the anomeric center of III possesses the $\alpha$-D configuration.

The structure for III was confirmed by the following chemical transformations. Permanganate oxidation afforded D-arabinonic acid characterized as the crystalline phenylhydrazide. Therefore, the position of the double bond is restricted to either the 1- and 2- or the 2- and 3-carbons and the isomerization of I to III did not involve carbons 4, 5, or 6. Hydrogenation of III afforded the tetraacetates of 3-deoxy-D-*ribo*-hexose and 3-deoxy-D-*arabino*-hexose as expected for the structure assigned to III on the basis of its n.m.r. spectrum. The n.m.r. spectrum of the resulting sirup, see Figure 2, showed absorption in the $\tau$ 6.2–6.7 region characteristic for the protons of *endo* cyclic methylene groups bonded both to oxygen and to carbon and suggesting that III underwent extensive hydrogenolysis at the 1-position. Lead tetraacetate oxidation of the crude sirup resulting from the hydrogenation of III followed by deacetylation led to the formation of 2-deoxy-D-*erythro*-pentose identified as its crystalline anilide derivative.

Spectra of isomer VII at both 60 and 100 Mc.p.s. are shown in Figure 3. The signals for the two C-6 protons and the C-5 proton are obviously overlapping at

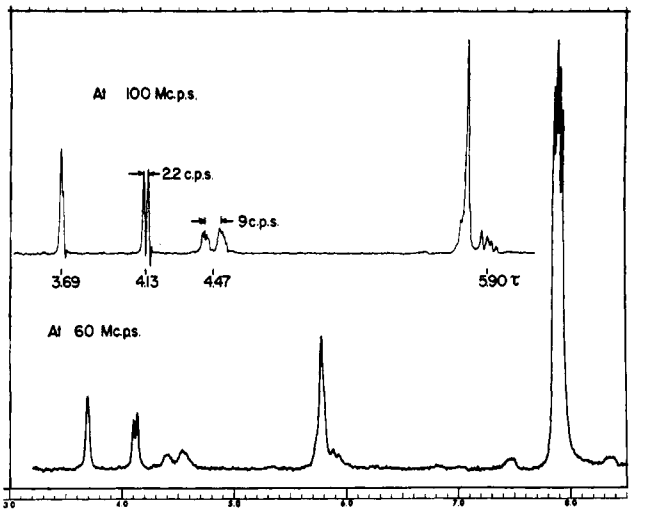


Figure 1.—The proton magnetic resonance spectra of tetra-*O*-acetyl-3-deoxy-$\alpha$-D-*erythro*-hex-2-enopyranose (III) in chloroform solution.

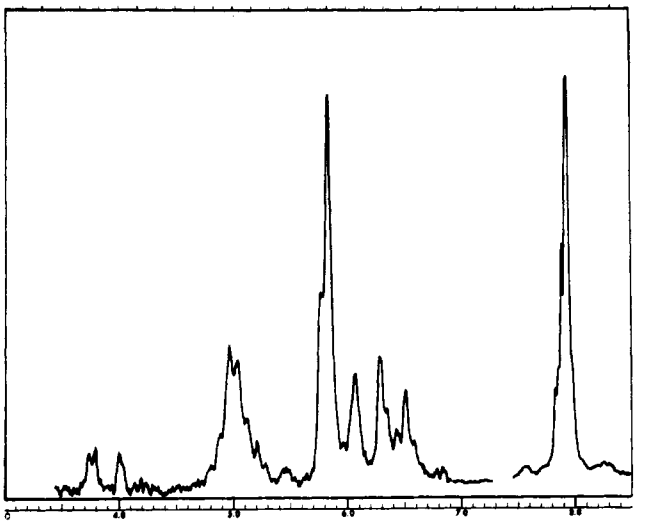

Figure 2.—The proton magnetic resonance spectrum at 60 Mc.p.s. of the product obtained on the catalytic hydrogenation of tetra-*O*-acetyl-3-deoxy-$\alpha$-D-*erythro*-hex-2-enopyranose (III) in chloroform solution.

$\tau$ 5.72. Irradiation of this position caused the quartet at $\tau$ 4.69 to collapse to a doublet with the larger spacing, 6.2 c.p.s. Therefore, the quartet arose from the C-4 proton. Similarly, double irradiation showed the C-4 proton to be coupled with the C-3 proton at $\tau$ 3.91, a conclusion already indicated by the spacing of 6.2 c.p.s. for the doublet at $\tau$ 3.91. In view of the lack of coupling, the singlet at $\tau$ 3.59 is assigned to the anomeric proton. Evidently, there is no hydrogen at the 2-position. As required by acetyl group analysis, the n.m.r. spectrum of the compound showed the presence of four *O*-acetyl groups. Therefore structure VII is assigned to this isomer. The coupling constant of 6.2 c.p.s. for the C-3 and C-4 protons of VII is the same as that found for the C-1 and C-2 protons of tri-*O*-acetyl-1,2-dideoxy-D-*arabino*-hex-1-enopyranoses and thus lends support to the olefinic nature of these protons. It is noteworthy that the coupling of the olefinic C-4 proton with the axial C-5 proton provides a spacing of 2.5 c.p.s. in the signal of the C-4 proton, a spacing in close agreement with that observed, 2.2 c.p.s., for the coupling of the olefinic C-3 proton with

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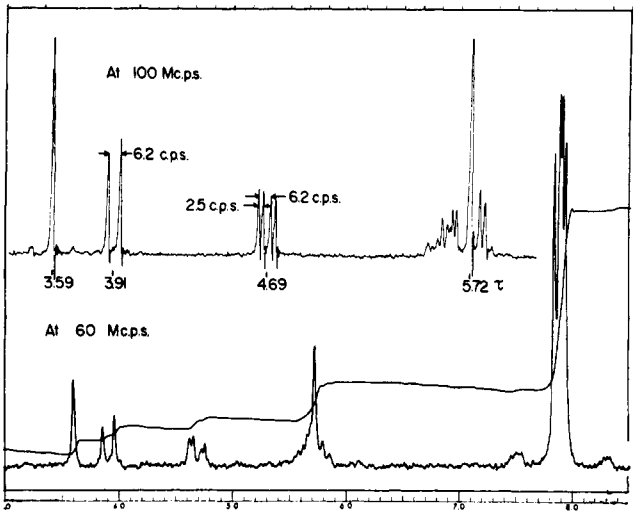
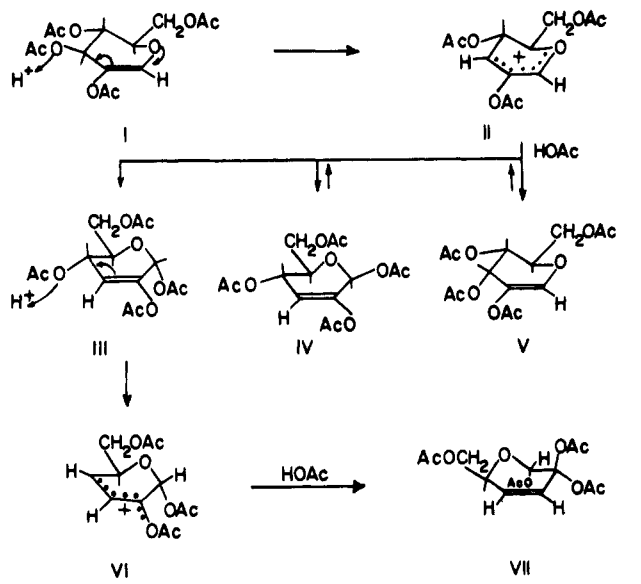



Figure 3.—The proton magnetic resonance spectra of tetra-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hex-3-enosulopyranose 2-hydrate (VII) in chloroform solution.

the axial C-4 proton in the spectrum (Figure 1) for compound III. Hydrogenation of VII, using a platinum catalyst, led to a rapid consumption of 2 moles of hydrogen/mole of VII. Deacetylation of the product liberated two compounds with mobilities on paper chromatograms 6.6 to 9.3 times that of glucose and 2 to 3 times those of the 3-deoxyhexoses derived from III. These high mobilities agree with the expectation that the hydrogenation of VII leads to the formation of 3,4-dideoxyhexoses. In view of the lack of asymmetry at the 4-position of the structure thus assigned to VII, it would be anticipated that VII would be formed on isomerization of the 4-epimer of I. In fact, treatment of tetra-*O*-acetyl-1-deoxy-D-*lyxo*-hex-1-enopyranose (2-acetoxy-D-galactal triacetate) with the zinc chloride in acetic anhydride afforded compound VII. Presumably, like its precursor (compound III), VIII has the α-D configuration. Very weak long-range coupling was observed between the 1- and 5-protons of VII. As indicated above, it was not possible to examine the structure of the isomer, m.p. 83.5–84°, obtained from the mother liquor from the isolation of III. Most likely the compound is either the β anomer IV of III




or the 3-epimer V of I, since the compound was rapidly converted to VII on treatment with zinc chloride in acetic anhydride. The compound is not expected to be the anomer of VII since, in view of the two electronegative acetoxy groups at the 2-position, the anomerization would be expected to be much slower than was the observed conversion to VII.

In conclusion, as expected, treatment of I with acid appears to lead to the allylic oxocarbonium ion II. It may have been anticipated, in view of the stereochemical route of reaction followed in SN2′ reactions,[15] that reaction of the ion with acetic acid would take place at the anomeric center and lead to the β anomer IV of a 2-enose structure. The evidence requires the α-D configuration for the main product (III) of the reaction. The anomerization of IV to III can be expected to be very rapid and, therefore, it is not possible to decide as to whether III or IV is the first product of the reaction. The cation II could of course accept acetic acid at the 3-position to form V. As indicated above, an isomer of undetermined structure likely possesses either structure IV or structure V. Once formed, III can be expected to undergo facile cleavage of the C-4 to acetoxy group bond to form the allylic oxocarbonium ion VI. Interaction of VI with acetic acid can then afford compound VII. The formation of VII from the 4-epimer VIII of I would follow an analogous route of reaction.

## Experimental

**N.m.r. Spectra.**—The spectra were measured either at 60 Mc.p.s. on a Varian A-60 spectrometer or at 100 Mc.p.s. on a Varian HR-100 spectrometer. The spin-decoupling experiments were performed as previously described.[16]

**Tetra-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranose (III). A. Using Zinc Chloride in Acetic Anhydride.**—Fifty grams of tetra-*O*-acetyl-1-deoxy-α-D-*arabino*-1-enopyranose (I)[6] was dissolved at room temperature (24°) in 200 ml. of redistilled acetic anhydride containing 10 g. of freshly fused zinc chloride and a sample was observed in the polarimeter. In 7 min. the specific rotation was +50° and dropped to +49° in 3 additional min. The solution was then poured into 2 l. of ice and water under vigorous stirring. The separated sirup crystallized and was removed by filtration and washed with water; yield 34 g., m.p. 62–66°. Pure material was obtained on recrystallization from hot ethanol; m.p. 70–71°, $[\alpha]^{21}D$ +50° (*c* 3, ethanol-free chloroform).

*Anal.* Calcd. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49; $CH_3CO$, 45.0; mol. wt., 330.3. Found: C, 50.80; H, 5.42; $CH_3CO$.[17] 47.7; mol. wt. (freezing point in $C_6H_6$), 332; no. of olefinic bond,[18] 0.9.

The aqueous solution above was extracted with four 100-ml. portions of chloroform and the extract was washed successively with 5% aqueous sodium bicarbonate and water. The sirup obtained on solvent removal from the dried (decolorizing carbon) extract was dissolved in 50 ml. of ether and hexane was added to incipient opalescence; yield 6.6 g., m.p. 53–60°. On recrystallization from hot ethanol a further amount of III was obtained; yield 4.3 g.

**B. Using Sulfuric Acid in Acetic Anhydride.**—Compound III was also obtained using concentrated sulfuric acid (0.30 ml.) to replace the zinc chloride in the above reaction. The reaction was stopped after 5 min. at room temperature (24°) and processed as above. The crude yield was 45 g.

**C. Using *p*-Toluenesulfonic Acid in Acetic Acid.**—On adding 24 g. of I to 150 ml. of a 1:5 mixture of acetic anhydride and acetic acid containing 1.38 g. of *p*-toluenesulfonic acid hydrate,

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the specific rotation changed from −17.3° to +57.3° in 24 hr. At this time, disappearance of I was complete as indicated by the n.m.r. spectrum of the solution. Isolation of the product as described above provided 15.0 g. of crude crystalline III, m.p. 59–60°. The n.m.r. spectra of a sample purified by recrystallization from ethanol are shown in Figure 1.

**Tetra-*O*-acetyl-1(3)-deoxy-D-hex-1(2)-enopyranose (IV or V).**—The mother liquor from the 6.6-g. crop of III described in A above was concentrated to a sirup which was dissolved in a small volume of warm ether. Crystallization ensued on standing at 15°; yield 1.8 g., m.p. 76–81°. Pure material was obtained on further recrystallization from hot methanol; m.p. 83.5–84°, $[\alpha]^{23}D$ +151° (*c* 4.8, chloroform).

*Anal.* Calcd. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49; mol. wt., 330.3. Found: C, 50.94; H, 5.54; mol. wt. (freezing point in $C_6H_6$), 328; no. of olefinic bonds,[18] 0.8.

**Tetra-*O*-acetyl-(3,4-dideoxy-α-D-*glycero*-hex-3-enosulopyranose 2-hydrate) (VII). A. From Tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I).**—I (17.6 g.) was dissolved at room temperature (24°) in 250 ml. of redistilled acetic anhydride containing 12 g. of freshly fused zinc chloride and a portion of the solution was observed in the polarimeter. At the end of 20 hr., the specific rotation had dropped to −50° and the brown solution was poured into 2 l. of ice and water. A low yield of sirup separated which crystallized and was removed by filtration and washed with water; yield 2.6 g. A further small amount of product was obtained by chloroform extraction of the aqueous filtrate followed by solvent removal from the washed (successively with 5% aqueous sodium bicarbonate and water) and dried extracts and crystallization of the resultant sirup from acetone–hexane. Pure material was obtained on further recrystallization effected in the same manner; m.p. 122–123°, $[\alpha]^{22}D$ −183° (*c* 3.3, ethanol-free chloroform). Spectra at 100 and 60 Mc.p.s. are reproduced in Figure 3.

*Anal.* Calcd. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49; mol. wt. 330.3. Found: C, 50.60; H, 5.24; mol. wt. (freezing point in $C_6H_6$), 323; no. of olefinic bonds,[18] 0.8.

**B. From Tetra-*O*-acetyl-1-deoxy-D-*lyxo*-hex-1-enopyranose (VIII).**[5]—VIII (2.0 g.) was treated with acetic anhydride and zinc chloride as described above for I. After only 10 min. standing at room temperature, the reaction mixture was poured into 400 ml. of ice and water. The crystalline product was removed by filtration and washed with water; yield 1.33 g., m.p. 93–96°. After two recrystallizations from acetone–hexane the melting point was 122–123°, undepressed on admixture with VII prepared from I.

**C. From Tetra-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranose (III).**—III (3.0 g.) was dissolved in 60 ml. of redistilled acetic anhydride containing 4% of freshly fused zinc chloride and the rotation was observed in a polarimeter at 25°. The initial $[\alpha]^{25}D$ +33° dropped to −27° in 7 hr. after which the solution was too dark for polarimetric observation. After 23 hr. at room temperature, the solution was poured into 600 ml. of ice and water and the separated crystalline material was removed by filtration and washed with water; yield 0.5 g. Pure material was obtained on recrystallization from acetone–hexane; m.p. 122–123°, undepressed on admixture with authentic VII.

**D. From Tetra-*O*-acetyl-1(3)-deoxy-D-hex-1(2)-enopyranose (IV or V).**—The isomer of undetermined structure (IV or V) (250 mg.) was treated with acetic anhydride and zinc chloride as described in the preceding section and the product was isolated in the same manner; crude yield 50 mg. Pure material was obtained on recrystallization from acetone–hexane and was identified as VII by melting point and mixture melting point.

**Permanganate Oxidation of III to D-Arabinonic Acid.**—III (2.0 g.) was dissolved in 50 ml. of 95% ethanol at 35–40° and a solution of 3.84 g. (4 molar ratio) of potassium permanganate and 0.68 g. of potassium carbonate in 300 ml. of water was slowly added dropwise under mechanical stirring. The stirring was maintained for 30 min. after the addition, the manganese dioxide formed was then removed by filtration and washed with aqueous ethanol, and the filtrate was concentrated to a sirup under reduced pressure. The sirup was then dissolved in 25 ml. of warm absolute ethanol and 1.83 ml. of concentrated sulfuric acid was added. After 25–30 sec. the potassium bisulfate formed was removed by filtration and phenylhydrazine was added dropwise. Phenylhydrazine sulfate separated and was removed by filtration. More phenylhydrazine (1 ml.) was added and the solution was refluxed for 30 min. Crystals formed on concentrating the solution to 5 ml. and adding 8–9 ml. of benzene; dec. pt. 190–194°. Pure D-arabinonic acid phenylhydrazide was obtained on recrystallization from ethanol–benzene; dec pt. 211–213° (uncor.), unchanged on admixture with authentic material, $[\alpha]^{24}D$ −14° (*c* 0.8, water); lit.[19] dec. pt. 213–214°, $[\alpha]D$ −14° (water).

*Anal.* Calcd. for $C_{11}H_{16}N_2O_5$: C, 51.55; H, 6.30; N, 10.93. Found: C, 51.42; H, 6.47; N, 10.96.

**Conversion of III to 2-Deoxy-D-*erythro*-pentose.**—A 0.500-g. amount of III was added to a suspension of 100 mg. of 10% palladium on charcoal in 20 ml. of acetic acid at equilibrium with hydrogen at room temperature. On stirring for 4 hr. in the hydrogen atmosphere, 1.5 moles of hydrogen were consumed per mole of III.

A 10-g. amount of III in 75 ml. of acetic acid was subjected to the action of the palladium catalyst, 750 mg., and hydrogen at 35 p.s.i. for 15 hr. The catalyst was removed and the filtrate was evaporated *in vacuo* to a sirup. Examination of the sirup by chromatography on dimethyl sulfoxide impregnated paper and elution with Skellysolve B[20] showed the presence of two main zones with $R_f$ values relative to that of I of 1.19 and 1.44. The starting material (III) moved at the relative rate of 1.04. Alkaline silver nitrate[21] was used as spray reagent. The n.m.r. spectrum (Figure 2) of the sirup in chloroform showed two signals at τ 3.77 and 4.00 in the region expected for absorption by the anomeric protons of acetylated sugars. The total intensities of these signals relative to the multiplet in the region τ 4.7–5.3 was 0.16. The latter multiplet, attributable to the two protons on secondary carbons bonded to acetoxy groups, had an intensity, relative to bands in the τ 5.7–6.2 region and assignable to the C-5 and the two C-6 protons, of 0.62. The rough doublet centered at τ 6.31 and the rough triplet centered at 6.51 together had an intensity 0.58 times that of the 5.7–6.2 bands. As normally found for acetylated deoxy sugars, signals attributable to the methylenic group are present in the region for the acetoxy group signals.

The sirup, 6.9 g., was deacetylated by allowing a solution in 20 ml. of 10% triethylamine in 1:1 water–methanol to stand for 8 hr. at room temperature. Evaporation of the solvents left 4.15 g. of a sirupy residue which was examined by chromatography on Whatman No. I paper using the 1-butanol–ethanol–water (5:1:4) system. Two spots were detectable by spraying with alkaline silver nitrate[21] with $R_f$ values relative to glucose of 3.1 and 3.7 after the chromatogram had run for 68 hr. Only the faster moving spot was readily detectable using the periodate–permanganate spray reagent.[22]

Titration of 32.8-mg. samples with aqueous sodium metaperiodate showed a rapid consumption of 0.125 mmole of the oxidant in 30 min. This was followed by the slow consumption of a further 0.14 mmole after 49 hr.

A 664-mg. sample was dissolved in 50 ml. of glacial acetic acid and 51.9 ml. of 0.085 *M* lead tetraacetate in glacial acetic acid was added. After 19 hr. at room temperature, a solution of 554 mg. of oxalic acid dihydrate in 20 ml. of glacial acetic acid was added. After 15 min., the precipitate was removed by filtration and washed with methanol. Evaporation of the combined filtrates left a sirup which gave, on paper chromatography as described above for the starting material, only one spot with alkaline silver nitrate spray. The $R_f$ value was indistinguishable from that found for 2-deoxy-D-*erythro*-pentose. The sirup was added to a 28-mm.-diameter column prepared from 30 g. of acid-washed Celite[23] using the 1-butanol–water system. Examination of the fractions showed the substance with the $R_f$ value of 2-deoxy-D-*erythro*-pentose to be in the 350–510-ml. fraction of the eluate. Concentration left 136 mg. of sirup which was exchanged with deuterium oxide for n.m.r. spectroscopy. The spectrum showed the signals present in a spectrum of 2-deoxy-D-*erythro*-pentose measured under the same conditions. The presence of a considerable amount of impurity was indicated by the presence of a multiplet in the τ 6.5–6.9 region nearly twice the intensity of the signals for the deoxypentose at τ 4.35 and 4.63.

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A sample of the sirup was treated with aniline in ethanol[24] at the reflux temperature for 4 hr. On concentration, cooling, and nucleation, a crystalline precipitate was deposited which was gathered by filtration, washed with ether, and dried. The melting point, 162–165°, was undepressed on admixture with authentic aniline of 2-deoxy-D-*erythro*-pentose. The infrared spectra were indistinguishable. The yield of the anilide was 8% based on the amount of sirup oxidized by lead tetraacetate.

**Hydrogenation of VII.**—VII (100 mg.) rapidly consumed 2 moles of hydrogen per mole of VII when hydrogenated in methanol using Adams platinum catalyst. The n.m.r. spectrum of the product was in good agreement with that expected for a crude dideoxyhexose diacetate. Deacetylation using triethylamine in aqueous methanol gave a sirup which on paper chromatography showed two spots using the alkaline silver spray of about equal intensities and with $R_f$ values relative to that of glucose of 6.6 and 9.3 after 21 hr. of development under the conditions described above for hydrogenated and deacetylated III.

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# Halogen and Nucleoside Derivatives of Acyclic 2-Amino-2-deoxy-D-glucose.[1,2] II

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A series of synthetic transformations is described involving mixed acyclic C-1 derivatives of 3,4,5,6-tetra-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucose aldehydrol. The 1-bromo-1,1-dideoxy-1-ethylthio derivative I can be readily converted, by replacement of bromine by an acetoxy group, into the compound II. Treatment of the *O*-ethyl (or methyl) *S*-ethyl thioacetal derivative III with chlorine gives the corresponding 1-*O*-alkyl-1-deoxy chloride IV. The chlorine atom of the latter readily undergoes replacement by nucleophiles, for example, the acetoxy group (to give V) and the 6-acetamido-9-purinyl group (to give VI). The acyclic nucleoside derivatives VI are readily *N*-deacetylated to give the acyclic adenine 1-*O*-alkyl nucleoside derivatives (VIII) by the way of the picrate salts (VII); *O*-deacetylation was effected with methanolic ammonia. All isolated products were obtained crystalline and in high yield.

In the preceding paper[3] we reported the preparation of acyclic 1-halogeno derivatives in the fully blocked 2-amino-2-deoxy-D-glucose structure, by halogenation of appropriate diethyl dithioacetal derivatives. Replacement of halogen by alkoxide or 6-acetamido-9-purinyl groups afforded acyclic mixed monothioacetal or acylic nucleoside derivatives, respectively, all having an ethylthio group at C-1. The present work describes the conversion of acyclic mixed monothioacetals in the 3,4,5,6-tetra-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucose structure into the corresponding 1-alkoxy-1-chloro derivatives by replacement of the 1-ethylthio group by chlorine. The chlorine atom can be replaced by an acetoxy group, to give 1-*O*-acetyl-1-*O*-alkyl aldehydrol derivatives, and, by a 6-acetamido-9-purinyl group, to give acyclic nucleoside derivatives having an alkoxy group at C-1. The formation of a 1-*O*-acetyl-1-ethylthioaldehydrol derivative is also demonstrated.

The acyclic bromo sugar I, which is readily prepared from 3,4,5,6-tetra-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucose diethyl dithioacetal by treatment with bromine,[3] is smoothly converted by the action of mercuric acetate in acetic acid into 1,3,4,5,6-penta-*O*-acetyl-1,2-dideoxy-2-(2,4-dinitroanilino)-1-ethylthio-D-glucose aldehydrol (II). Attempted replacement of the ethylthio group in this compound by halogen under the usual conditions[3,4] gave sirupy, unstable products which were not well suited for synthesis of acyclic nucleoside derivatives.

The acyclic monothioacetal derivative 3,4,5,6-tetra-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucose diethyl monothioacetal[3] (III, R = $C_2H_5$) underwent reaction in dichloromethane solution with an excess of chlorine to give 3,4,5,6-tetra-*O*-acetyl-1-chloro-1,2-dideoxy-2-(2,4-dinitroanilino)-1-*O*-ethyl-D-glucose aldehydrol (IV, R = $C_2H_5$) in high yield as a stable, crystalline compound. The crystalline 1-*O*-methyl analog IV (R = $CH_3$) could be prepared by a corresponding procedure. Both compounds could be stored up to several months at room temperature in a desiccator before darkening and decomposing. Each compound underwent reaction with mercuric acetate in acetic acid to give the corresponding crystalline 1,3,4,5,6-penta-*O*-acetyl-1-*O*-alkyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucose aldehydrol V (R = $C_2H_5$ or $CH_3$) in good yield.

Condensation of the chloro derivatives IV (R = $C_2H_5$ or $CH_3$) with 6-acetamido-9-chloromercuripurine, under the general conditions of Davoll and Lowy,[5] to give the fully blocked acyclic nucleoside derivatives VI (R = $C_2H_5$ or $CH_3$), followed by *N*-deacetylation[6] with picric acid in boiling methanol, gave the corresponding 3,4,5,6-tetra-*O*-acetyl-1-(9-adenyl)-1-*O*-alkyl-1,2-dideoxy-2-(2,4-dinitroanilino)-D-glucose aldehydrols as the crystalline picrate salts VII (R = $C_2H_5$ or $CH_3$), in good yield. Each of the picrate salts behaved as a single compound, was homogeneous by thin layer chromatography, exhibited a sharp melting point, and gave good elemental analytical values.

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