The Synthesis of 3-Deoxy-D-arabino-heptulosonic Acid 7-Phosphate*

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The demonstration that enolpyruvate-P plus D-erythrose 4-phosphate is converted enzymically to shikimic acid led to the suggestion (1) that the first intermediate in this process was 3-deoxy-D-arabino-heptulosonic acid 7-phosphate (Compound V, Fig. 1). It was postulated that the newly formed hydroxyl group on C-4 had the stereochemistry shown in Compound V since it would then correspond to that of C-3 of 5-dehydroquininate, the end product of the expected C-2-C-7 cyclization of 3-deoxy-D-arabino-heptulosonic acid 7-phosphate. In order to confirm the proposed structure of the intermediate (2) and to make it available for a study of its enzymic conversion to 5-dehydroquininate (3), it was decided to synthesize 3-deoxy-D-arabino-heptulosonic acid 7-phosphate by the series of reactions shown in Fig. 1.

Starting with 2-deoxy-D-arabino-hexose (2-deoxy-D-glucose), the cyanohydrin was prepared and hydrolyzed, and the methyl 3-deoxy-D-gluc-o-heptonate (I) was isolated. Tritylation and then benzylation of Compound I gave the tetra-O-benzoyl-D-O-trityl methyl ester (II). This compound was detritylated by catalytic hydrogenolysis and then esterified with diphenylphosphorochloridate to yield Compound III, which was not isolated. Unmasking of the phosphate group by catalytic hydrogenolysis (the benzene rings were reduced in this process) and saponification of the cyclohexylcarboxylic and methyl ester groups afforded 3-deoxy-D-glucose heptonic acid 7-phosphate (IV), which was isolated as a crystalline cyclohexylammonium salt. The latter was oxidized by a pyridine-vanadium pentoxide reagent, and the resulting 3-deoxy-D-arabino-heptulosonic acid 7-phosphate (V) was purified by ion exchange chromatography and isolated as a noncrystalline barium salt.

The hydroxyl group on C-2 of the methyl 3-deoxyheptonate (I) had the D-glycero configuration, since oxidation of Compound I with periodate to 2-oxysuccinaldehyde acid, followed by oxidation of the latter with silver oxide, gave 3-deoxy-D-glyceroxetaric (D-malic) acid. In the cyanohydrin synthesis from aldoses “the isomer which is more readily accessible is the one that carries its hydroxyl on carbon atoms 2 and 4 in trans relationship” (4). It would appear, therefore, that this rule may apply also to 2-deoxyaldoses.

In the aldonic acids it has been shown that the phenylhydrazides (6), amides (7), benzamidazoles (7), and alkali metal salts (8) are dextrorotatory if the hydroxyl group on C-2 is on the right, and vice versa. This relationship holds also for the methyl esters I and II, and the cyclohexylammonium salt IV, as well as the amide prepared from I. All of these compounds rotate to the right, as would be expected from derivatives of a 3-deoxy homologue of D-gluconic acid.

Attempts were made to prepare the tetrabenzoyl trityl derivative of methyl 3-deoxy-D-manno-heptonate from the oil remaining after the crystallization of I. However, a weakly levorotatory pentabenzoyl methyl ester was obtained instead. This was converted to a levorotatory deoxyheptonic amide, in contrast to the dextroretoratory amide derived from I, indicating that the pentabenzonate was derived from 3-deoxy-D-manno-heptonate acid formed in the cyanohydrin reaction as a minor product.

It is of interest that after decarboxylation of the salt of IV there was a rapid decrease in dextrorotation followed by a slower equilibration to a levorotatory solution. This would be expected from Hudson’s lactone rule (9), since formation of the more stable γ-lactone would involve a hydroxyl group of the D-glycero configuration; i.e. the lactone ring would be to the left of the Fischer projection with the carboxyl group placed uppermost.

The oxidation of IV to DAHP was at first achieved with potassium chlorate and vanadium pentoxide as in the procedure for the oxidation of gluconic and galactonic acids to their 2-keto analogues (10). It was found, however, that the yields were unpredictable, occasionally almost no DAHP being obtained. The modified conditions described under “Experimental Procedure” were found to be consistent and gave good yields. There was some evidence that the DAHP was decarboxylated to a small extent to a deoxyhexose phosphate. During chromatography of the oxidation mixtures on Dowex 1-C1, a small fraction showing an absorption maximum at 530 nm (11) in the thiobarbiturate assay appeared before elution of the unoxidized IV. Decarboxylation of α-keto acids to aldehydes has been observed recently in oxidations by vanadium pentoxide (12). The barium salt of DAHP was essentially pure as shown by its chromatographic behavior (2) and by its good elementary analysis. All attempts to prepare a crystalline cyclohexylammonium salt of DAHP failed. Crystalline sodium and ammonium salts could be obtained, but they were hygroscopic and difficult to handle.

In the dry state, infrared spectra of salts of DAHP show a band at 6.25 μ due to the carboxylate ion, but no bands between 5.5 and 6.0 μ. This would preclude the presence of a free carboxyl group and would suggest that DAHP exists in the pyranoid form. Because of its relative bulkiness, the carboxyl group of DAHP would probably assume the more stable equatorial position, corresponding to the α-anomer (V).

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† Career Investigator of the American Heart Association.

1 The abbreviation used is: DAHP, 3-deoxy-D-arabino-heptulosonic acid 7-phosphate.
The oxidation with periodate of DAHP, like that of ulosonic acids in general, gives rise to 2-oxosuccinaldehydeic acid (12, 13). Difficulties were encountered, however, in determining the periodate consumption. In the volumetric methods of determining periodate (14, 15), molecular iodine reacted with the products of DAHP oxidation. Attempts to use spectrophotometric methods (16-18) were complicated (19) by the appearance of a strong absorption at 279 m\(\mu\). On the assumption that 1 mole of absorbing material was produced per mole of DAHP, the molar absorbancy index of the product at 279 m\(\mu\) was 12,500 when the reaction was conducted at pH 7 or 8. At pH 4.6 this value was 9,400, and raising the pH to 8 restored the higher absorption. Under strongly acidic reaction conditions (20), a d-lactone produced from the p-anomer of DAHP would be a rather strained bicyclic structure. Alternative type of compound, the pentahydroxy acid produced by the hydroxylation of shikimic acid with osmium tetroxide. Treatment of this pentahydroxy acid with periodate is known to yield 2-oxosuccinaldehydic acid as shown by the isolation of its bis-2,4-dinitrophenylhydrazone (21).

It is of interest that the potassium salt of DAHP has a molar rotation of +6,300 whereas removal of cations by Dowex 50 (H\(^+\)) results immediately in a solution with a molar rotation of +12,100, exhibiting no mutarotation. Most aldonic acids show small rotations in comparison with their salts or lactones (8, 9). If Hudson's lactone rule (9) applies, this large increase in dextro-rotation may be due to the formation of a lactone involving a hydroxyl of the \(\alpha\)-configuration, i.e. a \(\delta\)-lactone. As shown by Dreiding models, a \(\delta\)-lactone produced from the \(\beta\)-anomer of DAHP would be a rather strained bicyclic structure. Alternatively, the increased rotation of the free acid relative to the salt may be due to the formation of a 5-membered hydrogen-bonded structure between the carbonyl oxygen of the carboxyl group and the hydrogen of the anomeric hydroxyl.

**EXPERIMENTAL PROCEDURE**

*Methyl 3-Deoxy-\(\beta\)-gluco-hepbnate (I)—* To 25.7 g (0.16 mole) of 2-deoxy-\(\beta\)-arabino-hexose dissolved in 80 ml of water and cooled in ice were added cold solutions of 40.0 g (0.23 mole) of calcium acetate monohydrate in 80 ml of water and 10.0 g (0.21 mole) of NaCN in 80 ml of water, and the reaction mixture was allowed to stand overnight in the refrigerator. After the addition of 11 g (0.15 mole) of Ca(OH)\(_2\), the mixture was heated for 4 hours on a steam bath with occasional shaking, and cooled. The above was combined with an identical second preparation of 2-deoxy-\(\alpha\)-arabino-hexose and all other reagents and solvents were “Reagent” grade.

The residue was taken up in 75 ml of dry methanol and 0.7 g of anhydrous HCl in 10 ml of dry methanol was added. Crystallisation began after several minutes, and after chilling for 3 hours in an ice bath, the crystals were collected (41 g, m.p. 169-172\(^{\circ}\)). On standing overnight at 0\(^{\circ}\), another 2.3 g were deposited, m.p. 169-172\(^{\circ}\). This material is sufficiently pure to be used in the next step. Analytical sample, recrystallized from methanol, m.p. 175-176\(^{\circ}\), exhibited no mutarotation and was used in the next step.

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Concerning periodate consumption (14, 15), molecular iodine reacted with the products of DAHP oxidation. Attempts to use spectrophotometric methods (16-18) were complicated (19) by the appearance of a strong absorption at 279 m\(\mu\). On the assumption that 1 mole of absorbing material was produced per mole of DAHP, the molar absorbancy index of the product at 279 m\(\mu\) was 12,500 when the reaction was conducted at pH 7 or 8. At pH 4.6 this value was 9,400, and raising the pH to 8 restored the higher absorption. Under strongly acidic reaction conditions (20), a d-lactone produced from the p-anomer of DAHP would be a rather strained bicyclic structure. Alternatively, the increased rotation of the free acid relative to the salt may be due to the formation of a 5-membered hydrogen-bonded structure between the carbonyl oxygen of the carboxyl group and the hydrogen of the anomeric hydroxyl.
and treated with 11.1 ml of 0.54 M solution of 0.45 g (2 mmoles) of ester (I) in 12 ml of H2O was kept at 10°C and treated dropwise with 1.6 g of SrCl2 in 4 ml of H2O. The precipitate was removed by centrifugation, and the supernatant solution was stirred magnetically for 1 hour at room temperature with thoroughly washed Ag2O (prepared from 5.0 g of AgNO3 and 30 ml of 1 N NaOH). The Ag2O was removed by centrifugation, and the supernatant solution and washings were passed through a column of Dowex 50 (H+). The eluate was evaporated to dryness in a vacuum, and the crystalline residue was extracted with acetone. Evaporation of the solvent and crystallization from ethyl acetate-ligroin gave 76 mg, m.p. 102–104°C. Recrystallization from the same solvent gave 40 mg, m.p. 103–105°C, no depression with authentic d-malic acid. \([\alpha]D +394°.\]

Configuration of I: Conversion of I to d-Malic Acid—A solution of 0.45 g (2 mmoles) of ester (I) in 12 ml of H2O was kept at 10°C and treated with 11.1 ml of 0.54 M solution of 0.45 g (2 mmoles) of ester (I) in 12 ml of H2O was kept at 10°C and treated dropwise with 1.6 g of SrCl2 in 4 ml of H2O. The precipitate was removed by centrifugation, and the supernatant solution was stirred magnetically for 1 hour at room temperature with thoroughly washed Ag2O (prepared from 5.0 g of AgNO3 and 30 ml of 1 N NaOH). The Ag2O was removed by centrifugation, and the supernatant solution and washings were passed through a column of Dowex 50 (H+). The eluate was evaporated to dryness in a vacuum, and the crystalline residue was extracted with acetone. Evaporation of the solvent and crystallization from ethyl acetate-ligroin gave 76 mg, m.p. 102–104°C. Recrystallization from the same solvent gave 40 mg, m.p. 103–105°C, no depression with authentic d-malic acid. \([\alpha]D +394°.\]

Methyl 3-Deoxy-2,4,5,6-tetra-benzoyl-7-trityl-D-gluco-heptonic Acid (II)—To 8.0 g (0.036 mole) of the thoroughly dried methyl ester in 200 ml of pyridine (dried over BaO) were added 10.8 g (0.039 mole) of triphenylmethyl chloride. The reaction mixture was allowed to stand at room temperature for 48 hours, 2 ml of water were added, and the rotation was determined. Authentic n-malic acid, \([\alpha]D +20.2 (c, 2.01 \text{ in } H_2O).\] The infrared spectrum was consistent with the structure of a primary amide.

Methyl 3-Deoxy-2,4,5,6,7-pentabenzoyl-D-manno-heptonic Acid—Attempts to apply the above procedure to 19 g of colored syrup remaining from the crystallization of Compound I did not give rise to a tetrabenzoyl trityl deoxyheptonic, but to a pentabenzoyl heptonic. Presumably tritylation of the syrup failed as a result of the difficulty of obtaining it sufficiently dry.

The chloroform solution obtained at the end of the procedure was evaporated to dryness, and the residue was treated with boiling methanol. Filtration while still hot yielded 11 g of a tan crystalline product, m.p. 160–171°C. (Much triphenylcarbinol was recovered from the mother liquors.) Two recrystallizations from hot methyl acetate with a little methanol yielded a product, m.p. 150–181°C, which gave an analysis for a methyl deoxypentabenzoylheptonate. \([\alpha]D +5° (c, 2.50 \text{ in } CHCl_3).\]

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The catalyst was removed by filtration and washed with methyl acetate. The filtrate and washings were evaporated to an oil under reduced pressure, and the residue was dried over P₂O₅ in a desiccator evacuated with a mechanical pump to yield a glassy solid (15 g).

The product was dissolved in 40 ml of dry pyridine, 10.2 g (0.038 mole) of diphenylphosphorochloridate were added slowly with chilling, and the mixture was placed in a refrigerator overnight.

After the addition of 0.5 ml of water to decompose excess reagent most of the pyridine was removed in a vacuum, and 200 ml of ether were added to the residue. The resulting solution was extracted with successive 200-ml portions of cold water, 1 M HCl, 1 M NaHCO₃, and water. The solvent was removed under reduced pressure, and ethanol was added several times and evaporated under reduced pressure.

The residual oil (containing crystals of triphenylmethane) was dissolved in 250 ml of absolute ethanol. 3.5 g of platinum oxide catalyst were added, and hydrogenation continued (overnight) until no additional hydrogen was taken up. The catalyst was filtered off and washed with ethanol, 200 ml of 1 M NaOH were added to the alcoholic solution (800 ml), and the mixture was allowed to stand at room temperature overnight. The solution was reduced at the water pump to 100 ml, 100 ml of water were added, and the mixture was extracted with ether to remove triphenylmethane. The aqueous solution was treated with 100 ml of Dowex 50 (H⁺) and stirred mechanically for 5 minutes. The resin was removed by filtration and washed with water, and the combined filtrate and washings were extracted three times with ether to remove cyclohexanecarboxylic acid. The aqueous solution was immediately brought to pH 9 with redistilled cyclohexylamine and reduced to dryness at the water pump, and the residue was dried over P₂O₅ under high vacuum. The white crystalline product (9.2 g, m.p. 152-157°) was dissolved in 40 ml of dry pyridine, 10.2 g of potassium acetate were added, and hydrogenation continued (overnight) in a current of hydrogen (100 liters per hour) with stirring at room temperature (22-25°). The solution was adjusted to pH 3.6 (pH meter) with HCl and pyridine and transferred to a small glass-stoppered Erlenmeyer flask with 1 ml of H₂O, and the suspension was stirred with a magnetic stirrer at room temperature (22-25°) for exactly 16½ hours. The dark gray-green clear solution was passed through a column (2 cm in diameter) of 15 ml of Dowex 50 (H⁺), and the green filtrate was passed through a second 15 ml of the resin, yielding a white, clear solution. The columns were washed thoroughly with water, the combined filtrate and washings were brought to pH 6 with NH₄OH, and 680 mg (2.7 mmoles) of barium acetate were added. The solution was evaporated in a vacuum to 15 ml at 30°, more NH₄OH was added to pH 8, and the barium salts were precipitated by the addition of 2 volumes of absolute alcohol. After cooling in an ice bath for several hours the precipitate was removed by centrifugation, washed three times with 5 ml of cold 70% ethanol and once with 5 ml of absolute ethanol, and dried in a vacuum at room temperature. The yield of crude barium salt was 850 to 900 mg, containing 65 to 75% of DAHP as shown by intensity of absorption maximum at 549 μm in the periodate-thiobarbiturate assay (13).

The crude barium salt was suspended in water and dissolved by the addition of 5 ml of Dowex 50 (H⁺). After removal of the resin by filtration, the filtrate was passed through a column of 5 ml of Dowex 50, and the resin was washed thoroughly with water. The combined filtrate and washings were brought to pH 8 with NH₄OH and the volume was adjusted to 300 ml. This solution was loaded at a rate of 1.5 to 2.0 ml per minute on a 10-ml column (1.3 cm in diameter and 7 cm high) of Dowex 1-X8 (chloride form, 200 to 400 mesh, finely divided and washed thoroughly with 3 N HCl and water). The column was washed with 100 ml of water and eluted with 0.01 N HCl on an automatic fraction collector, and the fractions (50 ml each) were neutralized with NH₄OH. The effluent became acid after three fractions, and Fractions 4 and 5 contained small amounts of inorganic phosphate and unidentified impurities showing an absorption maximum at 530 μm in the thiobarbiturate assay. Unoxidized IV (approximately 0.4 mmoles of organic phosphate) was eluted in Fractions 6 to 10, followed by four fractions devoid of any phosphate. Elution was now begun with 0.02 N HCl; 25-ml fractions were collected, neutralized with NH₄OH, and tested by the periodate-thiobarbiturate assay. After two fractions devoid of activity, 0.5 to 0.9 ml of DAHP was obtained in the subsequent nine fractions. The neutralized solutions containing IV and DAHP were treated with 165 and 290 mg, respectively, of barium acetate, and reduced in a vacuum to 15 and 20 ml, respectively. After adjusting to pH 8 with NH₄OH, adding absolute ethanol to 60% concentration (v/v), and chilling in an ice bath, the barium salts were collected by centrifugation, washed three times with cold 60% ethanol and once with absolute ethanol, and dried in a vacuum at room temperature.

Yield, 6 9.2° (c, 5.00 in water); 5 minutes after treatment of this solution of the salt with Dowex 50 (H⁺), [α]₂² +9.1° (c, 2.3), calculated for the lactone; after 25 minutes [α]₂² +5.6; after 4 hours [α]₂² -12.2°; after 20 or 28 hours [α]₂² -21°.

5-Deoxy-α-arabino-heptulosonic Acid 7-Phosphate (V)—The catalyst for the oxidation was prepared as follows: 750 mg of V₂O₅ were dissolved in 45 ml of concentrated HCl, and 45 ml of pyridine were added rapidly with cooling. The resulting suspension was adjusted to pH 3.2 with HCl and pyridine. It can be stored without special precautions for several months.

The tricyclohexylammonium salt of IV (1.6 g, 17 mmoles) and 0.10 g (0.82 mmoles) of KClO₃ were dissolved in 2 ml of water in a small beaker, and 3 ml of the catalyst suspension were added. The reaction mixture was adjusted to pH 3.6 (pH meter) with HCl and pyridine and transferred to a small glass-stoppered Erlenmeyer flask with 1 ml of H₂O, and the suspension was stirred with a magnetic stirrer at room temperature (22-25°) for exactly 16½ hours. The dark gray-green clear solution was passed through a column (2 cm in diameter) of 15 ml of Dowex 50 (H⁺), and the green filtrate was passed through a second 15 ml of the resin, yielding a white, clear solution. The columns were washed thoroughly with water, the combined filtrate and washings were brought to pH 6 with NH₄OH, and 680 mg (2.7 mmoles) of barium acetate were added. The solution was evaporated in a vacuum to 15 ml at 30°, more NH₄OH was added to pH 8, and the barium salts were precipitated by the addition of 2 volumes of absolute alcohol. After cooling in an ice bath for several hours the precipitate was removed by centrifugation, washed three times with 5 ml of cold 70% ethanol and once with 5 ml of absolute ethanol, and dried in a vacuum at room temperature. The yield of crude barium salt was 850 to 900 mg, containing 65 to 75% of DAHP as shown by intensity of absorption maximum at 549 μm in the periodate-thiobarbiturate assay (13).

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155 mg of the barium salt of IV, which can be used for the recovery of its cyclohexylammonium salt, and 400 to 600 mg of barium DAHP. Dried in a vacuum over P₂O₅ at room temperature, this salt was apparently a tetrahydrate which lost 6.3% of its weight in a vacuum at 100°C (calculated, 6.4%). The resulting dehydrated gave the following analysis.

\[
\text{C₉H₇O₇Ba₃·4H₂O}
\]

Calculated: C 15.94, H 2.66, P 5.88, Ba 39.09
Found: C 15.94, H 2.57, P 5.90, Ba 39.45

For polarimetric measurements 0.100 g of the barium salt (tetrahydrate) in water was converted to the potassium salt with twice the required amount of K₂SO₄ in a volume of 2 ml. \( [\alpha]_D^{20} +15.7^o \) (c, 3.82 as potassium salt). Similarly, 100 mg of the barium salt in water were treated with Dowex 50 (H⁺) and the solution of the free acid was made up to 3.7 ml. \( [\alpha]_D^{20} +42^o \) (c, 1.47 as free acid) read immediately or after 24 hours.

Infrared spectra of the barium salt in KBr showed a band at 6.25 μ (carboxylate ion), but no absorption between 5.5 and 6.0 μ (carbonyl region).

In the periodate-thiobarbiturate assay DAHP showed \( [\alpha]_D^{20} = 42,500 \) (13) or 45,500 (20). In the semicarbazide reaction (24) \( \lambda_{m} = 7,800 \).

**Oxidation of DAHP with Periodate**—A 1.82 mm solution (1 ml) of potassium DAHP prepared from the barium salt as described previously was added to 10 ml of 2.76 mm NaIO₄ in 0.1 M phosphate buffer, pH 8, and 2.8-ml aliquots were withdrawn at intervals and treated with 0.15 ml of 0.5 M sodium arsenite. After 15 minutes they were read in a Cary spectrophotometer against a similarly treated blank solution. (Fifteen minutes were required to destroy excess periodate at this pH, 90% of it being destroyed in 2 minutes.) A strong absorption appeared with a maximum at 279 μ and a minimum at 240 μ, which reached half-maximal intensity in 5 minutes and maximal intensity in 45 minutes. On the assumption that 1 mole of absorbing material was produced from 1 mole of DAHP, \( \lambda_{m} = 12,500 \). This material was further attacked by periodate, but was stable when excess reagent was destroyed with arsenite.

A similar study in 0.1 M acetate buffer, pH 4.6, gave \( [\alpha]_D^{20} = 9,400 \) (the rate of reaction being the same as at pH 8), which rose to the previous value of 12,500 after the addition of NaOH-Na₂HPO₄ buffer to pH 8. When the oxidation was carried out with periodate in 0.1 M H₂SO₄ and excess reagent was destroyed with arsenite under acidic conditions (29), \( \lambda_{m} \) was at 264 μ and \( [\alpha]_D^{20} = 1,600 \). After neutralization, \( \lambda_{m} \) shifted to 279 μ and \( [\alpha]_D^{20} \) was again 12,500.

**Oxidation of 1, 3, 4, 5, 6-Pentahydroxy cyclohexanecarboxylic Acid with Periodate**—A solution of 100 mg (0.58 mmole) of shikimic acid, 0.4 ml of 1% OsO₄, and 100 mg of NaClO₄ in 8 ml of H₂O was allowed to stand for 16 hours at room temperature, and was extracted four times with 5 ml of benzene. A periodate-thiobarbiturate assay (20) was performed on 0.04 ml of a solution diluted 1:5 (corresponding to 0.049 μmole of shikimic acid), and showed \( A_{420} \) at 2, 5, 20, and 40 minutes of 0.25, 0.35, 0.36, and 0.27, respectively. At 5 minutes this corresponded to a color development obtained (after 20 minutes) from 0.033 μmole of DAHP, or 72% of the shikimate originally present.

Oxidation of 1 ml of the same solution (0.825 μmole of pentahydroxy acid) for 5 minutes with 10 ml of 2.76 mm NaIO₄ at pH 8, as described for DAHP, gave a maximum with \( A_{280} = 1.14 \). This value corresponds to \( [\alpha]_D^{20} = 15,000 \), and is somewhat higher than that obtained with DAHP.

**2-Hydroxypyruvulinic Acid Derivative of 3-Deoxy-d-arabino-heptulosonic Acid—**The methyl ester (I) was oxidized as in the method of Regina and Coldwell (10), except that the solvent was methanol. The reaction mixture was shaken at room temperature for 4 days, and inorganic salts and starting material were removed by filtration. Evaporation of the filtrate in a vacuum left a sirup which reduced Fehling's solution. Recrystallized α-phenylenediamine (374 mg) in 1.2 ml of 1 N HCl was added to 280 mg of the sirup. After 2 days at room temperature the crude hydroxypyruvulinic (83 mg) was recrystallized twice from water (once with a little charcoal, m.p. 195-196°C. \( [\alpha]_D^{20} = 7,640; \]

\[ \text{C}_9\text{H}_7\text{N}_2\text{O}_4 \]

Calculated: C 55.7, H 5.75, N 10.0
Found: C 55.6, H 6.07, N 10.0

**SUMMARY**

1. 3-Deoxy-d-arabino-heptulosonic acid 7-phosphate was synthesized in good yield as a pure barium salt.
2. In the initial stage of the synthesis 3-deoxy-d-arabinoheptose is converted (via the cyanohydrin) into crystalline methyl 3-deoxy-d-gluco-heptonate, which is the major product, and sirup 3-deoxy-d-manno-heptonate.
3. A modified vanadium pentoxide method was developed for the oxidation of polyhydrosalic acid to ulosonic acids.
4. Salts of 3-deoxy-d-arabino-heptulosonic acid 7-phosphate exist in a pyranoid form, probably assuming the structure of the α-anomer (Fig. 1, V).
5. The ultraviolet-absorbing material produced by periodate oxidation of 3-deoxy-d-arabino-heptulosonic acid 7-phosphate, and of other compounds expected to give rise to 2-oxosuccin-aldehydic acid, has spectral properties consistent with the structure of the latter compound in enol form.

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The Synthesis of 3-Deoxy-d-arabino-heptulosonic Acid 7-Phosphate

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