$\Delta^{9(11)}$-Dehydro-21-norprogesterone.—A slurry of 0.08 g. of palladium-on-strontium carbonate containing 2% palladium in 4 ml. of isopropyl alcohol was hydrogenated at atmospheric pressure at 25°. Then 0.350 g. of $\Delta^{9(11),16}$-bisdehydro-21-norprogesterone (XVII) was added and washed in with 2 ml. of isopropyl alcohol, and the hydrogenation was continued until one molecular equivalent of hydrogen was added. The reaction mixture was filtered and the isopropyl alcohol was removed *in vacuo*. Trituration with ether yielded 0.17 g. of crystals, m.p. 127–131°, $[\alpha]^{25}D$ +120°.

$\Delta^{9(11)}$-Dehydro-21-norprogesterone-20-ethylene Glycol Acetal (XVI).—The procedure for the reaction between $\Delta^{9(11)}$-dehydro-21-norprogesterone and ethylene glycol was the same as for the preparation of XIII. A 71% yield of XVI was obtained, m.p. 173–176°. The analytical sample was recrystallized from methanol, m.p. 177–180°, $[\alpha]^{25}D$ +79.1°.

Anal. Calcd. for $C_{22}H_{30}O_3$: C, 77.2; H, 8.8. Found: C, 76.8; H, 8.9.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Occurrence of the (1 → 3)-Linkage in Starches[1]

BY M. L. WOLFROM AND A. THOMPSON[2]

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The presence of a small number of α-D-(1 → 3)-linkages in amylopectin is shown by the isolation, by means of carbon and silicate column chromatography, of 3-*O*-α-D-glucopyranosyl-D-glucose (nigerose), as its β-D-octaacetate, from the acid hydrolyzate of amylopectin under conditions in which its formation by reversion is negligible.

It is now generally accepted, on the basis of methylation[3–5] and rotational[6] studies, that the principal linkage in starch is α-D-(1 → 4), in agreement with the long known fact that enzymic degradation of starch produces maltose[7] as the major product. Freudenberg and co-workers[4] found that completely methylated potato starch, upon hydrolysis, yields 90% of 2,3,6-tri-*O*-methyl-D-glucose, 5% of 2,3,4,6-tetra-*O*-methyl-D-glucose and approximately 5% of a mixture of di-*O*-methyl-D-glucoses, consisting mainly of 2,3-di-*O*-methyl-D-glucose. These data indicate that a glycosidic linkage may occur at both carbons 6 and 4 in a small proportion of the D-glucose units later shown[8] to be located in the predominant amylopectin fraction of the starch. This observation has been confirmed by later workers[9] who have isolated isomaltose (6-*O*-α-D-glycopyranosyl-D-glucose) as its crystalline β-D-octaacetate from the acetylated acid hydrolyzate of amylopectin, prepared under conditions minimizing reversion products to a negligible quantity.[10]

Evidence obtained from periodate oxidation[11] indicates that some of the dextrans contain (1 → 2)- or (1 → 3)-linkages. Nigerose[12] ("sakebiose"[13] or the sugar of the "γ-acetate,"[14,15] 3-*O*-α-D-glucopyranosyl-D-glucose) has been isolated[12] from the acid hydrolyzate of the polysaccharide "mycodextran" or "nigeran" produced by the action of *Aspergillus niger* on sucrose. Periodate oxidation of amylopectin[16] followed by reduction and hydrolysis produces a small amount of D-glucose, which, assuming complete reaction, indicates the presence of either (1 → 3)-linkage alone or of both (1 → 2)- or (1 → 3)- and (1 → 4)-linkages in the same D-glucopyranose unit.

We wish to present herein definitive evidence for the presence of the 3-*O*-α-D-glucopyranosyl linkage in the amylopectin molecule. This evidence consists of the isolation of 3-*O*-α-D-glucopyranosyl-D-glucose as its crystalline β-D-octaacetate from an amylopectin (waxy maize starch) acid hydrolyzate produced under conditions in which the formation of this disaccharide during the hydrolysis is negligible.[10,14] Therefore, a small amount of an α-D-(1 → 3)-linkage exists preformed in the amylopectin molecule. The finding[17] that intestinal extracts hydrolyze nigerose offers further support for the presence of this linkage in starches.

Experimental

3-*O*-α-D-Glucopyranosyl-β-D-glucose Octaacetate from Amylopectin Acid Hydrolyzate.—Amylopectin (32.4 g. of waxy maize starch, equivalent to 36 g. of D-glucose) was suspended in 9000 ml. of 0.1 *N* hydrochloric acid solution and stirred in a boiling water-bath. The hydrolysis was followed by

(1) Preliminary communication: M. L. Wolfrom and A. Thompson, THIS JOURNAL, **77**, 6403 (1955).

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(3) W. N. Haworth, E. L. Hirst and J. I. Webb, *J. Chem. Soc.*, 2681 (1928).

(4) K. Freudenberg and H. Boppel, *Ber.*, **73**, 609 (1940); K. Freudenberg and G. Hüll, *ibid.*, **74**, 237 (1941); K. Freudenberg, *ibid.*, **76A**, 71 (1943).

(5) C. C. Barker, E. L. Hirst and G. T. Young, *Nature*, **147**, 296 (1941).

(6) K. Freudenberg, *Chem.-Ztg.*, **60**, 853, 875 (1936).

(7) C. O'Sullivan, *J. Chem. Soc.*, **25**, 579 (1872); **29**, 478 (1876).

(8) K. Meyer, M. Wertheim and P. Bernfeld, *Helv. Chim. Acta*, **23**, 865 (1940).

(9) M. L. Wolfrom, J. T. Tyree, T. T. Galkowski and A. N. O'Neill, THIS JOURNAL, **72**, 1427 (1950); **73**, 4927 (1951).

(10) A. Thompson, M. L. Wolfrom and E. J. Quinn, *ibid.*, **75**, 3003 (1953).

(11) Allene Jeans, W. C. Haynes, C. A. Wilham, J. C. Rankin, E. H. Melvin, Marjorie J. Austin, J. E. Cluskey, B. E. Fisher, H. M. Tsuchiya and C. E. Rist, *ibid.*, **76**, 5041 (1954).

(12) S. A. Barker, E. J. Bourne and M. Stacey, *J. Chem. Soc.*, 3084 (1953).

(13) K. Matsuda, G. Hiroshima, K. Shibasaki and K. Aso, *J. Fermentation Technol.* (Japan), **32**, 498 (1954); *Tohoku J. Agr. Research*, **5**, 239 (1954); *C. A.*, **49**, 8554 (1955).

(14) A. Thompson, Kimiko Anno, M. L. Wolfrom and M. Inatome, THIS JOURNAL, **76**, 1309 (1954).

(15) S. Peat, W. J. Whelan and Kathleen A. Hinson, *Chemistry & Industry*, 385 (1955).

(16) M. Abdel-Akher, J. K. Hamilton, R. Montgomery and F. Smith, THIS JOURNAL, **74**, 4970 (1952).

(17) J. Larner and R. E. Gillespie, *ibid.*, **78**, 882 (1956).

alkaline copper reduction and was stopped at 67% of completion by cooling to room temperature. Four such runs were made. The acid was removed from the cooled solution by passage through a column of Duolite A-4.[18] A preliminary separation was made on a column (900 × 70 mm.) of Unground Nuchar C[19] which had been pretreated by washing with 4 liters of 1% hydrochloric acid followed by 20 liters of water, 4 liters of 1% ammonium hydroxide solution and again with water until the effluent reached a *p*H of 7. The four amylopectin hydrolyzates were filtered successively through the carbon column, the D-glucose being removed by washing with water after the addition of each portion. The column was then washed with 5% ethanol (about 20 liters) until the effluent gave a negative Benedict test for reducing sugar. This effluent was concentrated to a sirup under reduced pressure, yield 24.5 g.

The dry sirup was acetylated by heating at the boiling point with 12 g. of sodium acetate and 200 ml. of acetic anhydride. After cooling, the reaction mixture was poured into 500 g. of ice and water, and after 3 hr. was extracted with chloroform. The chloroform solution was dried with anhydrous sodium sulfate and evaporated under reduced pressure to a sirup which was crystallized from ethanol (95%); yield 18.2 g. of β-maltose octaacetate which, after one recrystallization from ethanol (95%), showed m.p. 154–155°, $[\alpha]^{28}D$ +64° (*c* 4.5, chloroform). The mother liquor was evaporated under reduced pressure to a sirup, yield 22 g. This sirup was dissolved in benzene and chromatographed in 5-g. portions on Magnesol[20]–Celite[21] (5:1 by wt.) columns (275 × 75 mm., diam.) and developed with 4000 ml. of benzene–*t*-butyl alcohol (100:1 by vol.). The extruded and streaked (with 1% potassium permanganate in 10% sodium hydroxide) column showed a zone 190–220 mm. from the column top. A second zone occurred just above the first with only a slight interspace. The materials in these zones were eluted with acetone and evaporated to sirups under reduced pressure. The combined material from the bottom zone crystallized from ethanol (95%) as β-isomaltose octaacetate. The sirup (5 g.) from the combined upper zones was rechromatographed on Magnesol–Celite, as before, using 5000 ml. of benzene–*t*-butyl alcohol as developer. The bottom zone, 190–220 mm. from the top of the column, produced 200 mg. of β-isomaltose octaacetate; total yield from all columns 1.67 g., which, after one recrystallization from ethanol (95%), gave material of m.p. 144–146°, $[\alpha]^{28}D$ +98° (*c* 4.4, chloroform).

The material from the acetone eluate of the column section, located 110–190 mm. from the column top, was crystallized from ethanol (95%); yield 300 mg., m.p. 140–145°, $[\alpha]^{25}D$ +80° (*c* 3.2, chloroform). An additional yield of 50 mg. was obtained by rechromatography, performed in the manner described above, of the crystallization mother liquors. After further recrystallization from ethanol (95%), the melting point was 151–153°. The X-ray powder diffraction pattern was identical with that of known[14] β-nigerose octaacetate.

(18) A product of the Chemical Process Co., Redwood City, Calif.

(19) A product of the West Virginia Pulp and Paper Co., New York, N. Y.

(20) A product of the Westvaco Chemical Division of the Food Machinery and Chemical Corp., South Charleston, W. Va.

(21) A product of the Johns-Manville Co., New York, N. Y.

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[CONTRIBUTION FROM THE NATIONAL RESEARCH COUNCIL OF CANADA, PRAIRIE REGIONAL LABORATORY]

A Chemical Synthesis of Sucrose. A Conformational Analysis of the Reactions of 1,2-Anhydro-α-D-glucopyranose Triacetate[1]

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Sucrose was synthesized by reaction of 1,2-anhydro-α-D-glucopyranose triacetate with sirupy 1,3,4,6-tetra-*O*-acetyl-D-fructose. The ability of the anhydride to form α-D-glucopyranosides is rationalized on the basis of its conformation and the stereochemical requirements for opening of the epoxide ring.

The reaction of 1,2-anhydro-α-D-glucopyranose triacetate (Brigl's anhydride[4]) with sirupy 1,3,4,6-tetra-*O*-acetyl-D-fructose[5] has afforded a chemical synthesis of sucrose.[6] The synthesis was anticipated[7] on the basis of a conformational analysis of the properties of the anhydride. It is therefore of some interest to consider this matter in detail.

It can be assumed that the pyranose ring of Brigl's anhydride possesses the half-chair conformation of cyclohexene oxide.[8] On this basis, the conformation of the anhydride is either II or III. Which of these two forms is the more stable, and the height of the energy barrier which separates the two forms, cannot be anticipated. Nevertheless, it has become clear that the substance possesses an inherent tendency to react in form II. The anhydride very likely is liberated in the latter conformation from the reaction of 3,4,6-tri-*O*-acetyl-β-D-glucosyl chloride (I) with ammonia since the reaction most probably involves replacement of axial chlorine through nucleophilic attack at C_1 by anionic C_2-oxygen in axial orientation in accordance with the steric requirements for neighboring group participation[9] and elimination reactions.[10]

The anhydride clearly shows a strong preference for reaction at the anomeric center rather than at C_2 since glucopyranosides are formed in high yield when the substance reacts with alcohols.[4,11–13] This tendency is not surprising in view of the attachment of C_1 to the ring-oxygen atom. It appears well established[14] that the preferred reaction route in the opening of an epoxide situated on a

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(4) P. Brigl, *Z. physiol. Chem.*, **122**, 245 (1922).

(5) W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, **68**, 2171 (1946).

(6) A preliminary account of this work has been reported in Communications to THIS JOURNAL, **75**, 4118 (1953).

(7) R. U. Lemieux, *Can. J. Chem.*, **31**, 949 (1953).

(8) B. Ottar, *Acta Chem. Scand.*, **1**, 283 (1947).

(9) S. Winstein and R. M. Roberts, THIS JOURNAL, **75**, 2297 (1953).

(10) D. H. R. Barton and E. Miller, *ibid.*, **72**, 1066 (1950).

(11) W. J. Hickinbottom, *J. Chem. Soc.*, 3140 (1928).

(12) E. Hardegger and J. De Pascual, *Helv. Chim. Acta*, **31**, 281 (1948).

(13) Stig Veibel, *ibid.*, **31**, 736 (1948).

(14) A. Furst and P. A. Plattner, Abs. Papers, 12th International Congress of Pure and Applied Chemistry, p. 409 (1951).