uct from 1,2-benzanthracene is the 10-aldehyde, and this on Wolff–Kishner reduction affords the carcinogenic 10-methyl compound. The 10-nitrile and 10-α-hydroxyethyl derivatives have also been prepared and various reactions of 9-anthraldehyde investigated.

CONVERSE MEMORIAL LABORATORY
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The Preparation of α- and β-Gentiobiose Octaacetates

BY DELBERT DANIEL REYNOLDS AND WILLIAM LLOYD EVANS[1]

Recent investigations in this Laboratory gave rise to a need for considerable quantities of β-gentiobiose octaacetate. The five most important methods for its preparation are as follows: (1) isolation from gentian root,[2] (2) the action of emulsin on glucose to form gentiobiose, which is then connected to β-gentiobiose octaacetate,[3,4] (3) the catalytic hydrogenolysis of amygdalin followed by acetylation,[5] (4) separation from the commercial mother liquors ("Hydrol") obtained in the manufacture of glucose[6] and (5) the condensation of acetobromoglucose with β-*d*-glucose-1,2,3,4-tetraacetate by means of the Königs–Knorr reaction.[7]

The inferior quality of most gentian root renders the first method undesirable. The second method proved objectionable for two reasons, namely, (1) from ten to twelve weeks are required to complete the synthesis, and (2) emulsin is not readily available. The third method has not been tried in this Laboratory because of the relatively high cost of amygdalin. Since the percentage of gentiobiose in "Hydrol" varies greatly, this method leaves much to be desired.

A yield of 23.4% of the theoretical value has been reported for the fifth method.[7] This low yield may be attributed to numerous possible side reactions. The most probable of these is the reaction of acetobromoglucose with water in the presence of silver oxide to form β-*d*-glucose-2,3,4,6-tetraacetate, silver bromide and water. The water formed in this reaction may react with more acetobromoglucose, thus setting up a series of changes which would continually use up the acetobromo compound. Moreover, the β-*d*-glucose-2,3,4,6-tetraacetate may react with acetobromoglucose in the presence of silver oxide to form a trehalose octaacetate and more water. Accordingly, the yield of the β-gentiobiose octaacetate would be greatly lowered.

It was the purpose of this work to make the latter method a practical one for the preparation of β-gentiobiose octaacetate by reducing these side reactions to a minimum. This may be accomplished only if the reaction is carried out under anhydrous conditions. Such conditions are realized by (1) ensuring complete absence of water at the beginning of the reaction and (2) removal of the water from the reaction mixture as rapidly as it is formed, thus keeping the concentration of water in the reaction mixture relatively small at any given time. A preliminary stirring of the tetraacetate, silver oxide and chloroform with a large excess of Drierite assures complete absence of water when the reaction is begun. The addition of a chloroform solution of acetobromoglucose over a considerable period of time, as opposed to adding it in one large portion, permits only a small amount of water to be formed at any given time. The water formed during the reaction may be removed by employing an effective internal desiccant. Studies in this Laboratory[8] have shown that anhydrous calcium sulfate (Drierite) is an excellent substance for this purpose. Other investigators[9] have used powdered calcium chloride in similar reactions. By proceeding with the foregoing facts in mind, β-gentiobiose octaacetate has been obtained in yields as high as 82% of the theoretical value.

After β-gentiobiose octaacetate had been obtained in good yields, it seemed reasonable to believe that α-gentiobiose octaacetate might be prepared by the same method even though α-*d*-glucose-1,2,3,4-tetraacetate could be obtained

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(1) Presented at the Milwaukee Meeting of the American Chemical Society, September 8, 1938.

(2) E. Bourquelot and H. Herissey, *Compt. rend.*, **132**, 571 (1901); *Bull. Soc. chim.*, [3] **29**, 363 (1903).

(3) E. Bourquelot, H. Herissey and J. Coirre, *Compt. rend.*, **157**, 732 (1913).

(4) J. F. Leete, Ph.D. Dissertation, The University of Greifswald, Greifswald, 1929.

(5) M. Bergmann and W. Freudenberg, *Ber.*, **62**, 2783 (1929).

(6) H. Berlin, THIS JOURNAL, **48**, 2627 (1926).

(7) B. Helferich and W. Klein, *Ann.*, **450**, 219 (1926).

(8) L. C. Kreider and W. L. Evans, THIS JOURNAL, **58**, 797 (1936).

(9) B. Helferich, E. Bohm and S. Winkler, *Ber.*, **63**, 990 (1930).

only as a sirup. Since the preparation of 6-trityl-β-*d*-glucose-1,2,3,4-tetraacetate is always accompanied by the formation of the α-isomer, the sirupy α-*d*-glucose-1,2,3,4-tetraacetate may be prepared advantageously from this source. This affords a new and convenient method for the synthesis of α-gentiobiose octaacetate. Thus the over-all yield of gentiobiose octaacetate is greatly increased.

Experimental Part

Purification of Chloroform.—U. S. P. chloroform (500 cc.) was shaken with 12% sulfuric acid for one hour on a mechanical shaker. The chloroform layer was separated, neutralized by a saturated solution of sodium bicarbonate and washed well with water. It was then shaken for an hour with calcium chloride (100 g.), filtered and distilled. After drying for a short time over phosphorus pentoxide, the chloroform was redistilled and stored over Drierite.

Silver Oxide.—The silver oxide was prepared according to the method of Helferich and Klein.[7]

Trityl Chloride.—The trityl chloride was prepared after the method of Gomberg[10] in a modified apparatus and under such conditions that the pure compound was obtained. A mixture of anhydrous aluminum chloride (150 g.) and dry thiophene-free benzene (500 cc.) was placed in a two-liter wide-mouthed bottle equipped with a mercury-sealed stirrer, a dropping funnel and a side tube leading to a beaker of water. Stirring was begun and a mixture of dry carbon tetrachloride (100 cc.) and dry benzene (70 cc.) was added through the dropping funnel. The solution was stirred for an additional hour and then refluxed in a round-bottomed flask until hydrogen chloride was no longer evolved. It was then cooled and poured into a three-liter separatory funnel containing 350 g. of ice and 300 cc. of concentrated hydrochloric acid. The benzene layer was separated immediately and the water portion extracted with benzene. The combined benzene portions were washed with 1:1 hydrochloric acid solution and then dried over calcium chloride. The benzene solution was decolorized by heating it with Carboraffin. The benzene was removed completely under reduced pressure by heating on a water-bath. The residue was refluxed for twenty minutes with acetyl chloride (200 cc.) and allowed to cool. The trityl chloride crystallized at once in a very pure state: m. p. 112–113° (corr.); yield 230 g. (80%).

6-Trityl-β-*d*-glucose-1,2,3,4-tetraacetate.—6-Trityl-β-*d*-glucose-1,2,3,4-tetraacetate and the corresponding α-isomer have been prepared from both trityl chloride and trityl bromide. Experiments in which equivalent quantities of the trityl halide compounds were used gave approximately the same percentage yield of the 6-trityl-*d*-glucose-1,2,3,4-tetraacetates. Since trityl bromide is obtained quantitatively in the detritylation process, its re-use reduces both the cost and time of subsequent preparations.

The trityl chloride method as used by Helferich[11] was modified such that the time of preparation was shortened considerably.

A mixture of anhydrous glucose (120 g.), trityl chloride (193.2 g.) and anhydrous pyridine (500 cc.) was shaken mechanically at room temperature. Solution was effected within five hours. Acetic anhydride (360 cc.) was added in one portion without cooling. After standing for about twelve hours the reaction mixture was poured into ten liters of ice water and stirred vigorously for three hours with a mechanical stirrer. The water was renewed once in the meantime. The white granular precipitate was filtered, washed and air dried. It was then mixed with U. S. P. ether (500 cc.) and filtered. This treatment removed most of the 6-trityl-α-*d*-glucose-1,2,3,4-tetraacetate. The insoluble portion was taken up in hot 95% ethanol. Upon cooling, the 6-trityl-β-*d*-glucose-1,2,3,4-tetraacetate crystallized in fine needles usually of sufficient purity for subsequent use. Recrystallization yielded the pure compound: yield 175 g.; m. p. 166–166.5° (corr.).

The trityl bromide method was carried out as follows: 50 g. of trityl bromide (m. p. 130°) obtained by detritylation of the 6-trityl-*d*-glucose-1,2,3,4-tetraacetate was digested in U. S. P. ether (150 cc.) at room temperature for fifteen minutes to remove most of the impurities. It was then filtered and dried. Thirty-eight grams of trityl bromide was recovered which melted at 151–152° (corr.) with slight softening at 147°.

Thirty-seven grams of trityl bromide thus obtained was shaken for eleven hours at room temperature with anhydrous glucose (20 g.) in dry pyridine (200 cc.). Acetic anhydride (60 cc.) was then added and the reaction mixture allowed to stand for twelve hours, after which it was poured into four liters of ice water and stirred vigorously for about five hours. The water was changed twice during this time. The precipitate was filtered, washed and air dried. It was then dissolved in hot 95% ethanol (800 cc.). The crude product (20.6 g.) after one recrystallization from ethanol (400 cc.) melted at 166–166.5° (corr.); yield 19.7 g.

β-*d*-Glucose-1,2,3,4-tetraacetate.—β-*d*-Glucose-1,2,3,4-tetraacetate was prepared according to the method of Helferich and Klein[7] except for the method of crystallization. The chloroform solution was concentrated to a very thick sirup. Anhydrous ether was added and the sirup rubbed with a glass rod. The tetraacetate separated immediately as small white crystals. This was further purified by dissolving it in the least possible amount of chloroform and adding anhydrous ether until crystallization began, the crystallization being complete in a very short time.

β-Gentiobiose Octaacetate.—Thirty-five grams (1 mol.) of β-*d*-glucose-1,2,3,4-tetraacetate, silver oxide (25 g.), Drierite (100 g.) preheated at 240° for two hours, and dry, alcohol-free chloroform (100 cc.) were placed in a 500-cc. three-necked round-bottomed flask equipped with a mercury-sealed mechanical stirrer, a calcium chloride drying tube and a dropping funnel. The flask was wrapped in black paper. The contents of the flask were stirred for about one hour to ensure the complete absence of water. After the manner of Helferich, Bohm and Winkler[9] 5 g. of iodine was then added to the reaction mixture. Acetobromoglucose (41.3 g., *i. e.*, 1 mol.) was dissolved in dry, alcohol-free chloroform (150 cc.) and then added through the dropping funnel to the reaction mixture over a course of about one hour. The stirring was then continued for an additional twenty-four hours. The reaction mixture was filtered through a layer of "Filter-Cel" and the residue

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(10) M. Gomberg, *Ber.*, **33**, 3144 (1900).

(11) B. Helferich, L. Moog and A. Junger, *ibid.*, **58**, 877 (1925).

washed well with U. S. P. chloroform. The filtrate was concentrated under reduced pressure and the white crystalline residue taken up in two liters of hot absolute ethanol. Upon cooling, the β-gentiobiose octaacetate separated as very pure white crystalline needles: m. p. 195–196° (corr.); yield 50.5 g., 74.1%.

***α-d*-Glucose-1,2,3,4-tetraacetate.**—*α-d*-Glucose-1,2,3,4-tetraacetate was prepared in a manner similar to that of β-*d*-glucose-1,2,3,4-tetraacetate with the following exceptions. The chloroform extract of the tetraacetate was shaken with an ice-cold, saturated solution of sodium bicarbonate in order to remove all acetic acid. It was then washed with ice water, dried over anhydrous sodium sulfate, filtered and concentrated to a thick sirup. The concentrate was taken up in a small amount of methanol and the triphenylcarbinol allowed to separate out. After filtering, the methanol was removed under reduced pressure and the resulting sirup repeatedly taken up in chloroform, and reconcentrated. The sirup thus obtained was dissolved in dry ether and shaken with calcium chloride in order to remove any water or methanol still present. The sirup remaining after the removal of the ether under reduced pressure was used for the preparation of α-gentiobiose octaacetate.

α-Gentiobiose Octaacetate.—Thirty-eight grams of the *α-d*-glucose-1,2,3,4-tetraacetate sirup, silver oxide (15 g.), preheated "Drierite" (75 g.), iodine (5 g.), acetobromoglucose (20 g.) and dry, alcohol-free chloroform (300 cc.) were used in this preparation. The reaction was carried out according to the method described for β-gentiobiose octaacetate. The sirup obtained by concentrating the chloroform solution of the reaction products was taken up in absolute ethanol (250 cc.) and rubbed with a glass rod. Crystallization began after a few minutes. A yield of 50.9% (16.8 g.) of α-gentiobiose octaacetate was obtained. After two recrystallizations the product melted at 191–192° (corr.) and $[\alpha]^{29.5}\text{D}$ +51.6° (*c*, 4.29; *l*, 2; $CHCl_3$) C. S. Hudson and J. M. Johnson[12] reported a m. p. 188–189° (corr.) and $[\alpha]^{30}\text{D}$ +52.4° for the product obtained by the action of acetic anhydride and zinc chloride on β-gentiobiose octaacetate.

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Summary

1. An improved Königs–Knorr synthesis has increased the yield of β-gentiobiose octaacetate from 23.4 to 75–80% of the theoretical.

2. A 50% yield of α-gentiobiose octaacetate has been obtained by condensing acetobromoglucose with *α-d*-glucose-1,2,3,4-tetraacetate. So far as the authors are aware, this is the first time that a 6-linked α-octaacetate has been prepared by this method.

3. The complete synthesis of α- and β-gentiobiose octaacetates by this method may be completed in approximately one week.

4. Trityl bromide, a side product, has been introduced as a tritylating agent, thus decreasing both the time and cost of preparing the gentiobiose octaacetates.

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[12] C. S. Hudson and J. M. Johnson, THIS JOURNAL, 39, 1272 (1917).

COLUMBUS, OHIO RECEIVED SEPTEMBER 3, 1938

NOTES

The Activity Coefficient of Perchloric Acid, and a Correction to the Value of the Argentous-Argentic Oxidation Potential in Perchloric Acid

BY DON DEVAULT

The calculation of activity coefficients by Pearce and Nelson[1] from their measurements of the vapor pressure of perchloric acid solutions is apparently incorrect. Rosenfeld[2] has completely recalculated their data, obtaining results varying from 7.0% higher at 0.6 molal to 85.4% lower at 12 molal. Professor Redlich[3] has checked his values. Professor William C. Bray and I have also recalculated the data. The method which Pearce and Nelson report using gave us activity coefficients about 5% lower than those of Redlich and Rosenfeld. Although we examined a number of possibilities, we could not find the source of disagreement with Pearce and Nelson.

Our values of the activity coefficients agree with those of Redlich and Rosenfeld if we substitute, as did they, activity coefficients of hydrochloric acid for those of perchloric acid at 0.6 molal and lower concentration. This procedure receives justification from the electromotive force measurements of Popoff, Riddich, Wirth and Ough,[4]

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[1] Pearce and Nelson, THIS JOURNAL, 55, 3075 (1933).

[2] Landolt–Börnstein, "Physikalisch-chemische Tabellen," Erg. B. III, 2144 (1936).

[3] Private communication to Professor Bray. See also Redlich, Rosenfeld and Stricks, THIS JOURNAL, 58, 375 (1936).

[4] Popoff, Riddich, Wirth and Ough, *ibid.*, 53, 1195 (1931).