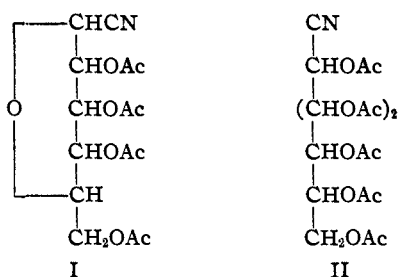


[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Researches on Nitrogenous Glycosides. III. Preparation of a Simple Cyanophoric Glycoside¹

BY LOUIS R. BUERGER

It is well known that alkyl halides interact with silver cyanide to form both nitrile and isonitrile derivatives. The author has applied this reaction with an halogenated sugar derivative, namely, tetraacetylbromoglycose, and finds that it interacts smoothly with silver cyanide to form a crystalline cyanophoric glycoside having the composition of 1-cyano-2,3,4,6-tetraacetyl-*d*-glycose. This glycoside does not exhibit the behavior of a normal cyanide on hydrolysis. It is characterized by the instability of the carbon-carbon linkage joining the cyanide radical to the glycoside and hydrocyanic acid is liberated under such conditions. The glycoside does not interact with mercury oxide at 75–80°, as would be expected if it had the structure of an isonitrile, and when treated with silver oxide in ammoniacal solution it does not undergo the reactions of Wohl² leading to the formation of lower sugar constructions. An explanation for this behavior is revealed by examination of the constitutional formulas of the glycosido-nitrile, and that of an acetylated cyanohydrin derivative of a sugar as represented in formulas I and II, respectively.



The glycosido-nitrile I is characterized by its behavior toward acetic anhydride and acetic acid. With both reagents it reacts to form pentaacetylglycose with loss of hydrocyanic acid. Albert³ has described a technique for the hydrolysis of acetylated cyanohydrins to acid amides which involves digesting of the cyanohydrin in acetic acid solution in the presence of zinc oxide. The

(1) This paper has been abstracted from a thesis presented by the author to the Faculty of the Graduate School of Yale University in June, 1934, in partial fulfillment of the requirements for the degree of Doctor of Philosophy (T. B. Johnson).

(2) Wohl, *Ber.*, **26**, 734 (1893); **32**, 3668 (1899).

(3) Albert, *ibid.*, **49**, 1384 (1916).

application of his procedure to 1-cyano-2,3,4,6-tetraacetylglycose leads to the formation of pentaacetylglycose. In fact, the cyanoglycoside is so unstable that it is decomposed by digesting with 50% acetic acid, 5% tartaric acid solution, and even by warming in water solution. The free hydrocyanic acid is easily detected by precipitation as silver cyanide.

Behavior toward Emulsin.—Some of the cyanoglycoside was dissolved in distilled water by warming at 80° and the concentration of the hydrogen ions adjusted to a pH of 4.2–4.4 by use of bromo cresol green as indicator. In each of two tubes 10 cc. of this solution was placed. To one was added 20 mg. of tested emulsin and the hydrogen-ion concentration properly adjusted. Both tubes were then incubated at 48–50° for one hour, and the course of the changes followed by the behavior of the respective solutions toward Fehling's solution.

It was observed that emulsin exercised no hydrolytic effect on the cyanoglycoside and that the latter slowly undergoes decomposition with loss of hydrocyanic acid by incubation at 45–50° when the hydrogen-ion concentration is 4.2.

1-Cyano-2,3,4,6-tetraacetyl-*d*-glycose, C₁₅H₁₉O₉N.—A solution of 41 g. of tetraacetylbromoglycose in 150 cc. of dry xylene was prepared, and in this was then suspended 15 g. of dry silver cyanide and the mixture refluxed for one hour under strong agitation by means of a motor stirrer. After cooling, the insoluble silver salts were separated by filtration, norite added to remove color, and finally the solution was diluted with petroleum ether until it became turbid. On standing at ordinary temperature the cyanoglycoside finally separated in crystalline form, but was contaminated by an oily residue. It was purified by repeated crystallizations from boiling ethyl alcohol and melted at 76°. The yield was 16 g.

The alcohol filtrates were combined and concentrated to remove excess of alcohol, when a thick oil was left behind. This distilled at 172° under 5 mm. pressure, and a yellow distillate was obtained with a carbonylamine odor which deposited crystals of the cyanoglycoside, melting at 76° on standing.

The cyanoglycoside is soluble in cold ethyl acetate, benzene, methyl alcohol, acetone, ether, chloroform and pyridine. It is slightly soluble in cold ethyl alcohol and water, and insoluble in petroleum ether.

Anal. Calcd. for C₁₅H₁₉O₉N: C, 50.40; H, 5.60; N, 3.93. Found: C, 50.37; H, 5.40; N, 3.93.

Conversion into β-Pentaacetylglycose.—A solution of 4 g. of 1-cyano-2,3,4,6-tetraacetyl-*d*-glycose was dissolved in 30 cc. of distilled acetic anhydride and the solution heated under pressure at 200° for two hours. The anhydride solution was then diluted with 150 cc. of chloroform,

washed with sodium bicarbonate solution and finally with cold water, and the chloroform solution then dried over calcium chloride. Addition of norite was necessary to clarify the solution. The solution was concentrated and finally diluted with petroleum ether, when the above acetyl derivative slowly separated in crystalline form. It was purified by crystallization from boiling ethyl alcohol and melted at 130°. The yield was 2.5 g. The compound did not contain nitrogen. The acetyl number was determined according to the method of Kunz.⁴ This same change with loss of the cyanide radical of the cyanoglycoside can also be brought about by heating 1-cyano-2,3,4,6-

triacylglycose with glacial acetic acid at 150° for two hours.

Anal. 0.1181 g. of substance required 16.2 cc. of 0.09495 *N* sodium hydroxide solution. The equivalent amount of β -pentaacetylglucose corresponds to 15.9 cc. of the alkali solution.

Summary

Tetraacetylglucose reacts with silver cyanide to form a cyanophoric glycoside, namely, 1-cyano-2,3,4,6-tetraacetyl-*D*-glucose melting at 76°.

NEW HAVEN, CONN.

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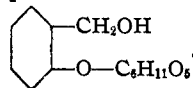
(4) Kunz, *This Journal*, **48**, 1982 (1926).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Structure of Populin

BY NELSON K. RICHTMYER AND ELEANOR H. YEAKEL

Populin, $C_{20}H_{22}O_8$, is a glucoside occurring in the bark, buds and leaves of certain species of poplar. It has long been known that alkaline cleavage produces benzoic acid and the glucoside salicin:



Since populin can be oxidized to benzoylhelicin, which contains a free aldehyde group, it follows that the benzoyl group is attached not to the ortho CH_2OH , but to one of the hydroxyl groups in the glucose residue.¹ Kitasato,² in 1927, attempted to determine the location of the benzoyl group by an enzymatic hydrolysis of populin with taka-diaxase, but was unsuccessful in obtaining the benzoyl glucose in a pure or crystalline form.

The following investigation was carried out with synthetic populin, prepared by the action of benzoyl chloride on salicin in the presence of aqueous alkali. The product, according to Dobbin and White,³ who devised the method, is identical with the naturally-occurring glucoside.

From the methylation of populin by means of methyl iodide and silver oxide, there was obtained a beautifully crystalline tetramethylpopulin. From this the benzoyl group was removed readily by the action of hot sodium methylate. The resulting crystalline tetramethylsalicin has one free hydroxyl group, which, barring a shift during the process of methylation, represents the point of

attachment of the benzoyl group in the original populin.

Acid hydrolysis of the tetramethylsalicin produced a sirupy trimethylglucose which was identified by conversion to the well-known 2,3,4-trimethyl- β -methylglucoside. Isolation of this derivative of 2,3,4-trimethylglucose shows that the benzoyl group was originally located on the sixth carbon atom of the glucose residue, and that populin may be designated as 6-benzoylsalicin.

That benzylation of other glucosides leads to the introduction of the first benzoyl group in the 6-position was established by the reaction of benzoyl chloride with *o*-cresylglucoside. The product, 6-benzoyl- β -*o*-cresylglucoside, was identical with desoxy populin; the latter was obtained by the hydrogenation of populin in the presence of palladium black, a reaction which is known to convert the ortho- CH_2OH to a $-CH_3$.

Experimental

Synthetic Populin.—A solution of 20 g. of salicin in 400 cc. of water was stirred vigorously while 25 g. of benzoyl chloride was added to it drop by drop in the course of about three hours; during that time the mixture was kept alkaline to phenolphthalein by the addition of aqueous potassium hydroxide. The product separated as a white granular solid which was filtered and washed well with water. The populin was separated from more highly benzoylated derivatives by extraction with boiling water; it crystallized from the cold solution in fine needles containing water of crystallization. A second crystallization, this time from alcohol, produced good-sized prisms which were solvent-free. The yield was only 8 g.; m. p. 178–179°, with sintering a few degrees lower. It showed $[\alpha]_D -2.0^\circ$ in pyridine ($c = 5$).

(1) See especially Piria, *Ann.*, **96**, 375 (1855).

(2) Kitasato, *Biochem. Z.*, **190**, 109 (1927).

(3) Dobbin and White, *Pharm. J.*, [IV] **19**, 233 (1904). See also Schiff, *Ann.*, **154**, 1 (1870).