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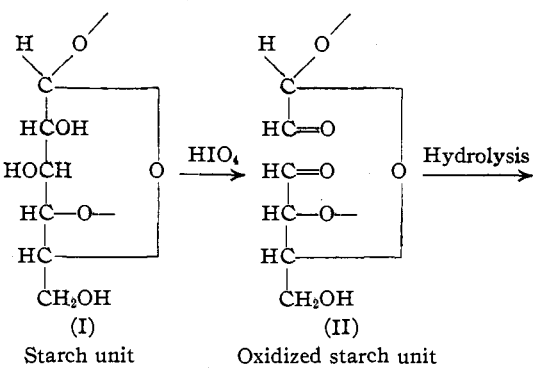
The Structure of the Products of the Periodic Acid Oxidation of Starch and Cellulose[1]

BY ERNEST L. JACKSON AND C. S. HUDSON

Cornstarch has been shown by us[2] to be oxidized readily by an aqueous solution of periodic acid with the consumption of about one mole of the oxidant per $C_6H_{10}O_5$ unit of starch. The quantity of the oxidant consumed was thus near the theoretical amount[3] required to oxidize the starch unit (I) to a product having structure (II). The structure of the product of the oxidation of cellulose by this reagent was suggested to be the same as (II), except that the glycosidic linkage at carbon atom 1 is beta for oxidized cellulose instead of alpha as in oxidized starch. The present article presents evidence to show that the products of the periodic acid oxidation of starch and cellulose possess the indicated structural units, respectively, as the principal component. This evidence does not exclude the possibility that other types of units may be present in minor quantities that have escaped detection.



The complete hydrolysis of (II) should yield glyoxal and *d*-erythrose. These two compounds have now been identified as products of the acid hydrolysis of both oxidized cornstarch and oxidized cotton cellulose. Glyoxal was identified as its phenylosazone and benzylphenylosazone. The presence of *d*-erythrose was established by the oxidation of the hydrolysis products with bromine water to produce oxalic and *d*-erythronic acids, the latter characterized as two well-known crystalline derivatives, brucine *d*-erythronate and *d*-erythronic lactone. The oxalic acid presumably was formed by the bromine oxidation of glyoxal. These results show that periodic acid breaks the carbon chain of the $C_6H_{10}O_5$ units of starch and cellulose between carbon atoms 2 and 3 to produce substances having the structures indicated. The smallness of the yields of the derivatives of glyoxal and *d*-erythrose, shown in Table I, is regarded as due, at least in part, to some destruction of the material, which evidently occurs during hydrolysis, and to incomplete degradation of the polymer; the presence of other types of units in minor quantities may also be a contributing factor.

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Jackson and Hudson, THIS JOURNAL, **59**, 2049 (1937).

(3) Jackson and Hudson, *ibid.*, **59**, 994 (1937).

TABLE I

DERIVATIVES OF GLYOXAL AND *d*-ERYTHROSE FROM OXIDIZED STARCH AND OXIDIZED COTTON

	Yield,[a] %	M.p. (uncorr.), °C	$[\alpha]^{20}D$ in water	Analyses, % Carbon Calcd.	Carbon Found		Hydrogen Calcd.	Hydrogen Found		Nitrogen Calcd.	Nitrogen Found
From oxidized starch											
Glyoxalphenylosazone[b] ($C_{14}H_{14}N_4$)	25	170–171	....	70.54	70.43	70.43	5.92	5.76	5.81	23.53	23.46
Glyoxalbenzylphenylosazone[c] ($C_{28}H_{26}N_4$)	33	199–200	....	80.33	80.41	80.41	6.27	6.13	6.18	13.40	13.24
Barium oxalate[d]	31	.....	....	...	.....		...	.....		...	...
Brucine *d*-erythronate[e] ($C_{27}H_{34}O_9N_2$)	22	211[f]	−22.6°[g]	61.10	60.77	60.59	6.46	6.47	6.36	...	...
d-Erythronic lactone[h] ($C_4H_6O_4$)	..	104–105[i]	−73.3°[j]	...	.....		...	.....		...	...
From oxidized cotton											
Glyoxalphenylosazone	18	170–171	....	70.54	70.58		5.92	5.93		...	...
Glyoxalbenzylphenylosazone	20	199–200	....	80.33	80.08		6.27	6.14		...	...
Barium oxalate[d]	20	.....	....	...	.....		...	.....		...	...
Brucine *d*-erythronate	15	211[f]	−22.5°[k]	61.10	60.80		6.46	6.38		...	...

[a] The yields refer to slightly impure first products; the other data were obtained after purification. [b] Fischer, *Ber.*, **17**, 575 (1884); **26**, 96 (1893); Harries and Temme, *ibid.*, **40**, 169 (1907); Hess and Uibrig, *ibid.*, **50**, 365 (1917); Karrer and Pfaehler, *Helv. Chim. Acta*, **17**, 363 (1934). [c] Ruff and Ollendorff, *Ber.*, **33**, 1809 (1900); Fenton, *J. Chem. Soc.*, 809 (1905); Karrer and Pfaehler, ref. *b*. [d] Oxalic acid was prepared and characterized by usual methods. [e] Ruff, *Ber.*, **32**, 3678 (1899); Jensen and Upson, THIS JOURNAL, **47**, 3021 (1925). [f] Decomposition. [g] *C*, 4.1. [h] Glattfeld, *Am. Chem. J.*, **50**, 149 (1913); Glattfeld and Forbrich, THIS JOURNAL, **56**, 1209 (1934); Jelinek and Upson, *ibid.*, **60**, 355 (1938); Erlbach, *Ber.*, **68**, 534 (1935); Ruff, ref. *e*; Jensen and Upson, ref. *e*. [i] A mixture with authentic *d*-erythronic lactone melted at 104–105° (uncorr.). *Anal.* Calcd. for $C_4H_6O_4$: 8.47 ml. of 0.1 *N* NaOH per 100 mg. Found: 8.61 ml. [j] *C*, 1.2. [k] *C*, 4.0.

Experimental

Glyoxal and *d*-Erythrose from Oxidized Starch.—Cornstarch[4] was oxidized under the conditions described in a previous paper[2] for the consumption of one mole of periodic acid.[5] The product was washed free from iodic acid with cold water and dried at 50°. A suspension of 10 g. of oxidized cornstarch in 400 ml. of distilled water was heated on the steam-bath for three hours. After filtration at 25° the solution was mixed with 50 ml. of *N* hydrochloric acid and then diluted to 500 ml. with water. The solution was kept at 98–99° in a stoppered flask for sixteen hours, then decolorized with activated carbon and neutralized with silver carbonate; the excess silver was removed as sulfide. Glyoxalphenylosazone was prepared by mixing 60% of this solution with 17 g. of phenylhydrazine and 75 ml. of ethanol, and keeping it at 50° for one hour. The product was recrystallized once from absolute ethanol and then from benzene. Glyoxalbenzylphenylosazone was prepared by the addition of cold concentrated aqueous solutions of 10.2 g. of sodium acetate trihydrate and 17.5 g. of benzylphenylhydrazine hydrochloride to 40% of the solution of the hydrolysis products. After about fifteen hours the gummy product was separated from the aqueous layer and purified by fractional crystallization from benzene.

For the identification of *d*-erythrose 9.8 g. of oxidized cornstarch was hydrolyzed as described above. After the solution had been decolorized with activated carbon, 12 ml. of bromine was dissolved in it and the mixture was kept in the dark at room temperature for four days. Excess bromine was removed by aeration and the solution was neutralized with barium hydroxide solution; this precipitated barium oxalate. The filtrate from the barium oxalate was freed from barium by sulfuric acid, from halogen ions by silver carbonate and from excess silver by hydrogen sulfide. The solution was concentrated *in vacuo* to 200 ml., mixed with 50 ml. of ethanol and heated on the steam-bath for three hours with excess of brucine. After removal of excess brucine by extraction with chloroform, the solution was concentrated *in vacuo* to a thick sirup which was crystallized from ethanol. *d*-Erythronic lactone was prepared in the usual way from the pure brucine *d*-erythronate. It was recrystallized from ethyl acetate.

Glyoxal and *d*-Erythrose from Oxidized Cotton.—Absorbent cotton was oxidized by aqueous periodic acid solution under the conditions described in the previous paper[2] for the consumption of 1.22 moles of the oxidant. A suspension of 6 g. of the product, which had been washed free from iodic acid with cold water and dried at 50°, in 240 ml. of water was heated on the steam-bath for twelve hours. The solution, after some insoluble material had been removed by filtration at 25°, was mixed with 30 ml. of *N* hydrochloric acid and then diluted to 300 ml. with water. The procedure for the hydrolysis and subsequent preparation of glyoxalphenylosazone and glyoxalbenzylphenylosazone was the same as that described for oxidized starch, one-half of the hydrolysis products being used to obtain each derivative.

Barium oxalate and brucine *d*-erythronate were prepared from the hydrolysis products of 6.1 g. of oxidized cotton. The procedure was the same as that used for oxidized starch.

The yields, analyses and characteristic physical constants of the various products from both oxidized starch and oxidized cotton are recorded in Table I.

(4) Potato starch is oxidized by periodic acid in a manner similar to cornstarch, except that under the same conditions the reaction proceeded more rapidly in the case of the potato starch which we used. A sample of potato starch (1.736 g. previously dried at 100° for eighteen hours), oxidized at 21–22° for twenty-four hours by 50 ml. of 0.535 *M* aqueous periodic acid solution, consumed 1.02 molecular equivalents of the oxidant. The product showed $[\alpha]^{20}D$ +8.6° in water which agrees with the value for oxidized cornstarch.[2]

(5) Preliminary experiments indicate that sodium metaperiodate ($NaIO_4$) may be substituted for periodic acid in the oxidation of starch; *cf.* Malaprade, *Bull. soc. chim.*, [5] **1**, 850 (1934).

We are indebted to Dr. J. W. E. Glattfeld of the University of Chicago for a sample of pure *d*-erythronic lactone and to Dr. W. T. Haskins of this Institute for carrying out some of the analyses.

Summary

The hydrolysis of the products of the periodic acid oxidation of cornstarch and cotton cellulose by 0.1 *N* aqueous hydrochloric acid at 98–99° has been shown to produce glyoxal and *d*-erythrose. These results prove that periodic acid breaks the carbon chain of the $C_6H_{10}O_5$ units of starch and cellulose between carbon atoms 2 and 3, and confirm the generally accepted structure of the predominating units in these polysaccharides. The possible presence of other types of units in minor quantities is not excluded by these results.

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CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE COLLEGE OF LIBERAL ARTS AND SCIENCES OF TEMPLE UNIVERSITY]

The Preparation of 3,7,12-Trioxy-23-aminonorcholane from Cholic Acid

BY WILLIAM T. CALDWELL

The remarkable role played by numerous derivatives of cyclopentanoperhydrophenanthrene in the initiation or maintenance of normal or abnormal growth imparts to them a peculiarly absorbing interest. However diverse the origins of sterols, bile acids, vitamin D, sex hormones, cardiac glycosides, toad poisons and carcinogenic hydrocarbons may be, their structural formulas suggest the possibility that various organisms may elaborate them from some common source or, at least, may be able to convert some of them into others. A comparison of the structures of such pairs of substances as pregnanediol and lithocholic acid, bufotalin and cholic acid or digitoxigenin and desoxycholic acid, makes clear the effect of changes involving, for the most part, the group attached to C-17; in the case of the last pair, it does not seem unreasonable to ascribe the marked difference in physiological action to the presence of the unsaturated lactone ring rather than to the change in position occupied by an hydroxyl group.

It seemed worth while, therefore, to attempt the preparation of various compounds by modifying the nature of the group attached to C-17. A consideration of the physiological activity of such substances as tyramine and histamine suggested that the introduction of an amino group into the radical attached to C-17 might result in the development of interesting pharmacological action; furthermore, if this could be done by a method such as the classic one due to Curtius, it would have the added value of an independent method of degradation made applicable to bile acids. This is no new thought as is quite clear from the statements made by Wieland, Schlichting and Jacobi[1] in the article in which they describe their very valuable method of degradation. After pointing out that attempts to degrade cholanic acid by way of the azide or amide had failed, they add, "So bestätigten zahlreiche Versuche—ein wenig erfreuliches und dem Aufwand an Arbeit nicht entsprechendes Ergebnis—nur wieder die mehrfach gemachte Erfahrung, dass an dem grossen Komplex des Gallensäure Moleküls die typischen Gruppenreaktionen häufig schwierig und regelwidrig ablaufen."[1a]

The application to cholic acid of Lindemann's modification of the Curtius reaction,[2] however, leads quite normally, as will be described below, to the formation of 3,7,12-trihydroxy-23-aminonorcholane.

A search of the literature disclosed the fact that Curtius himself had been interested in applying his method for the preparation of this same compound, reporting its preparation by E. Müller in the year 1906,[3] and giving to it the name "cholamine." However, many years later Borsche and Schwarz[4] called attention to the fact that the formation of this substance by Müller's method, involving, as it did, the

(1) Wieland, Schlichting and Jacobi, *Z. physiol. Chem.*, **161**, 80 (1926).

(1a) "Thus numerous experiments confirmed repeatedly the experience that, in the great complex of the bile acid molecule, the usual group reactions frequently proceed abnormally and with difficulty—a result giving little satisfaction and involving an incommensurate outlay of work."

(2) Lindemann, *Helv. Chim. Acta*, **11**, 1028 (1928).

(3) Curtius, *Ber.*, **39**, 1389 (1906).

(4) Borsche and Schwarz, *ibid.*, **60**, 1843 (1927).