concentrated to 25 cc. and cooled; long thick needles separated. It was recrystallized from 25 cc. of hot alcohol, in which it was very soluble; m. p. 175–176°; the yield was very good.

Anal. Calcd. for $C_8H_8O_2N_2$: C, 46.84; H, 6.30; N, 21.87. Found: C, 47.15, 46.93; H, 6.27, 6.21; N, 21.89.

Summary

1. Uracil-4-acetic acid was prepared by treating urea and citric acid with fuming sulfuric acid. This pyrimidine ring was easily ruptured by barium hydroxide solution and yielded the barium salt of β-carbamido-glutaconic acid.

2. Orotic acid was synthesized by oxidizing uracil-4-acetic acid in alkaline solution with potassium ferricyanide.

3. The possibility that orotic acid may be an intermediate in the synthesis of purines from histidine has been discussed.

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THE ACTION OF ACETIC ACID UPON CERTAIN CARBOHYDRATES[1]

BY H. T. CLARKE AND H. B. GILLESPIE

It has been shown[2] that native cellulose is esterifiable by the action of boiling acetic acid to a limited extent represented in the formula $C_{24}H_{39}$-$O_{20}(COCH_3)$, whereas hydrated cellulose under the same conditions can yield an ester of the limiting composition $C_{24}H_{36}O_{20}(COCH_3)_4$. A study of the behavior of other carbohydrates toward acetic acid was therefore undertaken in the hope of finding a clue to the nature of the factors which tend to restrict the esterifiability of cellulosic hydroxyl groups.

Reducing carbohydrates, such as glucose and fructose, caramelize under the influence of boiling acetic acid alone or in the presence of sodium acetate. This applies also to the two non-reducing carbohydrates of the furanose type which have been examined, namely, sucrose and inulin— a finding which need occasion no surprise, in view of the well-established ease with which the five-membered ring of sugars may be opened by acid reagents. The cyclic structure of non-reducing glycosides of the pyranose type, on the other hand, withstands the action of boiling acetic acid, and such compounds ultimately yield fully esterified products. Thus α-methylglucoside, β-methylglucoside and α-methylmannoside are converted into the corresponding tetraacetates, while potato starch yields a "tri-acetate." Similarly, mannitol is converted into its hexaacetate.

[1] Work supported by a research grant from The Chemical Foundation.

[2] C. J. Malm and H. T. Clarke, THIS JOURNAL, 51, 274 (1929).

These experiments thus throw little light upon the problems raised by the case of cellulose, beyond adding indirect confirmation of the view advanced by Hess and Trogus[3] that reactions with undissolved cellulose take place upon micellar surfaces.

The results obtained with potato starch nevertheless offer a certain intrinsic interest. This starch, which appears[4,5,6] to contain 96 to 98% of β-amylose, is at first esterified on treatment with boiling acetic acid in much the same way (though far more rapidly) as is hydrated cellulose, yielding as a primary product a "monoacetate" $C_6H_9O_5(COCH_3)$. At this stage the starch becomes soluble in acetic acid, and esterification continues until the composition approximates that of the "triacetate" $C_6H_7O_5(COCH_3)_3$.

The general properties of the products at various stages are shown in Table I. The faculty of yielding a blue color with iodine disappears when about 6% of acetyl has been introduced, but returns on removal of the acetyl groups by alkaline hydrolysis, the regenerated starch closely resembling ordinary "soluble starch." Progressive esterification is

TABLE I

Hours	% Acetyl	Acetic acid	Pyridine	Acetone	Ethyl acetate	Benzene	CHCl₃	85% CHCl₃ 15% EtOH	C₂H₂Cl₄	Ac₂O	Dioxane	75% EtOH-H₂O	50% EtOH-H₂O	25% EtOH-H₂O	H₂O	Color with iodine	$[\alpha]_{546}$ in pyridine	Reducing power (as % glucose)
1	4.6	−	−	−	−	−	−	−	−	−	−	−	−	−	±	Blue	−	−
2	6.0	−	±	−	−	−	−	−	−	−	−	−	−	−	+	Red	−	−
4	10.6	−	+	−	−	−	−	−	−	−	−	−	±	+	+	Brown		0
	20.5	+	+	−	−	−	−	−	−	−	−	±	+	+	+	Brown		−
8	19.7	−	+	−	−	−	−	−	−	−	−	±	+	+	+	Brown		−
	21.4	+	+	−	−	−	−	−	−	−	−	±	+	+	+	Brown		0
12	23.3	−	+	−	−	−	−	−	−	−	+	+	+	+	+	Brown	+163° (21)	−
	25.7	+	+	−	−	−	−	±	−	−	±	+	+	±	+	Brown	+172° (21)	−
18	27.7	+	+	+	−	−	−	+	−	−	+	+	+	±	±	Brown	+175° (22)	0
24	30.1	+	+	+	−	−	−	+	−	−	+	+	+	±	±	Brown	+187° (19)	−
36	31.3	+	+	+	−	−	−	+	−	−	+	+	+	−	−	Brown	+192° (19)	−
48	34.4	+	+	+	+	−	+	+	±	+	+	+	+	−	−	Brown	+187° (19)	0
72	35.4	+	+	+	+	−	+	+	+	+	+	+	+	−	−	Brown	+187° (21)	0.27
96	37.9	+	+	+	+	−	+	+	+	+	+	+	−	−	−	Brown		−
144	41.0	+	+	+	+	−	+	+	+	+	+	+	−	−	−	Brown		0.61
192	41.7	+	+	+	+	−	+	+	+	+	+	±	−	−	−	Brown		−
224	43.4	+	+	+	+	±	+	+	+	+	+	±	−	−	−	Brown		−
296	44.0	+	+	+	+	±	+	+	+	+	+	−	−	−	−	Brown		0.66
620	44.1	+	+	+	+	±	+	+	+	+	+	−	−	−	−	Brown		−

[3] Hess and Trogus, Z. physik. Chem., 15, 157 (1931).

[4] Taylor and Iddles, Ind. Eng. Chem., 18, 713 (1926).

[5] Haworth, Hirst and Webb, J. Chem. Soc., 2681 (1928).

[6] Baldwin, THIS JOURNAL, 52, 2907 (1930).

accompanied by increasing solubility in non-polar solvents, though in no case was solubility in 95% ethyl alcohol or ethyl ether observed. The lower esters are soluble in water; those of intermediate composition are soluble in aqueous ethyl alcohol of various ranges of concentration.

The products obtained by boiling potato starch with acetic acid alone for seventy-two hours and more yield, on alkaline hydrolysis, solutions possessing reducing power, the extent of this increasing with the duration of the treatment. This effect appears to be mainly due to the degrading action of the phosphoric acid which exists in combination with the 3% of α-amylose present in the starch, and may be largely suppressed by the addition of sodium acetate. In Table II are summarized the results of an experiment in which 110 g. of potato starch was boiled with 2200 cc. of acetic acid containing 1 g. of sodium acetate. The reducing power, estimated by the method of Folin and Wu,[7] is expressed as percentage of glucose in the starch acetate; detectable reduction occurred only with products obtained on boiling for 192 hours or more. Addition of the sodium acetate markedly retards the rate of esterification.

TABLE II

Time heated, hours	Acetyl, %	Solubility in acetic acid	Reducing power	Time heated, hours	Acetyl, %	Solubility in acetic acid	Reducing power
4	0.6	—	0	48	29.8	+	0
8	7.5	—	0	96	34.8	+	0
12	15.5	—	0	144	37.3	+	0
12	18.6	+	0	192	41.2	+	0.16
18	23.6	+	0	288	41.6	+	.32
24	27.1	+	0	384	43.3	+	.23

Apart from its reducing properties, the final product of the action of boiling acetic acid upon potato starch resembles the starch triacetates obtained by the methods of other workers, particularly that of Tsuzuki.[8] A triacetate of the same general properties, but lacking reducing power, may also be prepared by boiling the starch with acetic acid until it has dissolved and then completing the acetylation with acetic anhydride; we believe that this two-step process provides the most convenient method for preparing a starch triacetate. The products obtained by the methods of Haworth, Hirst and Webb[5] and of Hess and Smith[9] appear to be somewhat less degraded, inasmuch as they dissolve less readily and less completely in organic liquids.[10]

Table III shows the acetyl contents, reducing power and rotation in three solvents of triacetates obtained by various methods from the same

    [7] Folin and Wu, *J. Biol. Chem.*, **41**, 367 (1920). The authors are indebted to Miss Rhoda Howard for kindly making these determinations.

    [8] Tsuzuki, *Bull. Chem. Soc. Japan*, **3**, 276 (1928).

    [9] Hess and Smith, *Ber.*, **62**, 1619 (1929).

    [10] *Cf.* Brigl and Schinle, *ibid.*, **62**, 99 (1929).

sample of potato starch. With the exception of the product prepared according to the directions of Hess and Smith, which gelatinized rather than dissolved in pyridine and chloroform, the solubilities were roughly the same in every case.

TABLE III

Method of preparation	% Acetyl,	Reducing power	Pyridine	Chloroform	Acetic acid
Haworth, Hirst and Webb	41.2	0	+129° (28°)	Turbid	+142° (17°)
Hess and Smith	44.5	0	Turbid	Turbid	Turbid
Tsuzuki	46.1	0	179° (25°)	193° (25°)	183° (17°)
Boiled 28 hours AcOH then Ac₂O + C₅H₅N	44.5	0	174° (20°)	197° (21°)	184° (20°)
Boiled 384 hours AcOH + AcONa					
Fraction 1	43.0	0.52	194° (19°)	198° (21°)	196° (19°)
Fraction 2	43.5	0.17	189° (22°)	196° (22°)	189° (22°)

The $[\alpha]_{5461}$ columns are headed in Pyridine, Chloroform, Acetic acid.

Experimental

The method of acetyl determination was in all cases essentially the same as that adopted for the cellulose derivatives.

α-Methylglucoside Tetraacetate.—A mixture of 50 g. of α-methylglucoside and 500 cc. of glacial acetic acid was boiled under reflux in an all-glass apparatus. After twenty-four hours the acid was distilled through a column until the temperature of the vapor reached 115°. The distillate amounted to 175 cc.; this volume of glacial acetic acid was replaced in the reaction mixture and the boiling under reflux continued for forty-eight hours longer. On distilling off the moist acid up to 115°, 125 cc. of distillate was obtained and a similar volume of fresh acid replaced. This process was continued, moist acid being removed at increasing intervals until boiling had been continued for a total time of 240 hours. The acetic acid was then removed by distillation under reduced pressure, the dark brown viscous residue was dissolved in ethylene chloride and this solution shaken with dilute potassium carbonate, filtered, separated and distilled under reduced pressure from the steam-bath. The residue, weighing 81 g., was distilled under 4 mm. pressure, when 64 g. of a pale yellow, very viscous oil passed over at 158–160°. This contained 47.7% acetyl (calculated for $C_7H_{10}O_6(COCH_3)_4$, 47.5%). This distillate remained liquid almost indefinitely at room temperature if not inoculated. On addition of a crystal of α-methylglucoside tetraacetate it crystallized very slowly, becoming completely solid only after a lapse of several months. It was, however, rapidly converted into the crystalline form by rubbing under cold water with a crystal of the tetraacetate. After one recrystallization from alcohol it melted at 100.5–101.5° and showed no depression of melting point when mixed with authentic α-methylglucoside tetraacetate. On hydrolysis of a sample of the sirupy product by means of alcoholic barium hydroxide, α-methylglucoside. m. p. 166°, was regenerated.

β-Methylglucoside Tetraacetate.—By heating 10 g. of β-methylglucoside and 200 cc. of acetic acid, as above, for 240 hours (acetyl content after 144 hours, 41.0%). Distilled product (b. p. 185–187° (5 mm.)) analyzed 46.9% acetyl (calcd. 47.5%) and crystallized on inoculation, m. p. 101–102.5°, from toluene; did not depress melting point of a sample prepared with acetic anhydride.

α-Methylmannoside Tetraacetate.—From 50 g. of α-methylmannoside and 500 cc. of acetic acid for 144 hours; b. p. 204–207° (5 mm.), contained 47.6% acetyl; m. p. 65–66° from alcohol; mixed m. p. 65–66°.

Mannitol Hexaacetate.—From mannitol and 10 parts of acetic acid for 240 hours;

crystallized on concentrating the reaction mixture; m. p. 119°;[11] acetyl 59.2% (calcd.. 59.5%).

Acetylation of Potato Starch.—Commercial potato starch, containing about 12% of moisture, was suspended in twenty times its weight of glacial acetic acid and heated to boiling. Continual mechanical stirring was necessary to avoid bumping. The water was removed at the outset and then at frequent intervals, the distillates being replaced by equal volumes of glacial acetic acid. Samples were withdrawn periodically; during the first eighteen hours the undissolved portions were separated by centrifuging and well washed with acetic acid; the solution was freed of the bulk of the acetic acid by distillation under reduced pressure and the residue precipitated by means of 95% ethyl alcohol. Subsequently, samples of the homogeneous solution were merely concentrated under reduced pressure and precipitated with alcohol. The products were repeatedly washed with alcohol until free of acetic acid and then dried *in vacuo* over phosphorus pentoxide.

Rotations were determined on samples obtained after twelve to seventy-two hours' boiling; those secured after longer periods were too dark to read. The material produced by boiling for 384 hours in the presence of sodium acetate (Table II) was subjected to fractional precipitation, and so obtained free of color. The dark solution in acetic acid was slowly diluted with water until about half of the dissolved ester had precipitated. The supernatant liquor, containing 53% of acetic acid, was practically colorless; on dilution with much water it yielded Fraction 1. The first precipitate was then dissolved in ethyl acetate and ether added to the solution until the supernatant portion was colorless. This process was repeated six times with the dark coagulum. The clear solution was concentrated to a small volume and treated with excess of ether, when Fraction 2 precipitated. The dark, gummy residue was discarded. The properties of Fractions 1 and 2 are shown in Table III.

Preparation of Starch Triacetate.—A suspension of 50 g. of potato starch (containing 12% moisture) in 1000 cc. of acetic acid containing 1 g. of sodium acetate was boiled under reflux, with stirring, for twenty-eight hours, aqueous acetic acid being periodically removed and replaced with anhydrous acid. The volume was then reduced to 500 cc. by distillation under diminished pressure. The residual clear solution was mixed with 150 cc. of 95% acetic anhydride and 75 cc. of pyridine, and boiled for six hours. The volume was then reduced, by distillation under diminished pressure, to about 200 cc., and the sirupy residue was poured into a liter of ice water. The granular precipitate was well washed with water and then with alcohol, and dried *in vacuo* over phosphorus pentoxide. The starch triacetate (44.5% acetyl) weighed 76.6 g. (98% of the theoretical amount); it was readily soluble in acetic acid, chloroform, dioxane, ethyl acetate and pyridine, almost completely in acetone, slightly in benzene, insoluble in ethyl alcohol, ethyl ether and water. Other properties are recorded in Table III.

Summary

On treatment with boiling acetic acid:

1. Reducing carbohydrates and the non-reducing furanoses, sucrose and inulin, caramelize.

2. Mannitol and non-reducing glycosides of the pyranose type become fully esterified.

3. Potato starch yields a continuous series of amorphous acetates, the acetyl content of which increases with time of treatment and reaches

[11] Bouchardat, *Ann. chim.*, [5] 6, 107 (1875), reports 119°.

a limit with the introduction of three acetyl groups for each glucose residue.

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THE REACTIVITY OF ATOMS AND GROUPS IN ORGANIC COMPOUNDS. XII. THE PREPARATION AND PROPERTIES OF MIXED ALIPHATIC ETHERS WITH SPECIAL REFERENCE TO THOSE CONTAINING THE TERT.-BUTYL RADICAL

BY JAMES F. NORRIS AND GEORGE WAYNE RIGBY[1]

The influence of structure on the lability of bonds in organic molecules is shown in a marked degree by compounds which contain a tertiary radical. For example, the tert.-butyl alcohol reacts with concentrated hydrochloric acid over 200,000 times as rapidly as does n-butyl alcohol. It seemed of interest, therefore, to determine whether or not the facts accumulated in connection with the study of the lability of the carbon–oxygen and of the hydrogen–oxygen bonds in alcohols[2] by means of rates of reaction could be utilized in devising improved methods for the preparation of ethers and esters. A study of these classes of compounds from the standpoint of their relative reactivities with reagents would lead to a fuller understanding of the influence of structure on the lability of atomic linkings.

Certain tert.-butyl alkyl ethers have been prepared by the commonly used methods, but the results, as measured by yields and purity, have been far from satisfactory. One of the methods used is based on the view that the mechanism of ether formation from alcohols involves the intermediate formation of an alkyl sulfuric acid and consequently concentrated sulfuric acid was used to bring about the reaction between tert.-butyl alcohol and ethyl alcohol. Since the acid rapidly converts the tertiary alcohol into polymers of isobutylene, the yields obtained were very small.

When the Williamson synthesis is used difficulties are encountered as the result of the unique behavior of compounds containing a tertiary radical. Sodium tert.-butylate is formed very slowly and reacts very slowly with alkyl halides. The chief reaction between tertiary alkyl halides and the sodium derivatives of normal alcohols is the removal of hydrogen halide from the alkyl halide. When these methods are used the yields are also very small.

[2] (a) Norris, Rec. trav. chim., 48, 885 (1929); (b) Norris, Z. physik. Chem., 130, 662 (1927); (c) Norris and Ashdown, THIS JOURNAL, 47, 837 (1925); (d) Norris and Cortese, ibid., 49, 2640 (1927).