$C_{15}H_{20}N_2O$: C, 73.7; H, 8.3; N, 11.5. Found: C, 73.8; H, 8.2; N, 11.5.

9-Ketodecanenitrile.—Using the general procedure of Cason,[15] 43.7 g. (0.23 mole) of 8-cyanoöctanoyl chloride and dimethylcadmium [prepared from 0.5 mole of methylmagnesium bromide and 50 g. (0.27 mole) of cadmium chloride] were allowed to react and gave 27.0 g. of crude product, b.p. 130–135° (2 mm.). Fractionation through a one meter Podbielniak column separated this crude material into 2.5 g. of 2,10-hendecandione, b.p. 132–134° (4 mm.), and 23.5 g. (61%) of 9-ketodecanenitrile. After crystallization from methanol, the 2,10-hendecandione melted at 61.8–62.3° (reported[16] m.p. 65°) and formed a disemicarbazone melting at 183–184° (reported[16] m.p. 184°). The 9-ketodecanenitrile was refractionated and boiled at 161–162° (9–10 mm.): $n^{25}D$ 1.4430. *Anal.* Calcd. for $C_{10}H_{17}NO$: C, 71.8; H, 10.3; N, 8.4. Found: C, 72.0; H, 10.4; N, 8.3.

The semicarbazone was prepared in the usual manner and was crystallized from aqueous ethanol, m.p. 104.6–105.4°. *Anal.* Calcd. for $C_{11}H_{20}N_4O$: C, 58.9; H, 9.0; N, 25.0. Found: C, 58.8; H, 8.7; N, 25.0.

The 2,4-dinitrophenylhydrazone, prepared in the usual manner, was crystallized from 95% ethanol, m.p. 63–64° (dec.). *Anal.* Calcd. for $C_{16}H_{21}N_5O_4$: C, 55.3; H, 6.1; N, 20.2. Found: C, 55.2; H, 6.0; N, 19.8.

Hydrolysis of a sample of 9-ketodecanenitrile by warming with a mixture of equal volumes of glacial acetic acid and 6 *N* H_2SO_4 proceded overnight to give 9-ketodecanoic acid, m.p. 47.3–48.5° after crystallization from pentane containing a few drops of absolute ethanol (reported[17] m.p. 47.5–48.5°).

9-Methyl-9-hydroxytridecanenitrile.—To a solution of 6.61 g. (0.04 mole) of 9-ketodecanenitrile in 50 ml. of absolute ether, cooled in an ice-bath, was added over a one-hour period with rapid stirring 0.053 mole of *n*-butylmagnesium bromide in 150 ml. of ether. After addition was complete, the ice-bath was removed, rapid stirring was continued for one hour and the reaction mixture treated with ice and acidified with 3 *N* HCl. The layers were separated, the aqueous layer was washed with ether, and the combined ether solutions were dried and evaporated. Fractionation of the residue gave 2.76 g. of recovered keto nitrile, b.p. 124–126° (2 mm.), and 2.07 g. (40% yield based on keto nitrile consumed) of 9-methyl-9-hydroxytridecanenitrile, b.p. 156° (2 mm.); $n^{25}D$ 1.4550.

(15) Cason, THIS JOURNAL, **68**, 2078 (1946).

(16) von Braun, *Ber.*, **40**, 3943 (1907).

(17) Barger, Robinson and Smith, *J. Chem. Soc.*, 718 (1937).

9-Methyltridecanoic Acid.—A solution of 2.07 g. (9.2 millimoles) of 9-methyl-9-hydroxytridecanenitrile in 10 ml. of 2 *N* ethanolic potassium hydroxide was heated under reflux for 23 hours, at the end of which time 98% of the theoretical amount of ammonia had been evolved. After evaporating the ethanol, the residue was dissolved in water, acidified with hydrochloric acid to congo red and extracted with ether. The ether extracts were dried and evaporated, and the residue was heated with a few crystals of iodine at 190–200° for 2 hours and then distilled at 0.5 mm. The distillate, 1.9 g., dissolved in 10 ml. of absolute ethanol, absorbed 8.3 millimoles of hydrogen at room temperature using platinum oxide as the catalyst. Fractionation of the hydrogenated material gave 1.16 g. (55% yield based on nitrile) of 9-methyltridecanoic acid, b.p. 154° (2 mm.); $n^{25}D$ 1.4462. *Anal.* Calcd. for $C_{14}H_{28}O_2$: C, 73.6; H, 12.4; eq. wt., 228. Found: C, 73.8; H, 12.2; eq. wt., 228.

The 2,4,6-tribromoanilide was prepared as described above and crystallized from 95% ethanol, m.p. 105.5–106°. *Anal.* Calcd. for $C_{20}H_{30}Br_3NO$: C, 44.5; H, 5.6. Found: C, 44.5; H, 5.5.

The *p*-bromoanilide, prepared as described above, melted at 66.5–67°. *Anal.* Calcd. for $C_{20}H_{32}BrNO$: C, 62.8; H, 8.4. Found: C, 63.3; H, 8.5.

12-Methyltridecanoic Acid.—An authentic sample[18] of this acid melted at 52.5–53.4°.

The 2,4,6-tribromoanilide was prepared as described above and melted at 112.5–112.9°. *Anal.* Calcd. for $C_{20}H_{30}Br_3NO$: C, 44.5; H, 5.6. Found: C, 44.7; H, 5.6.

Myristic Acid.—A sample of pure myristic acid, kindly supplied by Dr. J. Cason, melted at 52.4–53.4°.

The 2,4,6-tribromoanilide and the ***p*-bromoanilide** were prepared as described above and melted at 124.3–125.5° and 108.4–109.3°, respectively (reported[19] m.p. 124° and 107°).

Summary

The carbon skeleton of carpaine has been shown to consist of a straight chain of fourteen atoms by degrading the alkaloid to myristic acid. This fact necessitates revision of the Barger–Robinson structure for carpaine.

9-Methyltridecanoic acid has been synthesized.

(18) Weitkamp, THIS JOURNAL, **67**, 447 (1945). We are indebted to Dr. Weitkamp for a sample of this material.

(19) Robertson, *J. Chem. Soc.*, **115**, 1210 (1919).

BERKELEY, CALIFORNIA RECEIVED JULY 28, 1950

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY[1]]

The Acylation of Corn Starch, Amylose and Amylopectin

BY IVAN A. WOLFF, DAVID W. OLDS AND G. E. HILBERT

In comparison with the amount of work on cellulose esters the study of starch esters has been most inadequate. Many of the data on starch esters revealed in the literature were obtained on materials degraded because of drastic conditions used in either the esterification reaction or the pretreatment of the starch. Recent literature reviews include those of Mullen and Pacsu[2a] and of Whistler.[2b] Carson and Maclay[3] have reported the esterification of white potato starch under mild conditions, using formamide as a solubilizing agent.

All whole starch esters (other than those of waxy or glutinous, starches) are mixtures of esterified linear and branched-chain polysaccharides. Organic esters of amylose and amylopectin, other than the acetate and carbanilate[4] are unreported in the literature. This paper deals with the preparation of the triacetates, tripropionates, tributyrates, tricaproates, tripalmitates and tribenzoates of whole starch, amylose and amylopectin.

It was found that the pretreatment of the polysaccharides was most important, both in determining their reactivity and in its effect on the solubilities of the resulting esters. For example, both amylose and starch whose granules had been disrupted ("disintegrated" starch) were more easily esterified and gave esters more soluble in organic solvents than did starches pretreated in liquid

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

(2) (a) Mullen and Pacsu, *Ind. Eng. Chem.*, **34**, 1209 (1942); (b) Whistler, in "Advances in Carbohydrate Chemistry," Vol. I, Pigman and Wolfrom, editors, Academic Press, New York, N. Y., 1945, pp. 279–307.

(3) Carson and Maclay, THIS JOURNAL, **68**, 1015 (1946).

(4) Wolff and Rist, *ibid.*, **70**, 2779 (1948).

ammonia or according to Mullen and Pacsu.[2a] The nature of the polysaccharide material (*i.e.*, whether it was whole starch or a starch fraction) was less significant than its physical form.

Experimental

The corn starch used in the acylations was a methanol-extracted commercial sample. The starch before extraction contained 0.05% nitrogen, 0.016% phosphorus, 0.08% ash and 0.68% methanol extractables. Maximum sulfur dioxide concentration used in steeping the corn prior to starch separation was 0.1%.

Preparation of Materials.—Starch was pretreated in liquid ammonia by preparing a 10% paste of the starch in the ammonia in a wide-mouthed Dewar vessel. The starch was precipitated with 95% ethanol, allowed to stand several days in an open glass vessel for evaporation of ammonia then filtered. The cake was resuspended in fresh 95% ethanol, stirred for several hours, filtered, air-dried and dried *in vacuo* at 70° to constant weight. This product was reactive toward esterification.

For the preparation of "disintegrated" starch granules a hot 7% corn starch paste was agitated for 15 minutes in a Waring Blendor, the paste cooled and the starch then precipitated in ethanol (100 ml. paste to 500 ml. ethanol) in the Blendor, washed three times with that solvent and finally dried *in vacuo*.

The fractionation of corn starch by use of *n*-butanol has been described in detail by Schoch.[5] Certain useful modifications of this procedure which have been made at this Laboratory will be described in a future publication. The recrystallized corn amylose for esterification absorbed from 190 to 200 mg. of iodine per gram.[6] Amylose was precipitated in ethanol in a Waring Blendor, washed twice more with ethanol and then dried *in vacuo*. The amylopectin solution was either chilled overnight in a refrigerator and precipitated in chilled absolute ethanol (1 part amylopectin solution to 5 parts ethanol) in a Waring Blendor or was first concentrated *in vacuo* to 12% solids content and then precipitated as described. Further washing and drying was carried out as reported for the amylose fraction.

Reagents.—The acetic, propionic and butyric anhydrides were redistilled commercial products with narrow boiling ranges coinciding with values reported in the literature. The benzoyl chloride and benzoic anhydride were Eastman Kodak Co. white label reagents. Eastman Kodak Co. "practical" grade quinoline was redistilled before use. Commercial pyridine with a 2° boiling range was dried for several weeks over solid sodium hydroxide and then distilled.

Palmitic anhydride was prepared in 80.5% yield by the reaction of acetic anhydride with commercial palmitic acid (Armour Neo-Fat No. 1-56, containing 90% palmitic, 6% stearic and 4% oleic acid).[7,8] The palmitic anhydride melted at 55–58° and gave the following analysis: calcd. for C, 77.7; found, C, 77.6, 78.0. The original palmitic acid had carbon 75.2; calcd., C, 75.0.

Caproic anhydride, prepared in similar fashion[9] in 71.8% yield, boiled at 125° (6 mm.) and had $n^{25}D$ 1.4262.

Palmitoyl chloride was prepared from Neo-Fat No. 1-56 and thionyl chloride.[10] A 94% yield of material boiling at 162–177° (3/4 mm.) was obtained.

Methods of Esterification.—When esterifications were carried out according to the method of Mullen and Pacsu,[2] vigorous stirring was needed during the distillation of the pyridine–water azeotrope to prevent caking of the starch on the sides of the flask. A heavy gel was formed during the esterification, causing stirring difficulties which often necessitated a somewhat longer reaction time.

Other esterifications were carried out by mixing the pyridine, carbohydrate and approximately 1.7 times the theoretical amount of acylating reagent at room temperature in a flask fitted with mechanical stirrer and calcium chloride drying tube. An oil-bath maintained at the desired temperature was placed around the flask and stirring was continued throughout the reaction interval. The times given in Table I refer to the time that the flask was immersed in the heated bath.

Isolation of the Esters.—All acetates, propionates, palmitates and benzoates were isolated from their reaction mixtures by precipitation in absolute ethanol, preferably in a Waring Blendor. The esters were given three successive washings with ethanol and were then dried, first in a vacuum desiccator over calcium chloride and finally in a vacuum oven at a temperature below their softening points. The butyrates usually dispersed in ethanol when their reaction mixtures were poured into that solvent. They were precipitated by pouring the ethanolic solution into water, and then were washed with water and dried as above. Caproyl esters were the most difficult to obtain in finely divided physical form. They were best precipitated in ice-cold 50% ethanol and were washed with that solvent. The caproates could be pulverized by grinding in a mortar with solid carbon dioxide.

Analysis of the Esters.—The analytical procedure used by Mullen and Pacsu[2] in our hands gave low and non-reproducible results. The Eberstadt procedure used for starch acetates[11] was not generally applicable to the wide variety of esters here reported. Saponification at room temperature in alcoholic potassium hydroxide for 48 hours, according to the general procedure of Genung and Mallatt[12] was employed in the analysis of acetates and propionates. The butyrates and caproates also could be analyzed by this method if a small amount of saturated sodium chloride solution and a wetting agent (Aerosol OT) were added to the ester prior to the addition of the alcoholic alkali. These addends prevented lumping of the ester on the sides and bottom of the flask and made consistent results obtainable.

Palmitoyl esters were completely saponified in forty-eight hours in the alcoholic potassium hydroxide. Lower precision between duplicate analyses was obtained than with the lower esters, due to difficulty in reading the end-point and to the relatively smaller total titration involved.

Butyrates and caproates were also analyzed by saponification in a mixture of pyridine and methanol with methanolic potassium hydroxide, in the presence of a small amount of water, using the technique of Malm, *et al.*[13]

Benzoates could be analyzed either by the 48-hour ethanolic alkali saponification or by the pyridine–methanol procedure. By the latter method a larger ratio of pyridine to methanol was necessary than recommended by the above authors. Enough excess pyridine was added so that *after* addition of the methanolic alkali a 1:1 pyridine–methanol ratio existed.

When the saponification methods described were applied to the analysis of the various esters prepared, good precision and accuracy were obtained. It is not considered that sufficient analytical data are available for critical analysis, so no probable errors are quoted. However, in most cases (Table I) the acyl values agreed rather closely with the theoretical amount of acyl calculated for the triesters.

Agreement between the calculated and observed percentage of acyl was poorest in the case of the benzoates and palmitates. Since reproducibility of the analyses was also poorest with these esters, the extent of esterification was measured also by carbon and hydrogen analysis. In all cases, the carbon content of the ester checked the calculated value for a trisubstituted product within 0.3%. Since there is considerable difference in calculated carbon content between a triester and a diester in these cases (*e.g.*, starch tribenzoate, calculated 68.3 C; starch dibenzoate calculated 64.9 C), any appreciable deviation from complete esterification would have been detected by these carbon analyses.

Effect of Excess Pyridine on the Acetylation of Amylose.—Although considerable latitude was possible in the quantity of pyridine used in the esterification, the retarding effect of too great an excess was shown by the following experiment. A mixture of 21 g. of amylose, 65 g. of acetic anhydride and 750 ml. of dry pyridine was heated for 3 hours at 100°. After cooling, the ester was precipitated in ethanol and washed with that solvent, as described above. Analysis for acetyl: found 43.2; calculated for a triacetate 44.8.

(5) Schoch, *ibid.*, **64**, 2957 (1942).

(6) Bates, French and Rundle, *ibid.*, **65**, 1942 (1943).

(7) Albitzky, *J. Russ. Phys.-Chem. Soc.*, **31**, 103–106 (1899); *Chem. Zentr.*, **70**, I, 1070 (1899).

(8) Wallace and Copenhaver, THIS JOURNAL, **63**, 699 (1941).

(9) Autenrieth, *Ber.*, **34**, 182 (1901).

(10) Ralston and Selby, THIS JOURNAL, **61**, 1019 (1939).

(11) Murray, Staud and Gray, *Ind. Eng. Chem., Anal. Ed.*, **3**, 269 (1931).

(12) Genung and Mallatt, *ibid.*, **13**, 369 (1941).

(13) Malm, Genung, Williams and Pile, *ibid.*, **16**, 501 (1944).

TABLE I

CONDITIONS OF ESTERIFICATION,[a] ANALYTICAL DATA AND OPTICAL ROTATIONS OF THE TRIESTERS

Ester	Pretreatment of polysaccharide	Polysaccharide,[b] g.	Pyridine, ml.	Acid anhydride, g.	Time, hr.	Acyl, % Calcd.	Acyl, % Found[f,g]	$[\alpha]^{25}D$	Molecular rotation
Starch acetate	[c]	26	200	81	3	44.8	44.8	+172.0	49,500
Starch acetate	[d]	23	350	80	4	44.8	44.6	171.5	49,400
Starch acetate	Liquid NH_3 pretreated	26	200	85	6	44.8	44.7	171.0	49,200
Amylose acetate	..	20	170	65	3	44.8	44.7	174.5	50,300
Amylopectin acetate	[d]	26	150	81	7	44.8	44.8	170.0	49,000
Amylopectin acetate	Pptd. from cold dil. soln.	11	100	45	8	44.8	44.9	...	....
Starch propionate	[c]	26	200	100	5	51.8	51.5	146.0	48,200
Starch propionate	[d]	28	300	100	6	51.8	51.5	144.5	47,700
Starch propionate	Liquid NH_3 pretreated	26	135	100	23	51.8	51.8	144.0	47,500
Amylose propionate	..	25	135	100	6	51.8	52.0	148.0	48,800
Amylopectin propionate	[d]	26	350	100	6	51.8	51.0	144.0	47,500
Amylopectin propionate	Pptd. from cold dil. soln.	11	100	66	8	51.8	52.0	...	....
Starch butyrate	[c]	26	135	125	5	57.3	56.5	137.0	51,000
Starch butyrate	[d]	28	350	125	17	57.3	57.0	134.5	50,000
Starch butyrate	Liquid NH_3 pretreated	26	135	125	22.5	57.3	57.0	134.5	50,000
Amylose butyrate	..	25	135	125	12	573.	57.0	138.0	51,300
Amylopectin butyrate	[d]	26	300	125	15	57.3	56.5	135.0	50,200
Amylopectin butyrate	Pptd. from cold dil. soln.	11	100	68.5	8	57.3	57.1	...	....
Starch caproate	[c]	20	185	150	15	65.1	64.7	106.0[h]	48,300
Amylose caproate	..	20	135	150	24	65.1	64.6	108.0[h]	49,200
Amylopectin caproate	[d]	20	350	160	24	65.1	65.5	106.0[h]	48,300
Starch palmitate	[c]	10	500	160	96	81.9	78.7	...	....
Amylose palmitate	..	6.5	350	110	101.5	81.9	81.3	58.0[h]	50,800
Amylopectin palmitate	[d]	15	500	235	88	81.9	80.6	...	....
Starch benzoate	[c]	26	300	121[e]	4	66.5	65.7	...	....
Starch benzoate	[d]	27	400	121[e]	4	66.5	66.1	...	....
Starch benzoate	Liquid NH_3 pretreated	26	300	121[e]	4	66.5	66.0	...	....
Amylose benzoate	..	26	300	121[e]	4	66.5	65.6	...	....
Amylopectin benzoate	Pptd. from concd. soln.	26	300	121[e]	4	66.5	65.8	...	....

[a] Esterifications were carried out at 100° excepting the benzoates, which were prepared at 80°. [b] The polysaccharides were not specially dried before esterification. From 4 to 10% moisture did not affect the reaction, so long as excess acylating reagent was present. [c] "Dintegrated" starch used. [d] Treated by the technique of Mullen and Pacsu.[2] [e] Benzoyl chloride as acylating reagent. [f] Average of duplicate determinations. [g] Calculated to a moisture-free basis. The esters at equilibrium with atmospheric moisture contain from 0.1 to 1.5% moisture. [h] Taken at 2% concentration. All other rotations were taken at 1% concentration. The solvent in every case was $CHCl_3$.

This incompletely esterified product, in contrast to the triester, was non-fibrous and completely acetone soluble.

Benzoylation with Benzoyl Chloride.—A typical preparation of the tribenzoates is illustrated by the following procedure. To 26 g. of amylopectin in 200 ml. of dry pyridine contained in a 1-liter, three-necked flask was added 20 ml. of benzoyl chloride, with stirring. The solution warmed up to about 60° and in about 10 minutes the starch seemed fairly well dispersed. A light yellow solution of high viscosity resulted. Over a period of 35 minutes an additional 80 ml. of benzoyl chloride was added and then 100 ml. more pyridine. Stirring was continuous. The color gradually turned a deeper yellow and then red, and a heavy precipitate formed. After addition was complete the reaction mixture was heated for four hours at 80° in an oil-bath. Isolation of the benzoates was carried out as described above.

Benzoylation with Benzoic Anhydride.—A mixture of 20 g. of amylose, 125 ml. of dry pyridine, and 140 g. of benzoic anhydride was heated for 12.5 hours with stirring in an oil-bath maintained at 100°. No change was apparent in the reaction mixture between the eighth and twelfth hours. After reaction was stopped the mixture was viscous, light yellow, and almost clear. The ester, which was fibrous, was precipitated and washed with ethanol in the Waring Blendor as usual. Per cent. benzoyl calculated for a tribenzoate 66.5, found 61.8, 61.7. Rebenzoylation of 20 g. of this product for 12 hours at 100° with 125 ml. of dry pyridine and 100 g. of benzoic anhydride gave a product which still contained less than the theoretical benzoyl content for a tribenzoate, per cent. benzoyl found 64.8, 65.1.

Palmitoylation with Palmitoyl Chloride.—To a mixture of 16.5 g. of amylose, 150 ml. of toluene and 175 ml. of quinoline contained in a 1-liter, three-necked flask was added with stirring a solution of 137.5 g. of palmitoyl chloride in 100 ml. of toluene. About one-third of the acid chloride mixture was added in 10 minutes after which time the reaction mixture had warmed to 40–50°. The flask was immersed in an oil-bath maintained at 100° and the remainder of the acylating mixture added in 10 minutes. At first, the mixture was yellow and fairly clear but the color gradually darkened and a fine precipitate formed. Reaction was carried out for 3 hours at 100° and for 2 hours more at 130°. After the reaction mixture had cooled the quinoline hydrochloride was separated by filtration through a coarse-fritted glass funnel, and the palmitate ester was precipitated by addition of ethanol to the filtrate. The amylose palmitate had 71.0% palmitoyl content, corresponding to approximately 1.65 palmitoyl groups per C_6 unit.

Solubilities of the Esters.—All of the esters were insoluble in water. The amylose, disintegrated whole starch and "reactive" amylopectin esters, within an ester class, had approximately the same solubilities in organic solvents. These were as follows (determined at 2% concentration): The solubility of the aliphatic esters reached a maximum with the butyrate; the higher and lower esters were less soluble. The benzoates had approximately the same solubility as the butyrates. The acetates were soluble in chloroform, pyridine and acetic acid; insoluble in the lower alcohols, ether, diethyl Cellosolve or petroleum ether; and partially soluble in benzene, dioxane, ethyl acetate, acetone and 2-nitropropane. The propionates were insoluble in the lower alcohols, Cellosolve, ether and petroleum ether, but soluble in all of the other solvents. The solubility of the butyrates had increased over that of the acetates and propionates to the extent that they were soluble in all solvents tried except cold ethanol, *n*-butanol and petroleum ether.

In the case of the first two solvents solubility was complete when the mixture was warmed. The butyrates could be "recrystallized" from ethanol or *n*-butanol (2% concentration). The caproyl esters were completely soluble in pyridine only but partially soluble in most other organic solvents. Palmitate esters were the most insoluble of all and were not completely soluble in any single solvent tried. They were partially soluble in chloroform, ethyl acetate, benzene, ether, petroleum ether, butanol and diethyl Cellosolve.

By contrast to the foregoing, whole starch esters prepared from liquid ammonia pretreated starch, or any esters prepared by the Mullen and Pacsu procedure, were much less soluble in organic solvents and the solubility differences between ester classes were non-existent. Acetates, propionates, butyrates and benzoates of the polysaccharides prepared by this method were insoluble in ether, diethyl Cellosolve, petroleum ether and the lower alcohols, and partially soluble in the other solvents. The esters were not completely soluble in any solvent.

In many cases the esters were highly swollen in organic liquids even though completely insoluble in those liquids. The large number of instances of "partial solubility" is analogous to the behavior of pectin esters noted by Carson and Maclay.[14]

Optical Rotations.—Since many of the esters were only partially soluble in chloroform when direct solution was attempted, the rotations were taken in a manner similar to that described by Mullen and Pacsu.[2] A 1 or 2% dispersion of the ester in chloroform was prepared in a Waring Blendor. This dispersion was filtered through a coarse-fritted glass funnel, the rotation taken, and the concentration determined by evaporating a 10-ml. aliquot to dryness and to constant weight under an infrared lamp. Where comparisons were possible, rotations obtained by this method agreed closely with those obtained by the direct-solution procedure. Noteworthy in Table I are the higher rotations of the amylose esters[15] compared with the same amylopectin ester and the approximate constancy of the molecular rotations with increasing length of the acyl radical.

The use of trade names in this publication does not necessarily constitute endorsement of these products nor of the manufacturers thereof.

Acknowledgment.—We are indebted to C. H. Van Etten and to T. A. McGuire for carrying out many of the acyl analyses. Dr. A. Jeanes developed the technique described for obtaining "disintegrated" starch.

Summary

1. Satisfactory techniques have been described for the preparation of whole corn starch, amylose and amylopectin triacetate, tripropionate, tributyrate, tricaproate, tripalmitate and tribenzoate.

2. Solubilities of the esters in a number of organic solvents were qualitatively determined. Solubility of an ester was shown to be dependent on the method used for pretreating the polysaccharide prior to its esterification.

3. The optical rotations of the triesters of amylose were higher than those of whole starch and amylopectin. The molecular rotations of the various aliphatic acid esters of the polysaccharides were approximately constant.

(14) Carson and Maclay, THIS JOURNAL, **67**, 787 (1945).

(15) A. Jeanes of this Laboratory (unpublished work) has previously measured the rotations of the acetates of amylose, amylopectin and disintegrated corn starch.

PEORIA, ILLINOIS RECEIVED JUNE 3, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGY AND VITAL ECONOMICS, UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE AND DENTISTRY]

Physiologically Active Substituted α-Glyceryl Phenyl Ethers[1]

BY JOHN P. LAMBOOY

The search for active analogs of 3-(*o*-toloxy)-1,2-propanediol which possess increased solubility or increased potency has not produced compounds which show therapeutic promise. As a result of interest in our department concerning the site and mode of action of the α-glyceryl phenyl ethers we undertook the preparation of analogs which might show greater solubility or potency. Any compound showing increased solubility would facilitate the study of permeability of this class of compounds and one of greater potency would reduce the complications introduced by disturbing the osmotic conditions which normally prevail in tissue.

It was felt that 3-(*o*-ethylphenoxy)-1,2-propanediol was worthy of more detailed study. Preliminary studies[2] had already been made on this compound but its synthesis had not been reported.

In view of the abnormal solubility of fluorobenzene when compared with the other halobenzenes it was thought that 3-(*o*-fluorophenoxy)-1,2-propanediol might show increased solubility. This compound was found to be soluble in less than an equal weight of water.

Since 3-(*o*-toloxy)-1,2-propanediol and 3-(*o*-chlorophenoxy)-1,2-propanediol had been found[2] to be about equal in potency we thought that their combination into 3-(2-methyl-6-chlorophenoxy)-1,2-propanediol might produce a compound of greater potency. This compound was found to be twice as potent as 3-(*o*-toloxy)-1,2-propanediol.

As can be seen in the summary of the pharmacological data (Table I), 3-(*o*-ethylphenoxy)-1,2-propanediol and 3-(2-methyl-6-chlorophenoxy)-1,2-propanediol are more potent and more toxic than 3-(*o*-toloxy)-1,2-propanediol, and these changes are accompanied by a somewhat reduced solubility.

A detailed report of the physiological properties of these compounds will be published by Dr. E. Wright and others in the near future.

The procedure outlined by Wheeler and Willson[3] was used for the preparation of the α-glyceryl phenyl ethers. The procedure was modified only in respect to purification and isolation of the product. *o*-Ethylphenol was prepared from *o*-nitroethylbenzene by reduction to the aniline and hydrolysis of the diazonium salt. 6-Chloro-*o*-cresol was prepared from *o*-cresol by adaptation of the method used by Brubaker and Adams[4] for the preparation of *o*-bromo-*o*-cresol with the result that the yield of

(1) This study was supported in part by a grant-in-aid from the Fluid Research Fund Committee of the University of Rochester School of Medicine and Dentistry.

(2) Berger, *J. Pharmacol.*, **93**, 470 (1948).

(3) Wheeler and Willson, "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1932, p. 290.

(4) Brubaker and Adams, THIS JOURNAL, **49**, 2290 (1927).