

acid placed in volumetric flasks, which were then filled to the mark with acetic acid. They were immediately transferred to 1-cm. stoppered quartz cells, which were placed in a cell compartment kept at 25° by circulating water from a constant temperature bath. The blank cells contained acetic and hydrochloric acids alone. The optical densities (D) at 311 $m\mu$, the absorption maximum of the end-product, were measured at regular intervals. Assuming first-order kinetics, the following equation holds for the rate constant k

$$kt = \ln(D_{\infty} - D_0/D_{\infty} - D)$$

where $D_{\infty} = 7530c$; $D_0 = 37c$ (for PP) and $56c$ (for EPP), with c being the initial molarities of the reactants and with the numerical values corresponding to the molar extinction coefficients of α -apoPP, PP and EPP, respectively, in glacial acetic acid. The following first-order rate constants were evaluated from the slopes of the straight-line portions of the graphs: PP, $k = 1.4 \times 10^{-3}/\text{min.}$ and EPP, $k = 1.5 \times 10^{-3}/\text{min.}$ (solutions 0.04 N in hydrochloric acid); PP, $k = 5.2 \times 10^{-3}/\text{min.}$ and EPP, $k = 5.5 \times 10^{-3}/\text{min.}$ (solutions 1.24 N in hydrochloric acid).

Picropodophyllin Ethyl Ether (I, R = OC₂H₅).—A solution of 0.20 g. of EPP in 2 ml. of absolute ethanol containing 0.06 ml. of concd. sulfuric acid was refluxed for 15 minutes. The felt-like colorless needles, which separated almost immediately, were collected, after diluting with another 6 ml. of absolute ethanol and chilling; they were washed with ethanol, water, and again ethanol, then dried. The yield was 0.17 g. (80%); in analogous experiments with PP and with EPP ethyl ether² it was 68% and 77%, respectively. The crude material melted at 243–245° with sintering at 196°, when immersed at room temperature;

when it was immersed at 210°, it melted with foaming, re-solidified and melted again at 243–245°; $[\alpha]^{25}_D + 58^\circ$ (c 0.50, chloroform). Two recrystallizations from chloroform-ethanol provided long colorless needles, m.p. 227–229°, $[\alpha]^{25}_D + 58^\circ$ (c 0.52, chloroform).

Anal. Calcd. for C₂₄H₂₆O₈: C, 65.15; H, 5.92; 4 alkoxy calcd. as OCH₃, 28.06. Found: C, 65.08; H, 5.97; OCH₃, 27.80.

The behavior of the crude material upon heating was apparently caused by the presence of residual sulfuric acid. Pyrolysis of the crude product at 225° gave α -apoPP, while the purified substance was recovered unchanged.

Conversion of Epipodophyllotoxin to Podophyllotoxin (Table I).—A solution of 1.0 g. of EPT in 6 ml. of acetone and 6 ml. of 2 N hydrochloric acid was refluxed for one hour, then diluted with water. The resulting oil (0.82 g.) solidified partly on chilling and completely after washing with water and drying at 60°; m.p. 167–178°, $[\alpha]^{25}_D - 94^\circ$ (c 1, chloroform). Epimerization with piperidine in aqueous ethanol² gave PP, m.p. 224–227.5° (acetate⁵ m.p. and mixed m.p. 214.5–216°). With N hydrochloric acid, the product (0.93 g.) had m.p. 164–175°, $[\alpha]^{25}_D - 85^\circ$ and was converted to impure PP, m.p. 207–222°.

Acknowledgments.—The authors are grateful to Dr. D. H. R. Barton and to several staff members of the National Institutes of Health for stimulating criticism and discussions. They wish to thank Dr. W. C. Alford and co-workers for microanalyses.

BETHESDA 14, Md.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

The Role of Chloroacetylpolyglycolic Acids in the Potassium Bromide Catalyzed Conversion of Chloroacetic Acid and Naphthalene into α -Naphthylacetic Acid¹

BY PHILIP L. SOUTHWICK, L. A. PURSGLOVE, BETTY M. PURSGLOVE AND WILLIAM L. WALSH²

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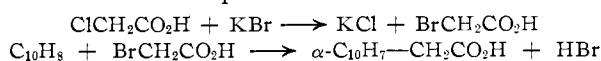
When heated at the reflux temperature in the presence of small amounts of potassium bromide, chloroacetic acid is converted into a mixture of chloroacetylpolyglycolic acids. This type of polyester will react with boiling naphthalene to yield α -naphthylacetic acid or products saponifiable to α -naphthylacetic acid. This sequence of two reactions is evidently involved in the conversion of naphthalene into α -naphthylacetic acid when naphthalene is heated with chloroacetic acid in the presence of potassium bromide. Mixtures of glycolide and chloroacetic acid also react with naphthalene to give α -naphthylacetic acid.

The reaction of chloroacetic acid with naphthalene to yield α -naphthylacetic acid was first reported in patents issued to Wolfram, Schörnig and Hausdörfer.³ The reaction was described as taking place when the reactants were kept for 48 hours at the reflux temperature of the mixture, and the use of catalysts was not mentioned. The reaction seemed remarkable in that alkylation of an aromatic hydrocarbon was achieved in the absence of any acid catalyst of the type used in Friedel-Crafts reactions.

When we investigated the utility of this reaction as a preparative method, we found that even when refluxing was continued for as long as 80 hours the yield of α -naphthylacetic acid reached only about 3%, and that large portions of both starting ma-

terials remained unchanged. Acids such as hydrogen chloride, hydrogen bromide and sulfuric acid, and typical Friedel-Crafts catalysts such as aluminum chloride and zinc chloride (which led to tar formation) did not improve the yield. Ferric chloride did appear to have a beneficial effect, but only to a minor degree.

On the other hand, we found that bromoacetic acid, mentioned in the patents as reacting in analogous fashion, gave higher yields. Experiments were then performed to test the possibility that by adding a mole of potassium bromide to a mole each of chloroacetic acid and naphthalene, bromoacetic acid might be formed *in situ* and might then react with naphthalene



Much improved yields (ca. 15%) were, in fact, obtained in this way, but when it was found that 0.1 mole of potassium bromide⁴ produced at least as favorable an effect on the yield as 1 mole, and

(4) Other bromides, such as sodium bromide and lithium bromide were ineffective, as were potassium chloride, lithium chloride and calcium chloride.

(1) The initial phase of this investigation was supported by a research grant from the Niagara Chemical Division, Food Machinery and Chemical Corporation. The major portion of this report was abstracted from a thesis submitted by William L. Walsh in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Carnegie Institute of Technology, June, 1953.

(2) Institute Fellow in Organic Chemistry, 1952–1953.

(3) A. Wolfram, L. Schörnig and E. Hausdörfer (to I. G. Farbenind. A.-G.), German Patent 562,391 (Feb. 1, 1929). U. S. Patent 1,951,686 (March 20, 1934).

that, moreover, yields in excess of 0.2 mole of product resulted from the use of 0.1 mole of potassium bromide, it was necessary to seek another explanation for the effect of potassium bromide.⁵ These initial observations on the potassium bromide catalysis were made in 1948.

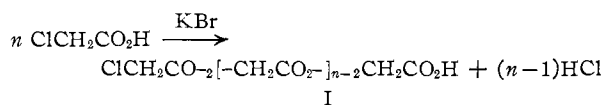
In 1950, Ogata and Ishiguro⁶ reported their discovery of the catalysis of the reaction by potassium bromide and by iron compounds. They placed particular emphasis upon the importance of the latter. They described a procedure which utilized small amounts of both potassium bromide and ferric oxide, called for a heating period of 24 hours, and led to yields as high as 34% (based on chloroacetic acid) of partially purified α -naphthylacetic acid (m.p. 124–126°). With potassium bromide as the only catalyst the yield was reported to be 4%; with ferric oxide as the only catalyst, 5%. Ogata and Ishiguro⁶ expressed the opinion⁷ that the beneficial effect of potassium bromide was due to its ability to convert chloroacetic acid into bromoacetic acid.

Since the stoichiometry of the reaction seemed to us to preclude any such simple explanation of the effect of potassium bromide, we investigated the effect of small amounts of potassium bromide on refluxing chloroacetic acid in the absence of naphthalene. The results of the experiments to be described here demonstrated (1) that potassium bromide promotes a fairly rapid conversion of chloroacetic acid into mixtures of chloroacetyl-polyglycolic acids and (2) that chloroacetyl-polyglycolic acids react with naphthalene at its boiling point to give α -naphthylacetic acid.

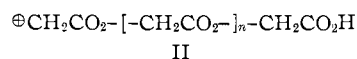
The addition of a small amount of potassium bromide to refluxing chloroacetic acid caused the evolution of hydrogen chloride and a gradual rise in the reflux temperature from 187° to 240° during a period 4 to 6 hours. When the mixture cooled, it solidified to a hygroscopic brown solid, over half of which was soluble in cold water. The insoluble portion, a light-brown amorphous powder, was freed of chloroacetic acid, of any bromoacetic acid which may have been formed, and of all traces of ionic halides by repeated washing with distilled water, and was then heated for 24 hours with naphthalene at the reflux temperature (218°). The usual extraction of the resulting mixture with hot sodium hydroxide produced α -naphthylacetic acid in a yield (22 g. of crude acid, 9 g. of fully purified acid, m.p. 132–33°, from 20 g. of the powder)⁸ exceeding on a weight basis the best yields we had previously obtained from chloroacetic acid with catalysis by potassium bromide. The powder produced α -naphthylacetic acid not only when

heated with naphthalene alone, but also when heated with naphthalene in the presence of chloroacetic acid.

The powder proved to have the properties expected of a polyester derived from glycolic acid. It had no definite melting point; the product of a typical run melted over the range 118–138°.⁹ A part of the material was soluble in sodium bicarbonate solution and almost all of it dissolved rapidly in dilute potassium hydroxide solution. A portion was also soluble in boiling water and was precipitated when the hot solutions were cooled. The substance was readily saponified with sodium hydroxide to give sodium glycolate. Covalently bound halogen was present, but only in small amount (4.5%, calculated as chlorine). A sample of polymer prepared as indicated above, except for the washing with water, was heated under reduced pressure, and glycolide was obtained as a distillation-product. These indications of the course of the reaction and the nature of the product suggest that the material consists mainly of chloroacetyl-polyglycolic acids (I), formed by elimination of hydrogen chloride from chloroacetic acid. Cal-



ulation of the average molecular weight from the chlorine content of the sample of water-insoluble polymer which was analyzed yielded a value of about 13 for n in formula I; *i.e.*, the average polymer molecule was formed from about 13 moles of chloroacetic acid. Decomposition of such polyesters at one or more of the methylene to oxygen bonds could result in the formation of carbonium ions of the type represented by formula II and



might thus account for an attack upon naphthalene at the α -position leading to α -naphthylacetic acid or products saponifiable to α -naphthylacetic acid.

Our results therefore suggest that in the potassium bromide catalyzed reaction of naphthalene with chloroacetic acid much of the α -naphthylacetic acid obtained is formed from chloroacetyl-polyglycolic acid intermediates. The results do not exclude the possibility of some direct reaction of chloroacetic acid, however. The question of whether the reaction of bromoacetic acid with naphthalene proceeds *via* a similar polymer has not been fully investigated, but the fact that the bromo acid reacts to an appreciable extent without the assistance of an added catalyst may point to a direct reaction. The reflux temperature of bromoacetic acid does rise gradually when heating is prolonged, but the increase is much slower than that observed for the reflux temperature of chloroacetic acid in the presence of potassium bromide.

(9) The material is apparently not the same as the substance known as "polyglycolide," m.p. ca. 220°, which has been prepared by heating salts of chloroacetic acid. See (a) C. A. Bischoff and P. Walden, *Ann.*, **279**, 45 (1894); (b) A. Sporzynski, W. Kocay and H. V. A. Briscoe, *Rec. trav. chim.*, **68**, 613 (1949).

(5) It is most unlikely that in these experiments hydrogen bromide formed in a reaction of bromoacetic acid with naphthalene participated to a significant extent in any reaction or reaction cycle leading to conversion of chloroacetic acid into bromoacetic acid. In the open systems used, the escape of hydrogen bromide from mixtures held above 200° should be very rapid. Moreover, addition of hydrogen bromide has been found to reduce yields of α -naphthylacetic acid obtained from chloroacetic acid with potassium bromide.

(6) Y. Ogata and J. Ishiguro, *THIS JOURNAL*, **72**, 4302 (1950).

(7) See also Y. Ogata, J. Ishiguro and Y. Kitamura, *J. Org. Chem.*, **16**, 239 (1951).

(8) Based on the assumption (*vide infra*) that the powder is essentially $\text{[-CH}_2\text{CO}_2\text{]}_n\text{-}$ and that all of the units $\text{-CH}_2\text{CO}_2\text{-}$ could be used, the crude yield was 34%, the pure yield, 14%.

Glycolide melts to form a liquid insoluble in molten naphthalene and, when used by itself, did not react with naphthalene at the reflux temperature to give α -naphthylacetic acid. However, mixtures of glycolide with chloroacetic acid are soluble in naphthalene, and by refluxing such mixtures, we obtained yields of α -naphthylacetic acid which were from two to seven times as large as those obtainable from the same amount of chloroacetic acid and naphthalene alone (without potassium bromide).

We have not investigated thoroughly the catalytic effect of iron compounds on these reactions. Iron compounds are apparently not essential for the reaction of chloroacetyl polyglycolic acids with naphthalene, for relatively good yields of α -naphthylacetic acid were obtained from reactants containing too little iron to be detected qualitatively with sodium thiocyanate. However, the addition of small amounts of ferric oxide to chloroacetyl polyglycolic acid-chloroacetic acid mixtures causes more complete reaction with naphthalene, and as Ogata and Ishiguro⁶ have reported, ferric oxide seems to have the same effect on the potassium bromide catalyzed reaction of chloroacetic acid with naphthalene.

The formation of tars often accompanies reactions of any of these compounds or mixtures with naphthalene, and in most instances the larger the yield of α -naphthylacetic acid, the less pure the crude acid will be when first obtained. As has been shown by Ogata, Ishiguro and Kitamura,⁷ naphthalene-1,5-diacetic acid is also a reaction product. Some unused naphthalene usually can be recovered, even when the other reactant is used in excess. Considerable variations in yield from the same procedure are also often encountered, possibly due to variations in the amount of heat supplied during the heating period. The reactions are nevertheless valuable because of the ease with which they can be carried out.

Experimental^{10,11}

Chloroacetyl polyglycolic Acid. A. Preparation.—In a flask fitted with a thermometer, stirrer and reflux condenser were placed 360 g. (3.81 moles) of chloroacetic acid and 36 g. (0.30 mole) of potassium bromide. Steam was passed through the condenser to keep it from being plugged with chloroacetic acid while the mixture was heated to the reflux temperature and stirred vigorously. Hydrogen chloride fumes were evolved and at the end of 6 hours the reflux temperature had reached 240°. The heating was interrupted and the mixture was poured out into a large evaporating dish, where it solidified. The dark brown, amorphous, hygroscopic solid weighed 274 g.

The solid was washed thoroughly with distilled water to remove chloroacetic acid and potassium bromide. The washing with distilled water was continued until the filtrate showed a negative test with silver nitrate. The resulting light brown powder, no longer hygroscopic, was dried. It weighed 125 g.; the m.p. was about 118–138°.

Anal. Found: Cl, 4.49.

A part of the material was soluble in dilute sodium bicarbonate solution and a portion was soluble in boiling water, from which it separated upon cooling as a sticky white precipitate which could be dried to an amorphous solid softening slightly at about 70° and melting at 123–125°. Nearly all

(10) Melting points are corrected.

(11) Microanalyses by Drs. G. Weiler and F. B. Strauss, Oxford, England.

of the material dissolved rapidly in dilute potassium hydroxide solution in the cold.

B. Saponification to Sodium Glycolate.—A 10-g. sample of the powder was saponified with 25% sodium hydroxide. After neutralization of the solution to pH 7 with hydrochloric acid, decolorization with charcoal, and removal of the water under reduced pressure the residue was extracted with absolute ethanol. When the ethanol extract was concentrated, crystalline sodium glycolate separated. A 1-g. sample was converted to the *p*-bromophenacyl ester,¹² m.p. 138–141° when crystallized from ethanol. A sample of the same derivative prepared from authentic glycolic acid melted at 138–141°¹³ and a mixed melting point showed no depression.

C. Pyrolysis to Glycolide.—A chloroacetic acid-potassium bromide mixture similar to that described above was refluxed for 4 hours and then distilled under reduced pressure. The first fraction collected (boiling range 110–210° at about 30 mm.) partially solidified. Addition of ether permitted the separation of a crystalline white solid, m.p. 79–81°. The substance was halogen free. Recrystallization from acetone and then from a dioxane-ether mixture raised the m.p. to 80–84°.¹⁴ A mixed m.p. with glycolic acid, m.p. 77–79°, was depressed to 61–64°. Analysis showed the compound to be glycolide.

Anal. Calcd. for C₄H₄O₄: C, 41.38; H, 3.45; sapon. equiv., 58. Found: C, 41.41; H, 3.31; sapon. equiv., 57.7.

Preparation of α -Naphthylacetic Acid from Chloroacetyl polyglycolic Acid. A. From Polymer and Naphthalene Alone.—A mixture of 40 g. (0.31 mole) of iron-free naphthalene and 20 g. of water-insoluble chloroacetyl polyglycolic acid, prepared as described above, was ground thoroughly in a mortar. It was then refluxed for 24 hours in a flask fitted with an air condenser and heated on a sand-bath. At the end of the heating period, the temperature of the refluxing liquid was 218°.

The reaction mixture was poured into a solution prepared from 20 g. (0.5 mole) of sodium hydroxide and 200 ml. of water. This mixture was boiled for 30 minutes, cooled and filtered (to remove unused naphthalene). Acidification of the filtrate with hydrochloric acid precipitated crude α -naphthylacetic acid, weight 22 g. when dried.

The crude product was extracted with 400 ml. of 15% sodium acetate solution at 70°. Some dark-colored, insoluble impurities were removed by decantation and filtration. The product was reprecipitated by acidification with hydrochloric acid, collected by filtration and dried. It was then extracted with hot benzene to dissolve the α -naphthylacetic acid and separate it from the benzene-insoluble naphthalene-1,5-diacetic acid. The insoluble material (2 g.) was removed by filtration and recrystallized three times from hot water to give 1 g. of the diacetic acid, m.p. 275–276°.¹⁵

Removal of the benzene from the filtrate and recrystallization of the residue from hot water gave 9 g. of pure α -naphthylacetic acid, m.p. 132–133°.

B. From Polymer with Chloroacetic Acid, Ferric Oxide and Naphthalene.—A mixture prepared from 7 g. of the same type of polymer, 5 mg. of ferric oxide, 7 g. of chloroacetic acid and 28 g. of naphthalene was refluxed for 24 hours. The mixture was carried through the procedure described above as far as precipitation from the sodium acetate extract. The yield was 10 g. of a crude product, m.p. 108–111°.

Preparation of α -Naphthylacetic Acid Using Glycolide-Chloroacetic Acid Mixtures. A. Without Ferric Oxide.—A mixture of 6 g. (0.052 mole) of glycolide, 6 g. (0.063 mole) of chloroacetic acid and 24 g. (0.187 mole) of naphthalene was refluxed under an air condenser for 24 hours. The reaction mixture was treated as described in the section above; acidification of the sodium acetate extract precipitated 2.5 g. of α -naphthylacetic acid, m.p. 123–125°.

(12) The procedure was that of Shriner and Fuson, "Identification of Organic Compounds," 3rd edition, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 157.

(13) W. L. Judefind and E. E. Reid, *THIS JOURNAL*, **42**, 1043 (1920), reported the m.p. 138°.

(14) Melting points quoted for glycolide are 86–87° (Bischoff and Walden, ref. 9a) and 82–83° (Sporzynski, *et al.*, ref. 9b).

(15) Y. Ogata, J. Ishiguro and Y. Kitamura, ref. 7, reported the m.p. 278–280°.

B. With Ferric Oxide.—A similar experiment conducted with a mixture prepared from 7 g. of glycolide, 7 g. of chloroacetic acid, 28 g. of naphthalene and 50 mg. of ferric oxide yielded 5 g. of less pure acid, m.p. 108–110°.

Acknowledgment.—The authors enjoyed the

benefit of consultation with Mr. John F. Les Veaux and Dr. O. H. Johnson during the initial phase of the investigation.

PITTSBURGH, PENNSYLVANIA

[CONTRIBUTION FROM THE STARCH AND DEXTROSE DIVISION, NORTHERN REGIONAL RESEARCH LABORATORY¹]

Polysaccharide Aryl Carbamates. IV. Partly Substituted and Cross-linked Starch Carbamates²

BY IVAN A. WOLFF, PAUL R. WATSON AND CARL E. RIST

RECEIVED SEPTEMBER 28, 1953

The preparation of partially substituted starch carbamates both in anhydrous pyridine and in aqueous medium is described. Gelatinization-resistant starches result when as little as one hexamethylenedicarbonyl cross-link for each 500 anhydroglucose units is introduced. Many of the starch carbamates still show the cross under polarized light and are microscopically indistinguishable from untreated corn starch.

In our recent publications the preparation and properties of completely substituted carbamate esters of several polysaccharides with phenyl isocyanate and with α -naphthyl isocyanate have been described.³ The general lack of information concerning the reactions of isocyanates with amylose polysaccharides also was indicated. This paper reports the reaction of starch with hexamethylene diisocyanate, 2,4-tolylene diisocyanate, and with quantities of phenyl isocyanate such that less than complete substitution occurs.

Experimental

Materials.—The corn starch used was a high-grade commercial product. The potato starch was extracted at this Laboratory with distilled water from No. 1 commercial-grade Michigan potatoes. Phenyl isocyanate was Eastman Kodak Company white label grade used without further purification. The difunctional isocyanates were obtained from E. I. du Pont de Nemours and Company and were redistilled under reduced pressure before use. Their purities, determined by the method of Stagg,⁴ were between 95 and 100%. Commercial pyridine (2° boiling range) was dried for several weeks over solid sodium hydroxide pellets and redistilled before use.

Preparation of Starch Carbamates in Pyridine.—Starch was usually dried by distilling pyridine from it until no more pyridine–water azeotrope could be removed. More anhydrous pyridine or other solvent was then added when desired, followed by the isocyanate, and reaction was carried out in an oil-bath, maintained at 100° for 6 hours. The product was isolated by pouring the reaction mixture into ethyl alcohol, washing the carbamated starch several times with ethyl alcohol, and drying. Analysis for nitrogen was by the Kjeldahl procedure.

Reaction of Starch with Isocyanates in Aqueous Medium.—To a stirred mixture of 100 g. of starch (as is basis) in 400 ml. of water, adjusted to the desired pH, was added the desired quantity of isocyanate. The suspension was allowed to stir for 2 hours, following which the product was separated by filtration, washed three times with water by alternate suspension and filtration, and finally allowed to air dry.

Measurement of Extent of Swelling of Products.—The amount of swelling undergone by starch carbamates in hot

water was measured as follows: Two grams (as-is basis) of the substance, contained in a graduated 40-ml. centrifuge tube, was suspended in sufficient water to make a total volume of 40 ml. and the mixture was stirred for 20 minutes in a steam-bath. The volume of the swollen granules was read after a 24-hour settling period.

Results

Reaction of Starch with Phenyl Isocyanate.—When 0.03 to 0.5 mole of phenyl isocyanate per base mole of starch was used, substantially all of the added reagent combined with the starch (see Table I). As the degree of substitution increased, progressively greater granule damage was evident. While sample C still appeared microscopically like unchanged starch, some of the granules in D showed an enlargement of the hilum. In E and F increasing amounts of amorphous material were noted although many granules containing the cross in polarized light were still present.

TABLE I

REACTION OF 25 G. (AIR-DRY BASIS) CORN STARCH WITH INSUFFICIENT AMOUNTS OF PHENYL ISOCYANATE FOR COMPLETE SUBSTITUTION (100°, 6 HOURS)

Product	Mole C ₆ H ₅ NCO/ anhydroglucose unit	N content of product ^a	Degree of substitution, acyl per C ₆
A	0.03	0.25	0.03
B	.07	.45	.05
C	.13	.48	.06
D	.27	1.56	.21
E	.40	2.51	.37
F	.53	3.28	.53

^a Corrected for 0.03% N in the original starch.

A progressive change was also noted in the X-ray diffraction patterns of these materials. Sample C had a typical "A" X-ray diffraction pattern. In D the "A" pattern was still present but the background was appreciably stronger and a ring close to the so-called 16 Å. ring of the "B" starch pattern appeared. This new ring became stronger in E, and in F it appeared to have the same intensity as the strongest line of the "A" part of the pattern.

All of the above materials had a hydrophobic surface, evidenced by their tendency to float on water and to become wetted only with difficulty. Products A through C pasted in hot water, although

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

(2) Presented before the Division of Carbohydrate Chemistry at the 124th national meeting of the American Chemical Society, Chicago, Illinois, September, 1953.

(3) I. A. Wolff and C. E. Rist, *THIS JOURNAL*, **70**, 2779 (1948); I. A. Wolff, P. R. Watson and C. E. Rist, *ibid.*, **74**, 3061, 3064 (1952); **75**, 4897 (1953).

(4) H. E. Stagg, *Analyst*, **71**, 557 (1946).