

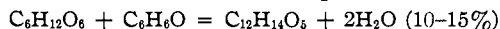
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Sugar-Phenol Condensations. The Condensation of *d*-Glucose with Phenol¹BY JOSEPH B. NIEDERL AND ROBERT K. MAURMEYER²**Introduction**

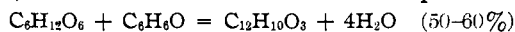
In a previous publication³ it was shown that aliphatic aldehydes condense mole for mole with phenols and that the condensation products thus formed undergo "disproportionation" to the respective saturated alkylphenols upon pyrolysis. These condensations are now extended to sugars. The results obtained by condensing *d*-glucose with equimolar quantities of phenol are set forth in this communication.

In 1894 Emil Fischer⁴ had shown that the polyhydric phenols, resorcinol and pyrogallol, are capable of condensing with reducing monosaccharides, but specifically stated that: "Monohydric phenols appear not to be able to undergo such condensations." His work was continued by C. Counciler,⁵ who used phloroglucinol. E. Fischer as well as C. Counciler did not go beyond establishing a general empirical formula for the reaction products. Both, however, emphasized the phenolic and the non-glucosidic nature of the condensation products. The third report in the literature deals with a baking process involving sugars and phenols, leading to undefined resinous materials and which has been patented by J. V. Meigs.⁶

Experimental results obtained in the condensation of molar quantities of *d*-glucose and phenol showed the formation of three distinct products: (A) a water-soluble product, (B) a water and benzene insoluble product, and (C) a benzene-soluble product. Quantitative elementary analysis showed that the products were formed as follows: (A) the water-soluble product:



(B) The water and benzene insoluble product:



(C) The benzene-soluble product:



(1) This paper was presented in part before the Division of Organic Chemistry at the Rochester meeting (Sept., 1937) and in full before the Division of Sugar Chemistry and Technology at the Baltimore meeting (April, 1939) of the American Chemical Society.

(2) The material presented in this paper is taken from the thesis presented by Robert K. Maurmeyer to the Faculty of the Graduate School of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) J. B. Niederl and co-workers, *THIS JOURNAL*, **59**, 1113 (1937).

(4) E. Fischer, *Ber.*, **27**, 1355 (1894).

(5) C. Counciler, *ibid.*, **28**, 24 (1895); *Chem. Ztg.*, **20**, 585 (1896).

(6) J. V. Meigs, U. S. Patents 1,877,417 (1933); 2,001,430 (1935).

The Condensation Products. (Derivatives and chemical properties.) (A) **The Water-soluble Product.**—This product gave the following derivatives:

- I Benzoate: insoluble in dilute alkalis;
- II Sodium salt: insoluble in ethyl alcohol;
- III Phenylsazone: soluble in Claisen solution, not precipitated from this solution by the addition of water ("Cryptophenol");⁷
- IV Dibromo compound: soluble in Claisen solution and reduces Fehling's solution.

Of this dibromo compound (IV) the following derivatives were prepared:

- IV (a) benzoate: insoluble in Claisen solution;
- (b) semicarbazone: soluble in Claisen solution;
- (c) 2,4-dinitrophenylsazone: soluble in Claisen solution;
- (d) nitro derivative: soluble in sodium carbonate solution, and reduces Fehling's solution;
- (e) picric acid: which indicates that the bromine must be in the side chain of the benzene ring.

In addition to the above, the water-soluble product (A) shows the following chemical properties:

- (α) It reduces Fehling's solution;
- (β) Exhaustive nitration yielded picric acid in amounts indicating a mol for mol addition of the phenol to *d*-glucose;
- (γ) Diazotization is positive.

(B) **The Water and Benzene Insoluble Product.**—This product possesses the following chemical characteristics:

- (α) It is soluble in aqueous alkalis and alcohol, insoluble in hydrocarbons;
- (β) It reduces Fehling's solution;
- (γ) It is unsaturated;
- (δ) Diazotization is positive.

Upon treatment with zinc dust in boiling glacial acetic acid solution, it is partially reduced, giving

(7) Claisen solution is a mixture of equal parts by volume of methyl alcohol and 50% aqueous potassium hydroxide solution, *L. Claisen, Ann.*, **418**, 96 (1919); **442**, 210 (1925). High molecular weight phenols may no longer be soluble in aqueous alkalis but must be soluble in Claisen solution ("Cryptophenols"). J. B. Niederl, *Ind. Eng. Chem.*, **30**, 1272 (1938); O. Behaghel and H. Freienselner, *Ber.*, **67**, 1368 (1934); **68**, 341 (1935); M. E. McGreal and J. B. Niederl, *THIS JOURNAL*, **57**, 2625 (1935). The expression "soluble in Claisen solution" means that the compound either *a priori* possesses a free phenolic hydroxyl group or forms such a group (keto-enol tautomerism), which then yields a potassium salt when treated with this reagent. Similarly the expression "insoluble in Claisen solution" denotes absence of a free phenolic hydroxyl group.

a water and benzene insoluble reduction product (B I) which yielded the following derivatives:

- B I (a) benzoates: simple and *p*-nitro, both are insoluble in alkalis;
- (b) dibromo compound: soluble in Claisen solution, and reduces Fehling's solution;
- (c) nitro compound: soluble in sodium carbonate solution, and also reduces Fehling's solution.

In addition to the above, the partially reduced product (B I) gives the following reactions:

- B I (α) It is soluble in aqueous alkalis and alcohol, insoluble in water, aromatic and aliphatic hydrocarbons;
- (β) It reduces Fehling's solution;
- (γ) It reacts unsaturated;
- (δ) Exhaustive oxidative nitration gave picric acid;
- (ε) Diazotization is positive.

(C) **The Benzene-soluble Product.**—This product gave the following crystalline derivatives:

- I Benzoate: insoluble in Claisen solution;
- II Phenylurethan: insoluble in Claisen solution.

In addition to this, the product exhibits the following physical and chemical properties:

- (α) It is soluble in Claisen solution and alcohol, ether, aromatic and aliphatic hydrocarbons, soluble in water 1:1000 (approx.);
- (β) It does not reduce Fehling's solution;
- (γ) Diazotization is positive;
- (δ) It is crystalline and not a polymer.

Discussion of Results

Although at present no final assignment of structure can be given to the three condensation products obtained by condensing *d*-glucose with phenol, nevertheless, certain conclusions as to the structure of these compounds might be attempted on the basis of the experimental results thus far obtained. The first step in this direction would be to select a known scheme of reaction into which the new products derived here would fit, so that they could be explained in terms of the old.

Condensation of phenols with carbonyl compounds fundamentally proceeds according to either one of the two reaction schemes thus far encountered in such types of condensations. Either one of the ring hydrogen atoms (ortho or para) or the hydroxyl hydrogen of the phenol adds to the carbonyl group. In the first case "phenolhydrins" form which usually undergo further reaction, yielding finally phenolic alkylene oxides, phenylalkylene dioxides, coumaranes or

alkylidene-diphenols depending what type of phenol, whether *o*-, *m*- or *p*-substituted, was employed.^{8,8} In the second case, oxygen heterocyclics, chromanols, chromenes, spirochromanes or flavanols are produced.⁹

The water-soluble compound (A) does not furnish any specific clue as to its structure, except that the compound possesses one phenolic radical, that it has four hydroxyl groups which can be esterified, and that it reduces and is unsaturated. Thus, any of the above enumerated types of condensation schemes would have to be considered.

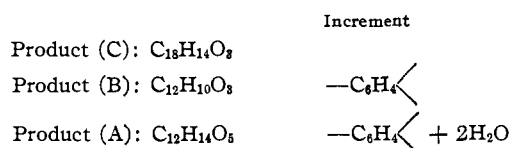
The water and benzene insoluble compound (B), however, limits these possibilities and definitely points to ring formation. Formation of carbocyclic compounds from *d*-glucose or other monosaccharides has never been observed; the formation, however, of oxygen heterocyclic compounds of the furan and pyran type is well known. If only one oxygen heterocyclic ring were formed, the compound would have to have a highly unsaturated side chain. Study of the derivatives of this compound precludes this possibility. Thus additional oxygen heterocyclic ring formation, of either type mentioned before, is indicated. There are, then, a number of ring combinations possible. Assuming usual ortho condensation, the three rings (one benzene and two oxygen heterocyclic rings) may be arranged linearly or angularly. Since the compound shows keto-enol tautomerism, a linear arrangement of the three rings becomes unlikely. There remains, then, an angular arrangement of the three rings. This makes possible the following combinations 6:5:5 (furanocoumarane); 6:6:5 (furanochromane) and 6:6:6 (pyranochromane). All three ring combinations have about an equal degree of validity.

The crystalline, benzene-soluble compound (C) possesses two phenyl radicals, a fact which distinguishes it from the products (A) and (B). Thus compound (C) may not be structurally related at all to these products and might be a diphenylmethane or terphenyl type of compound. The other view would be that all three products are structurally related, a view which appears particularly strengthened by the fact that the

(8) (a) M. E. McGreal and co-workers, *THIS JOURNAL*, **61**, 345 (1939); (b) J. B. Niederl and co-workers, *ibid.*, **61**, 348 (1939); (c) **58**, 657 (1936); (d) M. E. McGreal and J. B. Niederl, Baltimore meeting, Am. Chem. Soc., April, 1939; (e) H. Jordan, German Patent, 501,723 (1926).

(9) (a) A. Dianin, *J. Russ. Phys.-Chem. Soc.*, **46**, 1313 (1914); (b) J. B. Niederl, *THIS JOURNAL*, **50**, 2230 (1928); (c) **51**, 2426 (1929); (d) *Z. angew. Chem.*, **44**, 467 (1931); (e) *Monatsh.*, **60**, 150 (1932); (f) J. B. Niederl and co-workers, *ibid.*, **51**, 1038 (1929).

three products show a very simple relationship in their empirical formulas:

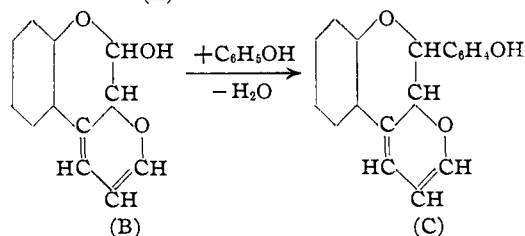
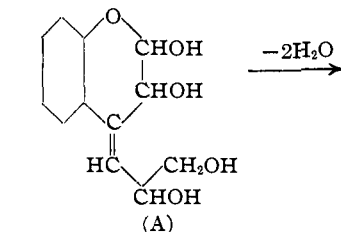
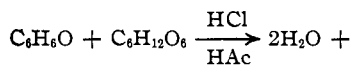


A condensation system involving a carbonyl compound and phenol, in which the products which are formed under identical reaction conditions, show a similar relationship to the one existing between products (C) and (B), is known. It is the condensation of mesityl oxide with phenol which yields a chromanol and a flavanol, respectively.^{9a,c}

Assuming a similar structural relationship between the water insoluble condensation products formed from *d*-glucose and phenol, then the water and benzene insoluble product (B) could either be a furano- or a pyranochromanol, and the water insoluble, but benzene soluble product (C) a furano- or pyranoflavanol, respectively. A furanoflavanol, since the product is formed from *d*-glucose, would retain the terminal methylol group and consequently would require four oxygen atoms. There are only three oxygen atoms present in this compound, a fact which would favor the pyranoflavanol configuration. This, however, would indicate "double addition" (addition of the phenolic hydroxyl hydrogen to the carbonyl group and addition of the phenyl group to an ethylenic linkage) and from this it would follow that *d*-glucose reacted not as a saturated carbonyl compound but unsaturated.

Condensation systems in which a saturated carbonyl compound reacted not as such, but rather as its alpha unsaturated aldol type of condensation product, are reported in the literature. Thus when acetone is condensed with *m*- or with *p*-cresol spirochromanes are produced, which are identical with the condensation products formed from phorone and these phenols.^{9b,d,e,f} By analogy, *d*-glucose also could have reacted as an alpha unsaturated carbonyl compound, such as the intermediates in the formation of methylol-furfural in acid medium (glucoseen-2,3, etc.).¹⁰ On the basis of all this, the establishment of tentative structural formulas for the three condensation products and their derivatives, might be attempted as indicated in the following

(10) H. Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, 1938, Vol. II, pp. 1493-1501.



Experimental

Condensation Methods. (a) **Fast Process.**—Ninety-four grams of phenol (1 mole) was dissolved in 250 cc. of glacial acetic acid and added to 180 g. (1 mole) of anhydrous *d*-glucose and placed in a 2-liter triple-necked round-bottomed flask provided with a reflux condenser, a thermometer, a gas inlet tube extending to the bottom of the vessel, and a mechanical stirrer. A vigorous stream of hydrogen chloride gas was passed through the system at 25°. After two and a half hours a dark reddish-brown mixture indicated the completion of the reaction. After this, the flask was well stoppered and set aside for forty-eight hours.

(b) **Slow Process.**—Ninety-four grams of phenol (1 mole) and 180 g. of *d*-glucose were placed in a 1-liter Erlenmeyer flask. To this mixture 500 cc. of concentrated hydrochloric acid (sp. gr. 1.18) was added. The mixture was well stirred while being further saturated with hydrogen chloride gas. The flask was then stoppered and allowed to stand for at least one month at room temperature. The reaction mixture was stirred occasionally and resaturated with hydrogen chloride gas until complete solution of the reactants had taken place.

Isolation of the Condensation Products.—The reaction mixture as obtained by either process (a or b) was poured into three liters of warm water under vigorous stirring. The water and benzene insoluble product (B) separated out in the form of a dark, semisolid mass; yield, about 50-60%. The supernatant aqueous solution was decanted and filtered several times until perfectly clear.

This filtered aqueous extract was then concentrated *in vacuo* at 15 mm. pressure and at a temperature not exceeding 50° to a total volume of 500 cc. This concentrated aqueous solution was then extracted four times with 100-cc. portions of benzene to remove unreacted phenol as well as the benzene-soluble product (C). The combined benzene extracts were filtered and concentrated *in vacuo* to about half the original volume. Upon standing at room temperature, the benzene-soluble condensation product (C) crystallized out in the form of large plates; yield, about 1%. The aqueous solution was further concentrated under diminished pressure (15 mm.) and at a tem-

perature not exceeding 50° to a viscous sirup and then poured into 250 cc. of absolute alcohol to remove any unreacted *d*-glucose which thus precipitated out. This precipitate was removed and the alcoholic solution was again concentrated *in vacuo* as described above. The resulting sirup was treated once more with 150 cc. of absolute alcohol and any precipitate which still might form was removed and the remaining alcoholic solution was again transferred to a vacuum desiccator containing phosphorus pentoxide and the desiccator was evacuated. The glassy, extremely hygroscopic residue was the water-soluble, benzene-insoluble product (A); yield, about 15%.

Condensations of *d*-glucose with other phenols (phenol homologs) polyhydric phenols, polynuclear phenols, etc., seem to follow an identical course of reaction with decreasing yields of the water-soluble product. Also, variation of the carbohydrate does not alter materially the above given reaction procedure, thus substitution of the *d*-glucose by isomeric aldohexoses (*d*-galactose, *d*-mannose, etc.) or ketoses (*d*-fructose) or pentoses (*d*-arabinose) or by hydrolyzable disaccharides (sucrose, lactose, maltose, etc.) or polysaccharides such as starch (potato or rice starch), cellulose (cotton, sawdust, etc.) produces materials of similar behavior and hence, apparently, of closely related structure.

Condensation Products. The Water-Soluble Benzene-Insoluble Product (A).—Solid, amorphous, hygroscopic; m. p. 115° (uncorr., dec.); $d_{25}^{24} + 79.2^\circ$ (in water). It is soluble in water in all proportions and reduces Fehling's solution. One gram of the substance was treated with 50 cc. of concentrated nitric acid, first in the cold and then boiled until a clear, straw-yellow colored solution resulted. This solution was evaporated on a steam-bath to dryness. Crystals of picric acid formed: m. p. 119°; mixed m. p. with a standard sample, 121°; yield, 0.8 g.

Anal. Calcd. for $C_{12}H_{14}O_5 \cdot H_2O$: C, 56.26; H, 6.25; H_2O , 6.87; mol. wt., 256. Found: C, 54.57; H, 6.37; H_2O , 6.71; mol. wt., 269, 272 (cryosc., in water).*

Derivatives. Benzoate (A I).—This compound was prepared according to Shriner and Fuson¹¹ following procedure 7, page 142. One gram of product (A) was dissolved in 3 cc. of pyridine. Half of one cc. of benzoyl chloride was added and the solution gently heated for several minutes. After cooling, the mixture was poured into 20 cc. of ice water and filtered. The precipitate was washed with 5 cc. of a 5% sodium carbonate solution and finally crystallized from 80% ethyl alcohol: yield, 60% of the theoretical; m. p., 130° (uncorr.).

Anal. Calcd. for $C_{40}H_{30}O_9 \cdot H_2O$: C, 71.42; H, 4.76; H_2O , 2.68. Found: C, 71.60; H, 5.08; H_2O , 3.30.*

(11) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935.

* It is herewith pointed out that in the case of the water-soluble product (A) and the water- and benzene-insoluble product (B) some of the products were non-crystalline and also did not give analytical results within the accustomed limits of errors. However, the deviations do not exceed the limits found tolerable by R. Willstätter and R. Robinson in their investigation of the structurally related anthocyanins. The same applies to the melting points given. [R. Willstätter and co-workers, *Ann.*, **401**, 224, 226, 227 (1913); **408**, 48, 49, 52, 71, 81, 109, 117, 119 (1915); **412**, 187, 193, 221, 228 (1917); *Ber.*, **51**, 1950 (1924); R. Robinson and co-workers, *J. Chem. Soc.*, 1437, 1438, 1444 (1932); 26, 29 (1933); 448 (1937).]

Sodium Salt (A II).—One gram of product (A) was dissolved in 25 cc. of absolute ethyl alcohol. Fifty cc. of a saturated solution of sodium ethylate was prepared by dissolving metallic sodium in absolute alcohol until the solution was saturated, as indicated by the formation of a film on the surface of the alcohol. This solution was filtered and 25 cc. of this filtered solution was added to the above solution of product (A) in absolute alcohol. A white precipitate formed which turned red on prolonged exposure to air. This precipitate was centrifuged and washed twice with 25-cc. portions of absolute alcohol. After these washings, the precipitate was quickly transferred to a desiccator and dried *in vacuo* over phosphorus pentoxide; yield, quantitative.

Anal. Calcd. for $C_{12}H_{13}O_5Na$: C, 55.38; H, 5.00; Na, 8.84. Found: C, 55.26; H, 5.12; Na, 8.34.*

Phenyllosazone (A III).—To a mixture of 3 g. of phenylhydrazine hydrochloride and 6 g. of sodium acetate 50 cc. of distilled water was added and the mixture heated to boiling. It was then quickly filtered. One gram of product (A) was dissolved in 5 cc. of distilled water and this solution was added to the filtered solution of the reagent. The mixture was then heated for six hours on a steam-bath, using a stopper valve to prevent excessive oxidation. Upon standing overnight the osazone precipitated out. The osazone was filtered off and dissolved in 5 cc. of Claisen solution. To this solution 50 cc. of distilled water was added and the mixture was allowed to stand overnight. Any phenylglucosazone present precipitated out and was filtered off. The filtrate was decomposed cautiously with dilute ice-cold hydrochloric acid. The precipitate was centrifuged, washed three times with distilled water, and transferred to a porous tile. When air dry, the precipitate was transferred to a desiccator and dried over phosphorus pentoxide: yield, about 10%; m. p., 183° (uncorr.).

Anal. Calcd. for $C_{21}H_{24}N_4O_7 \cdot H_2O$: C, 66.66; H, 6.00; N, 12.90; H_2O , 4.14. Found: C, 66.73; H, 6.09; N, 12.91; H_2O , 3.91.

Dibromo Compound (A IV).—To 25 cc. of a 4% aqueous solution of product (A), 25 cc. of bromine water was added. A brick-red precipitate formed immediately. The precipitate was centrifuged and washed three times with distilled water. It was then transferred to a porous tile and was dried in a desiccator over phosphorus pentoxide: yield, quantitative, m. p., 130° (uncorr., dec.).

The product is insoluble in water and sodium carbonate solution, but dissolves readily in sodium hydroxide solution and organic solvents. It forms a water-insoluble barium salt when treated with barium hydroxide solution. It reduces Fehling's solution. One bromine atom can be hydrolyzed easily by treating the compound with weak aqueous alkalis in the cold. For the removal of the remaining bromine atom, more drastic treatment is necessary. One gram of this compound was treated with 50 cc. of concentrated nitric acid first in the cold and afterward the reaction mixture was heated to boiling until a clear solution resulted. This solution was evaporated to dryness on a steam-bath. The remaining residue was extracted with 3 portions of 5 cc. each of benzene. The benzene extracts were combined, filtered and allowed to evaporate at room temperature. Large crystals of picric acid formed and no brominated nitrophenol could be found. This

indicates that the bromine must be in the side chain and not in the benzene ring of the compound, hence addition and not substitution had taken place.

Anal. Calcd. for $C_{12}H_{14}O_5Br_2$: C, 36.18; H, 3.51; Br, 40.20. Found: C, 36.22; H, 3.18; Br, 40.83.*

Derivatives of the Dibromo Compound (A IVa-d)

Benzoate (A IVa).—Eight grams of the dibromo compound (A IV) was dissolved in 50 cc. of pyridine. To this solution 10 cc. of benzoyl chloride was added slowly and the mixture well shaken. After this, the reaction mixture was poured into 500 cc. of ice water. A precipitate formed, which was allowed to settle. The supernatant aqueous layer was decanted and the residue crystallized from hot 90% alcohol: yield, about 60%; m. p., 155° (uncorr.).

The compound is insoluble in water, sodium carbonate and dilute sodium hydroxide solution, but soluble in organic solvents.

Anal. Calcd. for $C_{40}H_{50}O_9Br_2$: C, 58.96; H, 3.68; Br, 19.70. Found: C, 58.60; H, 3.72; Br, 19.80.

Semicarbazone (A IVb) and 2,4-Dinitrophenylosazone (A IVc).—Both compounds were prepared according to Shriner and Fuson, procedure 15 B (p. 145) and procedure 21 (p. 148); both compounds are soluble in Claisen solution; m. p., (A IVb) 210° (uncorr.); m. p., (A IVc) 181° (uncorr.).

Anal. Calcd. for $C_{13}H_{17}N_3Br_2O_5$ (A IVb): C, 34.36; H, 3.52; N, 9.20; Br, 35.24. Found: C, 35.24; H, 3.35; N, 8.89; Br, 34.35.* Calcd. for $C_{24}H_{30}N_3Br_2O_{11}$ (A IVc):¹² C, 38.10; H, 2.66; N, 14.81; Br, 21.16. Found: C, 37.25; H, 2.84; N, 14.48; Br, 21.79.*

Nitro Derivative (A IVd).—Five grams of the dibromo compound was dissolved in 50 cc. of concentrated nitric acid in the cold, and the resulting solution filtered, using a funnel with a glass sintered filter plate. To the filtrate 50 cc. of water was added and the mixture allowed to stand overnight. It was then filtered and the filtrate evaporated to dryness on a steam-bath. The residue was crystallized from hot water. In this process one of the bromine atoms appeared to have been replaced by a nitro group. The compound is somewhat soluble in water, very soluble in sodium carbonate solution, but insoluble in ether or benzene. It still reduces Fehling's solution; m. p. 107° (uncorr., dec.).

Anal. Calcd. for $C_{12}H_{10}N_3BrO_{11} \cdot H_2O$: C, 30.64; H, 2.55; N, 8.93; Br, 17.02. Found: C, 30.39; H, 2.39; N, 8.64; Br, 17.92.*

The Water and Benzene Insoluble Product (B).—This product as it is obtained in any of the two condensation methods, appears to be a pyrylium type of compound. Thus, it is soluble in concentrated hydrochloric acid, but precipitates out upon dilution with water. The compound itself is soluble in sodium hydroxide solution, in pyridine, in ethyl and amyl alcohol, but insoluble in water, sodium carbonate solution and benzene. The product itself was not further purified but immediately used for the preparation of derivatives more suitable for study.

(12) Caution is indicated in regard to the 2,4-dinitrophenylosazone (IVc), since no such types of compounds have thus far been reported. However, the product was obtained in following a standard procedure, and quantitative analysis of four different elements gave correct results.

Derivatives. Reduced Compound (B I).—One-half mole (101 g.) of the crude product (B) was dissolved in 1 liter of glacial acetic acid contained in a 2-liter round-bottomed flask provided with a water reflux condenser. The solution was heated to boiling. Zinc dust was added to the boiling solution in small portions until the originally dark solution became straw-yellow in color. This took several days. After this, the mixture was filtered either through glass wool or through a glass sinter funnel. The filtered solution was poured into 3 liters of warm water with vigorous stirring. The almost pure white precipitate was allowed to settle and was then filtered off, redissolved in glacial acetic acid and reprecipitated as described above. The product was then transferred to a desiccator and dried *in vacuo* over phosphorus pentoxide. The product is light yellow in color and no longer hygroscopic. It still shows the same reactions and solubility behavior as the unreduced product (B), with the exception that it does not seem to be able to form an osazone nor an alcohol insoluble sodium salt. The product is an amorphous, non-hygroscopic white powder; m. p., 120° (uncorr., dec.).

Anal. Calcd. for $C_{12}H_{12}O_3 \cdot H_2O$: C, 65.47; H, 6.31; H_2O , 8.10. Found: C, 65.54; H, 6.04; H_2O , 7.85.

Derivatives of the Reduced Compound (B I)

Benzoate (B Ia).—This benzoate was prepared in a manner exactly similar to the benzoates (A I) and (A IVa); m. p., 145° (uncorr.).

Anal. Calcd. for $C_{15}H_{16}O_4 \cdot H_2O$: C, 70.37; H, 4.94; H_2O , 5.55. Found: C, 70.09; H, 4.72; H_2O , 4.60.*

***p*-Nitrobenzoate (B Ia').**—This compound was prepared in a manner similar to the above simple benzoate (B Ia); m. p., 175° (uncorr.).

Anal. Calcd. for $C_{15}H_{13}NO_6 \cdot H_2O$: N, 3.63. Found: N, 3.53.

Dibromo Compound (B Ib).—This compound was prepared by dissolving 1 g. of product (B) in 1 liter of boiling water. The solution was filtered, and to the filtrate excess bromine water was added. The supernatant solution was decanted, the precipitate centrifuged and washed three times with distilled water, and then transferred to a porous tile and dried over phosphorus pentoxide. It is soluble in Claisen solution and still reduces Fehling's solution, but does not seem to be able to form carbonyl group derivatives: m. p., 138° (uncorr., dec.).

Anal. Calcd. for $C_{12}H_{12}Br_2O_3$: C, 39.77; H, 3.31; Br, 44.20. Found: C, 39.04; H, 3.04; Br, 44.13.*

Nitro Derivative (B Ic).—This product also was prepared in a manner analogous to the nitro derivative (A IVd); m. p., 130° (uncorr., dec.).

Anal. Calcd. for $C_{12}H_9N_3O_9 \cdot H_2O$: C, 40.59; H, 2.53; N, 11.83; H_2O , 5.04. Found: C, 40.86; H, 2.38; N, 11.70; H_2O , 5.27.

The Benzene-Soluble Product (C).—This compound can be crystallized either from benzene or from hot water. It is soluble in cold water approximately 1:1,000. It is insoluble in sodium carbonate solution, but soluble in Claisen solution. The compound no longer reduces Fehling's solution. It is soluble in organic solvents including ethers, aromatic and aliphatic hydrocarbons; m. p. 238–240° (uncorr.).

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.70; H, 5.04; mol. wt., 278. Found: C, 78.03; H, 5.17; mol. wt.,¹³ 275, 284.

Derivatives of the Benzene-Soluble Product (C). Benzoate (C I).—This benzoate was prepared like the benzoates (A I), (A IVa), and (B Ia); crystalline, m. p., 169° (uncorr.).

Anal. Calcd. for $C_{26}H_{18}O_4$: C, 78.53; H, 4.71. Found: C, 78.81; H, 4.52.

Phenylurethan (C II).—Two grams of product (C) was placed in a test-tube. Five cc. of phenyl isocyanate was added and the mixture heated to 150–160° for five minutes. The tube was then sealed and placed in boiling water for six hours, after which time the entire content of the tube solidified. The material was then placed on a porous tile and as soon as it was completely dry, it was crystallized repeatedly from alcohol. The product finally was crystallized from diisobutylene: crystalline, m. p., 195° (uncorr.).

Anal. Calcd. for $C_{26}H_{19}NO_4$: C, 75.75; H, 4.78. Found: C, 75.80; H, 4.64.

(13) The molecular weight determinations were performed cryoscopically, utilizing the method of K. Rast described in "Micro-methods of Quantitative Organic Elementary Analysis," by J. B. Niederl and V. Niederl, John Wiley and Sons, Inc., New York, N. Y., 1938, pp. 171–174.

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Summary

The condensation of *d*-glucose with phenol in the presence of hydrochloric acid has been described. Three types of condensation products were isolated: a water-soluble product, a benzene-soluble one, and a third product, insoluble in both water and benzene. Of these three products, numerous derivatives were prepared. The empirical formulas of these condensation products were established and probable structures discussed.

Variations of the phenol or the carbohydrate, which includes such materials as starch and cellulose, appear to produce condensation products of similar behavior. Thus, the condensation of *d*-glucose with phenol appears to be the prototype of all condensations in acid medium involving a carbohydrate and a phenolic compound.

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Hydrofluoric Acid as a Condensing Agent. II. Nuclear Alkylations in the Presence of Hydrofluoric Acid

BY WILLIAM S. CALCOTT, JOHN M. TINKER AND VIKTOR WEINMAYR

The replacement of one or more nuclear hydrogen atoms of an isocyclic compound with one or more alkyl or aralkyl radicals is referred to as nuclear alkylation. Such condensations take place under the influence of a great number of condensing agents of which acid condensing agents occupy the most prominent place. That hydrofluoric acid is a novel condensing agent was pointed out recently.¹

In view of the apparent interest in this field, this paper is presented in order to make available a background of experience which has been developed in E. I. du Pont de Nemours & Co. during the past years.

The isocyclic compounds which were alkylated belong to the classes of hydrocarbons, hydroxy compounds and their ethers, hydroxy nitro compounds and their ethers, carboxylic acids and hydroxy carboxylic acids, sulfonic acids, primary, secondary and tertiary hydroxy amines

and their ethers. It was possible to introduce into isocyclic compounds alkyl groups containing as few as two carbon atoms, but the best results were achieved when alkyl radicals containing three or more carbon atoms were used. Olefins or compounds which under the conditions of reaction would be expected to react like olefins, such as alcohols, ethers, esters or halides, were employed as alkylating agents. The alkyl radicals were aliphatic or isocyclic compounds, which might contain halogen, carboxy or hydroxy substituent groups. Condensation could take place with two isocyclic compounds, when more than one reactive group was present in the alkyl radical.

Nuclear alkylations in the presence of essentially anhydrous hydrofluoric acid proceeded smoothly and in the absence of side reactions. Migration or isomerization of alkyl groups was not observed. The alkyl groups appeared to replace nuclear hydrogen atoms directly whenever isocyclic hydroxy compounds were alky-

(1) J. H. Simons and S. Archer, *THIS JOURNAL*, **60**, 986 (1938).