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 $C_{25}H_{18}O_4$: 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 "Micromethods 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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[CONTRIBUTION FROM THE JACKSON LABORATORY, E. I. DU PONT DE NEMOURS & COMPANY]

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).

lated, and an ether formation was never noted. Isocyclic hydroxy ethers remained unchanged when treated with hydrofluoric acid under the usual experimental conditions. This indicates that ethers are not even formed as intermediates during the alkylation of isocyclic hydroxy compounds. The nuclear alkylation of aminophenols and aminophenol ethers took place in a similar manner without the intermediate formation of N-alkylated products.

The experiments were started using anhydrous technical hydrofluoric acid, but even 46% acid still acted in certain instances as a condensing agent. Of course the hydrofluoric acid was diluted to a certain extent during the condensation whenever alcohols, ethers or esters were used as the alkylating agent due to the elimination of water during the reaction.

We are not aware that isopropylnaphthols, isopropylnitronaphthalenes, alkylanthracenes and phenanthrenes, isopropylhydroxynaphthoic acids or isopropylbenzoic acid, or isopropylhydroquinones have been prepared by any other direct nuclear alkylation method. Tetraisopropylnaphthalene, tetraisopropylbenzene, their lower alkylated isomers, and isocyclic alkyl hydroxy compounds were obtained with practically quantitative yields in the presence of hydrofluoric acid.

Olefins, alcohols, ethers or esters were in general equally well adapted for the condensations, and only one instance was found where the alcohol did not react while the ether gave the normal alkylation. Dibenzyl ether gave benzyl isocyclic compounds while benzyl alcohol polymerized to 1,2,3,4,5,6-hexaphenylcyclohexane. A similar polymerization of benzyl alcohol takes place in the presence of boron trifluoride.[2]

Olefins usually were selected when a high yield of highly alkylated compounds was desired. In this connection it should be mentioned, however, that diisobutylene gave tertiary butyl compounds and not octyl compounds, when condensed with isocyclic compounds in the presence of hydrofluoric acid. Such a cleavage of diisobutylene also was observed in the presence of other acid condensing agents.[3]

Several interesting observations have been made on some of the alkylated products prepared in the course of the study. It was remarkable, for example, how labile some of the substituents of the isocyclic compounds became when alkyl groups were introduced into the nucleus. Good examples were the alkylated aminophenols and the alkylated aminophenol ethers. It is known that aminophenols and aminophenol ethers can be condensed under certain conditions to give the corresponding diphenylamines.[4] Dialkylated aminophenols and their ethers were so reactive that they gave off some ammonia at ordinary temperature and changed quite readily to the corresponding tetraisopropyldiphenylamines upon heating and distilling.

A related reaction was reported in the literature where 4,4′-dimethoxy-2,2′-dimethyl-5,5′-diisopropyldiphenylamine was isolated when the methyl ether of thymol was nitrated and reduced.[5]

Another illustration of the increase of the lability of substituents caused by the presence of alkyl groups was observed during the alkylation of hydroquinone. It was possible to isolate a monoisopropylhydroquinone, but a diisopropylhydroquinone could not be isolated. The next higher alkylated product obtained was always the 2,4,6-triisopropylphenol. Apparently, at the instant a second alkyl group had condensed with the hydroquinone, it made the second hydroxy group so unstable that it was replaced by a third alkyl group.

The constitution of new products obtained in the course of the alkylation in the presence of hydrofluoric acid was not determined, but there is no indication that the substitution rules of alkylation in the presence of hydrofluoric acid are not the same as those for other acid condensing agents. Whenever known alkyl compounds were formed, they were identical with those obtained in the presence of sulfuric acid, boron fluoride or other condensing agents.

The following isocyclic compounds were alkylated: benzene, toluene, xylene, naphthalene, tetrahydronaphthalene, mono- and diisopropylnaphthalene, α-nitronaphthalene, phenanthrene, anthracene, phenol, *o*- and *m*-cresol, diphenyl oxide, β-naphthol, 2,3-hydroxynaphthoic acid, naphthalene β-sulfonic acid, N-dimethyl-*p*-aminophenol, *p*-aminophenol, *p*-anisidine, diethylamino-3-ethoxybenzene and 1-amino-2-methoxynaphthalene.

The following alkylating agents were used:

(2) Cannizzaro, *Ann.*, **92**, 114 (1851).

(3) V. N. Ipatieff and H. Pines, THIS JOURNAL, **58**, 1056 (1936); R. P. Perkins and H. S. Nutting, U. S. Patent 2,091,565 (1937).

(4) R. Vidal, *Chem. Centr.*, **74**, I, 85 (1903).

(5) H. Decker and B. Solonina, *Ber.*, **38**, 64 (1905).

ethylene oxide, isopropyl alcohol, isopropyl ether, propylene, 3-chloro-2-methylpropene-1, *t*-butyl alcohol, hexene-3, 3-bromohexane, diisobutylene, cyclohexanol, dibenzyl ether, allyl alcohol, allyl formate, propylene oxide and oleic acid.

The following alkylated compounds were obtained: mono-, di- and tetraisopropylbenzene, mono-(1'-chloro)-*t*-butylbenzene and di-(1'-chloro)-*t*-butylbenzene, α,β-diphenylpropane, phenylethyl alcohol, *t*-butyltoluene, 1,3,5-*t*-butyl-*m*-xylene, tetraisopropylnaphthalene, di-*t*-butylnaphthalene, naphthylstearic acid, tetrahydropolyisopropylnaphthalene, diisopropylanthracene, di-(ethylbutyl)-anthracene, *t*-butylphenanthrene, diisopropyl-1-nitronaphthalene, 1-methoxy-2-nitro-4-isopropylbenzene, 1-methoxy-2-nitro-4-cyclohexylbenzene, 2,4,6-triisopropylphenol, mixed monoisopropyl-*m*-cresols, mono- and dibenzyl-*o*-cresol, monoisopropylhydroquinone, di-*s*-hexyldiphenyl oxide, diisopropyl-β-naphthol, mixed isopropyl-2,3-hydroxynaphthoic acid, triisopropylnaphthalene-2-sulfonic acid, mono-*m*-isopropylbenzoic acid, diisopropyl-*p*-aminophenol, 4,4'-dihydroxytetraisopropyldiphenylamine, monoisopropyl- and diisopropyl-N-dimethyl-*p*-aminophenol, diisopropyl-*p*-anisidine, 4,4'-dimethoxytetraisopropyldiphenylamine, monocyclohexyl-*p*-anisidine, monoisopropyl-1-diethylamino-3-ethoxybenzene and triisopropyl-1-amino-2-methoxynaphthalene.

Experimental Part

General Procedure.—The alkylations were run in a forged or stainless steel, copper or nickel vessel which was provided with a tightly fitting cover, agitator, thermometer well and charging hole. The latter was loosely covered during the condensations to minimize absorption of moisture from the air. Steel pressure vessels were used whenever the reaction temperature was higher than 20–25°. Liquid technical anhydrous hydrofluoric acid was poured from cooled steel cylinders into copper flasks, weighed, and transferred to the reaction vessels. No special precautions were taken to avoid the absorption of moisture from the air during this manipulation. The finished condensation mass was poured onto ice in Pyrex vessels and worked up by methods best suited for the different products obtained. Many of the alkylated products were insoluble in the dilute hydrofluoric acid and readily soluble in solvents. They were dissolved, washed in solution, and purified by crystallization or distillation. Solids were filtered, washed, and if necessary crystallized. Amines sometimes crystallized as hydrofluorides, and more frequently were precipitated from the dilute hydrofluoric acid solution through the addition of alkali, then dissolved in solvents and further purified. Unreacted starting materials frequently could be removed by extraction with water.

The isocyclic compounds as a rule were added as quickly as possible to the cooled hydrofluoric acid, while the temperature was kept below the boiling point of the hydrofluoric acid. The alkylating agent usually was introduced slowly over a certain period of time. If it were a gas it was led under the surface of the mixture of the isocyclic compound and the hydrofluoric acid. Liquids were added by means of Pyrex dropping funnels. It was of course not necessary to have a solution of the isocyclic compound and the hydrofluoric acid to obtain alkylation. Compounds like benzene, alkylated naphthalenes, or alkylated phenols are not miscible with the acid. Most of the condensations were allowed to stand overnight before being worked up, although they were usually finished in a much shorter time.

In the following list of experiments, the charge, the temperature and the time of addition of the alkylating compound, the temperature and the time at which the condensation was held until it was worked up, are given in the order mentioned.

Experimental

Benzene and Propylene.—Benzene (500 g., 6.4 *M*), propylene 80% (220 g., 4.18 *M*), H_2F_2, (375 g.) 10–15°, five hours, 15–20° eighteen hours. Obtained 376 g. (74.7%) of monoisopropylbenzene, b. p. 151°, 117 g. (17.23%) of diisopropylbenzene, b. p. 201–209°.

Benzene and Propylene.—Benzene (390 g. 5 *M*), 80% propylene (1200 g., 23 *M*), H_2F_2 (505 g.), 15° six hours, 20–25° twenty hours. Decomposition with water gave a precipitate (1155 g.) which was crystallized from 3000 cc. of alcohol. 1,2,4,5-Tetraisopropylbenzene (940 g., 76.7%) was obtained melting from 117–118° (lit. 118°).[6]

Benzene and 3-Chloro-2-methylpropene-1.—Benzene (250 g., 3.2 *M*), methallyl chloride (105.8 g., 1.17 *M*) (a product of the Shell Development Co. of California), H_2F_2 (150 g.), 5–10° thirty minutes, 0–5° twenty hours. 1'-Chloro-*t*-butylbenzene (130 g. 66%, b. p. 111° at 90 mm.) and di-(1'-chloro)-*t*-butylbenzene (31 g., 10.1%, b. p. 140° at 4 mm.) were obtained.

Anal. Calcd. for $C_{10}H_{13}Cl$: Cl, 21.05. Found: Cl, 21.5. Calcd. for $C_{14}H_{20}Cl_2$: Cl, 27.4. Found: Cl, 25.6.

The compounds distilled under reduced pressure practically without decomposition but gave off hydrogen chloride when heated to the boiling point (about 225 and 300°) at atmospheric pressure. Practically all of the 1'-chloro-*t*-butylbenzene was recovered unchanged after it had been heated with 13% alcoholic potassium hydroxide to 86° for twenty-four hours.

Benzene and Allyl Alcohol.—Benzene (132 g., 1.69 *M*), allyl alcohol (45.4 g., 0.78 *M*), H_2F_2 (200 g.), 4–7° two hours, 0–5° twenty hours. The reaction had for some time a pleasant odor, which was most likely due to the presence of hydratropic alcohol. α,β-Diphenylpropane (80 g., 52.3%, b. p. 109° at 2 mm.) was isolated.

Anal. Calcd. for $C_{15}H_{16}$: C, 91.8; H, 8.16. Found: C, 91.83; H, 8.0.

The identical compound was formed when allyl formate or propylene oxide was used in place of allyl alcohol.

Benzene and Ethylene Oxide.—Ethylene oxide was passed into the mixture of benzene and H_2F_2 at 6–12°.

(6) A. Kirrmann and M. Graves, *Bull. soc. chim.*, [5] **1**, 1494 (1934).

The characteristic odor of phenylethyl alcohol was noted, but the product could not be isolated in a pure state.

Toluene and Diisobutylene.—Toluene (400 g., 4.35 *M*), diisobutylene (224 g., 2 *M*) (product of the Shell Development Co.), H_2F_2 (100 g.), 3–6° two hours, 0–5° twenty hours. *p*-*t*-Butyltoluene (230 g., 77.2%, b. p. 190°, lit. 189–190°) and di-*t*-butyltoluene (81 g., 19.6%, b. p. 81.8–82.8° at 4 mm.), were obtained.

***m*-Xylene and *t*-Butyl Alcohol.**—*m*-Xylene (170 g., 1.6 *M*), *t*-butyl alcohol (88 g., 1.2 *M*), H_2F_2 (520 g.) −3 to −8° in a few minutes, 0–3° sixteen hours. *t*-Butyl-*m*-xylene, b. p. 56° at 44 mm., was obtained with a yield of 97.4% based on the amount of *t*-butyl alcohol used.

Naphthalene and Propylene.—Naphthalene (128 g., 1 *M*), 80% propylene (300 g., 5.7 *M*), H_2F_2 (525 g.), 0–8° six hours, 20° twenty hours. The alkylated naphthalenes precipitated from the hydrofluoric acid, making it necessary to finish the condensation without stirring. Crude tetraisopropylnaphthalene (290 g., m. p. 119–125°, lit. 127.5°) was separated by filtration of the diluted condensation mass; yield 98%. Crystallization from acetone gave the pure compound melting at 128°.

A tetrachlorotetraisopropylnaphthalene was prepared by chlorination in carbon tetrachloride in the presence of anhydrous ferric chloride at 0–5°. It distilled at 170° at 0.1 mm. without decomposition, but split off hydrochloric acid when heated to 340° at 760 mm.

Anal. Calcd. for $C_{22}H_{22}Cl_4$: Cl, 32.7. Found: Cl, 31.6.

Naphthalene and *t*-Butyl Alcohol.—Naphthalene (128 g., 1 *M*), *t*-butyl alcohol (233 g., 3.15 *M*), H_2F_2 (500 g.) 4–8° three hours, 0–5° twenty hours. Di-*t*-butylnaphthalene (184 g., 76%, m. p. 143°) was obtained.

Naphthalene and Oleic Acid.—Naphthalene (64 g., 0.5 *M*), oleic acid (141 g., 0.5 *M*), H_2F_2 (500 g.) 0–5° ten minutes, 0–5° twenty hours. The condensation product obtained was dissolved in carbon tetrachloride, washed, and freed of the excess of naphthalene and some low boiling impurities by heating to 290° at 4 mm. The residue (130 g., 61.9%) was naphthylstearic acid, a brown viscous oil, completely soluble in dilute aqueous sodium carbonate.

Anal. Calcd. for $C_{28}H_{42}O_2$: C, 81.8; H, 10.24. Found: C, 79.97; H, 10.87.

Tetrahydronaphthalene and Propylene.—Tetralin (132 g., 1 *M*), 80% propylene (280 g., 5.33 *M*), H_2F_2 (450 g.), 5–15° four hours, 5–15° sixteen hours. Mixed isopropyltetrahydronaphthalene (136 g., b. p. 136–270° at 4.6 mm.) was obtained forming a viscous oil at ordinary temperature.

Anthracene and Isopropyl Ether.—Anthracene (267 g., 1.5 *M* used as 80% anthracene), isopropyl ether (306 g., 3 *M*), H_2F_2 (1195 g.), 10° forty-five minutes. Cooling was discontinued and the reaction temperature rose to 30° after two hours. The condensation product was completely soluble in 500 cc. of benzene. Diisopropylanthracene (300 g.) distilled from 202–206° at 0.2 mm. forming a viscous oil which could not be crystallized. Oxidation with chromic acid in glacial acetic acid gave a small amount of a mixture of anthraquinone carboxylic acids (m. p. above 300°).

Anal. Calcd. for $C_{16}H_8O_6$: acid number, 189; C, 64.8. Found: acid number, 188.3; C, 65.6.

Anthracene and 3-Bromohexane. **Acknowledgment.**—We are obliged to Mr. L. Spiegler for permitting the publication of this experiment. Anthracene (48 g., 0.27 *M*), 3-bromohexane (42 g., 0.25 *M*), H_2F_2 (54 g.). This charge was heated to 120–125° for twenty hours. Di-(ethylbutyl)-anthracene was formed, distilling from 240–256° at 3 mm. A small amount of penta-(diethylbutyl)-anthracene melting from 89.2–101° was isolated by crystallization of the still residues.

Anal. Calcd. for $C_{44}H_{70}$: mol. wt., 598. Found: mol. wt., 595.

Phenanthrene and *t*-Butyl Alcohol.—70% Phenanthrene (133.5 g., 0.75 *M*), *t*-butyl alcohol (122 g., 1.65 *M*), H_2F_2 (433 g.), 15–20° thirty minutes, 15–20° eighteen hours. Mixed *t*-butylphenanthrenes (130 g.) were obtained, distilling from 200–250° at 0.5 mm. The product was a viscous, dark colored oil, beginning to boil at about 370° at atmospheric pressure.

α-Nitronaphthalene and Isopropyl Ether.—1-Nitronaphthalene (216 g., 1.25 *M*), isopropyl ether (122.5 g., 1.2 *M*), H_2F_2 (465 g.), 0–5° ninety minutes, 0–5° six hours and 20° fifteen hours. Monoisopropyl-1-nitronaphthalene (26 g., 9.6%) distilled from 145–155° at 2 mm.

Anal. Calcd. for $C_{13}H_{13}O_2N$: N, 6.50. Found: N, 6.62.

Diisopropyl-1-nitronaphthalene (264 g., 82.1%) distilling from 155–168° was the principal product. The product was 98.2% pure as determined by a titanium chloride titration. Its molecular weight was determined as 247 (calcd. 257).

Diisopropyl-1-nitronaphthalene (100 g., 0.39 *M*) was reduced with hydrogen at 100° and a pressure of 600 lb. (40 atm.), using a nickel catalyst. Diisopropyl-1-aminonaphthalene (75 g., 84.7%, b. p. 150–158° at 0.5 mm.) was obtained. Apparently, a slight loss of isopropyl groups had occurred during the reduction.

Anal. Calcd. for $C_{16}H_{21}N$: N, 6.17. Found: N, 6.74.

***o*-Nitroanisole and Isopropyl Alcohol.**—*o*-Nitroanisole (153 g., 1 *M*), isopropyl alcohol (60 g., 1 *M*), H_2F_2 (248 g.) 8–10° one hour, 20° eighteen hours. 1-Methoxy-2-nitro-4-isopropylbenzene (164 g., 84.1%) was formed distilling from 138.5–139.5° at 3 mm. The product analyzed as 98.9% pure by a titanium chloride titration.

***o*-Nitroanisole and Cyclohexanol.**—*o*-Nitroanisole (375 g., 2.45 *M*), cyclohexanol (225 g., 2.25 *M*), H_2F_2 (350 g.), 15–20° one hour, 20° twenty hours. 1-Methyl-2-nitro-4-cyclohexylbenzene (172 g.) was separated, distilling from 198–208° at 2 mm., analyzing 93.3% pure by a titanium chloride titration.

Phenol and Propylene.—Phenol (140 g., 1.49 *M*), isopropyl alcohol (405 g., 6.75 *M*), H_2F_2 (820 g.). The solution of phenol in isopropyl alcohol was added to the hydrofluoric acid at 2–8° in three hours. The charge was then held at 20–25° for sixteen hours. 2,4,6-Triisopropylphenol (310 g., 94.5%, b. p. 125° at 7 mm.) was obtained.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.8; H, 10.81. Found: C, 81.8; H, 10.92.

***m*-Cresol and Propylene.**—*m*-Cresol (324 g., 3 *M*) 80% propylene (158 g., 3 *M*), H_2F_2 (550 g.), 0–8° four hours, 20° sixteen hours. A mixture of mono-isopropylated *m*-cresol distilled at 102.5° at 4 mm. and crystallized at 43°.

o-Cresol and Dibenzyl Ether.—*o*-Cresol (162 g., 1.5 *M*), dibenzyl ether (178 g., 0.9 *M*), H_2F_2 (290 g.), 5–10° two hours, 20–25° eighteen hours. Monobenzyl-*o*-cresol (160 g., 53.9%, b. p. 160° at 5 mm.) and dibenzyl-*o*-cresol (30 g., 10.4%, b. p. 235° at 5 mm.) were obtained.

Hydroquinone and Isopropyl Alcohol.—Hydroquinone (550 g., 5 *M*), isopropyl alcohol (360 g., 6 *M*), H_2F_2 (830 g.), 5–10° two hours, 20° twenty-four hours. The oil which separated after decomposition with water was extracted three times with three liters of boiling water to remove any unreacted hydroquinone, and then distilled. The product boiling from 137–170° at 6 mm. (300 g., 39.4%, crystallizing point 128°) contained the monoisopropylhydroquinone, which was isolated in its pure form by a crystallization from benzene. It melted from 147–148°.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.1; H, 7.9; mol. wt., 152. Found: C, 71.9; H, 8.5; mol. wt., 151, by boiling point rise in alcohol.

When a large excess of isopropyl alcohol was used (165 g., 1.65 *M* hydroquinone, 458 g. 7.63 *M* isopropyl alcohol), there was not formed a polyisopropylhydroquinone, but 2,4,6-triisopropylphenol (300 g., 82.7%) distilling at 125° at 7 mm. was isolated instead.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.8; H, 10.81. Found: C, 81.38; H, 11.2.

Diphenyl Oxide and Hexene-3.—Diphenyl oxide (105.5 g., 0.62 *M*), hexene-3 (151 g., 1.8 *M*), H_2F_2 (130 g.) 5–10° two hours, 20° over the week end. Di-(*s*-hexyl)-diphenyl oxide (127 g., 60.8%, b. p. 200–230° at 5 mm.) was obtained.

Anal. Calcd. for $C_{24}H_{34}O$: C, 84.7; H, 10.58. Found: C, 85.2; H, 10.27.

β-Naphthol and Isopropyl Alcohol.—β-Naphthol (160 g., 1.11 *M*), isopropyl alcohol (267 g., 4.44 *M*), H_2F_2 (500 g.), 4–9° four hours, 0–5° twenty hours. Diisopropyl-β-naphthol distilling at 196° at 2 mm. was formed with a yield of 94%.

Anal. Calcd. for $C_{16}H_{20}O$: C, 84.2; H, 8.78. Found: C, 84.15; H, 8.82; purity by coupling value 96%.

2,3-Hydroxynaphthoic Acid and Isopropyl Alcohol.—2,3-Hydroxynaphthoic acid (188 g., 1 *M*), isopropyl alcohol (72 g., 1.2 *M*), H_2F_2 (650 g.), 15–20° thirty minutes, 15–20° twenty hours. The monoisopropyl-2,3-hydroxynaphthoic acid was isolated as a viscous mass which was purified by extracting it repeatedly with boiling water to remove unreacted starting material. The product was completely soluble in dilute aqueous sodium carbonate and formed a solid melting at about 50°. By using more isopropyl alcohol, a higher alkylated 2,3-hydroxynaphthoic acid was obtained which melted at 70–75°. Neither of these compounds could be isolated in a crystalline form.

Naphthalene-2-sulfonic Acid and Isopropyl Alcohol.—Naphthalene-2-sulfonic acid monohydrate (113 g., 0.5 *M*), isopropyl alcohol (90 g., 1.5 *M*), H_2F_2 (480 g.), 0–5° thirty minutes, 20° twenty hours.

The finished condensation mass was poured onto 800 g. of ice and 750 cc. 96% sulfuric acid was added (allowing the temperature to rise to 80°) to salt out the polyisopropylnaphthalene-2-sulfonic acid as an oil. This oil was dissolved in 500 cc. water at 80° and again precipitated through the addition of 250 cc. of 96% sulfuric acid. The polyisopropylnaphthalene-2-sulfonic acid was of light gray color and solidified at about 40°.

Benzoic Acid and Isopropyl Ether.—Benzoic acid (183 g., 1.5 *M*), isopropyl ether (306 g., 3 *M*), H_2F_2 (904 g.), 10–20° thirty minutes, 75° eight hours. An oil separated when the charge was decomposed with water. Unreacted benzoic acid was extracted with hot water. Some caustic insoluble matter was removed with ether from a caustic solution. The mono-*m*-isopropylbenzoic acid was precipitated with hydrochloric acid. It melted at about 20°. The mono-*m*-isopropylbenzoyl chloride was prepared with thionyl chloride. It distilled from 125–130° at 23 mm.

Anal. Calcd. for $C_{10}H_{11}OCl$: Cl, 19.45. Found: Cl, 20.1.

***p*-Aminophenol and Isopropyl Ether.**—*p*-Aminophenol (327 g., 3 *M*), isopropyl ether (510 g., 5 *M*), H_2F_2 (2000 g.), 10–20° one hour, 75° five hours. Some of the excess of H_2F_2 was removed by distillation. The charge was poured onto an excess of dilute ammonia in the presence of 1000 cc. of benzene, keeping the temperature at 50–70°. Diisopropyl-*p*-aminophenol (69 g., 11.8%) distilled at 120° at 2 mm. The product is a solid that gives off traces of ammonia upon storing.

Anal. Calcd. for $C_{12}H_{19}ON$: N, 7.26; Found: N, 6.75.

It forms a neutral sulfate which melts from 206–208°.

4,4'-Dihydroxytetraisopropyldiphenylamine (340 g., 61.5%) distilled at 228° at 4 mm. The product was a pale yellow solid which turned red readily when exposed to the air. It was 95% pure as a secondary amine.

Anal. Calcd. for $C_{24}H_{35}O_2N$: N, 3.76; mol. wt., 369; C, 78.0; H, 9.48. Found: N, 3.76; mol. wt., 347; C, 76.88; H, 9.4.

N-Dimethyl-*p*-aminophenol and Isopropyl Ether.—Neutral oxalate of N-dimethyl-*p*-aminophenol (364 g., 2 *M*), isopropyl ether (214 g., 2.1 *M*), H_2F_2 (1175 g.), 8–10° two hours, 20–25° twenty hours. Some of the hydrofluoric acid was removed by heating the finished charge to 75° for several hours. The experiment was worked up as described in the preceding experiment.

Monoisopropyl-N-dimethyl-*p*-aminophenol (150 g., 41.9%, b. p. 137° at 3 mm.) and diisopropyl-N-dimethyl-*p*-aminophenol (40 g., 9%, b. p. 148° at 3 mm.) were obtained. The monoisopropyl-N-dimethyl-*p*-aminophenol was crystallized from carbon tetrachloride and petroleum ether and melted at 99–104°.

Anal. Calcd. for $C_{11}H_{17}ON$: N, 7.82. Found: N, 7.48, 7.63. Calcd. for $C_{14}H_{23}ON$: N, 6.34. Found: N, 6.63.

***p*-Anisidine and Isopropyl Ether.**—*p*-Anisidine (246 g., 2 *M*), isopropyl ether (306 g., 3 *M*), H_2F_2 (1200 g.), 10–20° one hour, 20–25° twenty hours. Isolation as described before. Diisopropyl-*p*-anisidine (157 g., 37.9%) distilled at 128° at 3.6 mm. The compound was a crystalline solid, completely soluble in dilute hydrochloric acid.

Anal. Calcd. for $C_{13}H_{21}ON$: N, 6.76. Found: N, 6.60.

The second cut of the distillation was 200 g. of 4,4'-dimethoxytetraisopropyldiphenylamine (50.4%) distilling from 230–234° at 3 mm. It was a low melting, brittle solid, which turned red readily when exposed to the air and could not be crystallized.

Anal. Calcd. for $C_{26}H_{39}O_2N$: N, 3.52. Found: N, 3.82.

It was 95.5% pure as a secondary amine apparently still containing traces of diisopropyl-*p*-anisidine. The hydrochloride was prepared by dissolving the compound in ether and adding 36% hydrochloric acid.

Anal. Calcd. for $C_{26}H_{39}O_2N \cdot HCl$: N, 3.23; Cl, 8.18. Found: N, 3.63; Cl, 8.9.

p-Anisidine and Cyclohexanol.—*p*-Anisidine (95.5 g., 0.77 *M*), cyclohexanol (200 g., 2 *M*), H_2F_2 (386 g.), 10–20° thirty minutes, 20° eighteen hours. An oil separated when the condensation mass was poured onto water. It was dissolved in benzene, washed with water, clarified by filtration and concentrated to a small volume. Petroleum ether was then added to precipitate the product in a crystalline form. Monocyclohexyl-*p*-anisidine tetrahydrofluoride (50 g., 22.8%, m. p. 185–195°) was obtained. It was of interest that this hydrofluoride was soluble in benzene.

Anal. Calcd. for $C_{13}H_{19}ON \cdot H_4F_4$: N, 4.91. Found: N, 4.83.

The hydrofluoride was based and converted to the hydrochloride which melted from 225–230°.

Anal. Calcd. for $C_{13}H_{19}ON \cdot HCl$: N, 5.80; Cl, 14.7. Found: N, 5.75; Cl, 14.46. By nitrite absorption: 99% pure.

1-Diethylamino-3-ethoxybenzene and Isopropyl Ether.—N-Diethyl-*m*-phenetole (88 g., 0.45 *M*), isopropyl ether (51 g., 0.5 *M*), H_2F_2 (303 g.), 10–20° thirty minutes, 20° twenty hours. The finished reaction mass was poured onto an excess of aqueous ammonia and the product which separated was dissolved in benzene. Monoisopropyl-1-diethylamino-3-ethoxybenzene (84 g., 79.5%) distilled at 110° at 0.15 mm. as a dark colored oil which was only sparingly soluble in aqueous hydrochloric acid.

Anal. Calcd. for $C_{15}H_{25}ON$: N, 5.95. Found: 5.99.

1-Amino-2-methoxynaphthalene and Isopropyl Ether.—1-Amino-2-methoxynaphthalene (104 g., 0.6 *M*), isopropyl ether (102 g., 1 *M*), H_2F_2 (435 g.), 5–10° one hour, 20° twenty hours. The condensation product separated as an oil when poured onto water. Triisopropyl-1-amino-2-methoxynaphthalene (83 g., 46.3%, b. p. 169° at 0.14 mm.) was obtained as a viscous oil which was only sparingly soluble in aqueous hydrochloric acid, but diazotized and coupled.

Anal. Calcd. for $C_{20}H_{29}ON$: N, 4.68. Found: N, 4.52.

Summary

It has been shown that hydrofluoric acid is an effective acid condensing agent for the preparation of nuclear alkylated isocyclic compounds.

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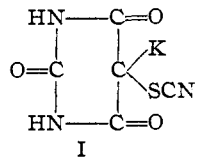
[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF MISSOURI]

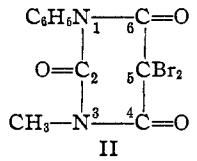
Phenyl Alkyl Nitrogen Substitution and Reactivity in the Barbituric Acid Series

BY DOROTHY NIGHTINGALE AND R. G. TAYLOR[1]

5,5-Dibromobarbituric acid reacts vigorously with ammonia to form an ammonium salt of 5-bromobarbituric acid,[2] with thiourea to form thiopseudo uric acid and with potassium thiocyanate to form (I)[3]



I



II

In this Laboratory, Morris[4] found that 1-phenyl-5,5-dibromobarbituric acid reacted with these same reagents but much less vigorously, to form the same derivatives. The amine salts of 1-phenyl-5-bromobarbituric acid were unstable as compared with the corresponding salts of 5-bromobarbituric acid. The 1,3-diphenyl-5,5-dibromobarbituric acid either did not react at all under the same conditions or formed some tarry material which would not yield crystals.

The progressive differences in reactivity of the halogen atoms as one or both of the hydrogens attached to nitrogen were replaced by phenyl groups led to the questions: is it the fact that the substituting groups on the nitrogens are aryl, which affects the reactivity, or would alkyl groups have the same effect?

To answer these questions, 5,5-dibromo-1-phenyl-3-methylbarbituric acid (II) and 5,5-dibromo-1-phenyl-3-butyl-barbituric acid (III) have been prepared and their reactions studied with amines, thiourea, and potassium thiocyanate.

Their behavior paralleled that of the corresponding diaryl nitrogen substituted barbituric acids. Replacement of an aryl group by an alkyl group increased the solubility of the acids in organic solvents and lowered the melting points.

Hepner and Frenkenberg[5] describe the prepa-

(1) Abstract of a dissertation presented by Richard G. Taylor in partial fulfilment of the requirements for the degree of Master of Arts at the University of Missouri.

(2) Biltz and Hamburger, *Ber.*, **49**, 635 (1916).

(3) Trzcinski, *ibid.*, **16**, 1057 (1883).

(4) Nightingale and Morris, THIS JOURNAL, **58**, 1469 (1936).

(5) Hepner and Frenkenberg, *J. prakt. Chem.*, **134**, 249 (1932).