[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE ROYAL HELLENIC NAVY]

o-AMINOPHENOL DERIVATIVES

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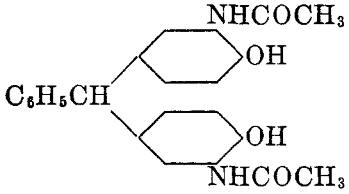
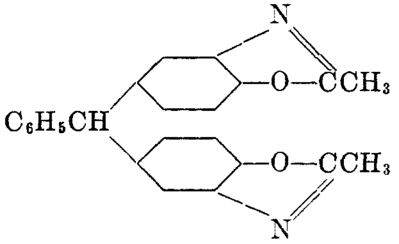
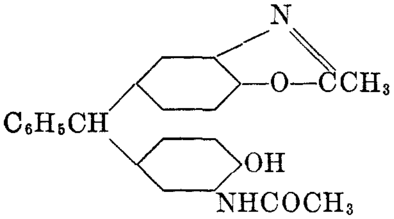
In a preceding paper (1) the opinion was expressed that by heating 3,3′-diacetylamino-4,4′-dihydroxytriphenylmethane (I), the corresponding anhydro base II could probably be obtained. The case was interesting in so far as the expected compound would contain two methylbenzoxazole groups connected through an atom of carbon, whilst the few condensed dioxazoles I was able to find in the literature available to me, bear the oxazole groups either on the same phenyl or symmetrically on the two phenyls of an anthraquinone. The experiment justified this opinion, for when heated at 275°, compound I readily gives off water, leaving a residue which consists principally of the anhydro base II, to which the indexing name 5,5′-*bis*-(2-methylbenzoxazolyl)phenylmethane can be given



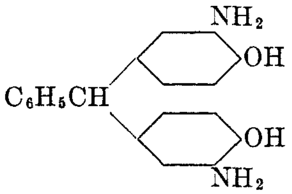
I



II



III



IV

The constitution of this base derives not only from the process of its formation, but also from the fact that when heated with 25% HCl, it yields the same aminophenol IV obtained from I by boiling with the same acid, as described in the preceding paper.[1]

The anhydro base is amorphous. It can be isolated either as a hard, colorless, and transparent resin, or in fine white flakes. As expected, it is insoluble in caustic alkalies and is precipitated from its solutions in strong HCl by dilution with

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[1] The identity of the two hydrolysis products was checked not only by their melting points but also by means of their respective benzylidene derivatives, which proved to be identical.

water. It seems to give no crystalline salts with aqueous acids. The only crystalline derivative obtained is a compound with $HgCl_2$.

While studying the conditions of the dehydration, it was noticed that if the flask was lifted from the oil-bath immediately after all solid matter had disappeared, the evolution of water continued for some time, although the temperature of the liquid had fallen considerably. In this particular case, it was found that the caustic alkali with which the benzene solution of the residue was washed in order to eliminate possible phenolic impurities, on acidifying precipitated a certain amount of a new crystalline substance which was converted by further heating into the anhydro base and gave, when heated with strong HCl, the same aminophenol as I and II. It was further found that when the dehydration of I was carried out from the beginning at lower temperatures the amount of this substance increased considerably, and it separated from the benzene solution of the residue on standing as a crystalline powder. When the temperature was kept at 230°, the yield reached 30% of the quantity of I worked up. These facts proved that under milder conditions only one molecule of water was split off and an intermediate product was formed, a semianhydride corresponding to formula III. But the dehydration cannot be conducted in such a manner that only this intermediate product is formed, and the residue is always more or less rich in the anhydro base, according to the temperature and time of heating.

The preparation of I by condensation of acetyl-*o*-aminophenol and benzaldehyde, as described previously gives a very poor yield. It was therefore considered necessary to improve the reaction. The principal reason for the low yield was found in the fact that the condensation is not complete at the end of the third day, as one is inclined to believe from the apparent amount of the precipitate formed, but after two weeks. In addition, the considerable quantity of unreacted benzaldehyde agglutinates the liberated base when the hydrochloride is hydrolyzed, and prevents it from separating in a fine, easily filtrable form. A description of the improved method, which gives a yield of 75–80% is given below.

EXPERIMENTAL[2]

3,3'-Diacetylamino-4,4'-dihydroxytriphenylmethane (*I*). Acetylaminophenol (151 g., 1 mole) is dissolved in 750 ml. of concentrated HCl in a glass-stoppered bottle, 55 ml. (0.5 mole) of freshly distilled benzaldehyde added, and the mixture left in a dark place. The next day a considerable deposit of the hydrochloride of the condensation product appears at the bottom of the vessel; this increases from day to day. Every morning the hard cake is broken up to a coarse powder with a flattened glass rod. After two weeks the condensation is practically complete. The light green hydrochloride is filtered through sintered-glass, washed with 2:1 hydrochloric acid (by volume), and hydrolyzed. For this purpose it is first treated with 2 liters of cold water, the resulting gray flakes left to settle, the supernatant liquid poured off, and the decantation repeated once more. The deposit is then steam-distilled in order to eliminate some unreacted benzaldehyde. After cooling, the fine grayish powder is washed by decantation until neutral, filtered, and dried on porous plates. It is

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[2] Corrections for Ref. (1): p. 335, read yield of *o*-aminophenol as 25 g., not 35 g. The statements on pp. 332, 333, and 340 concerning oxidation of the condensation product must be revised; the reaction is being reinvestigated.

finally purified by refluxing with alcohol or still better with acetone, to dissolve a red-brown impurity; yield, 75–80%.

Anhydro base (II). Compound I (20 g.) is heated at 275° and 10 mm. for 1.5 hours. By this time the powder is converted into a dark, red-brown oil which gathers at the bottom of the flask.[3] The transparent red-brown residue is extracted with boiling ligroin (b.p. 60–100°) and the combined extracts washed with 2 *N* KOH in order to eliminate all phenolic impurities. The light orange solution is concentrated, shaken with a few drops of concentrated HCl which absorb most of the coloring matter, filtered, washed with water, and transferred in portions into a distillation flask bearing a special side tube for materials which rapidly solidify. The rest of the ligroin is driven off and the anhydro base distilled under 1–2 mm. It appears as a thick, transparent, slightly colored oil which solidifies in the receiver to a hard resin. In order to obtain a colorless product it may be necessary to repeat the distillation.

If desired to have the base in the form of flakes, the decolorized ligroin solution is extracted with a cold mixture of 100 ml. of HCl and 200 ml. of water. The acid layer containing the base is then passed through a dry filter in order to keep back any trace of ligroin that could cause the flakes to stick together, and diluted gradually under stirring with five times its volume of cold water. The base separates in white flakes that are filtered and dried on a porous plate. It is absolutely necessary that all operations with the base, when in form of flakes, be carried out at a temperature as low as possible, always below 15°, otherwise the flakes will soften and stick together. Because of this tendency of the flakes to agglutinate it is not advisable to filter them by suction.

The anhydro base is sparingly soluble in boiling water, moderately so in ligroin at ordinary temperature, and soluble in all proportions in the other usual organic solvents. From these solutions it is obtained upon spontaneous evaporation as a hard transparent resin. When heated above room temperature it softens gradually and is liquid at about 130°. It can be distilled under 1–2 mm. at about 250°. At ordinary temperature the flakes agglutinate in the course of several months and are transformed into the resin. Chemically, the anhydro base is insoluble in caustic alkalies, but it is soluble in HCl stronger than 10%, from which it is precipitated upon dilution with water. However, after standing for several days at room temperature, the acid solutions will no longer yield a precipitate with water and upon evaporation give the hydrochloride of the aminophenol (IV). This hydrolysis can be performed in one hour by heating the base with 25% HCl on the water-bath. On cooling, especially after seeding or rubbing, the hydrochloride will separate in white needles.

Anal. Calc'd for $C_{23}H_{18}N_2O_2$: C, 77.97; H, 5.08; N, 7.91.
Found: C, 77.67, 77.91; H, 5.3, 5.36; N, 7.9, 7.91.

Compound with $HgCl_2$. Equimolecular amounts of the anhydro base and $HgCl_2$ in 5% alcoholic solutions are mixed. Soon a white crystalline precipitate is formed, that melts at 182° after crystallization from alcohol. For the determination of mercury it was recrystallized twice from alcohol (25 parts), dissolved in HCl (1:2), the mercury precipitated cold with H_2S and the HgS washed with the same dilute HCl.

Anal. Calc'd for $C_{23}H_{18}N_2O_2 \cdot HgCl_2$: Hg, 32.00; N, 4.48.
Found: Hg, 31.70; N, 4.59.

Reaction of the anhydro base with $FeCl_3$. A 5% solution of the anhydro base in concentrated HCl is poured into a similar solution of $FeCl_3$. Immediately a thick, pale yellow amorphous precipitate is formed, that is readily hydrolyzed by water or alcohol, and cannot be recrystallized from concentrated HCl. Heated above room temperature it softens grad-

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[3] During the dehydration a white sublimate of acetylaminophenol collects on the cooler parts of the flask and a few drops of the anhydro base are condensed in the receiver. At ordinary pressure some water, acetylaminophenol, and 2-methylbenzoxazole (formed by dehydration of the latter) fall back into the boiling liquid causing a continual bumping. It is therefore advisable to work under reduced pressure; however, below 10 mm. the losses by evaporation are excessive.

ually and is liquid at about 120°. Upon oxidation with sulfuric acid and KNO_3 the substance proved to have 13.58% Fe.

Semianhydride (III). The substance (I), 20 g., is heated at 230° and 10 mm. until all solid matter is converted into a dark red-brown liquid. This takes more than two hours. After cooling, the solidified transparent residue is dissolved in 40 ml. of boiling benzene, filtered, and left for two days. By this time 6–7 g. of the semianhydride separates as a reddish crystalline powder. Recrystallized twice from alcohol it is obtained perfectly white.

Anal. Calc'd for $C_{23}H_{20}N_2O_3$: N, 7.53. Found: 7.41.

In a capillary tube the semianhydride melts at 191°. Heated in a test tube under reduced pressure it begins to melt at 190–191°, and an intense boiling of the molten mass shows that dehydration has already begun. In the amorphous state, *e.g.*, as obtained by evaporation of a solution in an organic solvent, or by acidifying an alkaline solution, it is very soluble in ether, alcohol, benzene, and chloroform; scarcely so in ligroin, and insoluble in water. Its tendency to crystallize is not great, and the solutions need to be seeded and scratched to induce crystallization, and even then the separation takes one or two days. However, when crystalline it is very moderately soluble in the above mentioned solvents, even at the b.p. It behaves towards mineral acids like the anhydro base, but is more sensitive to their hydrolyzing action. Heating for half an hour with 20% HCl is sufficient to convert it into the aminophenol (IV). It is readily soluble in NaOH, but almost immediately the sodium salt begins to precipitate as a fine grayish powder, or if the alkali is concentrated (20%), as a greenish, viscous mass, that can easily be transformed by rubbing into a gray powder. The sodium salt is hydrolyzed by cold water. On the contrary the potassium salt is very soluble in an excess of KOH. This is of importance in case one wishes to extract the semianhydride from a solution in an organic solvent. From the solution in KOH, the sodium salt is precipitated by sodium chloride.

Reaction with $FeCl_3$. Under the same conditions as the anhydro base, the semianhydride gives a similar pale yellow amorphous precipitate with $FeCl_3$.

Supplementary notes concerning the aminophenol (IV). In addition to the description of IV given in the preceding paper, the following facts may be noted: The *hydrochloride,* as obtained by boiling I with HCl, is usually of a greenish gray color. It can be easily purified by adding ammonia dropwise and with shaking to its concentrated aqueous solution. The first flakes of the liberated aminophenol adsorb the coloring matter and the solution soon appears colorless. After filtration, 1.5 volumes of concentrated HCl are added. On cooling, the pure hydrochloride separates slowly in white needles. Should the original product be very dark, this treatment must be preceded by boiling with charcoal. The air-dried hydrochloride obstinately retains HCl that can only be eliminated by heating at 110°. It is further preferable, if one desires to isolate the free aminophenol from its hydrochloride, to add sodium acetate to the dilute solution instead of neutralizing with sodium bicarbonate. Here also, if the solution of the hydrochloride is colored, the acetate is first added dropwise until the solution is colorless, and the rest of the aminophenol precipitated after filtration.

Benzylidene derivative of IV. One mole of IV and 2 moles of benzaldehyde are heated together on a water-bath for one hour. The mixture first liquefies, then gradually becomes solid. Then 5 parts of benzene are added and the flask again heated until the cake, which meanwhile is transformed into a crystalline powder, is dissolved, and an equal volume of ligroin added. On cooling and standing, the thick precipitate formed is filtered, washed with a little benzene, and dried. The benzylidene derivative forms fine, pale yellow crystals that melt at 183°. It is very soluble in benzene and chloroform, scarcely so in alcohol and ligroin. It can be recrystallized from the two first-mentioned solvents but it is advantageous to use them diluted with an equal volume of ligroin.

Anal. Calc'd for $C_{33}H_{26}N_2O_2$: N, 5.81. Found: N, 5.5.

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REFERENCE

(1) GALATIS, *J. prakt. Chem.*, **151**, 331 (1938).