

SYNTHESIS OF PHENYLANTHRANILIC ACIDS

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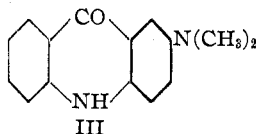
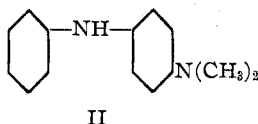
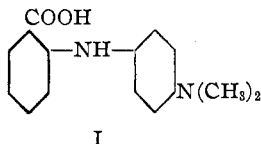
The discovery was made by Ullmann,¹ that the mobility of halogens in the benzene ring was greatly increased by the addition of copper as catalyst. The first reaction studied in detail was the formation of phenylanthranilic acid by the action of aniline on *o*-chlorobenzoic acid, as represented by the following equation: $C_6H_5.NH_2 + Cl.C_6H_4.COOH = C_6H_5.NH.C_6H_4.COOH + HCl$. Besides the copper, Ullmann added 2 equivalents of potassium carbonate, one to form the potassium salt of *o*-chlorobenzoic acid and the other to neutralize the hydrochloric acid resulting from the reaction. In this manner he obtained crude phenylanthranilic acid of exceptionally good quality in a yield of 97%.

In the years immediately following the discovery, this method was employed by Ullmann and his pupils in the synthesis of many substituted anthranilic acids, salicylic acids and naphthalene derivatives;² but since it attained commercial importance almost at once, it was soon buried in patents and has not often been applied in pure synthetic organic chemistry.

The present investigation deals with the action of the dialkyl-*p*- and *m*-phenylenediamines and piperidine on *o*-chlorobenzoic acid and its mono- and dinitro derivatives which are accessible by direct nitration. The ultimate object is the conversion of these substituted phenylanthranilic acids into unsymmetrical acridones and acridines, and the following is a brief summary of the results which have been obtained.

Action of Dialkylphenylene-Diamines

On *o*-Chlorobenzoic Acid.—Dimethyl-*p*-phenylenediamine reacts with *o*-chlorobenzoic acid in the presence of copper to give 4'-dimethylamino-diphenylamine-2-carboxylic acid (I).



By heating this acid a few degrees above its melting point, it is converted almost quantitatively into 4-dimethylamino-diphenylamine (II). The properties of this compound were found to agree with those previously reported.³

When treated with concd. sulfuric acid, 4'-dimethylamino-diphenyl-

¹ Ullmann, *Ber.*, **38**, 2211 (1905).

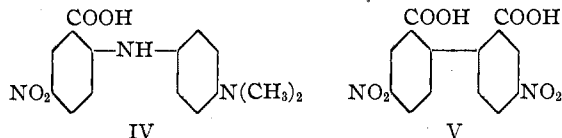
² Ullmann, *Ann.*, (a) **355**, 312 (1907); (b) **366**, 79 (1909); etc.

³ Fischer, *Ber.*, **21**, 2612 (1888).

amine-2-carboxylic acid is converted completely into 2-dimethylamino-acridone (III).

Similar results were obtained by the reaction of *o*-chlorobenzoic acid with diethyl-*p*-phenylenediamine as well as with both dimethyl- and diethyl-*m*-phenylenediamine.

On 5-Nitro-2-chlorobenzoic Acid.—Dimethyl-*p*-phenylenediamine reacts smoothly with 5-nitro-2-chlorobenzoic acid in the presence of copper to give 4-nitro-4'-dimethylaminodiphenylamine-2-carboxylic acid (IV).



It was expected that this reaction would be complete in a shorter time than the reaction between the same base and *o*-chlorobenzoic acid, since it is a well-established fact that a negative substituent in the *ortho* position with respect to the halogen in the benzene ring greatly increases its mobility, and that a negative group in *para* position to the halogen has a similar, though considerably smaller, labilizing effect.⁴

However, on investigating the action of dimethyl-*p*-phenylenediamine on 5-nitro-2-chlorobenzoic acid, the author found that the reaction required 2½ hours for completion, or approximately the same time as was required by *o*-chlorobenzoic acid. * In the action of dimethyl-*m*-phenylenediamine on these two acids, as will be shown later, 5-nitro-2-chlorobenzoic acid had to be digested more than twice as long as *o*-chlorobenzoic acid to complete the reaction. On account of these unexpected results, the relative reactivities of the chlorine in the two cases was tested by the digestion of the acids with sodium hydroxide solution, precipitation with nitric acid and testing the filtrates with silver nitrate. *o*-Chlorobenzoic acid was recovered unchanged, the filtrate giving only the slightest cloudiness with silver nitrate. The filtrate obtained by the same procedure with 5-nitro-2-chlorobenzoic acid gave, however, a voluminous precipitate with silver nitrate, and the recovered acid was identified as a mixture of 5-nitro-2-chlorobenzoic acid and 5-nitrosalicylic acid.

These results prove that the nitro group in the *para* position does make the chlorine more labile, and the discrepancies with the dimethyl-phenylenediamines are probably more apparent than real. The condensation products of *o*-chlorobenzoic acid with the dialkyl phenylenediamines decompose to some extent during the reaction, while those of 5-nitro-2-chlorobenzoic acid appear to be more stable at the temperature of the reaction, possibly because they melt at a higher temperature.

An unexpected result was obtained when diethyl-*m*-phenylenediamine

⁴ Schöpf, *Ber.*, 22, 3281 (1889).

acted on 5-nitro-2-chlorobenzoic acid in the presence of copper. The crude product was contaminated with a large amount of tar, as if the diamine had not entered into the reaction. After the tar had been removed by prolonged boiling of the sodium carbonate solution with animal charcoal, acidification yielded a white substance that melted sharply at 257°, without decomposition. On investigation it was found that this product had resulted from the elimination of 2 chlorine atoms from 2 molecules of 5-nitro-2-chlorobenzoic acid and was, in fact, 4,4'-dinitrodiphenyl-2,2'-dicarboxylic acid (V).

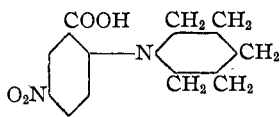
On 3,5-Dinitro-2-chlorobenzoic Acid.—As was to be expected, this acid acts so readily that the addition of copper is unnecessary.

Action of Piperidine

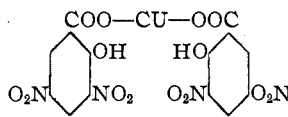
On *o*-Chlorobenzoic Acid.—When an amyl alcohol solution of piperidine and *o*-chlorobenzoic acid was digested in the presence of copper, a curious reaction occurred. The product was a white acid that crystallized from dil. alcohol in fine needles, melted at 155–156°, was free from chlorine and nitrogen, and proved to be salicylic acid.

Since the question immediately arose as to whether the salicylic acid owed its formation to the basic properties only of the piperidine, the process was repeated under the same conditions except that potassium hydroxide was substituted for the piperidine. In this case, however, most of the *o*-chlorobenzoic acid was returned unchanged, there being only qualitative indications that salicylic acid had been formed.

On 5-Nitro-2-chlorobenzoic Acid.—In amyl alcohol in the presence of copper, piperidine reacts with 5-nitro-2-chlorobenzoic acid, yielding 2-piperidino-5-nitrobenzoic acid (VI).



VI



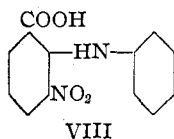
VII

On 3,5-Dinitro-2-chlorobenzoic Acid.—Before either of the two reactions just described had been studied, an aqueous solution of piperidine, 3,5-dinitro-2-chlorobenzoic acid and sodium acetate was digested in the presence of copper, in the expectation that the piperidine nucleus would not enter in place of the chlorine between the nitro and carboxyl groups. The mixture became orange-colored as soon as warmed, and after the liquid had digested for 2 hours it was filled with fine green needles. These were collected and it was then observed that all the copper had disappeared. Renewed digestion of the mother liquor in the presence of fresh copper yielded more of the same needles. At the end a small amount of the copper remained undissolved. An attempted determination of the melt-

ing point of the green needles resulted in disaster, for at 320° the substance exploded violently, shattering the melting-point tube to dust. The analysis, which was made with great difficulty on account of the explosive nature of the compound, ultimately proved that the substance was the copper salt of 3,5-dinitrosalicylic acid (VII).

Labilizing Influence of the Nitro Group on Chlorine in the Benzene Ring

During the course of the syntheses already described, the author has investigated the mobility of the chlorine in *o*-chlorobenzoic acid and the influence of a nitro group in each of the four possible positions, 3, 4, 5 and 6. Of these 4 acids, the chlorine of 3-nitro-2-chlorobenzoic acid is the most labile, as would be expected, since the nitro and carboxyl groups occupy the two most influential positions. In the presence of copper, aniline reacts with 3-nitro-2-chlorobenzoic acid in alcoholic solution, yielding 2-nitrodiphenylamine-6-carboxylic acid (VIII).



The second acid, in order of the lability of the chlorine, should be 5-nitro-2-chlorobenzoic acid, containing 1 negative group in the *ortho* position with respect to the chlorine and the other in the *para* position. This actually seems to be the case, for the chlorine, as previously described, is removed from 5-nitro-2-chlorobenzoic acid by bases at the temperature of boiling water.

In 4-nitro- and 6-nitro-2-chlorobenzoic acid the nitro group in *meta* position with respect to the chlorine would be expected to exert no influence on its mobility.⁴ Since Ullmann condensed 4-nitro-2-chlorobenzoic acid with a large number of bases without commenting on the mobility of the chlorine^{2b} it would appear that the nitro group of this acid is without influence on the chlorine. On the other hand, when the author digested 6-nitro-2-chlorobenzoic acid with excess of aniline in the presence of copper, it was wholly charred, and under other conditions was either charred or returned unchanged. These results seem to indicate that the nitro group in the 6 position makes the chlorine less labile than in *o*-chlorobenzoic acid. The difficulty of obtaining this 6-nitro acid, however, has prevented the author from completing the investigation.

The experimental part falls under the following headings: (I) dimethyl-*p*-phenylenediamine; (II) dimethyl-*m*-phenylenediamine; (III) diethyl-*p*-phenylenediamine; (IV) diethyl-*m*-phenylenediamine; (V) piperidine; (VI) investigation of the mobility of the chlorine in *o*-chlorobenzoic acid and its nitro derivatives.

Experimental Part

The *o*-chlorobenzoic acid was prepared at first by diazotization of *o*-toluidine and oxidation of the resulting *o*-chlorotoluene with potassium permanganate; but since the oxidation of *o*-chlorotoluene can be conveniently performed only with small quantities, this method was soon discarded in favor of the well-known process for the preparation of anthranilic acid from phthalimide.⁵ The anthranilic acid was always diazotized without being isolated.

The 5-nitro- and 3,5-dinitro-2-chloro-benzoic acids were prepared by direct nitration of *o*-chloro-benzoic acid.⁶

The dimethyl- and diethyl-phenylenediamines were prepared from the dialkyl anilines and were purified by distillation in a current of hydrogen. They were preserved in sealed tubes from the oxidizing action of the air.

Dimethyl-*p*-phenylenediamine

4'-Dimethylamino-diphenylamine-2-carboxylic Acid (I).—Three g. of *o*-chlorobenzoic acid, 2 g. of dimethyl-*p*-phenylenediamine, 3 g. of potassium carbonate, 35 cc. of amyl alcohol and about 0.2 g. of copper powder were digested over a free flame for 2 $\frac{1}{4}$ hours. After distillation of the amyl alcohol in a current of steam, the dark green solution was boiled for about an hour with animal charcoal. It was then filtered free from charcoal and copper powder and neutralized while still hot, whereupon all the product separated at once as an amorphous, green solid, that was dried (3.1 g.) and crystallized twice from alcohol, from which it separated in pale green prisms or needles.

In the first attempts to prepare this acid, copper was employed which had been made by the addition of zinc to a solution of copper sulfate, and no pure product could be isolated. Substitution of the so-called "molecular copper," which can be bought in the market, yielded a good product at once.

Since dimethyl-*p*-phenylenediamine becomes impure so rapidly in contact with the air, a steady stream of dry hydrogen was passed through the apparatus during the digestion.

Analyses. Subs., 0.1350: 12.5 cc. of N₂ (14°, 753 mm.). Subs., 0.1208: CO₂, 0.3109; H₂O, 0.0688. Calc. for C₁₅H₁₆O₂N₂: C, 70.5; H, 6.3, N, 10.9. Found: C, 70.2; H, 6.3; N, 10.8.

The substance melts at 216° with decomposition. It is practically insoluble in water and only slightly soluble in xylene and alcohol. It dissolves more readily in acetic acid but does not separate on cooling.

4-Dimethylamino-diphenylamine (II).—One g. of 4'-dimethylamino-diphenylamine-2-carboxylic acid was heated in an oil-bath at about 220° until the evolution of carbon dioxide ceased. When cold the dark residue was extracted with hot alcohol, and the purple solution decolorized by boiling with animal charcoal. Concentration and cooling yielded fine, white needles, and two more crystallizations raised the melting point to 130°, that found by O. Fischer.³

2-Dimethylamino-acridone (III).—Two g. of 4'-dimethylamino-diphenylamine-2-carboxylic acid was dissolved in 20 g. of concd. sulfuric acid and the solution heated to 100°. It became fluorescent at once, and after 10 minutes was poured into 500 cc. of

⁵ *Compt. rend.*, 10, 6 (1901); etc.

⁶ Graebe, *Ann.*, 276, 40 (1893). Holleman and de Bruyn, *Compt. rend.*, 20, 209 (1911). Ref. 2b.

water. Neutralization with ammonia yielded the acridone as a yellow, amorphous precipitate; yield, about 95%. It crystallized from alcohol in small, bright yellow clusters; m. p., 289–290°.

Analyses. Subs., 0.1024: CO₂, 0.2842; H₂O, 0.0550. Subs., 0.1054: 10.6 cc. of N₂ (16°, 760 mm.). Calc. for C₁₈H₁₄ON₂: C, 75.63; H, 5.88; N, 11.76. Found: C, 75.68; H, 5.96; N, 11.72.

This acridone is only slightly soluble in all organic solvents. In alcohol and concd. sulfuric acid the fluorescence is blue; in acetic acid, green.

4-Nitro-4'-dimethylamino-diphenylamine-2-carboxylic Acid (IV).—Three g. of 5-nitro-2-chlorobenzoic acid, 2 g. of dimethyl-*p*-phenylenediamine, 2 g. of potassium carbonate, 35 cc. of amyl alcohol and about 0.2 g. of copper were digested for 2½ hours. The amyl alcohol was then distilled with steam, and the red solution, after purification with charcoal, was neutralized with hydrochloric acid. The brown amorphous product was crystallized twice from alcohol, forming small, coppery needles; m. p., 234–235°.

Analyses. Subs., 0.1058: CO₂, 0.2330; H₂O, 0.0486. Subs., 0.1000: 11.8 cc. of N₂ (15°, 758 mm.). Calc. for C₁₅H₁₅O₄N₃: C, 59.8; H, 4.98; N, 13.95. Found: C, 60.05; H, 5.10; N, 13.8.

When the process just described was carried out in an atmosphere of hydrogen, the yield of crude product amounted to only 50%. Without the hydrogen, however, the yield was 75%.

This synthesis was also accomplished by digesting for 6 hours a solution of 2 g. of 5-nitro-2-chlorobenzoic acid, 1.35 g. of dimethyl-*p*-phenylenediamine and 2.7 g. crystallized sodium acetate in 20 cc. of water, with about 0.2 g. of copper. The product, however, was much more tarry and difficult to purify.

2,4-Dinitro-4'-dimethylamino-diphenylamine-6-carboxylic Acid.—One and six-tenths g. of dimethyl-*p*-phenylenediamine was added, drop by drop, to a solution of 3 g. of 3,5-dinitro-2-chlorobenzoic acid and 3.3 g. of crystallized sodium acetate in 20 cc. of water. A vigorous reaction took place, the mixture became brown, and a yellow precipitate separated; yield, 100%. The product was collected and purified by crystallization of the hydrochloride from dil. hydrochloric acid. The hydrochloride forms reddish-brown plates, is sparingly soluble in water and dil. hydrochloric acid, and melts gradually at 240–260°.

Analysis. Subs., 0.0806: 10.1 cc. of N₂ (13°, 754 mm.). Calc. for C₁₅H₁₅O₆N₄Cl: N, 14.64. Found: 14.81.

A part of the pure hydrochloride was dissolved in water and the free 2,4-dinitro-4'-dimethylamino-diphenylamine-6-carboxylic acid precipitated with sodium acetate. Obtained in this manner, the acid was a bright yellow, amorphous powder, melting at 253° with decomposition.

Analysis. Subs., 0.1132: 15.5 cc. of N₂ (16°, 760 mm.). Calc. for C₁₅H₁₄O₆N₄: N, 16.18. Found: 15.96.

Dimethyl-*meta*-phenylenediamine

3'-Dimethylamino-diphenylamine-2-carboxylic Acid.—Three g. of *o*-chlorobenzoic acid, 2 g. of dimethyl-*m*-phenylenediamine, 3 g. of sodium carbonate, 35 cc. of amyl alcohol and 0.2 g. of copper were digested in an atmosphere of hydrogen for 2:05 hours. After removal of the amyl alcohol with steam and treatment of the solution with a nimal charcoal, the clear brown solution was cooled in ice and neutralized. The pale brown precipitate was collected rapidly and dissolved in hot 50% alcohol. As this cooled, pale brown needles separated, which after two more crystallizations were colorless and melted at 155°, without decomposition.

Analyses. Subs., 0.1120: CO₂, 0.2880; H₂O, 0.0644. Subs., 0.1096: 10.5 cc. of N₂ (18°, and 755 mm.). Calc. for C₁₅H₁₆O₂N₂: C, 70.31; H, 6.25; N, 10.93. Found: C, 70.12; H, 6.38; N, 10.99.

4-Nitro-3'-dimethylamino-diphenylamine-2-carboxylic Acid.—This acid was obtained by digestion for 5 hours of a mixture of 3 g. of 5-nitro-2-chlorobenzoic acid, 2 g. of dimethyl-*m*-phenylenediamine, 2 g. of sodium carbonate, 35 cc. of amyl alcohol and about 0.2 g. of copper. After recovery of the amyl alcohol by distillation with steam and purification of the solution by boiling with animal charcoal, the product was precipitated by neutralizing the solution with hydrochloric acid. It was crystallized thrice from alcohol, forming small, greenish-brown needles without definite melting point. Heated gradually to 300°, it sintered and became black without actually melting, but when dipped into a bath at 247° it melted sharply, with decomposition.

Analyses. Subs., 0.1062: CO₂, 0.2336; H₂O, 0.0485. Subs., 0.1248: 15.3 cc. of N₂ (21°, 756 mm.). Calc. for C₁₅H₁₅O₄N₃: C, 59.80; H, 4.98; N, 13.95. Found: C, 59.98; H, 5.07; N, 13.88.

2,4-Dinitro-3'-dimethylamino-diphenylamine-6-carboxylic Acid.—This acid was prepared in two different ways. (1) A solution of 3.7 g. of 3,5-dinitro-2-chlorobenzoic acid and 2 g. of dimethyl-*m*-phenylenediamine in 80 cc. of absolute alcohol, was digested under a reflux condenser for 35 minutes. As the mixture cooled, fine green needles separated (3.5 g.), and cautious addition of water to the mother liquor yielded more needles (0.4 g.). Obtained thus, the acid is quite pure, as shown by analysis.

Analysis. Subs., 0.1445: 20.1 cc. of N₂ (19°, 766 mm.). Calc. for C₁₅H₁₄O₆N₄: N, 16.18. Found: 16.12.

The substance turned dark when heated above 300° but did not melt. It is very sparingly soluble in all organic solvents except alcohol. (2) A solution of 3 g. of 3,5-dinitro-2-chlorobenzoic acid, 1.6 g. of dimethyl-*m*-phenylenediamine, and 3.3 g. of crystallized sodium acetate in 20 cc. of water was digested under a reflux condenser for 1 hour. The product began to separate very soon and at the end entirely filled the volume of the liquid; yield, 100%. Made in this way, the acid is amorphous. In the present case it was dissolved in hot, dil. hydrochloric acid and as this solution cooled the hydrochloride separated in green needles.

Analysis. Subs., 0.1518: 19.2 cc. of N₂ (22°, 753 mm.). Calc. for C₁₅H₁₅O₆N₄Cl: N, 14.64. Found: 14.18.

When heated to 320° the hydrochloride sintered but did not melt.

Diethyl-*para*-phenylenediamine

4'-Diethylamino-diphenylamine-2-carboxylic Acid.—Two g. of *o*-chlorobenzoic acid, 2 g. of diethyl-*p*-phenylenediamine, 2 g. of sodium carbonate, 35 cc. of amyl alcohol and about 0.2 g. of copper were digested for 90 minutes. After distillation with steam and treatment with animal charcoal the clear brown solution was cooled to 0° and neutralized slowly. A light blue substance separated which did not become tarry on standing for 2 hours in the solution at 0°. As soon as it was collected, however, it became gummy and black. All attempts to crystallize the free acid, its sodium salt and its acid salts were unsuccessful.

4'-Diethylamino-4-nitro-diphenylamine-2-carboxylic Acid.—A mixture of 2.5 g. of 5-nitro-2-chlorobenzoic acid, 2 g. of diethyl-*p*-phenylenediamine, 2.5 g. of sodium carbonate, 35 cc. of amyl alcohol and about 0.2 g. of copper was digested for 2½ hours. The amyl alcohol was recovered by distillation with steam and the solution of the sodium salt freed from a small amount of tar by boiling it with animal charcoal. Neutralization then yielded an olive-green precipitate that weighed 3.1 g.; yield, 78%. This

was crystallized twice from alcohol, separating the second time in fine brown needles; m. p., 239–240°.

Analyses. Subs., 0.1112: CO₂, 0.2518; H₂O, 0.0601. Subs., 0.1125: 12.3 cc. of N₂ (17°, 750 mm.). Calc. for C₁₇H₁₉O₄N₃: C, 62.00; H, 5.77; N, 12.76. Found: C, 61.59; H, 5.98; N, 12.51.

4'-Diethylamino-2,4-dinitrodiphenylamine-6-carboxylic Acid.—A solution of 3 g. of 3,5-dinitro-2-chlorobenzoic acid, 2 g. of diethyl-*p*-phenylenediamine and 3.5 g. of crystallized sodium acetate in 20 cc. of water was warmed, whereupon a precipitate appeared, and after the liquid had been boiled for 5 minutes it was entirely filled with a brown amorphous solid. When this was cold, 4 g. of product was collected and dissolved in hot, dil. hydrochloric acid; the solution as it cooled deposited the hydrochloride in orange-colored flakes; m. p., 252–253°.

Analysis. Subs., 0.0950: 10.9 cc. of N₂ (13°, 754 mm.). Calc. for C₁₇H₁₉O₆N₄Cl: N, 13.64. Found: 13.44.

A portion of the pure hydrochloride was dissolved in hot water and the free acid precipitated with sodium acetate.

Analysis. Subs., 0.1135: 14.7 cc. of N₂ (16°, 760 mm.). Calc. for C₁₇H₁₈O₆N₄: N, 14.97. Found: 15.10.

The substance was a bright yellow powder; m. p., 259°. It is either insoluble or very sparingly soluble in ethyl alcohol, methyl alcohol, benzene, acetone, acetic acid, chloroform, xylene, toluene, ether, carbon tetrachloride or water. It dissolved in boiling pyridine but did not separate when the solution was cooled.

Diethyl-*meta*-phenylenediamine

3'-Diethylamino-diphenylamine-2-carboxylic Acid.—A mixture of 5 g. of *o*-chlorobenzoic acid, 5 g. of diethyl-*m*-phenylenediamine, 5 g. of sodium carbonate, 60 cc. of amyl alcohol and about 0.2 g. copper was digested for 1 hour. The amyl alcohol was recovered by distillation with steam and the solution was boiled with animal charcoal. After this had cooled to 0°, neutralization yielded a dark blue precipitate, which did not collect into a tar as long as it remained in suspension. When collected on the filter, however, it became black and gummy at once. As in the case of its isomer previously described, neither the acid nor any of its salts could be obtained in a pure state.

Action of Diethyl-*m*-phenylenediamine on 5-Nitro-2-chlorobenzoic Acid. 4,4'-Dinitrodiphenyl-2,2'-dicarboxylic Acid (V).—A mixture of 4 g. of diethyl-*m*-phenylenediamine, 5 g. of 5-nitro-2-chlorobenzoic acid, 5 g. of sodium carbonate, 60 cc. of amyl alcohol and about 0.2 g. of copper was digested for 3½ hours. After removal of the amyl alcohol with steam, the liquid contained a large amount of tarry matter which was completely removed by long boiling with animal charcoal. Acidification of the pale yellow solution thus obtained yielded an almost pure product. This was collected and crystallized twice from alcohol, from which it separated in thick, white needles. Dried at 100° the glossy needles lost water of crystallization and then melted at 257°.

Analyses. Subs., 0.1062: CO₂, 0.1961; H₂O, 0.0249. Calc. for C₁₄H₈O₈N₂: C, 50.6; H, 2.4. Found: C, 50.4; H, 2.6.

The substance is fairly soluble in hot water and crystallizes with 1 molecule of water of crystallization, which it loses completely only at 150–160°, as stated by Schultz,⁷

Analyses. Subs., 0.3457, 0.6397: loss at 160°, 0.0195, 0.0355. Calc. for C₁₄H₈O₈·N₂·H₂O: H₂O, 5.14. Found: 5.64, 5.55.

As final confirmation of the identity of this acid, the dimethyl ester was prepared by the addition of 5 cc. of dimethyl sulfate to a solution of 1 g. of anhydrous 4,4'-dinitro-

⁷ Schultz, *Ann.*, **196**, 26 (1879).

diphenyl-2,2'-dicarboxylic acid in 30 cc. of 2 *N* sodium hydroxide solution, vigorous agitation of the mixture for 4 hours and after 1 hour collection of the white solid which had separated; m. p., 166–172°. After two crystallizations of the substance from methyl alcohol the melting point was 177–178°, which is that reported by Schultz.⁷

3'-Diethylamino-2,4-dinitro-diphenylamine-6-carboxylic Acid.—A solution of 3 g. of 3,5-dinitro-2-chlorobenzoic acid and 2 g. of diethyl-*m*-phenylenediamine in 90 cc. of 99% alcohol, colorless at first, became red as soon as it was warmed, and after 2 minutes' boiling yellow needles separated. After 5 minutes the solution was cooled and 2 g. of bright yellow needles was collected, washed with alcohol and dried; m. p., 220° (decomp.).

Analysis. Subs., 0.1372: 17.5 cc. of N₂ (14°, 758 mm.). Calc. for C₁₇H₁₅O₆N₄: N, 14.97. Found: 14.96.

Piperidine

Action of Piperidine on *o*-Chlorobenzoic Acid in the Presence of Copper. Formation of Salicylic Acid.—A mixture of 5.6 g. of *o*-chlorobenzoic acid, 3 g. of piperidine, 6 g. of sodium carbonate, 35 cc. of amyl alcohol and about 0.2 g. of copper was digested with vigorous stirring for 6 hours. After recovery of the amyl alcohol by distillation with steam, the bright green solution, containing only the copper powder undissolved, was treated with animal charcoal, filtered and the filtrate evaporated to about 50 cc. When this concentrated solution was acidified with hydrochloric acid, a slightly yellow precipitate separated. To remove the color the product was dissolved in dil. sodium carbonate solution and again treated with animal charcoal. Acidification then yielded a pure white acid, which crystallized from 25% alcohol in fine, white needles; m. p., 155–156°.

Analyses. Subs., 0.1131: CO₂, 0.2566; H₂O, 0.0462. Calc. for C₇H₆O₃: C, 60.86; H, 4.34. Found: C, 61.87; H, 4.55.

A mixed melting point with pure, known salicylic acid of melting point 156.5° gave 156.5° unchanged.

2-Piperidino-5-nitrobenzoic Acid (VI).—A mixture of 2.4 g. of 5-nitro-2-chlorobenzoic acid, 1 g. of piperidine, 2 g. of sodium carbonate, 20 cc. of amyl alcohol and about 0.2 g. of copper was digested and vigorously stirred for half an hour. After the first 15 minutes the solution was orange-colored and filled with a white solid, and digestion for an additional 15 minutes made no apparent change. The amyl alcohol was then recovered by distillation with steam and the filtered solution acidified. The yellow precipitate thus formed was collected and crystallized thrice from alcohol, the hot solution being treated each time with animal charcoal. The 2-piperidino-5-nitrobenzoic acid was thus obtained as very pale yellow, well-formed rhombic crystals; m. p., 200–202°.

Analyses. Subs., 0.0908: CO₂, 0.1929; H₂O, 0.0467. Subs., 0.1221: 12 cc. of N₂ (15°, 758 mm.). Calc. for C₁₂H₁₄O₄N₂: C, 57.6; H, 5.6; N, 11.2. Found: C, 57.93; H, 5.71; N, 11.47.

Action of Piperidine on 3,5-Dinitro-2-chlorobenzoic Acid. Formation of 3,5-Dinitrosalicylic Acid.—A mixture of 3 g. of 3,5-dinitro-2-chlorobenzoic acid, 1 g. of piperidine, 3.3 g. of crystallized sodium acetate, 50 cc. of water and about 0.2 g. of copper was digested for 3 hours. The solution became orange colored at once, but gradually turned pale yellow, and green needles soon began to separate. After 2 hours, the process was interrupted to collect these needles (2 g.). Since the copper had entirely disappeared, more was added and the digestion continued for another hour. The total yield was 3 g. of the copper salt of 3,5-dinitrosalicylic acid.

The product was crystallized from very dilute alcohol and dried at 100°. As described in the introduction, this copper salt explodes violently at about 320°.

Analysis. Subs., 0.1309: 11 cc. of N₂ (17°, 747 mm.). Calc. for C₁₄H₆O₁₄N₄Cu: N, 10.8. Found: 9.6.

Since the analysis for nitrogen was of questionable accuracy on account of the explosive nature of the compound, an analysis for copper was undertaken. Difficulties arose at once, however. After a solution of the copper salt in concd. mineral acids had been boiled for some time, qualitative tests of the solution did not indicate the presence of copper. Furthermore, boiling with dil. sodium hydroxide deposited no copper oxide, and dry ignition was obviously out of the question. The procedure finally adopted was as follows.

In a porcelain crucible 0.4466 g. of substance was moistened with a few drops of concd. sulfuric acid and very cautiously ignited until all the organic matter had been decomposed. The black residue was then readily dissolved in about 5 cc. of concd. nitric acid and the solution transferred to a beaker. The nitric acid was expelled by several evaporations with excess of hydrochloric acid, the solution diluted with water and the copper precipitated with sodium hydroxide.

Analysis. Subs., 0.5001: CuO, 0.0682. Calc. for $C_{14}H_6O_{14}Cu$: Cu, 12.3. Found: 10.9.

Thus the percentages found for both nitrogen and copper were considerably lower than the calculated percentages for the copper salt of 3,5-dinitrosalicylic acid. In explanation of this discrepancy, it was found that the specimen employed in both analyses still contained 10.7% of water of crystallization, which it lost completely only at 180°. When allowance is made for this 10.7% in the calculations, the analyses may be restated as follows.

Analyses. Subs., 0.1169: 11 cc. of N_2 (17°, 747 mm.). Subs., 0.4466: CuO, 0.0682. Calc. for $C_{14}H_6O_{14}N_4Cu$: N, 10.8; Cu, 12.3. Found: N, 10.68; Cu, 12.19.

A later determination of the water of crystallization gave the following result.

Analysis. Subs., 0.8482: loss at 180°, 0.0870. Calc. for $C_{14}H_6O_{14}Cu \cdot 3H_2O$: H_2O , 10.1. Found: 10.2

In order to confirm the identity of this compound as the copper salt of 3,5-dinitrosalicylic acid, 1.9890 g., dried at 200°, was boiled with 50 cc. of 20% potassium hydroxide solution for 2 hours. The solution became a deep red almost at once and copper oxide soon began to separate. While the mixture was still hot, the copper oxide was removed (0.2760 g.; Cu, 11.1%). The filtrate and first wash waters were evaporated to a small volume and cooled, whereupon red needles separated. These were twice recrystallized from a small volume of water containing about 10% of alcohol, and dried at room temperature.

Analysis. Subs., 0.3999: loss at 170°, 0.0212. Calc. for $C_7H_2O_7N_2K_2 \cdot H_2O$: H_2O , 5.6. Found: 5.3.

This is in agreement with the statement of Hübner.⁸

When the mother liquors of the dipotassium salt were poured into an excess of dil. hydrochloric acid, the monopotassium salt separated as a yellow powder.⁸ After the solution of the monopotassium salt had been boiled for an hour with the excess of hydrochloric acid and concentrated to a small volume, cooling the mixture in ice deposited 3,5-dinitrosalicylic acid. Repeated crystallizations from very dilute hydrochloric acid raised the melting point only to 170°, in comparison with 173° found by previous investigators.

The pure acid was dissolved in 25 cc. of absolute alcohol, the solution saturated with dry hydrogen chloride and allowed to stand overnight. When the mixture was poured into water, a brown oil separated which soon solidified. This ethyl ester crystallized from alcohol in small coppery needles and melted at 99°, as stated by Hübner.⁸

⁸ Hübner, *Ann.*, **195**, 47 (1879).

Finally, the solutions of the copper salt, the free acid and the ethyl ester gave a red color with ferric chloride.

Investigation of the Mobility of the Chlorine in *ortho*-Chlorobenzoic Acid and its Nitro Derivatives

o-Chlorobenzoic Acid.—A mixture of 2 g. of *o*-chlorobenzoic acid (m. p., 141°), 2 g. of potassium hydroxide and 20 cc. of water was digested for 4 hours. The solution was acidified with nitric acid, yielding then *o*-chlorobenzoic acid which melted at 140°. The filtrate gave no precipitate with silver nitrate. When this experiment was carried out in the presence of copper the result was the same.

In this connection may be stated the results of an attempt to convert *o*-chlorobenzoic acid into salicylic acid by means of potassium hydroxide instead of piperidine.

One g. of potassium hydroxide, 2 g. of *o*-chlorobenzoic acid, 2 g. of sodium carbonate, 20 cc. of amyl alcohol and about 0.2 g. of copper were digested together for 6 hours. After the amyl alcohol had been removed by distillation with steam and the solution filtered to free it from undissolved copper, acidification with nitric acid yielded 1.9 g. of *o*-chlorobenzoic acid; m. p., 137–138°. Since the filtrate gave a slight precipitate with silver nitrate it was extracted with ether. Evaporation of the ether left about 0.1 g. of white acid, which after crystallization from water melted at 131–132°. Its solution gave a red coloration with ferric chloride; it was therefore probably a mixture of *o*-chlorobenzoic acid and salicylic acid. The amount was considered too small to permit a separation of the 2 acids.

5-Nitro-2-chlorobenzoic Acid.—Two g. of 5-nitro-2-chlorobenzoic acid, 2 g. of potassium hydroxide and 20 cc. of water were digested together for 4 hours. Acidification with nitric acid then yielded an acid which melted over a wide range, from 155° to 210°. By several crystallizations from a rather large amount of water, 5-nitrosalicylic acid was obtained in fine, pale yellow needles; m. p., 227°.

3-Nitro-2-chlorobenzoic Acid. Formation of 2-Nitrodiphenylamine-6-carboxylic Acid.—One g. of 3-nitro-2-chlorobenzoic acid, 5 g. of aniline, 0.7 g. of potassium carbonate, 10 cc. of ethyl alcohol and about 0.2 g. of copper were digested for 1 hour. After the excess of aniline had been removed by distillation with steam the solution was filtered and acidified with hydrochloric acid. The bright red alkaline solution hereupon became yellow, and the product separated in yellow clusters. After several crystallizations from dil. alcohol the substance melted at 194°.

Analysis. Subs., 0.0735: 6.7 cc. of N₂ (11°, 758 mm.). Calc. for C₁₃H₁₀O₄N₂: N, 10.85. Found: 10.89.

Summary

1. In most instances *o*-chlorobenzoic acid and its nitro derivatives reacted with the dimethyl- and diethyl-*p*- and *m*-phenylenediamines to yield the expected products. The only exception was the reaction of 5-nitro-2-chlorobenzoic acid with diethyl-*m*-phenylenediamine which gave 4,4'-dinitrodiphenyl-2, 2'-dicarboxylic acid.

2. With piperidine these acids yielded chiefly unexpected products. 5-Nitro-2-chlorobenzoic acid alone reacted in the expected manner. *o*-Chlorobenzoic acid yielded salicylic acid and 3,5-dinitro-2-chlorobenzoic acid yielded 3,5-dinitrosalicylic acid.