101 mv. lower than those of the corresponding naphthoquinones, while α-anthraquinone is 246 mv. higher in potential than 9,10-anthraquinone. These facts are consistent with the conception that α-anthraquinone is in every way comparable to α-naphthoquinone, but that its reduction product should be compared with 9,10-anthrahydroquinone.

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THE ISOMERISM OF PHENYLPHTHALIMIDE AND A STUDY OF THE NITRO AND CHLORO DERIVATIVES

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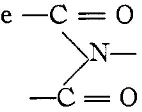
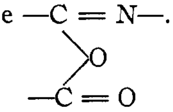
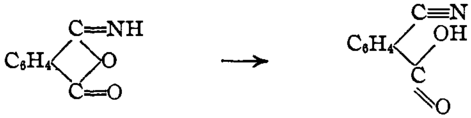
A critical study of the extensive work which has been done on phenylphthalimide or phthalanil, and its derivatives shows not only conflicting theoretical interpretations but contradictory experimental results. In addition to the closely related compounds the phthalanils, the phthalanilic acids, and the phthalamides which have not always been completely separated from one another, there are the two isomeric phthalimides—the symmetrical type  and the asymmetrical type 

These isomers differ so slightly in their physical and chemical properties that the separation and identification have been difficult and this accounts for much of the confusion and inaccuracy in the reported results. In the present study a complete survey of the literature was made and much of the experimental work repeated, duplicated in some cases and in the case of disputed points additional evidence has been obtained. The more general methods of preparation of the phthalanils and the phthalanilic acids have not been a matter of controversy, but this is not true of the preparation and isolation of the isomeric phthalanil derivatives.

The first evidence of the existence of an isomeric phthalimide was reported by Hoogewerff and van Dorp.[1] They found that o-cyanobenzoic acid was obtained by the action of ammonia on phthalyl chloride. Since neither phthalimide nor the phthaldiamide can be transformed by ammonia into the o-cyanobenzoic acid, they assumed the formation of an asymmetrical phthalimide as an intermediate compound—this evidently was unstable in alkaline solution and rearranged to the acid, thus



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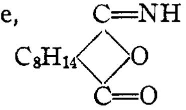
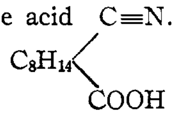
[1] Hoogewerff and van Dorp, *Rec. trav. chim.*, **11**, 84 (1892).

A year later the same authors[2] prepared compounds isomeric with the substituted camphorimides by treating the proper camphoramic acid with acetyl chloride or phosphorus oxychloride. These camphor-iso-imides were found to react with ammonia to give the corresponding cyano acid and therefore were assumed to have the following structure,  giving the acid  Iso-imides of other dicarboxylic acids could not be prepared but the iso-imide of phthalic acid was evidently obtained although not in a pure state; the substance obtained did give, with ammonia, *o*-cyanobenzoic acid. This work was one of the most important proofs of the existence of iso-imides and of the asymmetrical structure of the compounds obtained by the action of acetyl chloride on a dibasic acid. It stimulated interest in the preparation of various substituted iso-imides and phthalmethyl-iso-imide and phthalbenzyl-iso-imide were prepared in this way.[3] These iso-imides were crystalline products whose melting points were much lower than those of the ordinary imides; they were bases, but the salts were easily decomposed in the presence of water forming the corresponding acid. In 1896 van der Meulen,[4] working in the same laboratories, prepared the phthalphenyl-iso-imide by the action of acetyl chloride on phthalanilic acid. He isolated a crystalline compound which melted at 115–117°, while the melting point of the ordinary phenylphthalimide was 208°. These results were duplicated by other investigators.[5] Van der Meulen[6] found that when iso-imides were heated they were converted into the ordinary imides, that alcohols transformed them and their hydrochlorides into amidoic esters, sometimes into iso-esters and that amines formed with the iso-imides di-amides.

In 1901 Kuhara and Fukui[7] claimed to have prepared a substance isomeric with phthalanil which they called α-phenylphthalimide. This work was repeated by Kuhara and Komatsu;[8] the α-phenylphthalimide, however, was not isolated but normal phenylphthalimide, phthaldiphenyl-

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[2] Hoogewerff and van Dorp, *Rec. trav. chim.*, **12**, 12 (1893).

[3] Hoogewerff and van Dorp, *ibid.*, **13**, 93 (1894).

[4] Van der Meulen, *ibid.*, **15**, 282 (1896).

[5] (a) Hoogewerff and van Dorp, *ibid.*, **21**, 339 (1901); (b) Pummerer and Dorfmüller, *Ber.*, **45**, 292 (1912).

[6] Van der Meulen, *Rec. trav. chim.*, **15**, 323 (1896).

[7] Kuhara and Fukui, *Am. Chem. J.*, **26**, 454 (1901).

[8] Kuhara and Komatsu, *Mem. Coll. Sci. Eng. Kyoto Imp. Univ.*, 1, 391 (1908); **2**, 365 (1909–1910).

diamide and a hydrated di-amide were obtained. Then these investigators repeated the work of van der Meulen[4,6] and reported that they could not duplicate his work. They obtained two substances isomeric with phthalanil; one, yellow in color, they called the iso-imide; the other, white in color, they designated as β,α-phenylphthalimide.

Since the work of Kuhara is the last publication dealing with these isomers of phthalanil, his conclusions and results have remained unchallenged. A study of his methods seemed to indicate that the two isomers he reported were mixtures, so it was thought advisable to repeat the experiments of van der Meulen, Hoogewerff and van Dorp, Pummerer and Dorfmüller on the one hand and those of Kuhara, Fukui, Komatsu on the other, in order to prove as far as possible the existence or nonexistence of the various isomers mentioned above. Especial attention was given to the preparation of van der Meulen's phthalphenyl-iso-imide and to the preparation and isolation of the β,α-phenylphthalimide and the isomeric phenylphthalimide reported by Kuhara.

Early in the work in this Laboratory it was found that phenylphthalimide and phthalanilic acid could be completely separated from each other by a difference of solubility in chloroform. By this method it was found that a compound reported by Gabriel and Thorpe[9] as phthalanilic acid (m. p. 192°) was a mixture of phenylphthalimide (m. p. 208°) and phthalanilic acid (m. p. 169°, decompd.). It was found possible by the use of chloroform to separate phenylphthalimide from phthaldiphenyldiamide and thus some very clean cut separations were made possible. The results show that van der Meulen's phthalphenyl-iso-imide is the true isomer of phthalanil, that the iso-phthalanil of Kuhara and Fukui, designated as α-phenylphthalimide, is a mixture of phthaldiphenyldiamide, that the β,α-phenylphthalimide of Kuhara is a mixture of phthalphenyl-iso-imide and phthalanilic acid and that the yellow product obtained by Kuhara (m. p. 125–126°) was a mixture of the true isophthalanil (m. p. 116°) and small amounts of *n*-phthalanil.

The literature showed also some conflicting data with regard to the *o*-*m*-*p*-nitrophthalanils and indicated that investigation of some of the methods might prove of value. Accordingly, the work of various investigators, including Pawlewski, Dobreff and Kuhara was repeated in this Laboratory with the result that much of the confusion has been eliminated. The *p*-chlorophthalanilic acid and the *p*-chlorophthalanil[10] have been prepared but no reference is given in the literature to the corresponding *ortho* and *meta* compounds. These compounds, as well as the *para* compounds, have been prepared in this work.

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[9] Gabriel and Thorpe, *Ber.*, 11, 2260 (1878).

[10] (a) Tingle and Brenton, THIS JOURNAL, **31**, 1157 (1909); (b) Gabriel, *Ber.*, **11**, 2261 (1878).

Experimental

Phthalanilic acid was prepared[11] by the reaction of chloroform solutions of phthalic anhydride (50 g.) and aniline (31.4 g.). There was considerable heat of reaction and the white phthalanilic acid which precipitated out was found to be practically pure; it melted at 169° with evolution of steam, the residue resolidified and remelted at 207°, the melting point of phthalanil.

The effect of alcohol on phthalanilic acid has been studied[12] and the final product has been proved to be phthalanil. In this process, however, the alcohol solutions become yellow and this color has not been definitely accounted for. Since one of the isomers of phthalanil is yellow,[6] it was thought that some of the isomeric compound might be formed as an intermediate. A series of experiments was carried out in which the action of alcohol (95% and absolute) on the acid was studied. The concentration, temperature, length of contact and light conditions were varied. The color of the solution increased from pale yellow to a deep red directly as there was an increase in the temperature, in the concentration of the solution, in the length of time of reaction and in the volume of air above the solution. The results seemed to indicate a slow oxidation and the change was most rapid and extensive in the presence of an oxidizing agent, as shown by the addition of a small amount of hydrogen peroxide to the solution. No trace of the isomer could be obtained. The products isolated after the reaction were only phthalanilic acid and phthalanil, the quantity of the latter increasing with the time. The ultraviolet absorption spectra of alcoholic solutions of phthalanil and phthalanilic acid were also investigated and showed that even very dilute solutions of phthalanilic acid were gradullay transformed into phthalanil.

Phthalanil was prepared by the fusion of phthalic anhydride (50 g.) with aniline at a temperature of 250–260°.[13] The product was washed with alcohol, dissolved in chloroform and precipitated by alcohol in the form of glistening white needles (m. p. 207°). On account of the extreme solubility of phthalanil in chloroform and the complete insolubility of phthalanilic acid in this solvent it was found possible to make a complete separation of the two and the method was used throughout this investigation. There is no indication in the literature that chloroform would serve for this separation. Repetition of the work of Gabriel and of Thorpe[9,14] showed that the product they obtained of melting point 192°, thought to be pure phthalanilic acid, could be separated into pure phthalanil (m. p. 207°) and pure phthalanilic acid (m. p. 169°) by extraction with chloroform.

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[11] Anschütz, *Ber.*, **20**, 3214 (1887).

[12] Tingle, This Journal, **30**, 1882 (1908).

[13] Laurent and Gerhardt, *Ann.*, **68**, 34 (1848).

[14] Thorpe, *Ber.*, **26**, 1262 (1893).

Isomeric Phthalanils

The fundamental reaction involved in the preparation of the iso-imides[2] consisted in the action of acetyl chloride on phthalamic acid. Therefore, before any duplication of the methods used by previous investigators was undertaken, this reaction was carried out under varying conditions of time and temperature and a careful separation and identification of the products were made. A pale yellow product (melting between 160 and 203°) resulted from the action of acetyl chloride on phthalanilic acid either at ordinary temperature or at 40°. If the yellow product was allowed to stand in the air or dried at a temperature of 80°, the yellow color disappeared entirely. If, however, the product was. dried in a vacuum desiccator and then kept in an atmosphere of carbon dioxide, the yellow color persisted for several weeks. The reaction product was extracted with ether and the ether extract gave a white crystalline substance melting with decomposition between 157 and 202°. By extraction of this substance with chloroform, phthalanil was isolated (m. p. 207°), phthalanilic acid (m. p. 169°) was obtained and some phthalic acid, colorless plates (m. p. 184° with decomposition forming phthalic anhydride, m. p. 129–130°). The identification of these substances was checked by comparison with the pure substance; in each case mixed melting points showed no depression. The phthalic acid was further identified by the fluorescein test; phthalanil and phthalanilic acid gave negative tests under the same conditions. The residue left after the ether extraction was treated with chloroform, which removed a small amount of phthalanil and the residue melted at 237° with decomposition. This proved to be the phthaldiphenyldiamide,[6,5a,15] for when heated with glacial acetic acid it was transformed into phthalanil. These results show that the yellow product contained the hydrochloride of phthalphenyl-iso-imide. This hydrochloride was unstable in the air (more stable in dry air or in carbon dioxide), giving off hydrogen chloride and leaving the iso-imide. This iso-imide has been shown to be easily transformed into phthalanil.[5b] The presence of phthalic acid indicated the decomposition of some of the phthalanilic acid into phthalic acid and aniline. The reaction of aniline with the phenyl-iso-imide would account for the small amount of diamide formed.

An effort was made to prepare the α-phenylphthalimide of Kuhara.[7] The work was repeated in every detail, as follows. To an ethereal solution of 93 g. of aniline cooled to —10°, an ethereal solution of 50.75 g. of phthalyl chloride, also cooled to —10°, was added drop by drop. The temperature was kept below —6°. Hydrogen chloride was evolved and a white precipitate separated. The reaction mixture was kept in a freezing mixture for two hours. The precipitate was filtered and washed suc-

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[15] Rogow, *Ber.*, **30**, 1442 (1897).

cessively with hydrochloric acid, ammonia and water, as described by Kuhara. The product obtained melted at 215–219°. A chloroform extraction separated a very small amount of phthalanil (m. p. 207°); the main portion of the material was insoluble in chloroform and slightly soluble in alcohol. By recrystallization from alcohol a white crystalline product was obtained, m. p. 231° with decomposition. This was soluble in hot glacial acetic acid but was thereby converted into phthalanil and was therefore phthalanilide. This confirms the work of Hoogewerff and van Dorp,[5a] Chambers,[16] and Dunlap and Cummer,[17] who found that ethereal solutions of aniline and phthalyl chloride at low temperature formed, in the main, phthalanilide. Therefore, the original product, m. p. 215–219°, proved to be a mixture of *n*-phthalanil and phthalanilide and not an isomeric phthalanil.

Phthalphenyl-iso-imide, m. p. 116°, was prepared by careful duplication of the work of van der Meulen.[4] Five grams of phthalanilic acid was treated with 30 g. of acetyl chloride and the mixture heated at a temperature of 60° for seven minutes; the mixture turned yellow almost immediately. The cooled mixture was treated with carbon disulfide, the insoluble hydrochloride of phthalphenyl-iso-imide was filtered and immediately transferred to anhydrous ether. The iso-imide was freed by 30% potassium hydroxide, the flask was kept cold and the potash added only to bare alkalinity. The product was then practically all dissolved and the ether solution, yellow in color, was separated from the water layer and dried over solid potassium hydroxide for ten minutes. From this solution, filtered and evaporated in a desiccator over sulfuric acid, yellow needle crystals (m. p. 112–115°) were obtained. After one recrystallization from anhydrous ether, the crystals melted at 116°. This agreed with the results of van der Meulen[4] and Pummerer and Dorfmüller[5b] although Hoogewerff and van Dorp[5a] gave the melting point as 120–122°. Kuhara and Komatsu[8] claimed that they could not obtain the product which van der Meulen reported but that, on distillation, of part of the ether solution and then on spontaneous evaporation of the remainder phthalanil crystallized out first and then an amber-colored substance. The latter, on repeated recrystallization from anhydrous ether, gave amber-colored rhombic crystals, m. p. 125–126°. Kuhara also evaporated, as quickly as possible, the ethereal solution of the reaction product and obtained an almost colorless crystalline substance which, after one recrystallization from anhydrous ether, melted at 83–84°. This he designated as β,α-phenylphthalimide and believed both this and the amber-colored substance to be the true isomers of phthalanil rather than the yellow needles, m. p. 116°, of van der Meulen. In order to clear up these points the phthalphenyl-iso-imide was prepared as given above; a portion of the ether solution was evaporated in a desiccator over sulfuric acid and the yellow crystals, m. p. 116°, were obtained. A second portion of the same ether solution was partially distilled and then allowed to evaporate. The first product crystallizing out was phthalanil, m. p. 207°; further evaporation gave a very pale yellow residue which melted from 70–80°, resolidified and melted at 207°. A chloroform extraction of this mixture was made; the residue insoluble in chloroform proved to be pure phthalanilic acid, m. p. 169°. It melted with evolution of gas, resolidified and remelted at 207°. The chloroform extract evaporated in a desiccator over sulfuric acid gave clusters of yellow needles, m. p. 116°; therefore the reaction prod-

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[16] Chambers, This Journal, **25**, 601 (1903).

[17] Dunlap and Cummer, *ibid.*, **25**, 612 (1903).

uct, m. p. 70–80°, was a mixture of phthalphenyl-iso-imide and phthalanilic acid. This mixture obtained on heating the ethereal solution was probably caused by traces of alkali hydrolyzing the iso-imide into the acid.

The fact that a low melting reaction product (70–80°) was obtained in this Laboratory on repetition of Kuhara's work and that this proved to be a mixture indicates definitely that what Kuhara and Komatsu really had in the case of the substance melting at 83–84°, called β,α-phenylphthalimide was a mixture of van der Meulen's iso-imide and phthalanilic acid. Further confirmation lies in the fact that whenever the phenyl-iso-imide melting at 116° was mixed with phthalanilic acid, the mixture melted between 70 and 85°. Kuhara also states that when heated by itself β,α-phenylphthalimide was converted into the normal phenylphthalimide; this would be true of a mixture of phthalphenyl-iso-imide and phthalanilic acid since, on heating, both of these substances are converted into the ordinary phenylphthalimide.

Whenever the phthalphenyl-iso-imide prepared in this Laboratory was exposed to the air, it was found that the melting point became gradually higher, due to the fact that it was slowly transformed into the normal phthalanil. It was also proved that a mixture of a small amount of phthalanil with the iso-phthalanil melted at 120–126°, which accounts for the product of higher melting point obtained by Hoogewerff and van Dorp (120–122°) and that obtained by Kuhara (125–126°). When the phthalphenyl-iso-imide was allowed to stand in the presence of acid fumes, however, long, white needle crystals could be observed on the surface of the iso-imide. These were collected and found to be phthalic anhydride. The residue was found to consist of a mixture of the normal phenylphthalimide, the phthalphenyl-iso-imide and the phthaldiphenyldiamide. The two former substances were separated from the latter by extraction with ether and were then separated from each other by fractional crystallization from the ether solution.

Nitrophenylphthalimides

Preliminary to the checking of the work of various investigators on the isomeric nitrophenylphthalimides, nitro phthalanilic acids were prepared.

p-**Nitrophthalanilic acid** (m. p. 192° with decomposition) was prepared by the reaction of acetic ester solutions of *p*-nitraniline and phthalic anhydride.[18] The solvent was distilled off and the residue, after recrystallization from alcohol, gave a crystalline product which melted at 190–192° with evolution of gas, resolidified and melted again at 260° (melting point of *p*-nitrophthalanil, 262–263°). The method used in the preparation of phthalanilic acid was found to give better yields and more satisfactory material. Chloroform solutions of equimolecular quantities of *p*-nitraniline and phthalic anhydride were mixed and heated until the yellow color of the solution gradually faded. When cool the product was filtered, washed with cold chloroform and then recrystallized

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[18] (a) Meyer and Lüders, *Ann.*, **327**, 52 (1903); (b) *Ann.*, **415**, 29 (1917).

from hot chloroform. It formed white crystals which melted at 192°, evolved a gas, resolidified and melted at 262–263°.

m-**Nitrophthalanilic acid** (m. p. 202° with decomposition) was prepared by the reaction of acetic ester solutions of *m*-nitraniline and phthalic anhydride. Chloroform solutions of the reagents gave, as for the *para* compound, a theoretical yield and the product washed with chloroform consisted of white needles which melted at 202°, resolidified and melted at 240–242°.

o-**Nitrophthalanilic acid** (m. p. 149–151°) was also prepared by the action of *o*-nitraniline on phthalic anhydride in ethyl acetate solution and in chloroform solution. The acid is very soluble in both acetic ester and chloroform, so it did not precipitate out as in the case of the *para* and *meta* compounds. In order to isolate the *o*-nitrophthalanilic acid it was necessary to evaporate the solvent in each case to a small volume and stir until the acid crystallized. The product, washed with ether, was purified by precipitation with hydrochloric acid from a solution in sodium hydroxide. It formed yellow needles which melted at 149–151° (Meyer and Lüders[18b] give 146–148°) without evolution of gas and the liquid did not resolidify on further heating as in the case of the *para* and *meta* acids. If the melted product was cooled, however, and heated again it began to melt at 150° and water vapor came off at 200°, the melting point of the *o*-nitrophthalimides.

The normal nitrophenylphthalimides, *p*-nitrophenylphthalimide (m. p. 262–264°), *m*-nitrophenylphthalimide (m. p. 242–244°) and *o*-nitrophenylphthalimide (m. p. 202–203°) were prepared by the fusion of the proper nitraniline with phthalic anhydride, according to Meyer and Maier.[19] These corresponded in properties and melting points to the values given by other investigators[20] for their normal compounds, but did not correspond to the compounds reported by Dobreff.[21]

Since Kuhara, Komatsu and Nishiyori claimed to have obtained both the symmetrical and asymmetrical forms of the *o*-, *m*- and *p*-nitrophenylphthalimides by the reaction of ether solutions of the corresponding nitraniline and of phthalyl chloride at —10°, and since the work of van der Meulen and that done in this Laboratory showed that under these conditions the phthaldiphenyldiamides were formed, the work of Kuhara and that of Dobreff was carefully repeated.

According to Kuhara,[20c] ethereal solutions of 10 g. of *p*-nitraniline and 14.6 g. of phthalyl chloride were cooled and the chloride was added slowly to the aniline. After five minutes a precipitate gradually separated and the yellow color of the ether solution faded. The precipitate was almost white, faintly tinged with yellow. It was filtered, washed with hydrochloric acid, then with ammonia, whereupon it became deep yellow in color and some of it dissolved and then crystallized in the pores of the filter plate. It was finally washed with water and dried. Then the entire mass was extracted with alcohol. From the deep yellow alcoholic solution there crystallized first a small amount of a white substance, m. p. 262–263°. This was normal *p*-nitrophenylphthalimide; a mixed melting point with the pure compound showed no depression. A large quantity of this compound was obtained from the ether filtrate of the original reaction mixture. Next from the alcoholic solution a mass of fine, white needles crystallized

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[19] Meyer and Maier, *Ann.*, **327**, 42 (1903).

[20] (a) Pawlewski, *Ber.*, **27**, 3430 (1894); (b) Rupe and Thiess, *Ber.*, **42**, 4289 (1909); (c) Kuhara, Komatsu and Nishiyori, *Mem. Coll. Sci. Eng. Kyoto Imp. Univ.*, **5**, 342 (1912).

[21] Dobreff, *Ber.*, **28**, 940 (1895).

which melted at 192°. This substance was reported by Kuhara to be pale yellow and to be the asymmetrical *p*-nitrophenylphthalimide, identical with the product obtained by Dobreff.[21] It was noted in this Laboratory, however, that the product melted with the evolution of gas, resolidified and melted again at 262–263°, which indicated that it was probably the *p*-nitrophthalanilic acid. It dissolved in alkalies, giving a deep yellow solution from which the acid was reprecipitated as a white powder. A mixture of this compound with *p*-nitrophthalanilic acid (m. p. 192°), prepared as indicated above, showed no change in the melting point. The appearance of the yellow color on washing the reaction product with ammonia was due to the formation of an ammonium salt and it was traces of this which colored the Kuhara product and that of Dobreff. This ammonium salt was obtained in this Laboratory as a yellow, crystalline product which finally crystallized from the alcohol solution.

The portion of the original reaction product insoluble in alcohol was a pale yellow powder which melted at 232° and when dissolved in hot glacial acetic acid was converted into the *p*-nitrophenylphthalimide. This compound was, therefore, *p*-nitrophenylphthalamide, which had been obtained by Pawlewski[22] by the action of two molecules of *p*-nitraniline on one molecule of phthalyl chloride. Therefore, by following the exact details of Kuhara's work, the products obtained were white *p*-nitrophenylphthalimide, m. p. 262–263°, white *p*-nitrophthalanilic acid, m. p. 192°, yellow *p*-nitrophenylphthalamide, m. p. 232°, and the yellow ammonium salt of *p*-nitrophthalanilic acid. When the experiment was repeated and the original reaction product washed with ether instead of hydrochloric acid and ammonia the product did not change color and from it were isolated, as above, *p*-nitrophenylphthalimide, *p*-nitrophthalanilic acid and *p*-nitrophenylphthalamide.

Similarly the work of Dobreff[21] was repeated. The *p*-nitraniline (10 g.) and the phthalyl chloride (14.6 g.) were heated on a steam-bath until the mixture changed from brown to tan. A portion of the filtered product was boiled, according to Dobreff, a long time with water and then recrystallized from alcohol. The yellow substance, insoluble in alcohol, melted at 230–232° and was *p*-nitrophenylphthalamide. From the alcohol solution a small amount of normal *p*-nitrophenylphthalimide (m. p. 262–263°) crystallized first, then a creamy white powder (m. p. 192° with decomposition) which proved to be the *p*-nitrophthalanilic acid. A second portion of the filtered product was washed with ether and extracted with alcohol and exactly the same products were obtained as from the first portion except that in this case there was much more of the normal *p*-nitrophenylphthalimide and much less of the *p*-nitrophthalanilic acid. This work showed that Dobreff's method gives largely the normal *p*-nitrophenylphthalimide but that boiling with water hydrolyzed this to the acid and that the 190–190.5° yellow compound of Dobreff is the *p*-nitrophthalanilic acid. The yellow color must have been due to traces of the yellow nitrophthalanilide.

Kuhara[23] stated that the asymmetrical nitrophenylphthalimides could be obtained by the action of acetyl chloride on the corresponding nitrophthalanilic acid but gave no details. The Hoogewerff-van Dorp method[2] was carried out with the utmost care. The *p*-nitrophthalanilic acid and acetyl chloride were heated for twenty minutes at 60–75°. There was no color change. The product, however, was washed with carbon disulfide, filtered and added directly to anhydrous ether. A drop or two of 30% potassium hydroxide temporarily changed the white solid into the orange potassium salt. This color disappeared, however, as long as the mixture was slightly acid. The only substance which could be isolated was the *p*-nitrophthalanilic acid, m. p. 192°, which was recovered practically quantitatively. Variations in temperature and time of reaction

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[22] Pawlewski, *Ber.*, **28**, 1118 (1895).

[23] Ref. 20 c, p. 345.

gave no other results. Therefore, the asymmetrical *p*-nitrophenylphthalamide cannot be prepared by the method used in the preparation of phenylphthal-iso-imide.

Kuhara[24] prepared a mono-silver salt of *p*-nitrophthalanilic acid from a water solution of the ammonium salt by precipitation with silver nitrate. The ammonium salt was prepared in this Laboratory by passing dry ammonia gas into an alcoholic solution of the acid. A solution of this salt was treated with silver nitrate and the silver salt, pale yellow in color, was dried and analyzed.

Anal. Calcd. for $C_{14}H_9O_5N_2Ag$: Ag, 27.46. Found: 27.20, 27.26.

A di-silver salt of *p*-nitrophthalanilic acid was also prepared. The di-potassium salt was first formed by the reaction of alcoholic potash on an alcoholic solution of the *p*-nitrophthalanilic acid. The potassium salt was washed with alcohol and dried, then dissolved in a large volume of alcohol and to this solution alcoholic silver nitrate was added. A yellow precipitate was first formed but on addition of the calculated amount of silver nitrate the precipitate became brown. This brown di-silver salt was difficultly soluble in alcohol but could be recrystallized from it.

Anal. Calcd. for $C_{14}H_{18}O_5N_2Ag_2$: Ag, 43.17. Found: 43.20, 43.12.

The action of phthalyl chloride on *m*-nitraniline according to the Kuhara method was investigated as in the case of the *para* compound. One product crystallizing from the alcoholic extract was white and melted at 243°. This substance agreed in melting point and properties with the symmetrical *m*-nitrophenylphthalimide of other investigators.[20a,20c,22]. The substance which crystallized next was *m*-nitrophthalanilic acid, colorless needles melting at 202° with evolution of gas, resolidifying and melting again at 243°. This was identical with the acid previously prepared.[18b,25] A large amount of the acid was also obtained from the ether filtrate of the original reaction product. The portion least soluble in alcohol was pale yellow in color and melted at 230–232°. This was reported by Kuhara[23] as the asymmetrical *m*-nitrophenylphthalimide. It proved to be the *m*-nitrophenylphthalamide and when heated with glacial acetic acid it was converted into the asymmetrical *m*-nitrophenylphthalimide.[22]

The Dobreff method was repeated in this case too.[21] The product, after being boiled with water, was crystallized from hot alcohol and found to be a mixture of *m*-nitrophenylphthalamide, m. p. 230–232°, and *m*-nitrophthalimide, m. p. 240–245°. This mixture was separated by treatment with chloroform; the amide was insoluble and the imide dissolved and was recrystallized from alcohol. Phthalic anhydride was obtained from the original ether solution and red crystals of the hydrochloride of *m*-nitraniline separated from the water extract. The evidence of this work shows that the yellow compound reported by Dobreff and the asymmetrical *m*-nitrophenylphthalimide of Kuhara were identical and were the *m*-nitrophenylphthalamide.

The reaction of acetyl chloride on the *m*-nitrophthalanilic acid was studied as in the case of the *para* compound, but no trace of an asymmetrical compound could be obtained. The acid was recovered practically quantitatively. At high temperatures small amounts of the symmetrical *m*-nitrophthalanil were obtained.

The Kuhara work[20c] on the asymmetrical *o*-nitrophenylphthalamide was repeated. The following products were isolated from the alcoholic solution: first colorless needles, m. p. 198–200°, which proved to be the *o*-nitrophenylphthalimide;[18b,20b,22] then yellow crystals, m. p. 149–151°, which proved to be the *o*-nitrophthalanilic acid, and on the sides of the beaker yellow crystals of the hydrochloride of *o*-nitraniline, which melted from 140–150° with evolution of gas. The original ether filtrate when evaporated gave a yellow mixture that melted between 108–145° with evolution of a gas. This was

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[24] Ref. 20 c, p. 362.

[25] Tingle and Rolke, THIS JOURNAL, 30, 1882 (1908).

extracted with dilute sodium hydroxide and from the alkali solution *o*-nitrophthalanilic acid was obtained. The residue, insoluble in alkali, was washed with alcohol from which yellow crystals of the hydrochloride of *o*-nitraniline were obtained. The residue, insoluble in alcohol, dissolved completely in chloroform and proved to be *o*-nitrophenylphthalimide. Efforts to prepare an asymmetrical *o*-nitrophenylphthalimide as in the case of the other nitro compounds proved unsuccessful. No trace of an isomeric compound could be obtained.

Chlorophthalanilic Acids

The *p*-chlorophthalanilic acid was prepared by the action of chloroform solutions of phthalic anhydride on *p*-chloro-aniline. The acid crystallized out in white needles and was filtered, washed with chloroform and found to melt at 187.5°; after cooling, it resolidified and when reheated melted at 192°, the melting point of *p*-chlorophthalanil. Recrystallization of the acid did not change its melting point. In properties it corresponded with the *p*-chloro acid reported by Tingle and Brenton[26] (m. p. 180°).

The *m*-chlorophthalanilic acid was prepared in a similar way. It formed white crystals which melted at 183–184° with evolution of gas. When cooled it resolidified and remelted at 157°. The acid is very soluble in ethyl acetate, glacial acetic acid and dilute alkalies. It can be recrystallized from alcohol, chloroform or benzene, but if prepared in chloroform solution this is unnecessary as the product is obtained pure. Since this compound is not given in the literature an analysis was made.

Anal. Calcd. for $C_{14}H_{10}O_3NCl$: N, 5.08. Found: 4.94.

The *o*-chlorophthalanilic acid was obtained by the same method. The acid is somewhat soluble in ether and in chloroform. It can be recrystallized from chloroform or benzene but the best product was obtained by precipitation from a solution of the acid in dilute alkali. It crystallizes in white needles, m. p. 147–148°. If it is heated to 155° a gas is gradually evolved.

Anal. Calcd. for $C_{14}H_{10}O_3NCl$: N, 5.08. Found: 4.91.

Chlorophenylphthalimides

The chlorophenylphthalimides were prepared by the fusion of the corresponding chloro-aniline with phthalic anhydride. The *p*-chloro compound was dissolved from the reaction mass by chloroform and precipitated by alcohol in the form of long, white, silky needles, m. p. 192°, unchanged by recrystallization from hot alcohol. It agreed in properties with the *p*-chlorophthalanil of Gabriel.[9] The *m*-chlorophenylphthalimide was isolated by dissolving it in chloroform and precipitating it with alcohol. It is very soluble in chloroform, ether, benzene and ethyl acetate and insoluble in glacial acetic acid. It can be recrystallized from hot alcohol and the crystals melt at 183–184° with evolution of gas.

Anal. Calcd. for $C_{14}H_9O_2NCl$: N, 5.43. Found: 5.47, 5.39.

The *o*-chlorophenylphthalimide was found to be too soluble in alcohol to be precipitated by it from a chloroform solution. The residue obtained by evaporation of the chloroform solution could be recrystallized from hot alcohol. The product consisted of long, white, silky needles which melted at 132–140°. It was found to be soluble in chloroform, glacial acetic acid, benzene, ethyl acetate and ether.

Anal. Calcd. for $C_{14}H_9O_2NCl$: N, 5.43. Found: 5.34.

Attempts to prepare isomeric forms of these chlorophenylphthalimides by the action of acetyl chloride on the acids were not successful.

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[26] Ref. 10 a, p. 1161.

***p*-Chlorophenylphthalamide** was obtained by the action of *p*-chloro-aniline on phthalyl chloride. By benzene and alcoholic extraction of the reaction product, *p*-chlorophthalanil was recovered. The residue, insoluble in alcohol, was a white powder that melted at 233°. When it was recrystallized from hot alcohol or boiled with glacial acetic acid it was transformed into the imide. This indicates that it is the amide but because of the difficulty of getting a pure sample no analysis was made.

Summary

The results of these investigations lead to the following conclusions.

1. The phthalphenyl-iso-imide prepared by van der Meulen is the true asymmetrical phenylphthalimide. The α-phenylphthalimide of Kuhara is a mixture of phthalanil and diphenyldiamide. The β,α-phenylphthalimide (83–84°) of Kuhara is a mixture of phthalphenyl-iso-imide and phthalanilic acid. The α-phenylphthalimide (m. p. 125°) of Kuhara is a mixture of the iso-imide and the normal phenylphthalimide.

2. The *p*-isonitrophenylphthalimide of Kuhara and of Dobreff is *p*-nitrophthalanilic acid. The *m*-isonitrophenylphthalimide of Kuhara and of Dobreff is a mixture of *m*-nitrophenylphthalamide and *m*-nitrophenylphthalimide. The *o*-isonitrophenylphthalimide of Kuhara is *o*-nitrophthalanilic acid with traces of *o*-nitrophthalanil and the hydrochloride of *o*-nitraniline. The asymmetrical *o*-, *m*- and *p*-nitrophenylphthalimides could not be obtained by the action of acetyl chloride on the corresponding phthalanilic acid.

3. The *o*-, *m*- and *p*-chlorophthalanilic acids can be prepared best by the reaction of chloroform solutions of phthalic anhydride on the corresponding chloro-aniline. The *o*- and *m*- acids have not been previously recorded. The *o*-, *m*- and *p*-chlorophthalanils can be prepared by the fusion of the chloro-aniline with phthalic anhydride. The *ortho* and *meta* compounds have not been previously recorded.

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