

## 260. Union of Aryl Nuclei. Part IV. Phenylphthalic Acids and Some Derivatives.

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*3-Phenylphthalic acid* and its 4-isomeride are obtained on hydrolysis of the product from the action of diazotised methyl 3- and 4-aminophthalate respectively on benzene in the presence of aqueous sodium hydroxide. The latter acid is also obtained from a similar reaction between diazotised aniline and ethyl phthalate, as well as by the interaction of nitrosoacetanilide and ethyl phthalate. Mixtures of 4-(methoxyphenyl)phthalic acids and of 4-(chlorophenyl)phthalic acids are similarly obtained by using the diazotised 4-aminophthalic ester with anisole and chlorobenzene respectively. 3-Phenylphthalic acid gives fluorenone-1-carboxylic acid on treatment with sulphuric acid. *Methyl 4-phenylphthalate*, 4-phenylphthalic anhydride, and 4-phenylphthalimide are prepared from 4-phenylphthalic acid. Condensation of 4-phenylphthalic anhydride with benzene in the presence of aluminium chloride gives a mixture of 4- and 5-phenylbenzophenone-2-carboxylic acids, which on ring closure yields 2-phenylanthraquinone. 4-(*p*-Nitrophenyl)phthalic acid and its anhydride are obtained from the product of the nitration of 4-phenylphthalic anhydride.

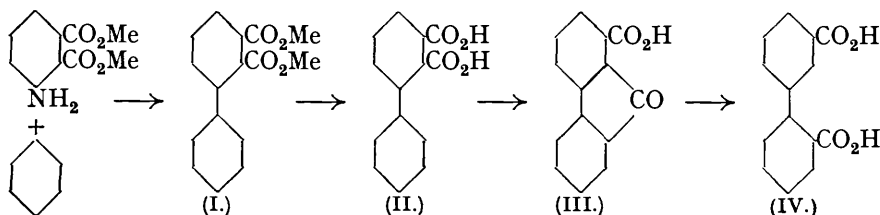
IN Part II (this vol., p. 113) a series of substituted diphenyl-2-carboxylic acids was prepared by means of the interaction of a diazotised substituted anthranilic ester with benzene in the presence of aqueous alkali, and the acids so obtained were converted by ring-closure into substituted fluorenones. The same reaction has now been applied to the preparation of the two phenylphthalic acids (diphenyl-2 : 3- and -3 : 4-dicarboxylic acid) by using diazotised aminophthalic esters in place of the anthranilic esters in the reaction with benzene.

4-Phenylphthalic acid (diphenyl-3 : 4-dicarboxylic acid) and its anhydride were first prepared by v. Auwers and Jülicher (*Ber.*, 1922, **55**, 2184), who obtained it by the action of sulphuric acid on 4-phenyl-1-trichloromethyl-1-methylcyclohexa-2 : 5-dien-4-ol; this gave 3-methyldiphenyl-4-carboxylic acid, which was then oxidised with potassium permanganate. More recently the acid has been obtained by Ghigi (*Ber.*, 1938, **71**, 684) by the oxidation of 3 : 4-dimethyldiphenyl. 3-Phenylphthalic acid (diphenyl-2 : 3-dicarboxylic acid) has not been previously reported.

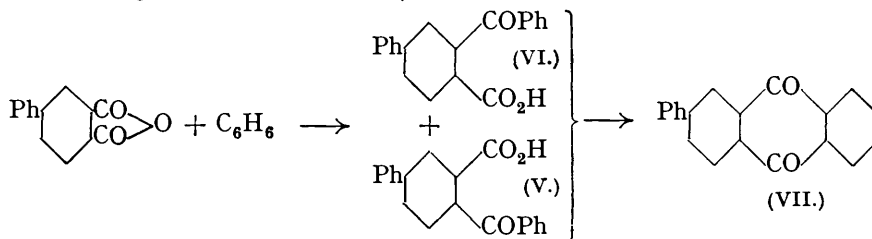
The preparation of the two phenylphthalic acids now described involves the union of two aromatic nuclei with the elimination of an amino-group from one of them. As in previous work (cf. Part II), it is again found that better results are obtained when the amino-group is attached to the more heavily substituted nucleus. This method of procedure is also advantageous in that the positions of the substituents, originally in the amine component, are fixed with reference to the internuclear bond in the reaction product.

The reaction between diazotised methyl 4-aminophthalate and benzene gave methyl 4-phenylphthalate in 37% yield (calculated on the weight of base), which afforded the acid on hydrolysis. Similar reactions were carried out but using (a) anisole and (b) chlorobenzene in place of benzene. These resulted in the formation of mixtures of 4-(methoxyphenyl)phthalic esters and 4-(chlorophenyl)phthalic esters in 32 and 45% yield respectively, which were hydrolysed to the corresponding acids. It was not found possible to separate completely the pure constituents from these mixtures; by analogy with similar reactions carried out previously (Grieve and Hey, J., 1934, 1797; Part II, *loc. cit.*), it is anticipated that they consist mainly of the 2'- and 4'-substituted diphenyl-3 : 4-dicarboxylic acids. The inverse reaction between diazotised aniline and ethyl phthalate gave mainly the 4-phenylphthalic ester, with indications of the presence of some of the 3-isomeride. A similar result was obtained in the cognate reaction between nitrosoacetanilide and ethyl phthalate. Methyl 4-phenylphthalate, 4-phenylphthalic anhydride, and 4-phenylphthalimide were prepared by standard methods from 4-phenylphthalic acid.

In similar manner the reaction between the diazotised dimethyl ester of 3-aminophthalic acid and benzene gave methyl 3-phenylphthalate (I) in 35% yield, which yielded the acid (II) on hydrolysis. The latter was converted by ring-closure with sulphuric acid into fluorenone-1-carboxylic acid (III). It cannot, however, be regenerated from that compound since the opening of the fluorenone ring by fusion with alkali gives diphenyl-2 : 3'-dicarboxylic acid (IV) (Fittig and Gebhard, *Annalen*, 1878, **193**, 155; Fittig and Liepmann, *ibid.*, 1880, **200**, 9).



Condensation of 4-phenylphthalic anhydride with benzene in the presence of aluminium chloride yielded a mixture of 4- and 5-phenylbenzophenone-2-carboxylic acids (V and VI), which when heated with zinc chloride gave 2-phenylanthraquinone (VII), obviously identical with that prepared by Scholl and Neovius (*Ber.*, 1911, **44**, 1079) by the action of phthalic anhydride on diphenyl in the presence of aluminium chloride and ring-closure of the resulting 4-phenylbenzophenone-2'-carboxylic acid by means of zinc chloride (cf. Groggins, *Ind. Eng. Chem.*, 1930, **22**, 626).



Nitration of 4-phenylphthalic anhydride gave a product from which 4-*p*-nitrophenylphthalic acid and its anhydride were obtained. The position of the nitro-group in these products was proved by the fact that oxidation of the acid with chromic anhydride gave *p*-nitrobenzoic acid (cf. Fittig and Bieber, *Annalen*, 1870, **156**, 242).

## EXPERIMENTAL.

*Methyl 4-Aminophthalate*.—4-Nitrophthalic anhydride (150 g.) was boiled under reflux with 300 c.c. of methyl-alcoholic hydrogen chloride for 12 hours. After standing overnight, the alcohol was removed by distillation, and the residue extracted with dilute aqueous sodium carbonate, filtered off, and washed with water. The crude methyl 4-nitrophthalate (158 g., m. p. 66—67°) was reduced to methyl 4-aminophthalate (117 g., m. p. 81°) by means of zinc and alcoholic hydrochloric acid, as described by Bogert and Renshaw (*J. Amer. Chem. Soc.*, 1906, **28**, 618).

*Methyl 3-Aminophthalate*.—An aqueous solution of silver nitrate (170 g.) was added to an aqueous solution of sodium 3-nitrophthalate prepared by neutralisation of the free acid (105 g.). The precipitated silver 3-nitrophthalate was filtered off, washed, dried in the steam-oven, and then boiled under reflux with a mixture of methyl iodide (280 g.) and benzene (200 c.c.) for 3—4 hours. The silver iodide was filtered off, and the excess methyl iodide and benzene removed by distillation (cf. Wegscheider and Lipschitz, *Monatsh.*, 1900, **21**, 791). The residual methyl 3-nitrophthalate (95 g., m. p. 67—68°) was reduced with zinc and alcoholic hydrochloric acid as described by Bogert and Renshaw (*loc. cit.*) for the reduction of the 4-nitro-ester, and the amino-ester was finally extracted with ether from the neutralised reaction mixture. Evaporation of the ether from the dried extract left methyl 3-aminophthalate as a brown oil (75 g.). Its hydrochloride melted at 171° (cf. Bogert and Jouard, *J. Amer. Chem. Soc.*, 1909, **31**, 487).

*Action of Diazotised Methyl 4-Aminophthalate on Benzene in Presence of Alkali*.—A mixture of methyl 4-aminophthalate (35 g.), concentrated hydrochloric acid (*d* 1.16, 67 c.c.), and water (15 c.c.) was diazotised in the normal manner by addition of aqueous sodium nitrite (12.5 g. in 50 c.c.). An aqueous solution of sodium hydroxide (25 g. in 100 c.c.) was added slowly over a period of 2 hours to a stirred mixture of the diazonium solution (filtered from a small residue of insoluble matter) and benzene (200 c.c.) at 5—10°. Stirring was continued overnight and the temperature was allowed to rise to about 20°. The benzene layer was separated, washed with water, dried, and distilled. The dark oily residue distilled at 140—160°/10<sup>-3</sup> mm., yielding a pale yellow oil which solidified (16.5 g., m. p. 55—60°). The crude ester was hydrolysed by boiling with 20% aqueous sodium hydroxide for 3 hours. After dilution and filtration, addition of acid precipitated 4-phenylphthalic acid, which crystallised from hot water or very dilute alcohol in needles, m. p. 194° (Found: C, 69.45; H, 4.4. Calc. for C<sub>14</sub>H<sub>10</sub>O<sub>4</sub>: C, 69.4; H, 4.1%). A portion of the acid was boiled under reflux for 2 hours with methyl-alcoholic hydrogen chloride. After removal of excess alcohol, the residue was poured into water, extracted with ether, and the extract washed with aqueous sodium carbonate and dried. Evaporation of the solvent left a residue, which, on sublimation in high vacuum and subsequent crystallisation from dilute alcohol or light petroleum (b. p. 40—60°), gave *methyl 4-phenylphthalate* in white needles, m. p. 62—63° (Found: C, 71.0; H, 5.4. C<sub>16</sub>H<sub>14</sub>O<sub>4</sub> requires C, 71.1; H, 5.2%).

*4-Phenylphthalic Anhydride*.—4-Phenylphthalic acid (5 g.) was boiled under reflux for 2 hours with acetic anhydride (10 c.c.). The anhydride of 4-phenylphthalic acid, which separated on cooling, was filtered off, and a further quantity was obtained on pouring the filtrate into ice-cold water. After purification by sublimation, 4-phenylphthalic anhydride was obtained in white needles, m. p. 138—139° (Found: C, 75.0; H, 3.7. Calc. for C<sub>14</sub>H<sub>8</sub>O<sub>3</sub>: C, 75.0; H, 3.6%).

*4-Phenylphthalimide*.—A mixture of 4-phenylphthalic anhydride (10.2 g.) and urea (1.6 g.) was heated to 130° on a sand-bath. The fused mass frothed and the temperature rose to 170°. After frothing had ceased the residual mass was purified by sublimation. *4-Phenylphthalimide* was obtained in white needles, m. p. 200° (Found: C, 75.4; H, 4.1. C<sub>14</sub>H<sub>9</sub>O<sub>2</sub>N requires C, 75.3; H, 4.0%).

*Action of Diazotised Aniline on Ethyl Phthalate in Presence of Alkali*.—A solution of aniline (50 g.) in a mixture of concentrated hydrochloric acid (*d* 1.16, 125 c.c.) and water (40 c.c.) was diazotised in the normal manner with aqueous sodium nitrite (40 g. in 100 c.c.). To a cold stirred mixture of the diazonium solution and ethyl phthalate (400 c.c.), a solution of sodium hydroxide (40 g.) in water (150 c.c.) was gradually added, and stirring was continued for 12 hours. After addition of sodium sulphate, the two layers were separated. The dried ethyl phthalate layer was distilled at 160—180°/10—12 mm., and, after removal of excess ethyl phthalate, the crude ethyl phenylphthalate (20 g.) was collected at 130—160°/10<sup>-3</sup> mm. Hydrolysis of the crude ester gave 4-phenylphthalic acid, m. p. 194° after repeated crystallisation from dilute alcohol. The crude product was less pure than that obtained as above, and was probably contaminated with a small quantity of the 3-phenyl isomeride.

*Action of Nitrosoacetanilide on Ethyl Phthalate*.—A solution of nitrosoacetanilide (22 g.) in

ethyl phthalate (400 c.c.) was stirred at room temperature for 24 hours. The solution darkened and nitrogen was evolved. The excess ethyl phthalate was removed by distillation mainly at 160—170°/12 mm., but distillation was continued up to 220°/12 mm. The dark residue on distillation at 160°/10<sup>-3</sup> mm. gave a deep-coloured oil (11 g.), which was hydrolysed by boiling under reflux with 20% aqueous sodium hydroxide. Acidification precipitated the crude phenylphthalic acid, which, after purification by repeated crystallisation from hot water (with charcoal) or very dilute alcohol, melted at 189—191°, both alone and admixed with an authentic specimen prepared as described above from methyl 4-aminophthalate and benzene.

*Action of Diazotised Methyl 4-Aminophthalate on Anisole in Presence of Alkali.*—This reaction was carried out with the ester (35 g.) and anisole (250 c.c.) as described above for the corresponding reaction with benzene. A mixture of 4-(2'- and 4'-methoxyphenyl)phthalic esters (16 g.) was obtained, which gave on hydrolysis a mixture of the corresponding two acids, m. p. 145—155° (Found : C, 66.4; H, 4.5. Calc. for C<sub>15</sub>H<sub>12</sub>O<sub>5</sub> : C, 66.2; H, 4.4%).

*Action of Diazotised Methyl 4-Aminophthalate on Chlorobenzene in Presence of Alkali.*—A similar reaction carried out between the ester (35 g.) and chlorobenzene (200 c.c.) gave a mixture of 4-(2'- and 4'-chlorophenyl)phthalic esters (22 g.), which on hydrolysis gave a mixture of the two acids, m. p. 140—150° (Found : C, 60.7; H, 3.4. Calc. for C<sub>14</sub>H<sub>9</sub>O<sub>4</sub>Cl : C, 60.8; H, 3.25%).

*Action of Diazotised Methyl 3-Aminophthalate on Benzene in Presence of Alkali.*—This reaction was carried out exactly as described above for the 4-amino-ester, 70 g. of the ester being used; the crude methyl 3-phenylphthalate (31.5 g.) was in part purified by crystallisation from light petroleum (b. p. 40—60°) and in part hydrolysed to the free acid. *Methyl 3-phenylphthalate* separated in white needles, m. p. 94° (Found : C, 71.3; H, 4.95. C<sub>16</sub>H<sub>14</sub>O<sub>4</sub> requires C, 71.1; H, 5.2%), and the *acid* separated from very dilute alcohol in fine needles, m. p. 181° (Found : C, 69.3; H, 4.4. C<sub>14</sub>H<sub>10</sub>O<sub>4</sub> requires C, 69.4; H, 4.1%). When this was heated in concentrated sulphuric acid solution at 40—50° for 10 minutes ring closure was effected, and when the mixture was poured into water, fluorenone-1-carboxylic acid separated, which crystallised from dilute alcohol in orange-red needles, m. p. 192° (cf. Fittig and Liepmann, *loc. cit.*, p. 18).

*2-Phenylanthraquinone.*—Powdered aluminium chloride (6.7 g.) was added to a solution of 4-phenylphthalic anhydride (5 g.) in dry benzene (13 c.c.) cooled in ice-water. When evolution of hydrogen chloride had slackened, the temperature was gradually raised to 80°, and the reaction flask, fitted with a reflux condenser, was maintained at this temperature for 2½ hours with constant stirring. The cold mixture was added to crushed ice, made strongly acid by addition of concentrated hydrochloric acid, and the excess benzene was removed with steam. The insoluble residue was filtered off, washed with water, and extracted with hot aqueous sodium carbonate. After filtration, addition of mineral acid precipitated a mixture of 4- and 5-phenylbenzophenone-2-carboxylic acids (5.5 g.), which after crystallisation from alcohol melted over the range 177—207° (Found : C, 79.3; H, 4.2. Calc. for C<sub>20</sub>H<sub>14</sub>O<sub>3</sub> : C, 79.4; H, 4.6%). Powdered anhydrous zinc chloride (1.0 g.) was added to the mixed acids (1.0 g.) heated in a nickel crucible at 230°, and heating was continued at this temperature for 2 hours. The cold mass was extracted first with boiling water, and then with hot alcohol. Concentration of the alcoholic extract deposited 2-phenylanthraquinone in yellow needles, m. p. 140—150°, which, after sublimation and recrystallisation, melted at 157° (Found : C, 84.7; H, 4.6. Calc. for C<sub>20</sub>H<sub>12</sub>O<sub>2</sub> : C, 84.5; H, 4.2%) (cf. Scholl and Neovius, *loc. cit.*; Groggins, *loc. cit.*).

*Nitration of 4-Phenylphthalic Anhydride.*—A mixture of fuming nitric acid (*d* 1.5, 20 c.c.) and glacial acetic acid (20 c.c.) was added to a solution of 4-phenylphthalic anhydride (2 g.) in glacial acetic acid (20 c.c.). After being heated for ¼ hour on the steam-bath, the solution was poured into water. The precipitated solid was boiled with water, cooled, filtered off, and crystallised from dilute alcohol. 4-(*p*-Nitrophenyl)phthalic acid separated in microcrystalline form, m. p. 178—179° (Found : C, 59.1; H, 3.5. C<sub>14</sub>H<sub>9</sub>O<sub>6</sub>N requires C, 58.9; H, 3.2%). A portion of the free acid was converted by sublimation into the *anhydride*; needles, m. p. 136—137° (Found : C, 62.4; H, 2.7. C<sub>14</sub>H<sub>7</sub>O<sub>5</sub>N requires C, 62.45; H, 2.6%). A second portion of the free acid was dissolved in glacial acetic acid and oxidised by gradual addition of chromic anhydride to the boiling solution. The reaction mixture was poured into water, from which ether extracted *p*-nitrobenzoic acid, identified by m. p. and mixed m. p. In the nitration of 4-phenylphthalic anhydride indications were obtained of the formation of isomeric nitro-compounds which were more soluble than the *p*-nitro-derivative, but these could not be obtained pure.

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