CCCXXXVIII.—*A New Reaction of Certain Diazosulphonates derived from β-Naphthol-*1*-sulphonic Acid. Part III. Preparation of Phthalazine, Phthalazone, and Phthalimidine Derivatives from* m-*Nitroaniline.*

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In Parts I and II of this series (J., 1926, 690; preceding paper), the preparation of phthalazine, phthalazone, and phthalimidine derivatives from 4′-nitrobenzene-2-naphthol-1-diazosulphonate has been described, and the constitution of the isomeric 4′-nitro- and -amino-phenylphthalazones discussed. The investigation has now been extended to the corresponding 3′-nitro- and amino-derivatives.

3′-Nitrobenzene-2-naphthol-1-diazosulphonate is formed quantitatively from diazotised *m*-nitroaniline and β-naphthol-1-sulphonic acid in acid solution, but conversion through *sodium* 1-3′-*nitrobenzeneazo*-β-*naphthaquinone*-1-*sulphonate* into *sodium hydrogen* 3-(3′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic acid*-1-*sulphonate* is accompanied by no marked change in colour and does not proceed so readily as in the case of the 4′-nitro-isomeride, owing to an increased tendency to the formation of 3′-nitrobenzeneazo-β-naphthol in appreciable quantities. This side reaction is limited by working at greater dilution, but under the best conditions the yield is 15% less than that obtained with the 4′-nitro-isomeride. Monosodium 3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid-1-sulphonate resembles the 4′-nitro-isomeride in general properties, although it is noteworthy that, whereas the latter is a level-dyeing, pure greenish-yellow, acid dye of good tinctorial power, the former possesses hardly any tinctorial properties. The replacement of the sodium-1-sulphonate group by hydroxyl gives 1-*hydroxy*-3-(3′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic acid* in a yield of about 10% less than was obtained with the 4′-nitro-isomeride. *Esters* and an *anilide* of this hydroxy-compound were obtained readily, but attempts to prepare an acetyl derivative failed, for although a variety of conditions was employed the product was always resinous and could not be crystallised. Unlike the 4′-nitro-isomeride, 1-hydroxy-3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid is not reduced satisfactorily by alkaline hydrosulphite [hyposulphite], for the compounds in the present series appear to be more sensitive to alkalis, and although the product resembled that anticipated in appearance and solubility in acids and alkalis, it could not be purified by crystallisation and was not converted into the corresponding aminophenylphthalazone by boiling with mineral acid. 1-*Hydroxy*-3-(3′-*aminophenyl*)*tetrahydrophthalazine*-4-*acetic acid* is obtained satisfactorily, however, by reduction with stannous chloride and hydrochloric acid, because its hydrochloride is so sparingly soluble in concentrated hydrochloric acid that the reaction does not proceed further even after prolonged boiling. On the other hand, by boiling 1-hydroxy-3-(3′-aminophenyl)tetrahydrophthalazine-4-acetic acid with aqueous sulphuric acid (b. p. 140°), acetic acid is eliminated and 3′-*amino*-3-*phenylphthalaz*-1-*one* is obtained in a 91% yield. When this is reduced with zinc dust and hydrochloric acid, one nitrogen atom is eliminated as ammonia and 3′-*amino*-N-*phenylphthalimidine* is produced. The replacement of the amino-group in the latter by hydrogen or by hydroxyl proceeds as with the 4′-amino-isomeride, except that, as the diazonium chloride obtained from 3′-amino-*N*-phenylphthalimidine is less stable to the action of boiling dilute sulphuric acid, 3′-*hydroxy*-N-*phenylphthalimidine* is formed with greater ease.

When 1-hydroxy-3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid is boiled with sulphuric acid (b. p. 140°), it loses acetic acid and 3′-*nitro*-3-*phenylphthalaz*-1-*one* is formed, but in a yield of 12% less than was obtained with the 4′-nitro-isomeride. 3′-Nitro-3-phenylphthalaz-1-one is much less acidic than the latter, but with mineral acids it also forms well-crystallised salts, decomposed by water, and it forms a more stable *picrate*. The product obtained from it by reduction varies with the conditions used. Thus, reduction with aqueous sodium sulphide gives 3′-amino-3-phenylphthalaz-1-one, although in a yield of 17% less than was obtained by the action of aqueous sulphuric acid on 1-hydroxy-3-(3′-aminophenyl)tetrahydrophthalazine-4-acetic acid, whereas zinc dust and hydrochloric acid give 3′-amino-*N*-phenylphthalimidine. 3′-Nitro-3-phenylphthalaz-1-one reacts with methyl sulphate in a similar manner to the 4′-nitro-isomeride, and the primary product behaves similarly with methyl or ethyl alcohol. After crystallisation from alcohol, heating gives 4-*keto*-1-*methoxy*-3-(3′-*nitrophenyl*)-3 : 4-*dihydrophthalazine*, but this is always accompanied by a more complex substance, especially if heating is too rapid at first. 1 : 4-*Diketo*-3-(3′-*nitrophenyl*)*tetrahydrophthalazine* is obtained from the methoxy-compound by the action of hydrobromic acid.

Finally, 3′-*nitro*-3-*phenylphthalaz*-4-*one* was prepared for purposes of comparison. The condensation of equimolecular proportions of phthalaldehydic acid and *m*-nitrophenylhydrazine in boiling alcoholic solution gives the *lactone* form of the *m*-nitrophenylhydrazone, and when a nitrobenzene solution of this is boiled, a molecule of water is eliminated with formation of 3′-nitro-3-phenylphthalaz-4-one. The latter, although very sparingly soluble in mineral acids, does not form salts either with them or with picric acid, is insoluble in sodium hydroxide, and is unaltered by treatment with methyl sulphate under conditions identical with those used in the case of 3′-nitro-3-phenylphthalaz-1-one.

The lactone form of *o*-carboxybenzaldehyde-*p*-nitrophenylhydrazone is converted into 4′-amino-3-phenylphthalaz-4-one by treatment with warm aqueous sodium sulphide, but the corresponding *m*-nitro-derivative is merely converted into 3′-nitro-3-phenylphthalaz-4-one, which separates and remains unaltered even after prolonged boiling. 3′-*Amino*-3-*phenylphthalaz*-4-*one*, however, is readily obtained by reducing 3′-nitro-3-phenylphthalaz-4-one with alkaline hydrosulphite.

Further work on this subject is in progress.

EXPERIMENTAL.

Sodium Hydrogen 3-(3′-*Nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetate*-1-*sulphonate*.—A filtered solution of 50 g. of commercial sodium β-naphthol-1-sulphonate in 220 c.c. of water was stirred into a cold solution of diazotised *m*-nitroaniline, obtained by adding a concentrated solution of 14 g. of sodium nitrite to a solution of 24 g. of *m*-nitroaniline in 60 c.c. of concentrated hydrochloric acid and 180 c.c. of water. The 3′-nitrobenzene-2-naphthol-1-diazosulphonate separated immediately as a yellowish-brown precipitate in theoretical yield (calculated on the *m*-nitroaniline). This was filtered off, washed free from acid with brine, made into a paste with 600 c.c. of cold water, and a cold solution of 50 g. of anhydrous sodium carbonate in 250 c.c. of water was added. The *sodium* 1-3′-*nitrobenzeneazo*-β-*naphthaquinone*-1-*sulphonate* formed does not separate from the solution at this dilution. The cold, clear, yellowish-brown solution was added immediately to a cold solution of 60 g. of sodium hydroxide in 120 c.c. of water, the temperature rose about 10°, and the deep reddish-brown mixture was left overnight. Conversion into sodium 3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid-1-sulphonate was accompanied by little change in colour. The mixture was rendered faintly acid with hydrochloric acid, then made alkaline with sodium carbonate, and a small amount of 3′-nitrobenzeneazo-β-naphthol (Metanitraniline Orange) filtered off. The latter should not be washed with hot water, as this renders the product resinous and difficult to coagulate. The filtrate was rendered faintly acid with hydrochloric acid, and salt added cautiously until the monosodium salt of the product separated completely as a yellowish-brown, semi-crystalline precipitate.

After drying, the product was separated from sodium chloride by extraction with absolute alcohol, from which it crystallised in orange-yellow prisms (yield 55 g.; 76·3%) (Found: S, 7·7. $C_{16}H_{12}O_7N_3SNa$ requires S, 7·7%). It is readily soluble in water, but less soluble in alcohol, forming yellow solutions, which are deepened in colour by the addition of alkalis. The aqueous solution is decolorised by zinc dust and ammonia, and on exposure to air a deeper colour returns. Unlike the 4′-nitro-isomeride (J., 1926, 699), it possesses but little tinctorial power.

1-*Hydroxy*-3-(3′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic Acid.*—An aqueous solution of monosodium-3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid-1-sulphonate (32 g.) was boiled with concentrated hydrochloric acid (aqueous sulphuric acid also can be used) as described for the 4′-nitro-isomeride (*ibid.*, p. 700). The product crystallised from ethyl acetate in pale yellow, prismatic needles, m. p. 234° (yield 21·3 g.; 83·5%) (Found: C, 58·9; H, 4·0; N, 12·9. $C_{16}H_{13}O_5N_3$ requires C, 58·7; H, 4·0; N, 12·8%). The substance is readily soluble in alcohol or glacial acetic acid, but less soluble in benzene, acetone, or ether. It is sparingly soluble in water, forming a solution acid to litmus, but dissolves readily in sodium carbonate with an orange-yellow colour, or in sodium hydroxide with a deep reddish-brown colour. It dissolves in cold concentrated sulphuric acid with a yellow colour and is reprecipitated unaltered on dilution, but when boiled with aqueous sulphuric acid it is converted into 3′-nitro-3-phenylphthalaz-1-one.

Derivatives of 1-*Hydroxy*-3-(3′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic Acid.*—The *methyl* ester, prepared as described for the 4′-nitro-isomeride (*ibid.*, p. 700), crystallised from methyl alcohol in pale yellow needles, m. p. 184° (Found: C, 59·7; H, 4·5; N, 12·2. $C_{17}H_{15}O_5N_3$ requires C, 59·8; H, 4·4; N, 12·3%). The *ethyl* ester, similarly prepared, crystallised from ethyl alcohol in pale yellow needles, m. p. 195° (Found: C, 61·1; H, 5·0; N, 11·9. $C_{18}H_{17}O_5N_3$ requires C, 60·8; H, 4·8; N, 11·8%). It is insoluble in sodium carbonate, but dissolves in sodium hydroxide with a reddish-brown colour. The *anilide* was prepared as described for the 4′-nitro-isomeride and, after several crystallisations from ethyl acetate, formed transparent, yellow prisms, m. p. 239° (decomp.) (Found: C, 65·8; H, 4·8; N, 13·9. $C_{22}H_{18}O_4N_4$ requires C, 65·7; H, 4·5; N, 13·9%). It is almost insoluble in cold sodium hydroxide, whereas the 4′-nitro-isomeride is readily soluble with a red colour, and it is also hydrolysed to the original acid by boiling concentrated hydrochloric acid.

1-*Hydroxy*-3-(3′-*aminophenyl*)*tetrahydrophthalazine*-4-*acetic Acid.*—1-Hydroxy-3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid

(20 g.) was boiled under reflux with a solution of stannous chloride (80 g.) in concentrated hydrochloric acid (200 c.c.) until it had all dissolved and been replaced by the hydrochloride of 1-hydroxy-3-(3′-aminophenyl)tetrahydrophthalazine-4-acetic acid, colourless cubic crystals. After a further 10 minutes' boiling, the hydrochloride was filtered off, washed with cold concentrated hydrochloric acid, and dissolved in water; tin was removed from the solution by means of hydrogen sulphide, and the product isolated by adding sodium carbonate until a white precipitate had separated completely. After being washed with cold water, it crystallised from boiling water in almost colourless, glistening prisms, m. p. 252° (yield 15·7 g.; 86%) (Found: C, 64·4; H, 5·4; N, 14·2. $C_{16}H_{17}O_3N_3$ requires C, 64·2; H, 5·7; N, 14·0%). This compound cannot be obtained satisfactorily by reduction with alkaline hydrosulphite. It is sparingly soluble in alcohol and benzene, more soluble in water than the 4′-amino-isomeride, and, unlike the latter, gives no coloration with ferric chloride. It dissolves readily in dilute alkalis or dilute acids, and can be diazotised. Direct esterification in this case also proved unsatisfactory, but there was no difficulty in preparing a pure *acetyl* derivative, which crystallised from boiling water in colourless prisms, m. p. 167° (Found: C, 63·5; H, 5·5; N, 12·1. $C_{18}H_{19}O_4N_3$ requires C, 63·3; H, 5·6; N, 12·3%).

3′-*Amino*-3-*phenylphthalaz*-1-*one*.—A solution of 5 g. of 1-hydroxy-3-(3′-aminophenyl)tetrahydrophthalazine-4-acetic acid in a mixture of 25 c.c. of concentrated sulphuric acid and 30 c.c. of water was boiled (b. p. 140°) under reflux for 1½ hours, acetic acid being eliminated during the reaction. After cooling, the solution was diluted with 50 c.c. of water, neutralised with sodium hydroxide, then made distinctly alkaline with sodium carbonate and filtered. The base crystallised from alcohol in stout, golden-yellow, spear-shaped prisms, m. p. 210° (yield 3·6 g.; 91%) (Found: C, 71·1; H, 4·8; N, 17·8. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·7%). It is soluble in hot water, sparingly soluble in acetone, and insoluble in benzene. It is insoluble in alkalis, but soluble in dilute acids and can be diazotised; the hydrochloride formed colourless needles, and the *acetyl* derivative crystallised from boiling water in fine, colourless needles, m. p. 204° (Found: C, 68·7; H, 4·9; N, 14·8. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%).

3′-*Amino*-N-*phenylphthalimidine*.—3′-Amino-3-phenylphthalaz-1-one was reduced with zinc dust and hydrochloric acid as described for the 4′-amino-isomeride (*loc. cit.*). After cooling, the product separated completely as colourless plates of the hydrochloride, together with a small proportion of colourless needles of the *zinc* double chloride; the filtrate contained ammonia. The crystals were dissolved in a little hot water and hydrochloric acid, the solution was rendered alkaline, and the dry precipitate extracted with alcohol. The base crystallised in almost colourless prismatic needles, m. p. 175° (Found: C, 75·1; H, 5·7; N, 12·8. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·4; N, 12·5%). The *acetyl* derivative crystallised from alcohol in colourless, silky needles, m. p. 204° (Found: C, 71·9; H, 5·6; N, 10·6. $C_{16}H_{14}O_2N_2$ requires C, 72·2; H, 5·4; N, 10·5%). *N*-Phenylphthalimidine, almost colourless plates, m. p. 160°, was obtained by diazotising 3′-amino-*N*-phenylphthalimidine sulphate, and boiling the sparingly soluble diazonium sulphate (almost colourless needles) with alcohol.

3′-*Hydroxy*-N-*phenylphthalimidine*.—This compound was prepared from 3′-amino-*N*-phenylphthalimidine (10 g.) as described for the 4′-hydroxy-isomeride (*loc. cit.*, p. 704), except that, as the diazo-compound in the present case was less stable, boiling for longer than ½ hour was unnecessary. The hydroxy-derivative crystallised from alcohol in colourless glistening leaflets, m. p. 268° (yield 9·5 g.; 95%) (Found: C, 75·0; H, 5·0; N, 6·4. $C_{14}H_{11}O_2N$ requires C, 74·7; H, 4·9; N, 6·2%). Its *methyl* ether, m. p. 122° (Found: C, 75·0; H, 5·5; N, 6·0. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·4; N, 5·9%), and *ethyl* ether, m. p. 115° (Found: C, 75·7; H, 5·9; N, 5·6. $C_{16}H_{15}O_2N$ requires C, 75·9; H, 5·9; N, 5·5%), crystallised from the corresponding alcohols in colourless leaflets.

3′-*Nitro*-3-*phenylphthalaz*-1-*one*.—A solution of 5 g. of 1-hydroxy-3-(3′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid in 25 c.c. of concentrated sulphuric acid was diluted with 30 c.c. of water, and the mixture boiled (b. p. 140°) under reflux. Solution was complete after ¾ hour, and boiling was continued for a further ¾ hour, acetic acid being eliminated during the reaction. The mixture was cooled, diluted with 120 c.c. of water, boiled, and filtered. After cooling, the sulphate (colourless needles) was filtered off and neutralised with sodium carbonate. A further quantity was isolated by neutralising the filtrate. The united product was purified through the sparingly soluble hydrochloride (long, colourless needles), and, after neutralisation with sodium carbonate, crystallised from pyridine in pale yellow needles, m. p. 324° (yield 2·3 g.; 56·5%) (Found: C, 63·2; H, 3·5; N, 15·7. $C_{14}H_9O_3N_3$ requires C, 62·9; H, 3·4; H, 15·7%). The substance is readily soluble in glacial acetic acid, soluble in nitrobenzene, sparingly soluble in alcohol and ethyl acetate, and very sparingly soluble in benzene. It is insoluble in sodium carbonate, and very sparingly soluble in boiling sodium hydroxide with a faint orange colour; with mineral acids it forms salts, which are readily decomposed by water. With an alcoholic solution of picric acid it forms a *picrate*, bright yellow needles, m. p. 234°, which can be recrystallised from alcohol without decomposition (Found : C, 48·6; H, 2·6; N, 16·8. $C_{20}H_{12}O_{10}N_6$ requires C, 48·4; H, 2·4; N, 16·9%).

Reduction of 3′-*Nitro*-3-*phenylphthalaz*-1-*one*.—(*a*) Reduction of 3′-nitro-3-phenylphthalaz-1-one (5 g.) with aqueous sodium sulphide as described for the 4′-nitro-isomeride (this vol., p. 2553) gave 3′-amino-3-phenylphthalaz-1-one (yield 3·3 g.; 74%), identical with that obtained from 1-hydroxy-3-(3′-aminophenyl)tetrahydrophthalazine-4-acetic acid (p. 2560).

(*b*) Reduction with zinc dust and hydrochloric acid gave 3′-amino-*N*-phenylphthalimidine (yield 83%), identical with that obtained from 3′-amino-3-phenylphthalaz-1-one (p. 2560).

Action of Methyl Sulphate on 3′-*Nitro*-3-*phenylphthalaz*-1-*one*.—A solution of 3′-nitro-3-phenylphthalaz-1-one in nitrobenzene was treated with methyl sulphate as described for the 4′-nitro-isomeride (*loc. cit.*), and the nitrobenzene removed by distillation with steam. The aqueous residue, after being filtered from a little resin, gave an orange-yellow, flocculent precipitate when rendered alkaline with sodium carbonate. This basic substance behaves with alcohol in a similar manner to the 4′-nitro-isomeride, becoming first resinous and then crystalline. Thus, crystallisation from methyl alcohol gave golden-yellow needles, m. p. 114—117° (Found : OMe, 18·5%), and crystallisation from ethyl alcohol gave large, golden prisms, m. p. 116—120° (Found : total OR, calculated as OMe, 18·1%). No definite conclusions as to the composition of these compounds could be based on these analyses, however, because the substance has combined with the alcohols, and the products are decomposed partially even by drying in a vacuum at the air temperature, as was done for the preparation of the analytical specimens; moreover, at 100° the crystals melt, then resolidify, and are converted gradually into 4-keto-1-methoxy-3-(3′-nitrophenyl)-3 : 4-dihydrophthalazine. The latter change was best effected by heating first at 100° and then at 140°, and, unlike the case of the 4′-nitro-isomeride, in this instance there was always simultaneous formation of a certain amount of a more complex substance, red needles, m. p. 289°, especially if heating was too rapid at first.

4-*Keto*-1-*methoxy*-3-(3′-*nitrophenyl*)-3 : 4-*dihydrophthalazine* crystallised from alcohol in long, colourless, prismatic needles, m. p. 182° (Found : C, 60·8; H, 3·9; N, 14·3; OMe, 10·2. $C_{15}H_{11}O_4N_3$ requires C, 60·6; H, 3·7; N, 14·1; OMe, 10·4%); it is readily soluble in chloroform, ethyl acetate, glacial acetic acid, and toluene, and insoluble in dilute mineral acids or alkalis. When 1 g. was heated with glacial acetic acid and twice the volume of hydrobromic acid in a sealed tube at 100° for ½ hour, 1 : 4-*diketo*-3-(3′-*nitrophenyl*)-*tetrahydrophthalazine* separated on cooling, and after crystallisation from alcohol formed colourless needles, m. p. 280° (Found : C, 59·6; H, 3·3; N, 14·8. $C_{14}H_9O_4N_3$ requires C, 59·4; H, 3·2; N, 14·8%). It is insoluble in dilute mineral acids, but soluble in dilute sodium carbonate with a pale yellow colour.

3′-*Nitro*-3-*phenylphthalaz*-4-*one*.—Alcoholic solutions of *o*-phthalaldehydic acid and *m*-nitrophenylhydrazine were boiled under reflux as described for the 4′-nitro-isomeride (*loc. cit.*). After removal of about one-half of the alcohol, the *lactone* form of the phenylhydrazone separated in small, orange crystals, m. p. 240° after becoming colourless at 200° (Found : C, 58·7; H, 4·0; N, 14·6. $C_{14}H_{11}O_4N_3$ requires C, 58·9; H, 3·9; N, 14·7%). It is sparingly soluble in dilute hydrochloric acid and soluble in dilute sodium carbonate, but acidification of the alkaline solution gave 3′-nitro-3-phenylphthalaz-4-one and not the hydrazone, and the same substance was obtained in attempts to recrystallise the lactone form from alcohol or pyridine. The *phthalazone* was prepared most conveniently by boiling a nitrobenzene solution for a short time, and, after cooling, crystallised in colourless needles, m. p. 240° (Found : C, 62·8; H, 3·5; N, 16·0. $C_{14}H_9O_3N_3$ requires C, 62·9; H, 3·4; N, 15·7%). It is soluble in alcohol, insoluble in sodium carbonate or hydroxide, and very sparingly soluble in hydrochloric acid. It neither forms a picrate nor reacts with methyl sulphate.

3′-*Amino*-3-*phenylphthalaz*-4-*one*.—To a fine suspension of 3′-nitro-3-phenylphthalaz-4-one in boiling water, made alkaline with sodium hydroxide, hydrosulphite was added until a clear solution was obtained. After cooling, 3′-*amino*-3-*phenylphthalaz*-4-*one* separated, and on recrystallisation from water formed colourless needles, m. p. 156° (Found : C, 71·2; H, 4·8; N, 17·5. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·7%). It forms a hydrochloride, clusters of colourless needles, and can be diazotised.

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