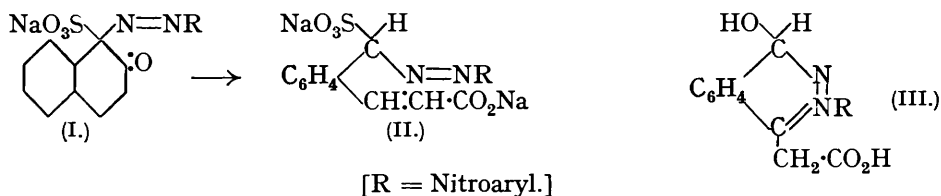


**254.** *A New Reaction of Certain Diazosulphonatēs derived from β-Naphthol-1-sulphonic Acid. Part XI. Constitution of the Phthalazine Derivatives.*

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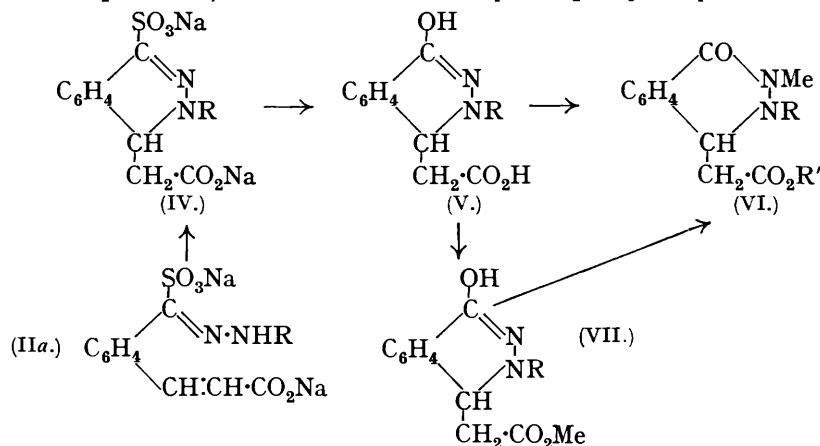
IN Part I of this series (J., 1926, 695) it was considered that diazosulphonates derived from β-naphthol-1-sulphonic acid react in aqueous sodium carbonate solution to form sodium aryl-1-azo-β-naphthaquinone-1-sulphonates (I), certain of which (with R=nitroaryl) are converted by sodium hydroxide into the carboxylic acids (II), and it was suggested that ring closure then occurred with formation of disodium 3-nitroaryl-1 : 3-dihydrophthalazine-1-sulphonate-4-acetates, which were subsequently hydrolysed to 1-hydroxy-3-nitroaryl-1 : 3-dihydrophthalazine-4-acetic acids (III).



In adopting the 1 : 3-dihydrophthalazine structure (III), we stated (*ibid.*, p. 698) that formulæ such as (IV) were not definitely excluded, but we provisionally decided in favour of (III) owing to our failure to prepare an *N*-methyl ether from it and to the results of our reduction experiments. Subsequently, however, B. Garforth and J. D. Pask (unpublished work) obtained *N*-methyl ethers (VI; R' = H) from those compounds where R = *o*-nitrophenyl and 4-chloro-*o*-nitrophenyl. Our views on the constitution of the phthalazines are therefore modified (cf. *Ann. Reports*, 1931, 28, 125), and the new structures assigned are confirmed by a repetition of the reduction experiments (see p. 1068).

The primary product of the action of sodium hydroxide on (I) may equally well be (IIa), but, in either case, ring closure occurs to give disodium 3-aryl-3 : 4-dihydrophthalazine-1-sulphonate-4-acetates (IV), which are hydrolysed to 1-hydroxy-3-aryl-3 : 4-dihydro- or 1-keto-3-aryltetrahydro-phthalazine-4-acetic acids (V, or corresponding CO·NH form). In agreement with this view, all of the compounds (V) in potassium hydroxide solution react readily with methyl sulphate to give *N*-methyl ethers (VI; R' = H), which are stable to hydrobromic acid at 180° and to hydriodic acid at 140°, and all of which form methyl esters (VI; R' = Me). On the other hand, the product of the action of methyl sulphate on the methyl esters (VII) in potassium hydroxide solution varies according to R. Where

R is *o*-nitrophenyl and 4-chloro-*o*-nitrophenyl, the sole product is (VI; R' = Me) (Garforth and Pask, unpublished), but where R is *m*- or *p*-nitrophenyl or *p*-nitrobenzeneazophenyl



[R = Nitroaryl or benzeneazophenyl.]

the sole product is (VI; R' = H), whilst where R is 4'-nitro-2'-methylphenyl, 2'-chloro- or 2':6'-dichloro(or dibromo)-4'-nitrophenyl, or benzeneazophenyl, the product is a mixture of the two compounds, the proportion depending upon the ease of hydrolysis of the ester. All of the *N*-methyl ethers (VI; R' = H) are soluble in both sodium carbonate and hydroxide, the colours of the solutions being much less deep than those of corresponding solutions of (V), but their methyl esters (VI; R' = Me) are insoluble.

There is no doubt that the reduction products of (V) are not 1-hydroxy-3-aminoaryl-tetrahydrophthalazine-4-acetic acids, as has been stated in the preceding parts of this series, but are 1-hydroxy-3-aminoaryl-3:4-dihydrophthalazine-4-acetic acids (V; R = aminoaryl). We have re-examined all the examples of this reduction and the products have been analysed by several independent workers. Moreover, the analyses by Bucherer and Fröhlich of "reduced yellow-II" (*J. pr. Chem.*, 1931, 132, 76), where R is *p*-amino-phenyl, provide further support. On this basis, the formation of nitro- and amino-3-arylphthalaz-1-ones with elimination of acetic acid by heating (V) and (V; R = aminoaryl) respectively in acid solution, followed by treatment with alkali, is strictly analogous in each case and easily explained (*J.*, 1928, 2553).

"Soluble yellow-I" and "yellow-II" (Bucherer and Fröhlich, *loc. cit.*) are (IV) and (V) respectively, where R is *p*-nitrophenyl (cf. *J.*, 1931, 1067). Those authors heated "yellow-II" with 10% hydrochloric acid in a sealed tube at 150° for 12 hours and obtained white needles, m. p. 229°, insoluble in acids and alkalis, for which they advanced the formula  $\text{C}_{15}\text{H}_{13}\text{O}_3\text{N}_3$ , implying mere decarboxylation. They obtained from "reduced yellow-II" by similar treatment a base, leaflets, m. p. 255°, for which they give no analytical data, but which they obtained also by reducing the above substance, m. p. 229°. As mere decarboxylation is contrary to any of our results with compounds in this series, we heated (V) (R = *p*-nitro- and *p*-amino-phenyl) with dilute hydrochloric acid (1:2) as described by Bucherer and Fröhlich, and obtained 4'-nitro- and 4'-amino-3-phenylphthalaz-1-one, m. p.'s 333° and 259°, respectively, as the sole products. Alteration of the conditions did not affect our result with the amino-compound, but by using weaker acid (1:7.5) at 175° for 6 hours, we obtained from the nitro-compound pale straw-coloured needles, insoluble in acids and alkalis, of variable m. p. (222—230°) after repeated crystallisation. If this is the product described by Bucherer and Fröhlich, our analyses do not agree with their empirical formula, and the product appears to be a difficultly separable mixture of 4'-nitro-3-phenyl- (*J.*, 1928, 2555) and 4'-nitro-3-phenyl-1-methyl-phthalaz-4-one (*J.*, 1931, 1923). If so, it involves the possibility of the formation of phenylphthalaz-4-ones in a new way and also of the conversion of phenylphthalaz-1-ones into the latter. We intend to investigate these points fully.

EXPERIMENTAL.

**1-Keto-3-aryl-2-methyltetrahydrophthalazine-4-acetic Acids** (VI;  $R' = H$ ).—A fine aqueous suspension of 1-hydroxy-3-aryl-3 : 4-dihydrophthalazine-4-acetic acid (3 g.; 1 mol.) (V) was treated gradually and simultaneously with (i) a solution of potassium hydroxide (10 mols.) and (ii) methyl sulphate (1.4 mols.) during 15 mins. with continuous vigorous shaking. Methylation was complete when addition of (i) gave no further characteristic coloration. The mixture was poured on ice-water, neutralised with dilute hydrochloric acid, the pale yellow precipitate collected, dissolved in sodium carbonate, and the clear alkaline solution neutralised. Better yields are obtained if methyl alcohol is used as solvent, but it tends to combine with some of the products. Methyl iodide (2 mols.) may be used instead of the sulphate.

**Esters, etc.**—A solution of (VI) in the minimum of dry methyl alcohol was saturated with dry hydrogen chloride at 0° and left over-night (heating causes resinification). A series of *N*-methyl ethers (VI;  $R' = H$ ) and their methyl esters (VI;  $R' = Me$ ) was prepared by these methods, the former being in all cases soluble in sodium carbonate and hydroxide, and the latter insoluble. The description of compounds (V) and (VI;  $R' = H$ ) in brackets refers to the colour of solutions in (a) sodium carbonate and (b) sodium hydroxide. Methylation of the methyl 1-hydroxy-3-aryl-3 : 4-dihydrophthalazine-4-acetates (VII) under standard conditions (above) gave (VI;  $R' = H$ ) or (VI;  $R' = Me$ ), or mixtures of the two, according to the particular compound employed.

1-Hydroxy-3-(4'-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid (V) crystallised from ethyl acetate in yellow prisms, m. p. 241° [(a), (b), deep wine-red]; its methyl ester (VII) crystallised from methyl alcohol in large yellow prisms, m. p. 166° (not 153° as previously given; J., 1926, 700).

1-Keto-3-(4'-nitrophenyl)-2-methyltetrahydrophthalazine-4-acetic acid crystallised from methyl alcohol in pale yellow prismatic needles, m. p. 207°, containing solvent which was difficult to remove (Found, in material dried in a vacuum : C, 57.9, H, 5.0; dried at 130° : C, 58.0, 58.1; H, 4.8, 4.95.  $C_{17}H_{15}O_5N_3 \cdot CH_3 \cdot OH$  requires C, 57.9; H, 5.1%), or from glacial acetic acid in pale yellow prisms, m. p. 207° (yield, 2.7 g.; 86%), difficult to analyse satisfactorily (Found, in material dried at 130° : C, 59.5; H, 5.0; N, 12.2.  $C_{17}H_{15}O_5N_3$  requires C, 60.0; H, 4.4; N, 12.3%) [(a) orange-brown, (b) deep orange-brown]. It was unchanged after heating with hydrobromic acid (*d* 1.7) in a sealed tube at 180° for 40 mins. or with hydriodic acid (*d* 1.7) at 140° for 1 hour under Zeisel's conditions. The methyl ester (VI;  $R' = Me$ ) crystallised from methyl alcohol, ethyl acetate, or glacial acetic acid in pale yellow prisms, m. p. 188° (Found, in material from ethyl acetate dried at 125° : N, 12.1.  $C_{18}H_{17}O_5N_3$  requires N, 11.85%). Methylation of (VII) gave solely (VI;  $R' = H$ ).

$R = 3'$ -Nitrophenyl (V) [(a) orange-yellow, (b) deep reddish-brown] (J., 1928, 2559). The corresponding methyl keto-acid (VI;  $R' = H$ ) crystallised from methyl alcohol in pale yellow needles, or from acetic acid or ethyl acetate in pale yellow prisms, m. p. 235° (yield, 2.7 g.; 86%) (Found, in material from ethyl acetate dried at 140° : C, 59.6, 60.0; H, 4.8, 4.7; N, 12.25.  $C_{17}H_{15}O_5N_3$  requires C, 60.0; H, 4.4; N, 12.3%) [(a), (b), yellow]. The methyl ester (VI;  $R' = Me$ ) crystallised from dilute acetic acid or ethyl acetate in pale yellow prisms, m. p. 180° (Found : N, 12.05.  $C_{18}H_{17}O_5N_3$  requires N, 11.85%). Methylation of (VII) gave solely the acid (VI).

$R = 4'$ -Nitro-2'-methylphenyl (V) [(a), (b) deep red] (J., 1932, 477). The derived acid of type (VI) crystallised from acetic acid or ethyl acetate in straw-coloured prisms, m. p. 211° (yield, 2.9 g.; 93%) (Found, in material dried at 120° : C, 60.7; H, 5.2; N, 12.05.  $C_{18}H_{17}O_5N_3$  requires C, 60.8; H, 4.8; N, 11.8%) [(a) yellow, (b) orange-brown]. The methyl ester crystallised from ethyl acetate in straw-coloured prisms, m. p. 201° (Found : C, 61.8; H, 5.3; N, 11.75.  $C_{19}H_{19}O_5N_3$  requires C, 61.8; H, 5.15; N, 11.4%). Methylation of (VII) gave the ester (VI;  $R' = Me$ ) and a little of the acid.

$R = 2'$ -Chloro-4'-nitrophenyl [(a), (b), deep orange-red] (J., 1932, 14). The corresponding methylated acid (VI;  $R' = H$ ) crystallised from acetic acid in straw-coloured glistening prisms, m. p. 218° (yield, 2.7 g.; 87%) (Found : C, 54.6; H, 4.0; Cl, 9.3.  $C_{17}H_{14}O_5N_3Cl$  requires C, 54.3; H, 3.7; Cl, 9.45%) [(a) yellow, (b) brownish-yellow]. The methyl ester crystallised from ethyl acetate in pale yellow glistening prisms, m. p. 210—211° (Found : C, 55.7; H, 4.3; Cl, 9.0.  $C_{18}H_{16}O_5N_3Cl$  requires C, 55.5; H, 4.1; Cl, 9.0%). Methylation of (VII) gave rather more ester than acid.

$R = 2' : 6'$ -Dichloro-4'-nitrophenyl [(a), (b), deep red] (J., 1931, 1079). The acid (VI;  $R' = H$ ) crystallised from acetic acid in straw-coloured prisms, m. p. 216° (yield, 2.6 g.; 84%) (Found : C, 50.3, 50.2; H, 3.2, 3.2; Cl, 17.1, 17.2.  $C_{17}H_{13}O_5N_3Cl_2$  requires C, 49.8; H, 3.2;

Cl, 17.3%) [(a) yellow, (b) orange-yellow]. The *methyl* ester, large pale yellow prisms from ethyl acetate, m. p. 186° (Found: Cl, 16.55.  $C_{18}H_{15}O_5N_3Cl_2$  requires Cl, 16.75%), is much more stable to alcoholic potassium hydroxide than the corresponding derivatives from *p*- and *m*-nitroaniline, which are hydrolysed readily to the *N*-methyl compounds. Methylation of (VII) gave the ester and a trace of acid.

R = 2': 6'-Dibromo-4'-nitrophenyl [(a), (b), brownish-red] (J., 1931, 1079). The *acid* (VI; R' = H) crystallised from acetic acid in pale yellow, transparent, rectangular prisms, m. p. 240°, containing 1 mol. of acetic acid removed at 140°, the crystals becoming opaque (yield, 2.7 g.; 87.5%) (Found, in material dried at 140°: C, 41.1; H, 2.9; N, 8.3; Br, 32.3.  $C_{17}H_{13}O_5N_3Br_2$  requires C, 40.9; H, 2.6; N, 8.4; Br, 32.1%) [(a), (b), orange]. The *methyl* ester crystallised from acetic acid in pale yellow prisms, m. p. 215° (Found: Br, 31.4.  $C_{18}H_{15}O_5N_3Br_2$  requires Br, 31.2%). Methylation of (VII) gave mainly (VI; R' = Me) with some acid (VI), the amount of the latter being greater than with the corresponding dichloro-compound, but less than with the 2'-chloro-4'-nitrophenyl derivative.

R = Benzeneazophenyl (V) [(a) orange-brown, (b) deep red] (J., 1932, 1122). 1-Keto-3-(benzeneazophenyl)-2-methyltetrahydrophthalazine-4-acetic acid crystallised with difficulty from a small amount of dry ethyl acetate in yellow prisms, m. p. 189° (yield, 2.3 g.; 74%) (Found: C, 69.25; H, 5.3; N, 13.8.  $C_{23}H_{20}O_3N_4$  requires C, 69.0; H, 5.0; N, 14.0%) [(a) yellow, (b) deep orange], soluble in concentrated hydrochloric acid with a deep magenta-red colour, but reprecipitated on dilution. The methyl ester (impure) was obtained as a pale yellow amorphous solid (methyl alcohol), insoluble in alkalis, decomposing at 105°. Methylation of (VII) gave almost wholly the acid (VI).

R = *p*-Nitrobenzeneazophenyl (V) [(a) brownish-red, (b) deep blue] (*ibid.*, p. 1124). The methyl ester (VII) crystallised from dilute acetic acid with difficulty and in small yield in red prisms, m. p. 105–109°, insoluble in sodium carbonate, but soluble in sodium hydroxide with a bluish-violet colour, becoming deep blue on warming owing to hydrolysis.

1-Keto-3-(4'-nitrobenzeneazophenyl)-2-methyltetrahydrophthalazine-4-acetic acid crystallised from acetic acid in brownish-red prisms, m. p. 246° (yield, 2.4 g.; 77%) (Found: C, 61.8; H, 4.5; N, 15.35.  $C_{23}H_{19}O_5N_5$  requires C, 62.0; H, 4.3; N, 15.7%), soluble in concentrated hydrochloric acid with a magenta colour [(a) brownish-yellow, (b) brown to olive-brown, the latter colour being particularly evident in alcoholic solution and indicating the completion of methylation in comparison with the blue colour of the unmethylated compound]. The methyl ester, obtained with difficulty and in minute yield, separated from dilute acetic acid on long standing as reddish-brown irregular prisms, becoming amorphous and insoluble in alkalis. Methylation of (VII) gave solely the acid (VI).

1-Hydroxy-3-aminoaryl-3:4-dihydrophthalazine-4-acetic Acids (V).—R = 4'-Aminophenyl (J., 1926, 702). The analytical specimen was not recrystallised, but was obtained pure in colourless prisms, m. p. 239°, by addition of hydrochloric acid to a hot solution in sodium carbonate (Found: C, 64.6, 64.55, 64.7; H, 5.05, 5.05, 5.1; N, 14.2.  $C_{16}H_{15}O_3N_3$  requires C, 64.65; H, 5.05; N, 14.1%).

R = 3'-Aminophenyl (J., 1928, 2560). The *acid* was purified similarly; colourless prisms, m. p. 252° (Found: C, 64.7; H, 5.05; N, 14.2.  $C_{16}H_{15}O_3N_3$  requires C, 64.65; H, 5.05; N, 14.1%).

R = 4'-Amino-2'-methylphenyl (J., 1932, 477). When purified similarly, the *acid* formed colourless prisms, m. p. 217° (Found: C, 65.4; H, 5.7; N, 13.6.  $C_{17}H_{17}O_3N_3$  requires C, 65.6; H, 5.5; N, 13.5%).

The compounds with R = 2': 6'-dichloro(or dibromo)- and 2'-chloro-4'-aminophenyl also undoubtedly possess the constitution (V) (cf. analytical data, J., 1931, 1081; 1932, 15).