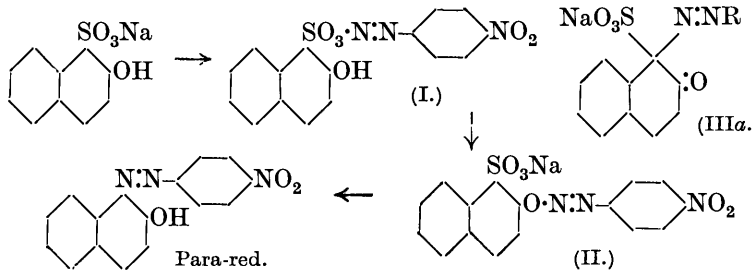
XCVI.—*A New Reaction of Certain Diazosulphonates derived from β-Naphthol-1-sulphonic Acid. Part I. Preparation of Phthalazine, Phthalazone, and Phthalimidine Derivatives from 4′-Nitrobenzene-2-naphthol-1-diazosulphonate.*

By Frederick Maurice Rowe, Esther Levin, Alan Chamley Burns, John Stanley Herbert Davies, and Wolfe Tepper.

Some β-naphtholsulphonic acids condense with diazo-compounds in acid solution to form stable diazosulphonates; thus, β-naphthol-1-sulphonic acid or oxy-Tobias acid (Bayer & Co., Brit. Pat. 11757 of 1895) gives diazosulphonates which Grant Hepburn (Brit. Pat. 116360) found to possess interesting properties. For example, Para-red is obtained in substance quantitatively by dissolving one molecular proportion of 4′-nitrobenzene-2-naphthol-1-diazosulphonate in an aqueous solution of sodium carbonate or of one molecular proportion of sodium hydroxide, and then acidifying the cold solution. Diazosulphonates derived from β-naphthol-1-sulphonic acid appear to be the only examples in which the stabilising component can provide subsequently an azo-coupling component. Bucherer (*Ber.*, 1909, **42**, 47; "Lehrbuch der Farbenchemie," 1914, 125), without giving experimental details, explains this reaction thus :



Wahl and Lantz (*Bull. Soc. chim.*, 1923, **33**, 97) have re-examined the above reaction and agree with Bucherer's conclusion that compound (II) is a diazo-oxide, but were unable to isolate an analogous compound from 1-bromo-(or chloro)-β-naphthol, although the latter reacts with diazotised *p*-nitroaniline to form Para-red as shown by Hewitt and Mitchell (J., 1906, **89**, 1169).

As Wahl and Lantz state that they propose to study the diazo-oxides which can be prepared from β-naphthol-1-sulphonic acid and other diazo-compounds, we must mention here that we began our present investigation in 1918 with an examination of these compounds. Diazosulphonates derived from β-naphthol-1-sulphonic acid are stable, whereas the compounds formed from them by the action of one molecular proportion of alkali are unstable and particularly sensitive to acids. If the latter are diazo-oxides, it is not clear why they should be more reactive and unstable than diazosulphonates, and, in view of our other results, we suggest that they are sodium aryl-1-azo-β-naphthaquinone-1-sulphonates of the general formula (III*a*). Compounds of this type would be hydrolysed readily by cold dilute acid, forming azo-β-naphthol derivatives. It might be anticipated that such compounds would give different reduction products from those obtained from corresponding diazo-oxides, but they are so unstable that the reduction products more probably would be derived from the corresponding azo-β-naphthol derivative, owing to the preliminary elimination of the sulphonic group. In support of this, we find that even the more stable diazosulphonates give 1-amino-2-naphthol on reduction.

Grant Hepburn (*loc. cit.*) observed that although Para-red is obtained by acidifying a solution of 4′-nitrobenzene-2-naphthol-1-diazosulphonate in one molecular proportion of aqueous sodium hydroxide, this is not the case if an excess of sodium hydroxide is used, and he handed over the investigation of this interesting reaction to one of us (F. M. R.).

When the orange solution of 4′-nitrobenzene-2-naphthol-1-diazosulphonate in aqueous sodium carbonate is added to an excess of cold aqueous sodium hydroxide, or vice versa, the temperature

rises and a crimson colour is developed immediately, which changes slowly to orange-brown, or more rapidly when warmed on the water-bath. There is no evolution of nitrogen, and no formation of sodium β-naphthol-1-sulphonate or sodium *p*-nitrophenylnitrosoamine. Subsequent acidification gives traces only of Para-red, and, consequently, a reaction has occurred in which the whole of the diazosulphonate has taken part. No organic by-products can be detected and a homogeneous yellow compound can now be isolated in excellent yield.

In order to test the generality of this reaction, various diazosulphonates were prepared, using other diazo-compounds in place of diazotised *p*-nitroaniline. Each diazosulphonate was converted by sodium carbonate into a sodium aryl-1-azo-β-naphthaquinone-1-sulphonate, many of which were isolated in a well-crystalline condition, and all of which were converted quantitatively into the corresponding azo-derivative of β-naphthol, with elimination of the sulphonic group, by the action of cold dilute acid. On the other hand, only certain diazosulphonates give rise to the new reaction with sodium hydroxide. For example, the compounds from aniline, *o*- and *p*-toluidine, 2 : 5-dichloroaniline, tribromoaniline, sulphanilic acid, *p*-aminoacetanilide, anthranilic acid, *p*-aminobenzonitrile, α- and β-naphthylamine, and benzidine are decomposed by sodium hydroxide with formation of sodium β-naphthol-1-sulphonate and evolution of nitrogen or formation of the nitrosoamine, although the reaction was examined under a variety of conditions. On the other hand, the compounds, for example, from *o*- and *m*-nitroaniline, 2 : 4-dinitroaniline, 4-nitroaniline-2-sulphonic acid, 4-chloro-2-nitroaniline, 4-nitro-2-chloroaniline, 2 : 6-dibromo-4-nitroaniline, and 3-nitro-4-aminotoluene give rise to the new reaction with sodium hydroxide, accompanied usually by the development of a transient intense colour, and new compounds are formed with properties similar to those of the compound derived from *p*-nitroaniline. In fact, the only compounds which have yet been found to give rise to the new reaction, and which do not contain a nitro-group, are aminoazo-compounds, such as 4-aminoazobenzene and its sulphonic acid. The suitability of a diazo-compound for participation in the new reaction depends mainly on the formation of a condensation product with β-naphthol-1-sulphonic acid, sufficiently stable to react further with sodium hydroxide without decomposition.

The possibility of using other compounds in place of β-naphthol-1-sulphonic acid was examined next. Diazotised *p*-nitroaniline condenses with β-naphthylamine-1-sulphonic acid, but the product does not react in the new way, nor is there any evidence of the

occurrence of the new reaction with β-naphthol-8-sulphonic acid or phenol-*o*-sulphonic acid. Naphthalene-α-sulphonic acid condenses with diazotised *p*-nitroaniline (Becker, D.R.-P. 89998) and the diazosulphonate dissolves in aqueous sodium carbonate, but the addition of sodium hydroxide to the solution causes decomposition with formation of sodium naphthalene-α-sulphonate and sodium *p*-nitrophenylnitrosoamine. Consequently, the presence of a hydroxyl group in the *o*-position with respect to the sulphonic group in the naphthalene nucleus is an essential feature of the new reaction. 1-Methyl-β-naphthol condenses with diazotised *p*-nitroaniline and its *o*-sulphonic acid, probably with formation of diazo-oxides, but these also are decomposed by sodium hydroxide. Finally, there was no evidence of the occurrence of the new reaction when diazotised *p*-nitroaniline and 1-bromo-β-naphthol were used, for the halogen atom in the latter compound is so labile that Para-red is produced under all conditions. Consequently, β-naphthol-1-sulphonic acid stands alone in giving rise to the new reaction.

From this point our attention has been confined to a detailed study of the compound formed by the action of an excess of sodium hydroxide on a solution of 4′-nitrobenzene-2-naphthol-1-diazosulphonate in aqueous sodium carbonate.

This compound has the formula $C_{16}H_{12}O_7N_3SNa$ and is the sodium salt of a sulphonic acid. Aqueous solutions are decolorised by zinc dust and ammonia, and are reoxidised to a deeper colour, indicating, *inter alia*, that a nitro-group has been reduced to an amino-group. Reduction proceeds further with hydrosulphite [hyposulphite] or acid stannous chloride, and, although concordant results were obtained with difficulty in titrations with titanous chloride or sulphate, the figures indicated that 8 atoms of hydrogen were required for complete reduction as compared with 6 for the mere reduction of a nitro- to an amino-group. When an aqueous solution of the compound $C_{16}H_{12}O_7N_3SNa$ is boiled with aqueous mineral acid, the sulphur is eliminated as sulphur dioxide, thus :

$$R{\cdot}SO_3H + H_2O = R{\cdot}OH + SO_2 + H_2O.$$

This behaviour is not confined to this compound, but is a common property of all the analogous compounds which we have yet prepared, and gave the first clue to the actual mechanism of the new reaction, for although the sulphonic group in β-naphthol-1-sulphonic acid is hydrolysed by similar treatment, β-naphthol is formed and not 1 : 2-dihydroxynaphthalene. The hydroxy-derivative has the formula $C_{16}H_{13}O_5N_3$ and with alkaline hydrosulphite a compound $C_{16}H_{17}O_3N_3$ is formed as the sole reduction product, *i.e.*, not only

has a nitro-group been reduced to an amino-group, but an additional two hydrogen atoms have been introduced. Reduction with acid stannous chloride, alone or in presence of granulated tin, however, gave varying results according to the duration and temperature of the reaction, and two further compounds were obtained. Closer investigation showed that whether alkaline hydrosulphite or acid stannous chloride is used, the initial reduction product is the compound $C_{16}H_{17}O_3N_3$. The latter, however, reacts with boiling hydrochloric acid, forming the compound $C_{14}H_{11}ON_3$, which is capable of undergoing further change with acid-reducing agents, forming the compound $C_{14}H_{12}ON_2$. Thus, although several derivatives and degradation products were obtained, we failed to bring about fission into two aromatic products by these reactions.

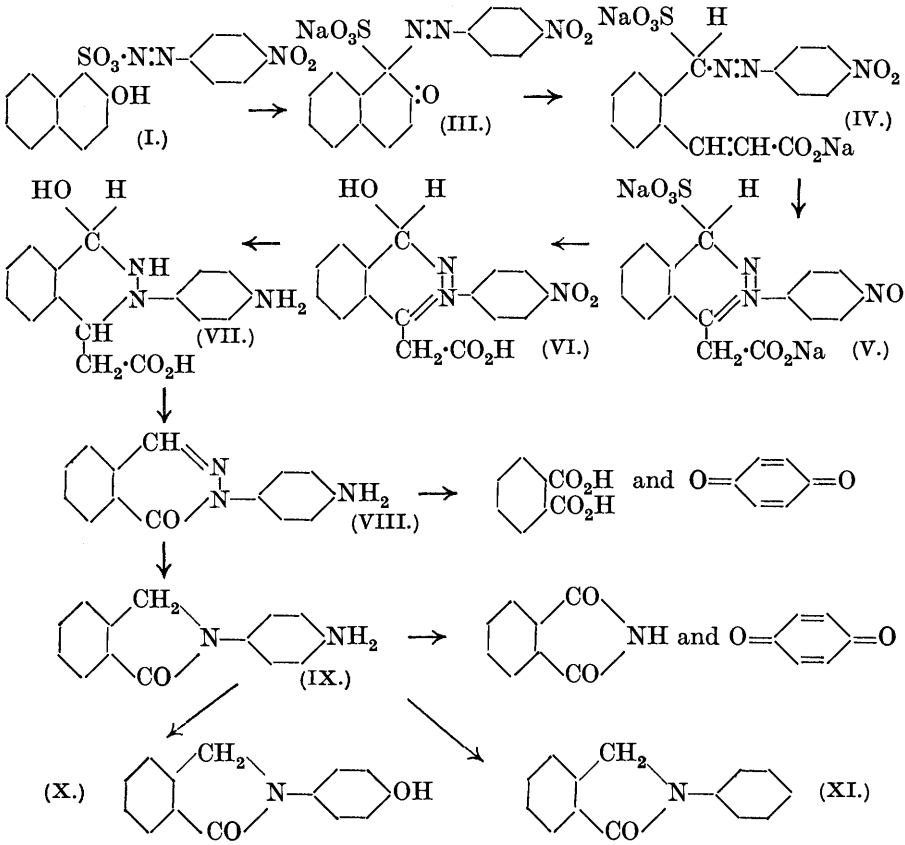
We wish to acknowledge here our great indebtedness to Professor Arthur Lapworth, F.R.S., and to Professor Robert Robinson, F.R.S., who first propounded the explanation of the mechanism of the new reaction upon which our constitutional formulæ are based, and to whom our warmest thanks are due for their interest in this investigation.

The course of the reaction in the case of 4′-nitrobenzene-2-naphthol-1-diazosulphonate (I) is outlined in the scheme on p. 695.

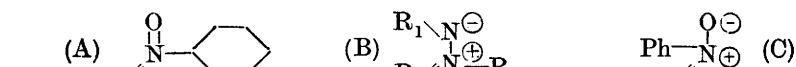
Reference has been made already to the compounds formed by the action of aqueous sodium carbonate on diazosulphonates derived from β-naphthol-1-sulphonic acid, and regarded hitherto as diazo-oxides. It would not be anticipated that diazo-oxides would react with alkali hydroxides in the manner outlined on p. 695, and it is upon the occurrence of this new reaction and the properties of the compounds to which it leads, that our opinion is based that the former compounds are really *sodium aryl-1-azo-β-naphthaquinone-1-sulphonates*. It is considered that sodium hydroxide opens the ring * of *sodium 4′-nitrobenzene-1-azo-β-naphthaquinone-1-sulphonate* (III) with addition of sodium hydroxide, forming the intermediate carboxylic acid (IV), which is not isolated, and a quinonoid modification of which would account for the transient intense coloration. The next step is a rearrangement and closing of the ring which we believe occurs as shown in (V) with formation of *disodium 3-(4′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetate-1-sulphonate*, and when the mixture is rendered faintly acid, the *monosodium* salt separates. The replacement of the sodium-1-sulphon-

* The opening of the naphthalene ring forming a carboxylic acid has also been effected by Werner and Piguet (*Ber.*, 1904, **37**, 4310), who prepared *o*-cyanocinnamic acid by the very vigorous reaction which occurs when a pyridine solution of 1-nitroso-β-naphthol is treated with benzenesulphonyl chloride or sulphuryl chloride.

ate group by hydroxyl gives 1-*hydroxy*-3-(4′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic acid* (VI). Formula (VI) is in agreement with the behaviour of this compound on reduction, whereby 1-*hydroxy*-3-(4′-*aminophenyl*)-*tetrahydrophthalazine*-4-*acetic acid* (VII) is formed.



N.B.—Formulæ (V) and (VI) above correspond with the familiar formula for nitrobenzene (A), but the formulæ may be expressed equally well as containing the semi-polar bond (B), corresponding with the form (C) for nitrobenzene.



Attempts to degrade compound (VI) by oxidation with acid dichromate were unsuccessful and gave an apparently more com-

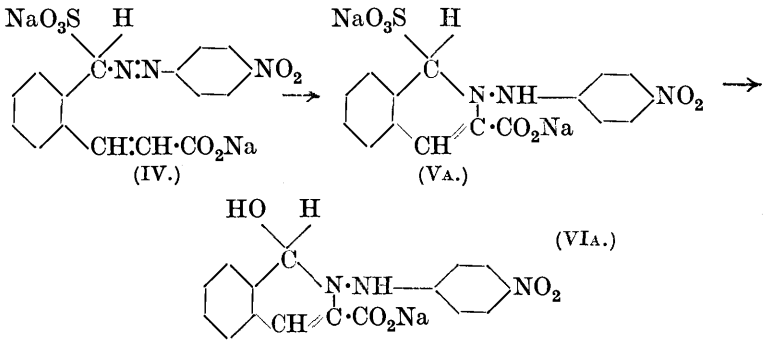
plex compound, which has been set aside for future investigation, as has also a compound formed by boiling with aqueous sulphuric acid.

The oxidation of compound (VII) with acid dichromate proceeded satisfactorily only if limited, and the compound formed has also been set aside for future investigation.

When compound (VII) is boiled with aqueous mineral acid, it is converted into 4′-*amino*-3-*phenylphthalaz*-4-*one* (VIII), the latter constitution being supported by the fact that oxidation with hot acid dichromate gives phthalic acid and benzoquinone.

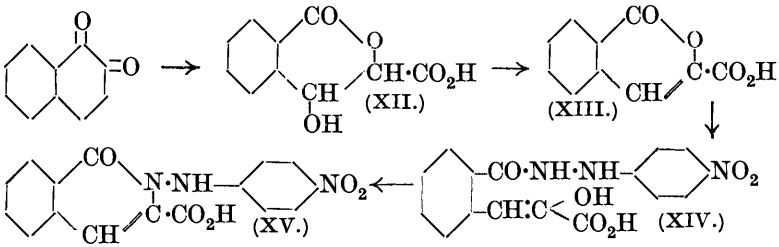
When compound (VIII) is reduced with zinc dust and hydrochloric acid, one nitrogen atom is eliminated as ammonia and 4′-*amino*-N-*phenylphthalimidine* (IX) is produced. Thus, this reaction is similar to that observed by Racine (*Annalen*, 1887, **239**, 78) in the preparation of *N*-phenylphthalimidine (XI) from 3-phenylphthalaz-4-one by reduction with tin and hydrochloric acid. The constitution of compound (IX) was confirmed by the preparation from it of *N*-phenylphthalimidine (XI), and also by oxidation with cold acid dichromate, when phthalimide and benzoquinone were obtained. The fact that phthalimide was obtained in this case suggests that it was also the primary oxidation product of compound (VIII), but that hydrolysis then occurred at the temperature necessary for satisfactory oxidation in the latter case.

At an early stage in our investigation it appeared possible that the rearrangement and closing of the ring in passing from compound (IV) might occur with the formation of *N*-arylimino-derivatives of *iso*quinoline thus :



In order to determine which of the two schemes for the final stage in the reaction is correct, the compound (VI) or (VIA) was studied closely. It might be argued that a compound such as (VIA) would give *p*-phenylenediamine as one of its reduction products, whereas we failed to obtain any trace of *p*-phenylenediamine by the reduc-

tion of this compound. As the literature appeared to contain no reference to *N*-arylimino-derivatives of *iso*quinoline, for purposes of comparison with compound (VI) or (VIA), a related compound undoubtedly of the type of the latter was synthesised thus :



β-Naphthaquinone was oxidised by calcium hypochlorite (Zincke and Scharfenberg, *Ber.*, 1892, **25**, 399; compare Zincke, *ibid.*, 1168, 1493; Bamberger and Kitschelt, *ibid.*, 888) to the δ-lactone of *o*-carboxyphenylglyceric acid (XII), and this was converted into *iso*coumarin-3-carboxylic acid (XIII) by heating with hydrochloric acid at 160—165°. It was anticipated that the latter would condense with *p*-nitrophenylhydrazine in alcoholic solution with elimination of water, forming N-4′-*nitrophenyliminoisocarbostyril*-3-*carboxylic acid* (XV), as Bamberger and Frew (*Ber.*, 1894, **27**, 198) prepared *N*-phenyl*iso*carbostyril-3-carboxylic acid in this way, using aniline. Actually, this condensation gave in our case the *hydrazide* (XIV), and the final stage of the synthesis was completed only by boiling a suspension of the latter in toluene in presence of phosphorus trichloride.

Compound (VI) or (VIA) dissolves in alkalis with a deep wine-red colour, and is reduced by hydrosulphite to compound (VII) in almost theoretical yield. Compound (XV) dissolves in alkalis with a deep red colour, but when reduced with hydrosulphite under exactly the same conditions, although no *p*-phenylenediamine could be detected and the sole reduction product was an *amino-acid*, the yield of the latter was much inferior to that obtained in the former case. This is probably due to the fact that compound (XV) is much more sensitive to alkalis than compound (VI) or (VIA). Other noteworthy differences between the properties of the two compounds were observed. Thus, whereas compound (VI) or (VIA) is esterified readily by passing hydrogen chloride through a solution in the requisite alcohol, or by means of the alcohol and sulphuric acid, or by the action of alkyl halides on the silver salt, we failed to esterify the carboxyl group in compound (XV). Further, compound (VI) or (VIA) forms an *anilide* when boiled with aniline in toluene solution in presence of phosphorus trichloride, but

compound (XV) is unaffected by this treatment. These differences in the properties of the two carboxylic acids are probably due to the proximity of the imino- and carboxyl-groups in compound (XV), and indicate the improbability of formula (VIA), particularly as we failed to prepare a nitroso-derivative of the compound, or to detect an imino-group in it by alkylation. In order to arrive at a definite conclusion on this point, the behaviour of compound (VI) or (VIA), when heated with an excess of zinc dust, was examined next, as Bamberger and Frew (*loc. cit.*) found that *N*-phenyl*iso*carbostyril-3-carboxylic acid gives *iso*quinoline when treated in this manner. In our case, however, we failed to obtain any trace of *iso*quinoline, a fact which appeared definitely to exclude formula (VIA). This is supported also by the fact that one of our later degradation products (VIII) undoubtedly contains two nitrogen atoms in the ring, and it is difficult to conceive how such a compound could be formed from an *iso*quinoline derivative. Further support of formula (VI) is afforded by the fact that when this compound is heated carefully above its melting point, nitrobenzene is formed, together with a basic residue which has not yet been examined closely; this behaviour is analogous to that of *p*-nitroazoxybenzene, which also gives nitrobenzene and a basic residue under similar conditions.

Consequently, formulæ (VA) and (VIA) have been discarded and it appears that formulæ (V) and (VI) are correct, although the possibility of tautomeric forms of these, such, for example, as (VIB), $C_6H_4<\begin{matrix}C(OH):N\\ |\\ CH\text{—}N\cdot C_6H_4\cdot NO_2\\ |\\ CH_2\cdot CO_2H\end{matrix}$, must not be overlooked. This is virtually an *iso*amide of a carboxylic acid, however, and it is improbable that such a compound would be reduced by alkaline hydrosulphite in the manner shown in (VII).

In the present state of our investigation, formulæ (V) and (VI) appear the most probable and agree best with the formulæ assigned to their derivatives and degradation products which we have yet prepared, although it is possible that the former may require slight modification in the light of future work. The closing of the ring which occurs in passing from (IV) to (V) is a condensation of a type closely allied to the condensation of nitrosobenzene and ethyl methylenemalonate recently described by Burkhardt and Lapworth (**J.** 1925, **127**, 1749).

Noteworthy features of the new reaction described in this communication are the simplicity and neatness with which certain naphthalene derivatives are converted into complex phthalazine derivatives. The latter by simple means are capable of almost

quantitative conversion into many other interesting compounds, which are now rendered readily accessible for further study.

Further work on this subject is in progress and the investigation will be extended in the various directions indicated.

EXPERIMENTAL.

Monosodium 3-(4′-Nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid-1-sulphonate (compare V).—A filtered solution of 48 g. of commercial sodium β-naphthol-1-sulphonate in 220 c.c. of water was stirred into a cold solution of diazotised *p*-nitroaniline, obtained by adding a concentrated solution of 14 g. of sodium nitrite to a solution of 24 g. of *p*-nitroaniline in 60 c.c. of concentrated hydrochloric acid and 240 c.c. of water. The 4′-nitrobenzene-2-naphthol-1-diazosulphonate (I) separated immediately as an orange precipitate in theoretical yield (calculated on the *p*-nitroaniline). This was filtered, washed free from acid with brine, made into a paste with 150 c.c. of cold water, and stirred into a cold solution of 48 g. of anhydrous sodium carbonate in 120 c.c. of water. A solution was produced but, if kept, crystals of *sodium 4′-nitrobenzene-1-azo-β-naphthaquinone-1-sulphonate* (III) separated. The cold orange solution was added immediately to a cold solution of 40 g. of sodium hydroxide in 80 c.c. of water, the temperature rose about 15°, and the deep crimson mixture was left overnight until the colour had changed completely to yellowish-brown. It was rendered faintly acid with hydrochloric acid, then made alkaline with sodium carbonate, and a trace of Para-red filtered off. The filtrate was rendered faintly acid with hydrochloric acid and, under these conditions, the product separated completely as a yellow, semi-crystalline precipitate. (N.B.—Many experiments were carried out to determine the best conditions for the preparation of this compound, and although the yield was not affected materially, variations of temperature, excess of sodium hydroxide, and duration of the reaction, gave a resinous product which coagulated slowly.) After drying, sodium chloride was removed by extraction with absolute alcohol, from which solvent the product crystallised in orange, prismatic needles (yield 66 g.; 91·5% of the theoretical) (Found : C, 46·3; H, 2·9; N, 10·4; S, 7·5; Na, 5·2. $C_{16}H_{12}O_7N_3SNa$ requires C, 46·5; H, 2·9; N, 10·2; S, 7·7; Na, 5·5%). It is readily soluble in water, but less soluble in alcohol, forming yellow solutions, which are deepened by the addition of alkalis. The aqueous solution is decolorised by zinc dust and ammonia, and on exposure to air a deeper colour returns. It is a level-dyeing, pure greenish-yellow acid dye of good tinctorial power and of good fastness to other influences, but fugitive to light, even when dyed

in admixture with a fast blue. When heated with concentrated nitric acid at 105° in a sealed tube for 8 hours, decomposition occurs and picric acid was isolated in yellow needles, m. p. 122°.

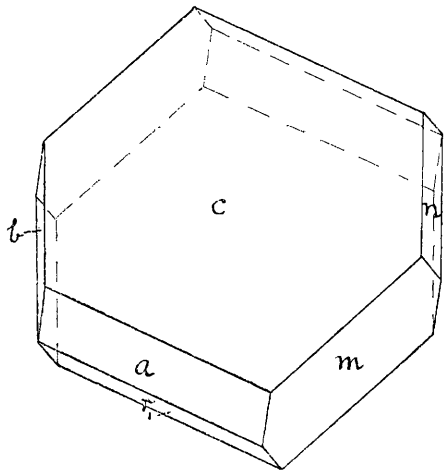
1-*Hydroxy*-3-(4′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic Acid* (VI).—A solution of 32 g. of monosodium 3-(4′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid 1-sulphonate in 120 c.c. of water was boiled with 64 c.c. of concentrated hydrochloric acid (aqueous sulphuric acid also can be used) until evolution of sulphur dioxide had ceased, and the product, which separated first as an oil, had formed yellowish-brown crystals. The latter were washed with boiling water and crystallised from ethyl acetate in pale yellow, vitreous, irregular prisms, m. p. 241° (yield 24 g.; 94%). Sulphur dioxide evolved during the reaction was determined quantitatively in the usual manner and was equivalent to one molecular proportion (Found : C, 58·9; H, 4·2; N, 12·8. $C_{16}H_{13}O_5N_3$ requires C, 58·7; H, 4·0; N, 12·8%). When the substance was heated carefully above its melting point, nitrobenzene (confirmed by conversion into aniline) was obtained, together with a basic residue which has not yet been examined closely. This behaviour is analogous to that of *p*-nitroazoxybenzene, which also gives nitrobenzene under similar conditions. The substance is readily soluble in alcohol, acetone, or glacial acetic acid, but less soluble in benzene or ether. It is sparingly soluble in water, forming a solution acid to litmus, but dissolves readily in sodium carbonate or hydroxide with a deep wine-red colour, and prolonged boiling of the alkaline solution causes decomposition. It forms a reddish-brown *silver* salt and a yellowish-brown *barium* salt, and decolorises bromine water. It dissolves in cold concentrated sulphuric acid with an orange colour and is reprecipitated unaltered on dilution, but when 5 g. were dissolved in 50 c.c. of sulphuric acid, then diluted with 60 c.c. of water, and the solution boiled under reflux for 1 hour, there was no precipitate on further dilution. A substance (4 g.) was isolated and crystallised from alcohol in fine yellow needles, m. p. 331°, but this has not yet been examined closely.

Derivatives of 1-*Hydroxy*-3-(4′-*nitrophenyl*)-1 : 3-*dihydrophthalazine*-4-*acetic Acid.*—*Methyl ester.* A solution of 5 g. in 50 c.c. of dry methyl alcohol was saturated with dry hydrogen chloride at 0°, left over-night, and then boiled under reflux for 2 hours. The *ester* crystallised from methyl alcohol in yellow prisms, m. p. 153° (Found : C, 59·8; H, 4·6; N, 12·5. $C_{17}H_{15}O_5N_3$ requires C, 59·8; H, 4·4; N, 12·3%). *Ethyl ester.* (*a*) A solution of 3 g. in 30 c.c. of dry ethyl alcohol was boiled with 1·5 g. of concentrated sulphuric acid under reflux for 4 hours. (*b*) The dry, reddish-brown, amorph-

ous silver salt, precipitated by the addition of silver nitrate to a neutral solution of 5 g. in sodium hydroxide, was boiled with 2 g. of ethyl iodide and 50 c.c. of dry ethyl alcohol under reflux for 1 hour. (*c*) As described above for the methyl ester, except that 60 c.c. of dry ethyl alcohol were used. The three products were identical in all respects and crystallised from ethyl alcohol in yellow crystals, tabular in character and with hexagonal outline; m. p. 180°. We have been furnished with the following crystallographic description of the substance by Mr. H. E. Buckley of the Department of Crystallography, University of Manchester, to whom we express our grateful thanks :

" The symmetry is anorthic (triclinic) pinacoidal, with $a : b : c = 1{\cdot}387 : 1 : 0{\cdot}626$ and $\alpha = 78° 15'$, $\beta = 40° 10'$, $\gamma = 117° 6'$.

FIG. 1.



The forms usually developed are *a*(100), *b*(010), *c*(001), tabular, *n*(011) and *r*($\bar{1}$01) (Fig. 1).

Angles measured: $a:b = 118° 11'$, $a : c = 39° 42'$, $a : m = 54° 53'$, $c : m = 56° 42'$, $c : n = 57° 53'$, $c : b = 103° 19'$, $n : r = 68° 19'$, $m : n = 35° 45'$, and $c : r = 89° 10'$ " (Found : C, 61·1; H, 4·7; N, 12·1. $C_{18}H_{17}O_5N_3$ requires C, 60·8; H, 4·8; N, 11·8%). It dissolves in sodium carbonate with an orange-brown colour, and is hydrolysed to the original acid by boiling with alcoholic potassium hydroxide. Attempts to acetylate the ester gave a yellow, resinous product which could not be crystallised. *Acetyl derivative.* A solution of 5 g. of the acid in 10 c.c. of glacial acetic acid was boiled with 5 c.c. of acetic anhydride under reflux for 8 hours, and then poured on to ice. The *acetyl* derivative crystallised from ethyl alcohol in greenish-yellow, vitreous prisms, m. p. 212° (Found : C, 58·8; H, 4·2; N, 11·7. $C_{18}H_{15}O_6N_3$ requires C, 58·5; H, 4·1; N, 11·4%). It dissolves in sodium carbonate with an orange-brown colour or in sodium hydroxide with a wine-red colour, and attempts to esterify it gave resinous products which could not be crystallised. *Anilide.* A fine suspension of 4 g. of the acid in 400 c.c. of toluene was boiled with 2·3 g. of aniline and 1 g. of

phosphorus trichloride under reflux for 5 hours with stirring. When cold, the residue was washed with a little sodium carbonate and, after several crystallisations from ethyl acetate, formed yellow needles, m. p. 190—192° (decomp.) (Found : C, 65·4; H, 4·6; N, 13·9. $C_{22}H_{18}O_4N_4$ requires C, 65·7; H, 4·5; N, 13·9%). The anilide dissolves in sodium hydroxide with a red colour and is hydrolysed to the original acid by boiling concentrated hydrochloric acid. *Oxidation of* (VI). A fine suspension, obtained by dissolving 20 g. in 200 c.c. of cold concentrated sulphuric acid and pouring on to 800 g. of ice, was oxidised by adding gradually 10 g. of powdered sodium dichromate. Next day the product was precipitated completely by nearly neutralising with sodium hydroxide and, after several crystallisations from ethyl alcohol and ethyl acetate, yellow leaflets (11·5 g.), m. p. 247°, were obtained, but this substance requires further investigation.

1-*Hydroxy*-3-(4′-*aminophenyl*)-*tetrahydrophthalazine*-4-*acetic Acid* (VII).—Hydrosulphite was added to a solution of 12 g. of 1-hydroxy-3-(4′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid in 150 c.c. of water and 10 g. of sodium hydroxide at about 90° until the deep wine-red colour had disappeared, the mixture being kept alkaline throughout by the addition of sodium hydroxide. The yellow solution was filtered and, if the filtrate was cooled, fine yellow needles of the *sodium* salt separated incompletely. The product was best isolated, therefore, by the addition of hydrochloric acid until a white precipitate had separated completely. The end-point is readily determined, because too much acid redissolves the precipitate with a brown colour. It was washed with cold water and crystallised from a large volume of boiling water in colourless prisms, m. p. 239° (yield 10·7 g.; 97·5%) (Found : C, 64·3; H, 5·7; N, 14·2. $C_{16}H_{17}O_3N_3$ requires C, 64·2; H, 5·7; N, 14·0%). This compound can also be obtained by rapid reduction with acid stannous chloride, but the yield is not so good owing to the subsequent action of acid upon it. It is soluble in alcohol, insoluble in benzene, and gives a transient wine-red colour with ferric chloride. It dissolves readily in dilute alkalis or dilute acids and can be diazotised. The esters could not be obtained by the reduction of the esters of 1-hydroxy-3-(4′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid with alkaline hydrosulphite, for hydrolysis also occurred, nor did direct esterification prove satisfactory. The fact that the compound is affected by acids interfered with the preparation of a pure *acetyl* derivative, for, after crystallisation from dilute acetic acid, colourless plates, softening at 145—165° and melting sharply at 266°, were obtained (Found : C, 64·3; H, 5·2; N, 12·3. $C_{18}H_{19}O_4N_3$ requires C, 63·3; H, 5·6;

N, 12·3%). *Oxidation of* (VII). Powdered sodium dichromate (7 g.) was added in small portions during 3 hours to a solution of 20 g. in 400 c.c. of water and 100 c.c. of concentrated sulphuric acid at the air temperature. A transient wine-red colour was produced after each addition, but any further addition did not produce this colour. The mixture was rendered just alkaline with sodium hydroxide, diluted with water to 2 litres, boiled, filtered, the filtrate neutralised, and concentrated. After crystallisation from alcohol and then from water, yellow, prismatic needles (15 g.), m. p. 276°, were obtained, but this substance requires further investigation.

4′-*Amino*-3-*phenylphthalaz*-4-*one* (VIII).—A solution of 12 g. of 1-hydroxy-3-(4′-aminophenyl)-tetrahydrophthalazine-4-acetic acid in 300 c.c. of concentrated hydrochloric acid (25—30% aqueous sulphuric acid also can be used) was boiled under reflux. A less soluble *hydrochloride* separated progressively in colourless needles after 1 hour and the reaction was completed by boiling for 18 hours. After cooling, the hydrochloride was filtered off and converted into the base, which crystallised from alcohol in deep straw-coloured, prismatic needles, m. p. 259° (yield 8·8 g.; 92·5%) (Found: C, 71·0; H, 4·7; 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, insoluble in alkalis, but soluble in dilute acids and can be diazotised, although we have not yet succeeded in removing the amino-group or replacing it by a hydroxyl group without the compound undergoing further change. *Acetyl derivative.* A solution of 1 g. in 10 c.c. of glacial acetic acid was boiled with 0·5 c.c. of acetic anhydride. After a few minutes the colourless acetyl derivative separated completely; it crystallised from a large volume of boiling water in almost colourless plates, m. p. 348° (Found: C, 68·9; H, 4·8; N, 14·9. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%). *Oxidation of* (VIII). A solution of 5 g. in 400 c.c. of water and 80 c.c. of concentrated sulphuric acid was oxidised at the air temperature by adding gradually 16 g. of powdered sodium dichromate. A brown precipitate separated and next day benzoquinone, yellow needles, m. p. 115°, was isolated by extraction with ether. The other oxidation product could not be obtained satisfactorily under these conditions, but was obtained in a second oxidation in which a further 14 g. of dichromate were added and the mixture heated. In this case extraction with ether gave phthalic acid, colourless needles, m. p. 197° (confirmed by conversion into phthalic anhydride, colourless needles, m. p. 129°, and by the formation of fluorescein).

4′-*Amino*-N-*phenylphthalimidine* (IX).—A solution of 20 g. of 4′-amino-3-phenylphthalaz-4-one in 1 litre of water and 100 c.c. of

concentrated hydrochloric acid was boiled, and 300 c.c. of concentrated hydrochloric acid were added, followed by 30 g. of zinc dust in small portions during 2½ hours with vigorous boiling so that the volume was reduced to 700 c.c. 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*. Completion of the reaction was indicated by the pink colour of the filtrate, and the latter 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. 198° (yield 16·5 g.; 87%) (Found: C, 75·1; H, 5·5; N, 12·4. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·4; N, 12·5%). *Acetyl derivative.* A solution of 1 g. in 10 c.c. of glacial acetic acid was boiled with 0·5 c.c. of acetic anhydride and poured into water; the product crystallised from dilute acetic acid in fine, colourless needles, m. p. 196° (Found: C, 72·0; H, 5·5; N, 10·7. $C_{16}H_{14}O_2N_2$ requires C, 72·2; H, 5·4; N, 10·5%). *Oxidation of* (IX). This was effected as described in the first example under oxidation of (VIII), except that a fine suspension of the *sulphate* was used, and dark green needles separated at first and disappeared subsequently. Ether extraction gave benzoquinone, yellow needles, m. p. 115°. The other oxidation product was obtained best in a second oxidation in which a further 16 g. of dichromate were added at the air temperature. In this case extraction with ether gave phthalimide, flat, colourless needles, m. p. 234° (confirmed by conversion into phthalamide, colourless crystals, m. p. 222° with evolution of ammonia and reformation of the imide).

N-*Phenylphthalimidine* (XI).—A fine suspension of the sulphate, obtained by grinding 10 g. of the amino-derivative with sulphuric acid, was diazotised with a concentrated solution of 3·6 g. of sodium nitrite. The sparingly soluble *diazo-sulphate*, almost colourless needles, was boiled with 1 litre of alcohol until the evolution of nitrogen had ceased; the *N*-phenylphthalimidine crystallised in almost colourless plates, m. p. 160° as given by Racine (*loc. cit.*)

4′-*Hydroxy*-N-*phenylphthalimidine* (X).—A fine suspension of the hydrochloride, obtained by grinding 20 g. of the amino-derivative with 36 c.c. of concentrated hydrochloric acid and 800 c.c. of water, was diazotised with a concentrated solution of 7·2 g. of sodium nitrite. Carbamide was added to remove excess nitrous acid, the solution poured into 640 c.c. of dilute sulphuric acid (1 : 3) at 90°, and the mixture boiled for 2 hours until the stable diazo-compound had decomposed completely. The hydroxy-

derivative crystallised from alcohol in colourless needles, m. p. 228° (yield 18·2 g.; 90·5%) (Found: C, 74·8; H, 5·1; N, 6·1. $C_{14}H_{11}O_2N$ requires C, 74·7; H, 4·9; N, 6·2%). *Methyl ether.* A solution of 2 g. in 50 c.c. of dry methyl alcohol was boiled with methyl iodide and sodium. The ether crystallised from methyl alcohol in colourless plates, m. p. 134° (Found: C, 75·2; H, 5·5; N, 6·0. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·4; N, 5·9%). The *ethyl ether* crystallised from ethyl alcohol in colourless needles, m. p. 148° (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%).

N-4′-*Nitrophenyliminoisocarbostyril*-3-*carboxylic Acid* (XV).—β-Naphthaquinone (3 g.) was oxidised by calcium hypochlorite to the δ-lactone of *o*-carboxyphenylglyceric acid (2 g.) (XII), colourless leaflets, m. p. 202—203°, as described by Zincke and Scharfenberg (*loc. cit.*), who give m. p. 202°, whereas Bamberger and Kitschelt (*loc. cit.*) give m. p. 204·5°. This acid (12 g.) was heated with concentrated hydrochloric acid (60 c.c.) at 160—165° and gave *iso*coumarin-3-carboxylic acid (8·2 g.) (XIII), colourless, quadrilateral plates, m. p. 238—239° (Zincke, *Ber.*, 1892, **25**, 1493 gives m. p. 235°, whereas Bamberger and Kitschelt give m. p. 237°). An alcoholic solution of *iso*coumarin-3-carboxylic acid (5 g.) and *p*-nitrophenylhydrazine (4·05 g.) was boiled under reflux for ½ hour, and gave o-*carboxy*-α-*hydroxycinnamic acid* p-*nitrophenylhydrazide* (8·5 g.) (XIV), which crystallised from alcohol in fibrous, yellow needles, m. p. 189—190° (decomp.) (Found: C, 55·9; H, 4·0; N, 12·5. $C_{16}H_{13}O_6N_3$ requires C, 56·0; H, 3·8; N, 12·2%). The hydrazide is hydrolysed into its constituents by heating with dilute mineral acids. The elements of water were removed by boiling the finely divided hydrazide (4 g.) suspended in toluene (800 c.c.) with phosphorus trichloride (1 g.) under reflux for 5 hours. N-4′-*Nitrophenyliminoisocarbostyril*-3-*carboxylic acid* (2·24 g.) crystallised from ethyl acetate in small, pale yellow needles, m. p. 287° (decomp.). This compound is formed also by condensing *iso*coumarin-3-carboxylic acid with *p*-nitrophenylhydrazine in presence of phosphorus trichloride and boiling toluene, but the yield is much inferior (Found: C, 58·8; H, 3·6; N, 13·0. $C_{16}H_{11}O_5N_3$ requires C, 59·1; H, 3·4; N, 12·9%). It is readily soluble in acetone or glacial acetic acid, but less soluble in alcohol or ether, and dissolves in alkalis with a deep red colour, the alkaline solution decomposing when heated. It is unaltered by boiling with dilute mineral acids, and is neither esterified nor converted into an anilide when treated under the conditions described for the preparation of these derivatives of 1-hydroxy-3-(4′-nitrophenyl)-1 : 3-dihydrophthalazine-4-acetic acid (VI). Reduction of the acid (4 g.) with alkaline hydro-

sulphite gave an *amino-acid* (2 g.), almost colourless, crystalline powder, m. p. 265°, which was not examined closely, and no trace of *p*-phenylenediamine could be detected in the reduction mixture.

We desire to thank (1) the Society of Dyers and Colourists for a grant which enabled one of us (A. C. B.) to take part in this investigation, and also for permission to publish the detailed results elsewhere than in the Journal of that Society, (2) Professor F. L. Pyman, F.R.S., for his kindly interest during the progress of the investigation, and (3) Alliance Colour and Chemical Co., British Dyestuffs Corporation, and the Gas Light and Coke Co., for gifts of sodium β-naphthol-1-sulphonate.

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MANCHESTER. [*Received, December 1st*, 1925.]