420. *A Reaction of Certain Diazosulphonates derived from β-Naphthol-1-sulphonic Acid. Part XIII. Fission of the Naphthalene Nucleus and Subsequent Closure in Two Directions.*

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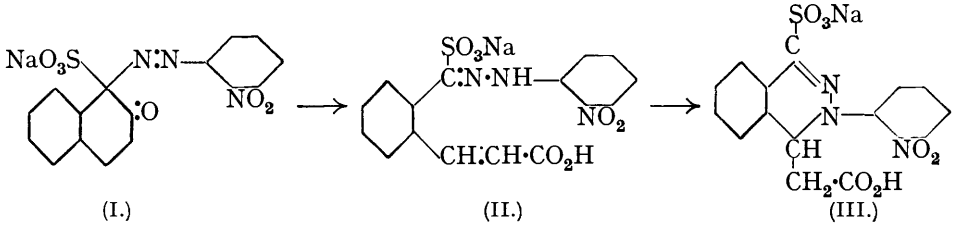
In previous Parts of this series the conversion of a number of 4'-substituted aryl-2-naphthol-1-diazosulphonates (J., 1926, 690; 1928, 2550; 1931, 1065, 1067, 1073, 1918; 1932, 11, 473, 1118; 1933, 1067; 1934, 1134) and of one 3'-substituted compound (J., 1928, 2556) into complex phthalazine derivatives, and the determination of the constitution of the latter, as well as of the derived phthalazones and phthalimidines, have been described. The investigation has now been extended to 2'-substituted compounds with noteworthy results.

In the formation of disodium 3-aryl-3 : 4-dihydrophthalazine-1-sulphonate-4-acetates from suitable diazosulphonates derived from β-naphthol-1-sulphonic acid, *via* the sodium 1-arylazo-β-naphthaquinone-1-sulphonates, it has been considered that the naphthalene ring of the latter is opened with addition of sodium hydroxide, forming a disodium benzaldehydearylhydrazone-ω-sulphonate-2-β-acrylate (J., 1926, 694; 1933, 1067), although hitherto there has been no evidence for the existence of such an intermediate compound. Consequently, it was most desirable that such a compound should be obtained, particularly as it was anticipated that under suitable conditions ring closure could then be effected to yield either a phthalazine derivative or an isomeride. With arylamines containing an *o*-nitro-group, we have now found, not only that these open-chain compounds exist, but that they are so stable that they can be isolated readily and preserved as the monosodium salts, and that, in fact, ring closure can be effected subsequently in either of two ways.

Thus, 2'-nitrobenzene-2-naphthol-1-diazosulphonate dissolves in sodium carbonate solution and then sodium 1-(2'-nitrobenzeneazo)-β-naphthaquinone-1-sulphonate (I) separates rapidly. Addition of this suspension to cold concentrated aqueous sodium hydroxide, followed by acidification after 1 minute, gives *sodium benzaldehyde-2'-nitrophenylhydrazone-ω-sulphonate-2-β-acrylic acid* (II), whereas acidification after 2 days (room temperature) gives *sodium hydrogen* 3-(2'-*nitrophenyl*)-3 : 4-*dihydrophthalazine*-1-*sulphonate*-4-*acetate* (III) as a result of the further action of sodium hydroxide on (II) :

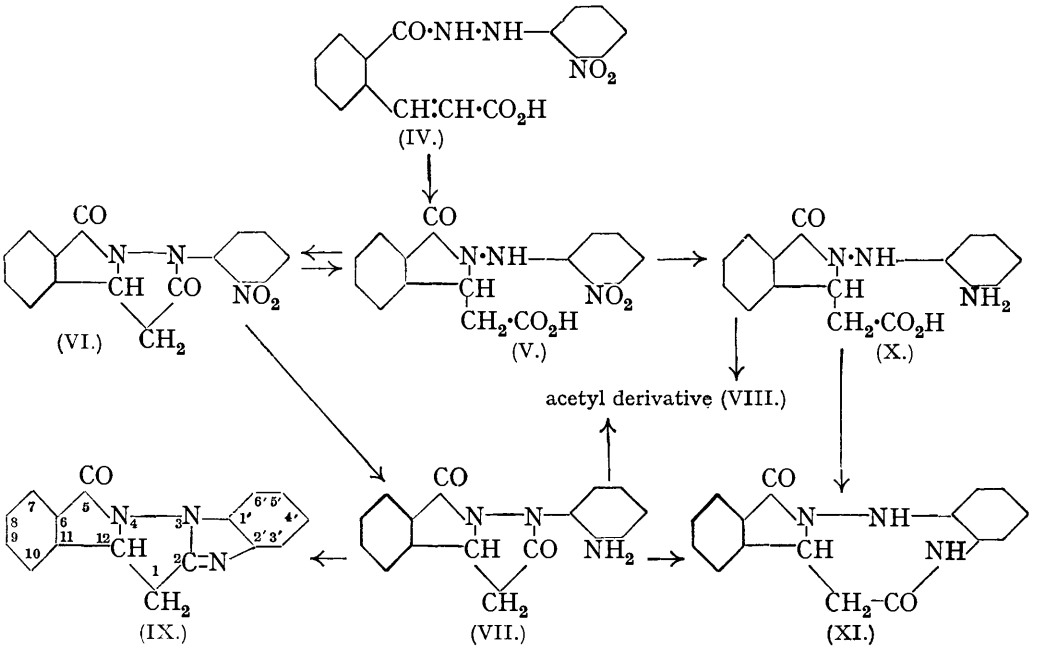


(I.) (II.) (III.)

Compound (II) is converted by boiling dilute hydrochloric acid into a mixture of *benzo-2'-nitrophenylhydrazide-2-β-acrylic acid* (IV) and 2-(2'-*nitrophenylamino*)iso*indolinone*-3-*acetic acid* (V), soluble in sodium carbonate solution with bluish-violet and yellow colours, respectively. Both *o*-carboxybenzo-2'-nitrophenylhydrazide (following paper) and β-benzoyl-*o*-nitrophenylhydrazine (Bischler, *Ber.*, 1889, **22**, 2808) also dissolve in sodium carbonate solution with a bluish-violet colour, so this appears to be a characteristic property of compounds containing the group $CO{\cdot}NH{\cdot}NH{\cdot}C_6H_4{\cdot}NO_2(o)$. Compound (IV) is converted into (V) by heat, boiling dilute sodium carbonate solution, or boiling nitrobenzene, and attempts to prepare esters and an anilide of (IV) lead to corresponding derivatives of (V). Unlike the isomeride in the phthalazine series (XII), compound (V) neither forms an *N*-methyl ether, nor is the acetic acid side-chain affected by refluxing with dilute sulphuric acid.

When 2-(2'-nitrophenylamino)*iso*indolinone-3-acetic acid is boiled with acetic anhydride,

with or without addition of pyridine, or is refluxed with toluene in presence of phosphorus trichloride, 1 molecule of water is eliminated, giving 2 : 5-*diketo*-3-(2′-*nitrophenyl*)iso*indolinopyrazolidocoline* (VI), which is hydrolysed readily to (V), preferably by acids, but also by rapid dissolution in aqueous-alcoholic sodium hydroxide.



Reduction of the nitro-compound (VI) with iron and acetic acid yields 2 : 5-*diketo*-3-(2′-*aminophenyl*)iso*indolinopyrazolidocoline* (VII), convertible by boiling acetic anhydride into the *acetyl* derivative (VIII). When (VII) is dissolved in dilute sulphuric acid (1 : 1) at 70°, 1 molecule of water is removed and the sulphate of a new base separates progressively on standing. The possibility that condensation occurs in this case between the amino-group and the keto-group in position 5 cannot be definitely excluded at present and this point is to be investigated further. Nevertheless, it is more probable that the keto-group in position 2 is involved in the condensation, which would then be analogous to the formation of benziminazoles, *e.g.*, (XV). If this is correct, the base is 2 : 2′-*anhydro*-2 : 5-*diketo*-3-(2′-*aminophenyl*)iso*indolinopyrazolidocoline* (IX), which is unaffected by boiling acetic anhydride. It forms a *picrate*, which can be obtained also by the action of alcoholic picric acid on (VII). In fact, any attempt to prepare a salt of (VII) actually results in a salt of (IX). The conversion of (VII) into (IX) is effected also by hot concentrated hydrochloric acid or by refluxing with toluene in presence of phosphorus trichloride. [A. S. Haigh (unpublished work), during the investigation of the 2′-nitro-4′-methyl analogues, has found that the homologue of (IX) can be obtained also from the homologues of (X) and (XI) by refluxing with toluene in presence of phosphorus trichloride, although these conversions into (IX) are not possible with the compounds at present under discussion.]

Although dilute sulphuric acid at 70° converts (VII) into the 2 : 2′-anhydro-derivative (IX), refluxing (VII) with similarly dilute sulphuric acid for 3—4 hours results in the formation of the *lactam* (XI) of 2-(2′-*aminophenylamino*)iso*indolinone*-3-*acetic acid*. This base forms a hydrobromide and a *picrate*, from which it is recovered unaltered by treatment with alkali, in contrast to the behaviour of (VII), which with acids yields salts of (IX). The eight-membered ring in compound (XI) has considerable stability.

Compound (V) is reduced to 2-(2′-*aminophenylamino*)iso*indolinone*-3-*acetic acid* (X), convertible by boiling acetic anhydride into the acetyl derivative (VIII), and the lactam (XI) is also obtained by refluxing compound (X) with dilute sulphuric acid for 1 hour.

All the formulæ proposed are supported by analysis, except those of (VII) and (VIII), the analytical results of which under all conditions and with numerous distinct samples consistently require the presence of H_2O and $\frac{1}{2}H_2O$, respectively.

All the reactions already described occur also with the analogous derivatives of 4'-chloro-2'-nitrobenzene-2-naphthol-1-diazosulphonate, but with the chloro-compounds all the analytical results support the constitutions proposed.

In general, the 2'-nitro- and 2'-amino-compounds in the phthalazine and phthalazone series are similar in properties to corresponding 4'- and 3'-nitro- and 4'- and 3'-amino-compounds, although naturally the presence of the 2'-amino-group in certain of the compounds leads to further ring formation with elimination of water.

1-*Hydroxy*-3-(2'-*nitro*- and 4'-*chloro*-2'-*nitro-phenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* (XII) are prepared from the corresponding 1-sodium sulphonates (*e.g.*, III) in the usual way. Unlike the 4'- and 3'-nitro-analogues, however, they do not form acetyl derivatives (regarded as *O*-acetates owing to the ease of hydrolysis), but prolonged boiling with acetic anhydride and pyridine has the remarkable effect of giving solely 2 : 5-diketo-3-(2'-nitro- and 4'-chloro-2'-nitro-phenyl)*iso*indolinopyrazolidocoline (as VI), although in lower yield than is obtained from the isomerides (*e.g.*, V), with which the use of pyridine is not essential as it is in the present case. As the compounds (*e.g.*, VI) are hydrolysed readily to compounds (*e.g.*, V), this new reaction affords the only known means of converting a phthalazine derivative into the isomeric *iso*indolinone derivative.

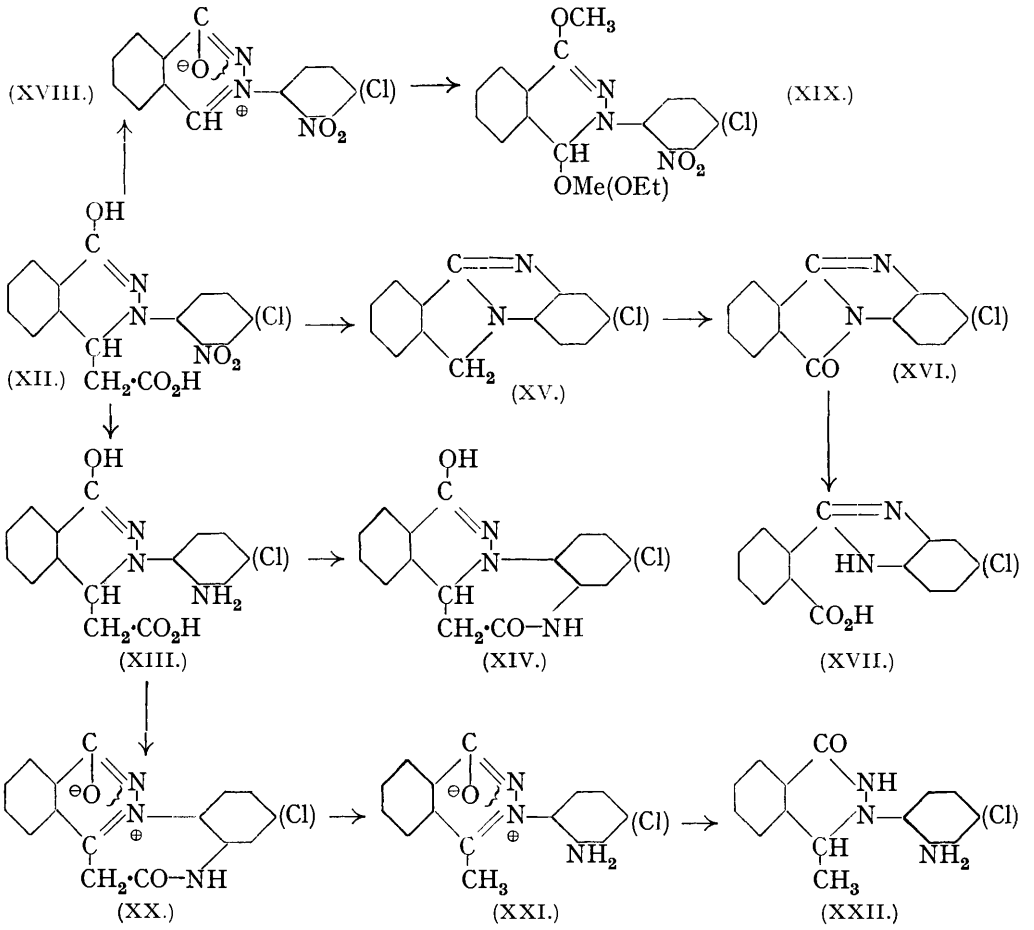
The N-*methyl* ethers of (XII) are reduced to the corresponding *amino-acids*, which are converted into the *lactams* of 1-*keto*-3-(2'-*amino*- and 4'-*chloro*-2'-*amino-phenyl*)-2-*methyltetrahydrophthalazine*-4-*acetic acid* by boiling dilute hydrochloric acid; compounds (XII) are best reduced by iron and acetic acid to the corresponding *amino-acids* (XIII), which are so unstable that even attempts to crystallise them yield the *lactams* (XIV).

4'- and 3'-Amino-3-arylphthalaz-1-ones are prepared by the action of boiling dilute mineral acids on 1-hydroxy-3-(4'- and 3'-aminoaryl)-3 : 4-dihydrophthalazine-4-acetic acid, respectively. Although similar treatment of 1-hydroxy-3-(2'-aminophenyl)-3 : 4-dihydrophthalazine-4-acetic acid or its lactam gave a *substance* which had the properties of the anticipated 2'-amino-3-phenylphthalaz-1-one, repeated analyses of numerous samples of the base, and of the product of the attempted acetylation of it, did not support this constitution. The base is unusually unstable and reactive, and even with hot solvents is converted into a colourless substance, m. p. above 360°, of undetermined constitution. On the other hand, 4'-*chloro*-2'-*amino*-3-*phenylphthalaz*-1-*one* is definitely obtained from the chlorinated compound (XIII) or its lactam (XIV) in the usual manner.

Compounds (XII) and (XIII) are converted by stannous chloride, tin, and hydrochloric acid into *o*-benzylene- and 5-*chloro*-o-*benzylene-benziminazole* (XV), identical with synthetic specimens prepared from *o*-phthalaldehyde and *o*-phenylenediamine (Thiele and Falk, *Annalen*, 1906, **347**, 125) or 4-chloro-*o*-phenylenediamine, respectively. The constitution was confirmed by oxidation to *o*-benzoylene- and 5-*chloro*-o-*benzoylene-benziminazole* (XVI), and conversion of these into 2-phenylbenziminazole- and 5-*chloro*-2-*phenylbenziminazole*-o-*carboxylic acid* (XVII), respectively.

2'-*Nitro*- and 4'-*chloro*-2'-*nitro*-3-*phenylphthalaz*-1-*one* (XVIII), prepared in the usual way (the yield of the unchlorinated compound is very small), react with methyl sulphate in a similar manner to the 4'- or 3'-nitro-analogues. The oxygen atom in the keto-group is methylated and the primary products combine similarly with alcohols (*loc. cit.*). Owing to the ease with which a portion of the alcohol is lost from the resulting compounds, however, only in the case of the derivative from 2' : 6'-dibromo-4'-nitro-3-phenylphthalaz-1-one (J., 1931, 1085) has it hitherto been possible to support by analysis the formulæ for these products. Compounds (XIX) also are sufficiently stable to enable their formulæ to be confirmed by analysis. On the other hand, these compounds are merely decomposed by heat without formation of 4-keto-1-methoxy-3-(2'-nitro- and 4'-chloro-2'-nitro-phenyl)-3 : 4-dihydrophthalazine. 2'-*Nitro*- and 4'-*chloro*-2'-*nitro*-3-*phenyl*-4-*methylphthalaz*-1-*one* also are obtained in the usual way, but their methylation products (cf. J., 1931, 1071, 1921) resist crystallisation and do not have the properties to be expected of compounds containing a reactive methylene group.

As a result of the presence of an amino-group in the 2′-position, it has been possible to isolate for the first time compounds intermediate between a 1-hydroxy-3-(aminoaryl)-



3 : 4-dihydrophthalazine-4-acetic acid and an amino-3-aryl-4-methylphthalaz-1-one. Thus, (XIII) and (XIV) are converted by acid dichromate into the *lactams* (XX) of *2′-amino-* and *4′-chloro-2′-amino-3-phenylphthalaz-1-one-4-acetic acid*, from which *2′-amino-* and *4′-chloro-2′-amino-3-phenyl-4-methylphthalaz-1-one* (XXI) are best obtained by the action of hot aqueous sodium sulphide, and in this instance the formula of the unchlorinated compound (XXI) is confirmed by analysis, although, as already mentioned, that was not the case in the absence of the 4-methyl group. Compounds (XXI) are also obtained by reducing the corresponding nitro-compounds with aqueous sodium sulphide, but reduction of these nitro- or amino-compounds with zinc dust and dilute sulphuric acid gives only *1-keto-3-(2′-amino-* and *4′-chloro-2′-amino-phenyl)-4-methyltetrahydrophthalazine* (XXII) and there was no evidence of the formation of methyl derivatives of compounds (XV).

Some derivatives of 5-chloro-*o*-nitroaniline also are described, but further investigation of these compounds was abandoned when it was clear that it would lead to unnecessary repetition.

Further work on this subject is in progress to support the constitutions and interrelationships of compounds of the types (V)—(XI), and confirmatory synthetic work leading to compounds of the type (V) is well advanced, as is also the preparation of 2-(4′-nitroarylamino)*iso*indolinone-3-acetic acids and their derivatives.

Experimental.

The methods of preparing the analogous compounds from *o*-nitroaniline and 4-chloro-*o*-nitroaniline are so similar that separate descriptions are unnecessary. Single details in parentheses apply to both cases, but where more than one figure, etc., is given, the first refers to the derivative of *o*-nitroaniline and the second to the derivative of 4-chloro-*o*-nitroaniline. Derivatives of 5-chloro-*o*-nitroaniline are prepared exactly as described for the 4-chloro-isomerides.

Sodium Benzaldehyde-2′-nitro- or *-4′-chloro-2′-nitro-phenylhydrazone-ω-sulphonate-2-β-acrylic Acid* (II).—A filtered solution of commercial 50% sodium β-naphthol-1-sulphonate (60 g.) in water (250 c.c.) was stirred slowly at 0° into a solution of diazotised *o*-nitroaniline or 4-chloro-*o*-nitroaniline, prepared by adding rapidly a cold solution of the base (13·8 g.; 17·25 g.) in concentrated sulphuric acid (60 c.c.; 75 c.c.) to a mixture of ice (250 g.) and sodium nitrite (7·7 g.) with good stirring. 2′-Nitro- or 4′-chloro-2′-nitro-benzene-2-naphthol-1-diazosulphonate separated (brownish-red; dark red). It was washed free from acid, mixed with cold water (150 c.c.), and stirred into a cold solution of anhydrous sodium carbonate (25 g.) in water (100 c.c.). Almost colourless prisms of sodium 1-(2′-nitro- or 4′-chloro-2′-nitro-benzeneazo)-β-naphthaquinone-1-sulphonate separated from the orange solution in 1 minute and the suspension was then added to a cold solution of sodium hydroxide (25 g.) in water (100 c.c.); the temperature rose by about 5° and a deep colour (reddish-violet; bluish-violet) began to change quickly (to brown; orange-brown). In order to obtain the maximum yield, after only 1 minute the solution was acidified rapidly with concentrated hydrochloric acid, then made alkaline with sodium carbonate, heated to 90° (charcoal), and filtered. The cold filtrate was rendered faintly acid with hydrochloric acid; the sodium salt separated in crystals (yellow; orange).

Sodium benzaldehyde-2′-nitrophenylhydrazone-ω-sulphonate-2-β-acrylic acid crystallised from alcohol or ethyl acetate in orange-red leaflets with a yellow reflex (yield, 33·8 g.; 81·8%, calculated on the *o*-nitroaniline) (Found: S, 7·4. $C_{16}H_{12}O_7N_3SNa$ requires S, 7·7%). It is sparingly soluble in cold water, and dissolves in sodium carbonate with a yellow colour and in cold dilute sodium hydroxide with an orange-brown colour changing to violet on heating, or in more concentrated cold sodium hydroxide with a violet colour. It is an orange acid dye of good tinctorial power, but fugitive to light.

Sodium benzaldehyde-4′-chloro-2′-nitrophenylhydrazone-ω-sulphonate-2-β-acrylic acid crystallised from aqueous alcohol in yellow needles, which became red on drying (yield, 42 g.; 93·9%, calculated on the 4-chloro-*o*-nitroaniline) (Found: Cl, 7·8; S, 6·9. $C_{16}H_{11}O_7N_3ClSNa$ requires Cl, 7·9; S, 7·15%). It has similar properties to those of the unchlorinated analogue.

Sodium benzaldehyde-5′-chloro-2′-nitrophenylhydrazone-ω-sulphonate-2-β-acrylic acid crystallised from aqueous alcohol in red leaflets with a yellow reflex (Found: Cl, 7·7; S, 7·0%).

Benzo-2′-nitro- or *-4′-chloro-2′-nitro-phenylhydrazide-2-β-acrylic Acid* (IV) *and* 2-(*2′-Nitro-* or *-4′-chloro-2′-nitro-phenylamino*)iso*indolinone-3-acetic Acid* (V).—The preceding sodium salt (II) (20 g.) was dissolved in boiling water (500 c.c.), concentrated hydrochloric acid (20 c.c.) added gradually, and boiling continued until evolution of sulphur dioxide had ceased (8 hours). The *acid* separated as a yellow crystalline mass consisting of a mixture of the two isomerides, the proportion varying with the conditions (total yield, 15·7 g.; 99·4% : 15·3 g.; 94·7%). The individual components can be recognised readily by sprinkling the dry powdered mixture on filter-paper moistened with dilute sodium carbonate solution; part dissolves with a deep bluish-violet colour (IV) and part dissolves with a yellow colour (V).

Benzo-2′-nitrophenylhydrazide-2-β-acrylic acid was separated as the less soluble portion of the mixture by rapid fractional crystallisation from glacial acetic acid in orange-yellow prismatic needles, m. p. 220—225° with conversion into (V) (Found: C, 58·6; H, 4·0; N, 12·8. $C_{16}H_{13}O_5N_3$ requires C, 58·7; H, 4·0; N, 12·8%). It, or the above mixture containing it, by boiling with nitrobenzene, or by boiling the violet sodium carbonate solution until yellow, was converted completely into 2-(*2′-nitrophenylamino*)iso*indolinone-3-acetic acid*, which crystallised from glacial acetic acid in greenish-yellow prisms, m. p. 224—225° (Found: C, 58·8; H, 4·3; N, 13·1. $C_{16}H_{13}O_5N_3$ requires C, 58·7; H, 4·0; N, 12·8%), soluble in cold dilute sodium carbonate solution with a pale yellow colour and in sodium hydroxide solution with a bluish-red colour.

Benzo-4′-chloro-2′-nitrophenylhydrazide-2-β-acrylic acid was separated similarly to the unchlorinated analogue in small orange prisms, m. p. 272—278° with ring closure (Found: C, 52·9; H, 3·5; N, 11·3; Cl, 10·0. $C_{16}H_{12}O_5N_3Cl$ requires C, 53·1; H, 3·3; N, 11·6; Cl, 9·8%). 2-(*4′-Chloro-2′-nitrophenylamino*)iso*indolinone-3-acetic acid* crystallised from glacial acetic acid or ethyl acetate in small yellow needles, m. p. 278° (Found: C, 53·1; H, 3·3; N, 11·3; Cl,

9·65. $C_{16}H_{12}O_5N_3Cl$ requires C, 53·1; H, 3·3; N, 11·6; Cl, 9·8%). The colour reactions of both compounds with cold dilute alkali solutions are similar to those of the unchlorinated analogues.

2-(5′-*Chloro*-2′-*nitrophenylamino*)iso*indolinone*-3-*acetic acid* crystallised from ethyl acetate in yellow needles, or from glacial acetic acid in yellow prisms, m. p. 248° (Found: C, 52·9; H, 3·5; N, 11·6; Cl, 10·05%).

Derivatives of the 2-(*Phenylamino*)iso*indolinone*-3-*acetic Acids*.—The following derivatives were obtained whether (IV) or (V) was used: *2′-Nitro-compounds*. The *methyl* ester, obtained by the hydrogen chloride–methyl alcohol method or by refluxing the acid in aqueous methyl-alcoholic potassium hydroxide solution with methyl iodide or sulphate, crystallised from methyl alcohol in yellow prisms, m. p. 164° (Found: C, 59·8; H, 4·7; N, 12·5. $C_{17}H_{15}O_5N_3$ requires C, 59·8; H, 4·4; N, 12·3%), stable to boiling acetic anhydride (compare the behaviour of the acid below). The *ethyl* ester crystallised from ethyl alcohol in yellow prisms, m. p. 153° (Found: C, 60·6; H, 4·9; N, 12·0. $C_{18}H_{17}O_5N_3$ requires C, 60·8; H, 4·8; N, 11·8%). Both esters are insoluble in sodium carbonate solution, but dissolve in boiling dilute sodium hydroxide solution with a magenta colour. The *anilide* crystallised from glacial acetic acid in yellow prisms, m. p. 272° (Found: C, 65·4; H, 4·05; N, 13·8. $C_{22}H_{18}O_4N_4$ requires C, 65·7; H, 4·5; N, 13·9%), insoluble in alkali.

4′-Chloro-2′-nitro-compounds. The *methyl* ester crystallised from methyl alcohol in small, yellow, prismatic needles, m. p. 152° (Found: C, 54·4; H, 3·7; N, 10·9; Cl, 9·7. $C_{17}H_{14}O_5N_3Cl$ requires C, 54·3; H, 3·75; N, 11·2; Cl, 9·45%). The *anilide* crystallised from glacial acetic acid in orange-yellow prisms, m. p. 268° (Found: N, 13·1; Cl, 7·7. $C_{22}H_{17}O_4N_4Cl$ requires N, 12·8; Cl, 8·1%).

5′-Chloro-2′-nitro-compounds. The *methyl* ester crystallised from methyl alcohol in stout yellow prisms, m. p. 182° (Found: C, 54·6; H, 3·8; N, 11·05%), and the *ethyl* ester from ethyl alcohol in yellow prisms, m. p. 184° (Found: C, 55·3; H, 4·2; N, 10·8. $C_{18}H_{16}O_5N_3Cl$ requires C, 55·45; H, 4·1; N, 10·8%).

2 : 5-*Diketo*-3-(2′-*nitro-* or 4′-*chloro*-2′-*nitro-phenyl*)iso*indolinopyrazolidocoline* (VI).—(*a*) 2-(2′-Nitro- or 4′-chloro-2′-nitro-phenylamino)*iso*indolinone-3-acetic acid (38 g.) was refluxed with acetic anhydride (180 c.c.) alone, or better with addition of pyridine (20 c.c.; 15 c.c.), for 3 hours; the product crystallised on cooling (yield, 29 g.; 80·7% : 21·1 g.; 61·2%). (*b*) The acid (2 g.) was refluxed with toluene (250 c.c.) and phosphorus trichloride (2 c.c.) for 2 hours (yield, 1·6 g.; 84·7% : 1·6 g.; 84·2%). Benzo-2′-nitro- or -4′-chloro-2′-nitro-phenylhydrazide-2-β-acrylic acid also can be used in both methods. 2 : 5-Diketo-3-(2′-nitro- or 4′-chloro-2′-nitro-phenyl)*iso*indolinopyrazolidocoline is hydrolysed to 2-(2′-nitro- or 4′-chloro-2′-nitro-phenylamino)*iso*indolinone-3-acetic acid best by dissolving it in concentrated sulphuric acid and pouring the solution into water, or by boiling a glacial acetic acid solution with hydrochloric acid for ¼ hour, or by boiling the substance with aqueous-alcoholic sodium hydroxide for a few minutes and then acidifying the solution.

2 : 5-*Diketo*-3-(2′-*nitrophenyl*)iso*indolinopyrazolidocoline* crystallised from glacial acetic acid in pale yellow prisms, m. p. 209° (Found: C, 62·2; H, 3·5; N, 13·6. $C_{16}H_{11}O_4N_3$ requires C, 62·1; H, 3·55; N, 13·6%), insoluble in cold dilute mineral acids and alkalis.

2 : 5-*Diketo*-3-(4′-*chloro*-2′-*nitrophenyl*)iso*indolinopyrazolidocoline* crystallised from glacial acetic acid in pale yellow prisms, m. p. 248—249° (Found: C, 55·75; H, 2·9; N, 12·3; Cl, 10·5; *M* in phenol, 331. $C_{16}H_{10}O_4N_3Cl$ requires C, 55·9; H, 2·9; N, 12·2; Cl, 10·3%; *M*, 343·5).

2 : 5-*Diketo*-3-(5′-*chloro*-2′-*nitrophenyl*)iso*indolinopyrazolidocoline* crystallised from glacial acetic acid in pale yellow prisms, m. p. 209° (Found: C, 56·1; H, 3·1; N, 12·2; Cl, 10·45%).

2 : 5-*Diketo*-3-(2′-*amino-* or 4′-*chloro*-2′-*amino-phenyl*)iso*indolinopyrazolidocoline* (VII).—The nitro-compound (VI) (5 g.) was dissolved in boiling glacial acetic acid (25 c.c.; 50 c.c.) and water (25 c.c.; 15 c.c.), and iron powder (3 g.) added gradually during 10 minutes. The green mixture was then boiled for a further 10 minutes, boiling water (40 c.c.) added (charcoal), and the liquid filtered; almost colourless crystals separated on cooling.

2 : 5-*Diketo*-3-(2′-*aminophenyl*)iso*indolinopyrazolidocoline* crystallised from alcohol, aqueous acetic acid, or ethyl acetate in colourless, asbestos-like, prismatic needles, m. p. 234—236° (yield, 3·7 g.; 82%) (Found: in material crystallised from dry ethyl acetate and dried at 120°: C, 64·7, 64·9; H, 5·0, 5·0; N, 14·2, 14·0. Found in material from aqueous acetic acid: C, 65·1; H, 5·05; N, 13·95. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·65; N, 15·05%. $C_{16}H_{13}O_2N_3,H_2O$ requires C, 64·65; H, 5·05; N, 14·1%). The *acetyl* derivative (VIII), prepared by boiling with acetic anhydride and a little pyridine for ¼ hour, crystallised from dry alcohol in large, almost

colourless prisms, from ethyl acetate or acetic anhydride in smaller prisms, and from glacial acetic acid in transparent flat prisms, all m. p. 175—176° (Found in material crystallised from ethyl acetate: C, 65·2, 65·4; H, 4·9, 4·9; N, 12·6, 12·6. Found in material from dry alcohol: C, 65·25; H, 4·8; N, 12·45. Found in material from acetic anhydride: C, 65·1; H, 4·9; N, 12·6. $C_{18}H_{15}O_3N_3$ requires C, 67·3; H, 4·7; N, 13·1. $C_{18}H_{15}O_3N_3,\frac{1}{2}H_2O$ requires C, 65·4; H, 4·85; N, 12·7%), insoluble in dilute mineral acids and alkalis.

2 : 5-*Diketo*-3-(4′-*chloro*-2′-*aminophenyl*)iso*indolinopyrazolidocoline* crystallised from aqueous acetic acid or ethyl acetate in small, colourless, fine needles, m. p. 253—254° (yield, 2·8 g.; 61·4%) (Found: C, 61·1, 61·15; H, 3·9, 3·9; N, 13·0, 13·2; Cl, 11·0, 11·0. $C_{16}H_{12}O_2N_3Cl$ requires C, 61·2; H, 3·9; N, 13·4; Cl, 11·3%). The *acetyl* derivative crystallised from ethyl acetate in colourless prisms, m. p. 242—243° (Found: C, 60·4; H, 4·1; N, 11·3; Cl, 9·8. $C_{18}H_{14}O_3N_3Cl$ requires C, 60·6; H, 4·2; N, 11·7; Cl, 10·0%).

2 : 2′-*Anhydro*-2 : 5-*diketo*-3-(2′-*amino*- or 4′-*chloro*-2′-*amino-phenyl*)iso*indolinopyrazolidocoline* (IX).—(*a*) The amino-compound (VII) (2 g.) was dissolved in dilute sulphuric acid (1 : 1) (16 c.c.) at 70° and left at room temperature. The crystalline sulphate which separated (2—3 hours; immediately) was collected on a glass filter and basified with warm dilute sodium hydroxide solution (yield, 1 g.; 53·5% : 1·4 g.; 74·5%). (*b*) The amino-compound (2 g.) was refluxed with toluene (250 c.c.) and phosphorus trichloride (2 c.c.) for 2 hours, the toluene then removed, and the residue ground with warm dilute sodium hydroxide solution (yield, 0·8 g.; 42·8% : 1 g.; 53·2%).

2 : 2′-*Anhydro*-2 : 5-*diketo*-3-(2′-*aminophenyl*)iso*indolinopyrazolidocoline* crystallised from aqueous acetic acid in colourless prismatic needles, m. p. 219—221° (Found: C, 73·5; H, 4·3; N, 16·1. $C_{16}H_{11}ON_3$ requires C, 73·6; H, 4·2; N, 16·1%), soluble in hot dilute mineral acids and insoluble in alkalis. The *picrate* crystallised from alcohol in small yellow needles, m. p. 234—236° (Found: C, 53·95; H, 3·1. $C_{22}H_{14}O_8N_6$ requires C, 53·9; H, 2·9%), and was also obtained directly from 2 : 5-diketo-3-(2′-aminophenyl)*iso*indolinopyrazolidocoline; the base (IX) was recovered on warming the picrate with aqueous ammonia.

2 : 2′-*Anhydro*-2 : 5-*diketo*-3-(4′-*chloro*-2′-*aminophenyl*)iso*indolinopyrazolidocoline sulphate* crystallised from glacial acetic acid in colourless prisms, m. p. 278° [Found: C, 55·4; H, 2·9; N, 11·9; Cl, 9·9; S, 4·65. $(C_{16}H_{10}ON_3Cl)_2,H_2SO_4$ requires C, 55·7; H, 3·2; N, 12·2; Cl, 10·3; S, 4·6%]. The *base* crystallised from aqueous acetic acid in colourless prismatic needles, m. p. 238—239° (Found: C, 65·0; H, 3·4; N, 14·2; Cl, 12·0. $C_{16}H_{10}ON_3Cl$ requires C, 65·0; H, 3·4; N, 14·2; Cl, 12·0%).

2-(2′-*Amino*- or 4′-*chloro*-2′-*amino-phenylamino*)iso*indolinone*-3-*acetic Acid* (X).—The nitro-acid (V) (5 g.) was dissolved in 10% aqueous sodium hydroxide (100 c.c.) and alcohol (10 c.c.), and maintained at constant temperature (70°; 50°) during the careful addition of hydrosulphite (7 g.) until the deep bluish-red colour had disappeared, the mixture being kept alkaline throughout by the addition of sodium hydroxide. After 20 minutes, the alcohol was removed by boiling, the liquid filtered (charcoal), and the excess of alkali in the cold filtrate neutralised very carefully. A green resinous precipitate was filtered off and discarded, and the mass of cream prisms which separated from the filtrate after 8 hours was filtered off and washed with cold water. Acid stannous chloride can also be used for this reduction, but is less satisfactory.

2-(2′-*Aminophenylamino*)iso*indolinone*-3-*acetic acid* crystallised from aqueous alcohol in colourless plates, m. p. 182—183° (decomp.) (yield, 3·5 g.; 77·1%) (Found: C, 64·0; H, 5·25; N, 14·2. $C_{16}H_{15}O_3N_3$ requires C, 64·6; H, 5·05; N, 14·15%), which rapidly turn brown in air. It is soluble in cold dilute mineral acids and alkalis.

2-(4′-*Chloro*-2′-*aminophenylamino*)iso*indolinone*-3-*acetic acid* crystallised from aqueous alcohol in colourless plates, m. p. 195° (decomp.) (yield, 2·2 g.; 48%) (Found: C, 58·2; H, 4·5; N, 13·0. $C_{16}H_{14}O_3N_3Cl$ requires C, 57·9; H, 4·3; N, 12·7%).

These amino-acids do not form acetyl derivatives, but with acetic anhydride, alone or with pyridine, yield 2 : 5-diketo-3-(2′-acetamido- or 4′-chloro-2′-acetamido-phenyl)*iso*indolinopyrazolidocoline (above).

2-(2′-*Amino*- or 4′-*chloro*-2′-*amino-phenylamino*)iso*indolinone*-3-*acetic Acid Lactam* (XI).—(*a*) The amino-acid (X) (5 g.) was refluxed with concentrated sulphuric acid (12 c.c.) and water (15 c.c.) for 1 hour; the mixture was then diluted with water (20 c.c.), boiled (charcoal), and filtered. A brown tarry mass separated when the cold filtrate was rendered alkaline with sodium carbonate, and was crystallised (yield, 1·2 g.; 25·6% : 1·3 g.; 27·5%). (*b*) 2 : 5-Diketo-3-(2′-amino- or 4′-chloro-2-amino-phenyl)*iso*indolinopyrazolidocoline (5 g.) was refluxed with dilute sulphuric acid (1 : 1) (50 c.c.) for 3—4 hours, and the product isolated as described under (*a*) (yield, 2·3 g.; 49% : 1·5 g.; 31·7%).

2-(2′-*Aminophenylamino*)iso*indolinone*-3-*acetic acid lactam* crystallised from ethyl acetate in colourless needles, or from aqueous acetic acid in colourless prisms, m. p. 227° (Found: C, 68·6; H, 4·6; N, 15·05. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·65; N, 15·1%), readily soluble in cold dilute mineral acids and insoluble in alkalis. Cold hydrobromic acid (*d* 1·7) gave the hydrobromide, colourless prisms, m. p. 264—265°, from which the base was recovered with warm aqueous sodium carbonate. The *picrate* crystallised from alcohol in fine yellow needles, m. p. 229—230° (Found: N, 16·2. $C_{22}H_{16}O_9N_6$ requires N, 16·5%), so that, unlike (VII), compound (XI) is not converted into (IX) by picric acid; the base (XI) was recovered by warming the picrate with aqueous ammonia.

2-(4′-*Chloro*-2′-*aminophenylamino*)iso*indolinone*-3-*acetic acid lactam* crystallised from ethyl acetate or dry alcohol in small colourless needles, m. p. 237° (Found: C, 61·05; H, 4·0; N, 13·1; Cl, 11·6. $C_{16}H_{12}O_2N_3Cl$ requires C, 61·2; H, 3·9; N, 13·4; Cl, 11·3%).

Sodium Hydrogen 3-(2′-*Nitro-* or 4′-*Chloro*-2′-*nitro-phenyl*)-3 : 4-*dihydrophthalazine*-1-*sulphonate*-4-*acetate* (III).—(*a*) A solution of sodium 1-(2′-nitro- or 4′-chloro-2′-nitro-benzeneazo)-β-naphthaquinone-1-sulphonate in sodium hydroxide, prepared exactly as described under sodium benzaldehyde-2′-nitro- or 4′-chloro-2′-nitro-phenylhydrazone-ω-sulphonate-2-β-acrylic acid (p. 1800), instead of being acidified after 1 minute, was kept at room temperature (2 days; 3—4 days) and then acidified. After separation from 2′-nitro- or 4′-chloro-2′-nitro-benzeneazo-β-naphthol (0·9 g.; 2 g.), the product was isolated in the usual manner (yield, 28·8 g.; 69·8%, calculated on the *o*-nitroaniline: yield, 42·5 g.; 94·8%, calculated on the 4-chloro-*o*-nitroaniline). (*b*) A solution of sodium benzaldehyde-2′-nitro- or 4′-chloro-2′-nitro-phenylhydrazone-ω-sulphonate-2-β-acrylic acid in sodium hydroxide was kept at room temperature for 3 days or at 60° for 3½ hours. The yield was almost quantitative and the identity of the product was confirmed by conversion into 1-hydroxy-3-(2′-nitro- or 4′-chloro-2′-nitro-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid.

Sodium hydrogen 3-(2′-*nitrophenyl*)-3 : 4-*dihydrophthalazine*-1-*sulphonate*-4-*acetate* crystallised from ethyl acetate in yellow needles, or from aqueous alcohol in orange-yellow irregular prisms (Found: S, 7·9. $C_{16}H_{12}O_7N_3SNa$ requires S, 7·7%), readily soluble in water or alcohol with a yellow colour, deepened by addition of alkali. It is a level-dyeing orange-yellow acid dye of less tinctorial power than the *p*-isomeride, and fugitive to light.

Sodium hydrogen 3-(4′-*chloro*-2′-*nitrophenyl*)-3 : 4-*dihydrophthalazine*-1-*sulphonate*-4-*acetate* crystallised from water in yellow prisms (Found: Cl, 8·2; S, 7·5. $C_{16}H_{11}O_7N_3ClSNa$ requires Cl, 7·9; S, 7·15%). It has similar properties to those of the unchlorinated analogue.

Sodium hydrogen 3-(5′-chloro-2′-nitrophenyl)-3 : 4-dihydrophthalazine-1-sulphonate-4-acetate was obtained only in a resinous condition by either method (*a*) or (*b*) and could not be purified for analysis, but it was converted in a normal manner into 1-hydroxy-3-(5′-chloro-2′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid in good yield.

1-*Hydroxy*-3-(2′-*nitro-* or 4′-*chloro*-2′-*nitro-phenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic Acid* (XII).—A solution of the preceding sodium hydrogen salt (32 g.; 42·5 g.) in water (200 c.c.) was boiled, and concentrated hydrochloric acid (60 c.c.; 50 c.c.) added gradually until evolution of sulphur dioxide had ceased. The product separated in yellowish-brown crystals, which were washed with boiling water.

1-*Hydroxy*-3-(2′-*nitrophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* crystallised from ethyl acetate in yellow prismatic needles, or from glacial acetic acid in orange-yellow prisms, m. p. 248° (yield, 23·5 g.; 92·8%) (Found: C, 59·0; H, 4·15; N, 12·7. $C_{16}H_{13}O_5N_3$ requires C, 58·7; H, 4·0; N, 12·8%), sparingly soluble in alcohol or ethyl acetate, but more soluble in glacial acetic acid. It is sparingly soluble in water, but dissolves readily in sodium carbonate or hydroxide solution with a deep violet-red colour, and dissolves in cold concentrated sulphuric acid with a yellow colour, being reprecipitated unaltered when this solution is diluted.

1-*Hydroxy*-3-(4′-*chloro*-2′-*nitrophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* crystallised from ethyl acetate in orange-yellow prismatic needles, m. p. 229—230° (yield, 28·7 g.; 83·3%) (Found: C, 53·0; H, 3·6; N, 11·55; Cl, 9·8. $C_{16}H_{12}O_5N_3Cl$ requires C, 53·1; H, 3·3; N, 11·6; Cl, 9·8%), soluble in alkalis with a deep reddish-violet colour.

1-*Hydroxy*-3-(5′-*chloro*-2′-*nitrophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* crystallised from ethyl acetate in fine yellow needles, m. p. 241—242° (yield, 26·3 g.; 72·8%, calculated on 17·25 g. of 5-chloro-*o*-nitroaniline) (Found: C, 53·2; H, 3·4; N, 11·55; Cl, 9·85%).

Derivatives of the 1-*Hydroxy*-3-*phenyl*-3 : 4-*dihydrophthalazine*-4-*acetic Acids.*—2′-*Nitro-compounds.* The *methyl* ester crystallised from methyl alcohol in yellow prismatic needles, m. p. 146° (Found: C, 59·7; H, 4·6; N, 12·5. $C_{17}H_{15}O_5N_3$ requires C, 59·8; H, 4·4; N, 12·3%), and the *ethyl* ester from aqueous ethyl alcohol in yellow prisms, m. p. 163° (Found:

C, 60·7; H, 4·9; N, 11·9. $C_{18}H_{17}O_5N_3$ requires C, 60·8; H, 4·8; N, 11·8%); both esters dissolve in boiling sodium carbonate and boiling sodium hydroxide solutions with a brownish-red and deep reddish-violet colour, severally. The *anilide* crystallised from ethyl acetate in orange-yellow prisms, m. p. 128° (Found: C, 65·5; H, 4·6; N, 13·75. $C_{22}H_{18}O_4N_4$ requires C, 65·7; H, 4·5; N, 13·9%), soluble in boiling sodium hydroxide solution with a magenta colour. The *N*-methyl ether, 1-*keto*-3-(2′-*nitrophenyl*)-2-*methyltetrahydrophthalazine*-4-*acetic acid* (cf. J., 1933, 1067), crystallised from methyl alcohol in yellow prisms, m. p. 207° (Found: C, 60·0; H, 4·5; N, 12·4. $C_{17}H_{15}O_5N_3$ requires C, 59·8; H, 4·4; N, 12·3%), soluble in cold dilute alkali solutions with a yellow colour. Its *methyl* ester crystallised from methyl alcohol in large orange-yellow prisms, m. p. 133—134° (Found: C, 60·7; H, 5·0; N, 11·8. $C_{18}H_{17}O_5N_3$ requires C, 60·8; H, 4·8; N, 11·85%), insoluble in alkalis and not hydrolysed as readily as the 4′- and the 3′-nitro-isomeride (J., 1933, 1069); it can also be prepared directly by methylating 1-hydroxy-3-(2′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid or its methyl ester with methyl sulphate in alkali hydroxide solution.

1-*Keto*-3-(2′-*aminophenyl*)-2-*methyltetrahydrophthalazine*-4-*acetic acid and its lactam.* A fine suspension of the preceding nitro-acid (5 g.) in glacial acetic acid (20 c.c.) and water (20 c.c.) was boiled, iron powder (3 g.) added slowly, the mixture boiled for 5 minutes and filtered hot, and the cold filtrate poured into water (100 c.c.); the product separated as a white flocculent precipitate (yield, 3 g.; 65·8%). Analyses of the amino-acid were variable owing to the ease of formation of the *lactam*, which was obtained readily by boiling a solution of the amino-acid in dilute hydrochloric acid until the separation of crystals ceased; it crystallised from alcohol in almost colourless, rectangular prisms, m. p. 315—317° (Found: C, 69·4; H, 5·1; N, 14·25. $C_{17}H_{15}O_2N_3$ requires C, 69·6; H, 5·1; N, 14·3%), insoluble in dilute mineral acids and alkalis.

2 : 5-*Diketo*-3-(2′-*nitrophenyl*)iso*indolinopyrazolidocoline* (VI). 1-Hydroxy-3-(2′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid (5 g.) was refluxed with acetic anhydride (25 c.c.) and pyridine (3 c.c.) for 15 hours, and the mixture poured into water; the product crystallised from glacial acetic acid in pale yellow prisms, m. p. and mixed m. p. 209° (yield, 2·5 g.; 52·9%). Pyridine is essential to this conversion, as unaltered 1-hydroxy-3-(2′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid was recovered after similar treatment with acetic anhydride, alone or in conjunction with glacial acetic acid.

4′-*Chloro*-2′-*nitro-compounds.* The *methyl* ester crystallised from methyl alcohol in yellow prismatic needles, m. p. 163—164° (Found: C, 54·3; H, 4·0; N, 11·1; Cl, 9·45. $C_{17}H_{14}O_5N_3Cl$ requires C, 54·3; H, 3·75; N, 11·2; Cl, 9·45%), and the *ethyl* ester from ethyl alcohol in yellow prisms, m. p. 145° (Found: C, 55·6; H, 4·4; N, 10·85; Cl, 9·0. $C_{18}H_{16}O_5N_3Cl$ requires C, 55·45; H, 4·1; N, 10·8; Cl, 9·1%); both esters dissolve in boiling sodium carbonate and warm sodium hydroxide solutions with a reddish-violet colour. The *anilide* crystallised from alcohol in golden-yellow plates of indefinite m. p., containing alcohol of crystallisation, and becoming opaque on exposure to air; recrystallisation from toluene gave pale yellow needles, m. p. 130° (Found: C, 60·3; H, 4·1; N, 12·95; Cl, 8·0. $C_{22}H_{17}O_4N_4Cl$ requires C, 60·5; H, 3·9; N, 12·8; Cl, 8·1%), soluble in boiling sodium hydroxide solution with a magenta colour, rapidly turning reddish-brown.

1-*Keto*-3-(4′-*chloro*-2′-*nitrophenyl*)-2-*methyltetrahydrophthalazine*-4-*acetic acid* crystallised from methyl alcohol in yellow prisms, m. p. 207° (Found: C, 54·4; H, 4·0; N, 11·4; Cl, 9·3. $C_{17}H_{14}O_5N_3Cl$ requires C, 54·3; H, 3·7; N, 11·2; Cl, 9·45%). Its *methyl* ester crystallised from methyl alcohol in large orange-yellow prisms, m. p. 129—130° (Found: C, 55·7; H, 4·2; N, 10·5. $C_{18}H_{16}O_5N_3Cl$ requires C, 55·5; H, 4·1; N, 10·8%).

1-*Keto*-3-(4′-*chloro*-2′-*aminophenyl*)-2-*methyltetrahydrophthalazine*-4-*acetic acid and its lactam.* The preceding nitro-acid (5 g.) was dissolved in dilute sodium hydroxide, hydrosulphite added to the reddish-violet solution at 50° until colourless, the mixture being kept alkaline throughout by the addition of sodium hydroxide, and filtered. The excess of alkali in the cold filtrate was neutralised; the *amino-acid*, which separated, crystallised from aqueous alcohol in almost colourless, flat, rectangular prisms, m. p. 225°, resolidifying and melting again at 300° (decomp.) (yield, 3·2 g.; 69·5%) (Found: C, 58·3; H, 4·8; N, 11·9. $C_{17}H_{16}O_3N_3Cl$ requires C, 59·0; H, 4·6; N, 12·15%), soluble in dilute mineral acids and alkalis, and diazotisable. The *lactam*, obtained by boiling a solution of the amino-acid in dilute hydrochloric acid, crystallised from alcohol in colourless prisms, m. p. 321° (Found: C, 62·1; H, 4·4. $C_{17}H_{14}O_2N_3Cl$ requires C, 62·3; H, 4·3%); it does not react with nitrous acid.

2 : 5-Diketo-3-(4′-chloro-2′-nitrophenyl)*iso*indolinopyrazolidocoline, obtained from 1-hydroxy-3-(4′-chloro-2′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid (5 g.) in a similar

manner to the unchlorinated compound, crystallised from glacial acetic acid in pale yellow prisms, m. p. and mixed m. p. 248—249° (yield, 1·75 g.; 36·9%).

5′-Chloro-2′-nitro-compounds. The *methyl* ester crystallised from methyl alcohol in yellow prisms, m. p. 163° (Found: C, 54·4; H, 3·6; N, 11·2; Cl, 9·45%), the *ethyl* ester from ethyl alcohol in yellow prisms, m. p. 153° (Found: C, 55·75; H, 4·1; N, 10·85; Cl, 9·25%), and the *anilide* from toluene in pale greenish-yellow needles, m. p. 223° (Found: C, 60·3; H, 3·85; N, 12·7; Cl, 8·2%).

1-*Keto*-3-(5′-*chloro*-2′-*nitrophenyl*)-2-*methyltetrahydrophthalazine*-4-*acetic acid* crystallised from toluene or aqueous acetic acid in orange-yellow prisms, m. p. 225° (Found: C, 54·1; H, 3·8; N, 11·4%). Its *methyl* ester, which was obtained even by crystallising the preceding acid from methyl alcohol, formed almost colourless plates, m. p. 143° (Found: C, 55·25; H, 4·0; N, 10·85%).

2 : 5-Diketo-3-(5′-chloro-2′-nitrophenyl)*iso*indolinopyrazolidocoline, obtained from 1-hydroxy-3-(5′-chloro-2′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid in the usual manner, crystallised from glacial acetic acid in pale yellow prisms, m. p. and mixed m. p. 209°.

1-*Hydroxy*-3-(2′-*amino*- or 4′-*chloro*-2′-*amino*-*phenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* (XIII) *and its lactam* (XIV). Iron powder (3 g.; 2·5 g.) was added gradually to a boiling solution of 1-hydroxy-3-(2′-nitro- or 4′-chloro-2′-nitro-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid (5 g.) in glacial acetic acid (25 c.c.; 50 c.c.) and water (25 c.c.), the mixture boiled for 10 minutes and filtered hot, and the cold filtrate poured into ice-water (100 c.c.). The precipitate was collected and extracted with cold dilute aqueous sodium carbonate, and the amino-acid precipitated carefully from the filtered solution with hydrochloric acid. Reduction with acid stannous chloride is less satisfactory. The lactam was best prepared by boiling a solution of the amino-acid (5 g.) in very dilute hydrochloric acid for 1 hour, colourless needles progressively separating.

1-*Hydroxy*-3-(2′-*aminophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* formed an almost colourless powder, m. p. 160°, resolidifying at 170°, and melting again at 293—294° (yield, 3·7 g.; 81·5%) (Found: C, 64·4; H, 5·1; N, 14·15. $C_{16}H_{15}O_3N_3$ requires C, 64·6; H, 5·05; N, 14·15%), soluble in dilute mineral acids and alkalis. All attempts to crystallise it gave the *lactam*, colourless needles, m. p. 293° (yield, 4 g.; 85·2%) (Found: C, 69·15; H, 4·7; N, 15·0. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·05%), insoluble in dilute mineral acids and sodium carbonate solution, but soluble in hot aqueous sodium hydroxide with a yellow colour and reprecipitated unaltered on acidification.

1-*Hydroxy*-3-(4′-*chloro*-2′-*aminophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid* formed an almost colourless powder, m. p. 214°, resolidifying at 220°, and melting again at 304° (yield, 3 g.; 65·9%) (Found: C, 58·5; H, 4·6; N, 12·35. $C_{16}H_{14}O_3N_3Cl$ requires C, 57·9; H, 4·2; N, 12·65%). The *lactam* crystallised in fine colourless needles, m. p. 304° (yield, 3·75 g.; 79·7%) (Found: C, 61·2; H, 4·0; N, 13·35; Cl, 11·1. $C_{16}H_{12}O_2N_3Cl$ requires C, 61·2; H, 3·8; N, 13·4; Cl, 11·3%).

1-*Hydroxy*-3-(5′-*chloro*-2′-*aminophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic acid lactam* crystallised from alcohol in colourless needles, m. p. 303—304° (Found: C, 60·9; H, 4·1; N, 13·2%).

Action of Sulphuric Acid on 1-*Hydroxy*-3-(2′-*aminophenyl*)-3 : 4-*dihydrophthalazine*-4-*acetic Acid.*—The acid (10 g.) or its lactam (9·4 g.) was refluxed with concentrated sulphuric acid (25 c.c.) and water (25 c.c.) for 1½ hours, the solution then diluted with water (100 c.c.) and filtered, and the cold filtrate almost neutralised with sodium carbonate. The product separated in orange needles which, recrystallised from water with addition of a little sulphuric acid, formed long straw-coloured needles (7 g.), softening at 95—100° and decomposing at 190—215°. This sulphate was basified by grinding with warm sodium carbonate solution; the substance then melted at 165°. It is soluble in water, but interference colours soon appear on the surface of the solution and eventually a dark precipitate separates; mere boiling with alcohol, nitrobenzene, pyridine, or aqueous sodium carbonate converts it into colourless needles which do not melt at 360°. On the other hand, it is soluble in mineral acids and alkalis, and is converted into *o*-benzylenebenziminazole (see below) by boiling with acid stannous chloride and tin. Although the substance thus has the properties of 2′-amino-3-phenylphthalaz-1-one, repeated analyses did not support this constitution and the results of the analysis of the product of an attempted acetylation also could not be interpreted.

4′-*Chloro*-2′-*amino*-3-*phenylphthalaz*-1-*one.*—1-Hydroxy-3-(4′-chloro-2′-aminophenyl)-3 : 4-dihydrophthalazine-4-acetic acid (20 g.) or its lactam (19 g.) was refluxed with dilute sulphuric acid (55 c.c., b. p. 140°) for 2 hours, and the base isolated as described for the preceding substance. 4′-*Chloro*-2′-*amino*-3-*phenylphthalaz*-1-*one* crystallised from alcohol in pale greenish-yellow

prisms, darkening at 200° and subliming slowly at 300—350° (yield, 12 g.; 73·2%) (Found: C, 61·9; H, 4·0; N, 15·6; Cl, 13·3; *M* in phenol, 284. $C_{14}H_{10}ON_3Cl$ requires C, 61·9; H, 3·7; N, 15·5; Cl, 13·1%; *M*, 271·5), soluble in dilute mineral acids with an orange colour and insoluble in alkalis. The *acetyl* derivative crystallised from aqueous alcohol or dilute acetic acid in pale yellow needles, m. p. 130—131° (Found: C, 61·6; H, 4·0. $C_{16}H_{12}O_2N_3Cl$ requires C, 61·2; H, 3·8%).

o-*Benzylene-* or 5-*Chloro*-o-*benzylene-benziminazole* (XV).—(*a*) Finely powdered 1-hydroxy-3-(2′-nitro- or 4′-chloro-2′-nitro-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) was added gradually to a boiling solution of stannous chloride (50 g.; 40 g.) in concentrated hydrochloric acid (120 c.c.; 100 c.c.). After refluxing (2 hours; 1 hour), granulated tin (30 g.; 20 g.) and concentrated hydrochloric acid (50 c.c.) were added to the solution, and the mixture was refluxed for a further 6 hours. The product separated progressively in colourless needles, which were filtered off and dissolved in boiling water containing a little hydrochloric acid (charcoal). Tin was removed with hydrogen sulphide, and the filtered solution basified with sodium carbonate (yield, 3 g.; 47·6% : 1 g.; 15%). (*b*) A solution of 1-hydroxy-3-(2′-amino- or 4′-chloro-2′-amino-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) in concentrated sulphuric acid (25 c.c.) and water (30 c.c.) was refluxed (2 hours; 1 hour), then zinc dust (6 g.; 12 g.) added gradually, and refluxing continued for 1 hour. The mixture was diluted with water (60 c.c.), boiled (charcoal), and filtered, the filtrate rendered strongly alkaline with ammonia with ice-cooling, and the product crystallised (yield, 4·4 g.; 63·4% : 4·9 g.; 67·5%).

o-Benzylenebenziminazole crystallised from aqueous alcohol in colourless, transparent, rectangular plates, m. p. 212° (Found: C, 81·6; H, 5·05; N, 13·4. Calc. for $C_{14}H_{10}N_2$: C, 81·55; H, 4·85; N, 13·6%), identical with that obtained by Thiele and Falk (*Annalen*, 1906, **347**, 125) by condensing *o*-phthalaldehyde with *o*-phenylenediamine. In confirmation it was oxidised in acetic acid solution by potassium permanganate to *o*-benzoylenebenziminazole, long, fine yellow needles, m. p. 211°, converted by dissolution in boiling sodium carbonate solution and acidification into phenylbenziminazole-*o*-carboxylic acid, colourless needles, m. p. 270°.

5-*Chloro*-o-*benzylenebenziminazole* crystallised from aqueous alcohol in colourless transparent plates, m. p. 242° (Found: N, 11·35. $C_{14}H_9N_2Cl$ requires N, 11·6%), identical with the product obtained by boiling a solution of *o*-phthalaldehyde (1 g.) in water (400 c.c.) with 4-chloro-*o*-phenylenediamine (1·5 g.), and then adding sodium carbonate.

5-Chloro-*o*-benzylenebenziminazole (2 g.) was dissolved in boiling glacial acetic acid (25 c.c.), 3% potassium permanganate solution added, and the mixture warmed on the water-bath until a faint pink colour persisted. The mixture was cooled in ice, sulphur dioxide introduced to dissolve the manganese dioxide, and the yellow precipitate filtered off.

5-*Chloro*-o-*benzoylenebenziminazole* (XVI) crystallised from alcohol or toluene in fine yellow needles, m. p. 156° (Found: N, 11·25. $C_{14}H_7ON_2Cl$ requires N, 11·0%).

5-*Chloro*-2-*phenylbenziminazole*-o-*carboxylic acid* (XVII), obtained by dissolving the preceding compound in boiling aqueous sodium carbonate and acidifying the cold colourless solution with acetic acid, crystallised from glacial acetic acid in small, colourless, prismatic needles, m. p. 285° (Found: N, 10·2. $C_{14}H_9O_2N_2Cl$ requires N, 10·3%).

2′-*Nitro-* or 4′-*Chloro*-2′-*nitro*-3-*phenylphthalaz*-1-*one* (XVIII).—A solution of 1-hydroxy-3-(2′-nitro- or 4′-chloro-2′-nitro-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) in concentrated sulphuric acid (25 c.c.) was diluted with water (30 c.c.) and refluxed for 2 hours; solution was then almost complete. The hot liquid was filtered through glass wool into ice (150 g.) and neutralised with sodium hydroxide with ice-cooling. The yellow precipitate was ground with cold dilute sodium carbonate solution, and the residue filtered off and washed with water.

2′-*Nitro*-3-*phenylphthalaz*-1-*one* crystallised from methyl alcohol in yellow prisms, m. p. 266° (yield, 0·4 g.; 4·9%) (Found: C, 63·1; H, 3·3; N, 16·05. $C_{14}H_9O_3N_3$ requires C, 62·9; H, 3·4; N, 15·7%), insoluble in sodium carbonate, but soluble in warm dilute sodium hydroxide solution with a purple colour; it was soluble in mineral acid, but no salt could be isolated from the solution. Reduction with aqueous sodium sulphide gave an intractable resin. The *picrate* crystallised from ethyl acetate or methyl alcohol in yellow prisms, m. p. 214—215° (Found: N, 16·75. $C_{20}H_{12}O_{10}N_6$ requires N, 16·9%).

4′-*Chloro*-2′-*nitro*-3-*phenylphthalaz*-1-*one* crystallised from methyl alcohol in yellow prismatic needles, m. p. 233° (yield, 3·8 g.; 45·6%) (Found: C, 53·1; H, 3·25; N, 14·2; Cl, 11·85. $C_{14}H_8O_3N_3Cl$ requires C, 53·4; H, 3·4; N, 13·9; Cl, 11·8%), soluble in warm dilute sodium

hydroxide solution with a magenta colour, and sparingly soluble in mineral acids. Reduction with aqueous sodium sulphide gave a resinous product, but reduction with zinc dust and dilute sulphuric acid gave 4′-chloro-*o*-benzylenebenziminazole.

Action of methyl sulphate. 2′-Nitro- or 4′-chloro-2′-nitro-3-phenylphthalaz-1-one (1 g.) in dry nitrobenzene (20 c.c.; 25 c.c.) was heated (110—120°; 140°), and methyl sulphate (0·6 g.) added slowly. After ¾ hour, the orange product was isolated (cf. J., 1928, 2554).

The 2′-*nitro*-derivative (XIX) crystallised from methyl alcohol in yellow needles, m. p. 135° (Found: C, 61·25; H, 4·9; N, 13·6. $C_{16}H_{15}O_4N_3$ requires C, 61·35; H, 4·8; N, 13·4%), and from ethyl alcohol in yellow needles, m. p. 150°. Both compounds are decomposed by heat, but without formation of 4-keto-1-methoxy-3-(2′-nitrophenyl)-3 : 4-dihydrophthalazine.

The 4′-*chloro*-2′-*nitro*-derivative (XIX) crystallised from methyl alcohol in yellow plates, m. p. 138° (Found: C, 55·6; H, 4·1; N, 11·6; OMe, 17·8. $C_{16}H_{14}O_4N_3Cl$ requires C, 55·25; H, 4·0; N, 12·1; OMe, 17·8%), and from ethyl alcohol in yellow plates, m. p. 110° (Found: C, 56·6; H, 4·5; N, 11·2. $C_{17}H_{16}O_4N_3Cl$ requires C, 56·4; H, 4·4; N, 11·6%). Both compounds are decomposed by heat, but without formation of 4-keto-1-methoxy-3-(4′-chloro-2′-nitrophenyl)-3 : 4-dihydrophthalazine.

2′-*Nitro- or* 4′-*Chloro*-2′-*nitro*-3-*phenyl*-4-*methylphthalaz*-1-*one*.—A solution of 1-hydroxy-3-(2′-nitro- or 4′-chloro-2′-nitro-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) in cold concentrated sulphuric acid (75 c.c.) was poured into ice-water (300 g.), and a solution of sodium dichromate (7 g.; 8·5 g.) in water (20 c.c.) added at 30° during ¼ hour with good agitation. After 3 hours' stirring, the mixture was left over-night at 30° and then neutralised with anhydrous sodium carbonate with ice-cooling. The yellow precipitate was washed with warm dilute sodium carbonate solution and then with water.

2′-*Nitro*-3-*phenyl*-4-*methylphthalaz*-1-*one* crystallised from alcohol in yellow prisms, m. p. 226° (decomp.) (yield, 7·5 g.; 87·3%) (Found: C, 64·3; H, 3·65; N, 15·0. $C_{15}H_{11}O_3N_3$ requires C, 64·1; H, 3·9; N, 14·9%), insoluble in sodium carbonate, but soluble in hot dilute sodium hydroxide solution with a brownish-red colour, and soluble in warm dilute mineral acids. The *picrate* crystallised from methyl alcohol in small yellow prisms, m. p. 217° (Found: N, 16·4. $C_{21}H_{14}O_{10}N_6$ requires N, 16·5%).

4′-*Chloro*-2′-*nitro*-3-*phenyl*-4-*methylphthalaz*-1-*one* crystallised from alcohol in greenish-yellow prismatic needles, m. p. 237° (yield, 6 g.; 68·7%) (Found: C, 57·3; H, 3·4; N, 13·7; Cl, 10·9. $C_{15}H_{10}O_3N_3Cl$ requires C, 57·1; H, 3·2; N, 13·3; Cl, 11·1%), soluble in hot sodium hydroxide solution with a dull purple colour, and soluble in dilute mineral acids. The *picrate* crystallised from alcohol in small, yellow, prismatic needles, m. p. 233° (Found: N, 15·4. $C_{21}H_{13}O_{10}N_6Cl$ requires N, 15·4%).

Action of methyl sulphate. A solution of 2′-nitro- or 4′-chloro-2′-nitro-3-phenyl-4-methylphthalaz-1-one (1 g.) in dry nitrobenzene (20 c.c.) was kept at 110—120°, and methyl sulphate (0·5 g.) added. After ¾ hour, the reddish-brown base was isolated, but it resisted crystallisation. It was insoluble in alkalis, but very soluble in dilute mineral acids, and the crude material contained a methoxy-group (Found: OMe, 10·0. $C_{16}H_{13}O_3N_3$ requires OMe, 10·5%) (Found: OMe, 8·0. $C_{16}H_{12}O_3N_3Cl$ requires OMe, 9·4%), but the properties were not those of a compound containing a reactive methylene group.

2′-*Amino*- or 4′-*Chloro*-2′-*amino*-3-*phenylphthalaz*-1-*one*-4-*acetic Acid Lactam* (XX).—A solution of 1-hydroxy-3-(2′-amino- or 4′-chloro-2′-amino-phenyl)-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) in concentrated sulphuric acid (50 c.c.; 150 c.c.) was poured on ice (250 g.; 500 g.), and a solution of sodium dichromate (12 g.; 10 g.) in water (50 c.c.) was added slowly to the resulting suspension at constant temperature (20°; 0°) with rapid stirring. The colourless precipitate dissolved at first with colour development (deep red; intense violet), the mixture then became orange-brown and an orange-brown precipitate separated, which was filtered off, ground with warm dilute sodium carbonate solution, and washed with hot water. The same product was obtained by using the amino-acid lactam (XIV) and carrying out the treatment with acid dichromate at 50°.

2′-*Amino*-3-*phenylphthalaz*-1-*one*-4-*acetic acid lactam* crystallised from dilute acetic acid in colourless prisms, or from glacial acetic acid in colourless fine needles, m. p. 302° (yield, 7·5 g.; 80·4%) (Found: C, 69·45; H, 4·1; N, 14·9. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·15%), sparingly soluble in alcohol or benzene. It is insoluble in sodium carbonate, but dissolves in warm dilute sodium hydroxide solution with an orange colour, and is soluble in moderately concentrated mineral acids.

4′-*Chloro*-2′-*amino*-3-*phenylphthalaz*-1-*one*-4-*acetic acid lactam* crystallised from dilute acetic acid in colourless needles, m. p. 314° (yield, 6 g.; 63·8%) (Found: C, 61·2; H, 3·35;

N, 13·8; Cl, 11·25. $C_{16}H_{10}O_2N_3Cl$ requires C, 61·6; H, 3·2; N, 13·5; Cl, 11·4%). It is similar in properties to the unchlorinated analogue, but when it is dissolved in hot dilute sodium sulphide solution and cooled, the amino-acid separates as a yellow precipitate, m. p. 287°, resolidifying and then melting at 314°, from which the lactam is regenerated on keeping or washing with dilute acetic acid.

2′-Amino- or *4′-Chloro-2′-amino-3-phenyl-4-methylphthalaz-1-one* (XXI).—(*a*) A solution of sodium sulphide crystals (10 g.) in water (10 c.c.; 25 c.c.) was added to a fine suspension of the preceding lactam (5 g.) in boiling water (200 c.c.; 50 c.c.). An orange solution was obtained in 1 minute and the product separated progressively on concentration of the solution (yield, 2·8 g.; 61·8% : 3·1 g.; 67·7%). Sodium hydroxide can be used in place of sodium sulphide, but is less satisfactory. (*b*) A solution of sodium sulphide crystals (10 g.) in water (20 c.c.) was added to a suspension of 2′-nitro- or 4′-chloro-2′-nitro-3-phenyl-4-methylphthalaz-1-one (5 g.) in boiling water (200 c.c.). A solution was obtained and then the amino-compound separated progressively on continued boiling (yield, 3·2 g.; 71·6% : 3 g.; 66·3%).

2′-Amino-3-phenyl-4-methylphthalaz-1-one crystallised from pyridine in pale yellow, prismatic needles, m. p. 218° (Found: C, 71·8; H, 5·3; N, 16·7. $C_{15}H_{13}ON_3$ requires C, 71·7; H, 5·2; N, 16·7%), insoluble in alkalis, but readily soluble in dilute mineral acids. The *acetyl* derivative crystallised from alcohol in pale pink prisms, m. p. 274° (Found: C, 69·6; H, 5·3; N, 14·15. $C_{17}H_{15}O_2N_3$ requires C, 69·6; H, 5·1; N, 14·3%).

4′-Chloro-2′-amino-3-phenyl-4-methylphthalaz-1-one crystallised from alcohol in pale yellow, prismatic needles, m. p. 257° (Found: C, 63·2; H, 4·3; N, 14·8; Cl, 12·4. $C_{15}H_{12}ON_3Cl$ requires C, 63·1; H, 4·2; N, 14·7; Cl, 12·4%). The *acetyl* derivative crystallised from aqueous alcohol in colourless plates, m. p. 296° (Found: C, 62·2; H, 4·6. $C_{17}H_{14}O_2N_3Cl$ requires C, 62·3; H, 4·3%), rapidly turning blue on exposure to light.

1-Keto-3-(2′-amino- or *4′-chloro-2′-amino-phenyl)-4-methyltetrahydrophthalazine* (XXII).—A solution of 2′-nitro- or 4′-chloro-2′-nitro-3-phenyl-4-methylphthalaz-1-one (5 g.) in concentrated sulphuric acid (25 c.c.; 20 c.c.) and water (30 c.c.) was boiled, and zinc dust (5 g.; 10 g.) added gradually during 10 minutes. Water (50 c.c.; 100 c.c.) was then added, the mixture boiled until almost colourless and filtered, the filtrate rendered strongly alkaline with ammonia with ice-cooling, and the product crystallised. It was also obtained by using the amino-compound in place of the nitro-compound in a similar reduction.

1-Keto-3-(2′-aminophenyl)-4-methyltetrahydrophthalazine crystallised from ethyl acetate in pale yellow prisms, m. p. 221° (yield, 1·5 g.; 33·3%) (Found: C, 71·4; H, 6·0; N, 16·4. $C_{15}H_{15}ON_3$ requires C, 71·15; H, 5·9; N, 16·6%), insoluble in alkalis, but soluble in dilute mineral acids.

1-Keto-3-(4′-chloro-2′-aminophenyl)-4-methyltetrahydrophthalazine (yield, 3 g.; 65·8%) crystallised from benzene in colourless needles, containing associated solvent and rapidly becoming opaque, m. p. 200° (Found: C, 63·0; H, 5·05; N, 15·4; Cl, 12·6; *M* in naphthalene, 270. $C_{15}H_{14}ON_3Cl$ requires C, 62·6; H, 4·9; N, 14·6; Cl, 12·3%; *M*, 287·5).

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