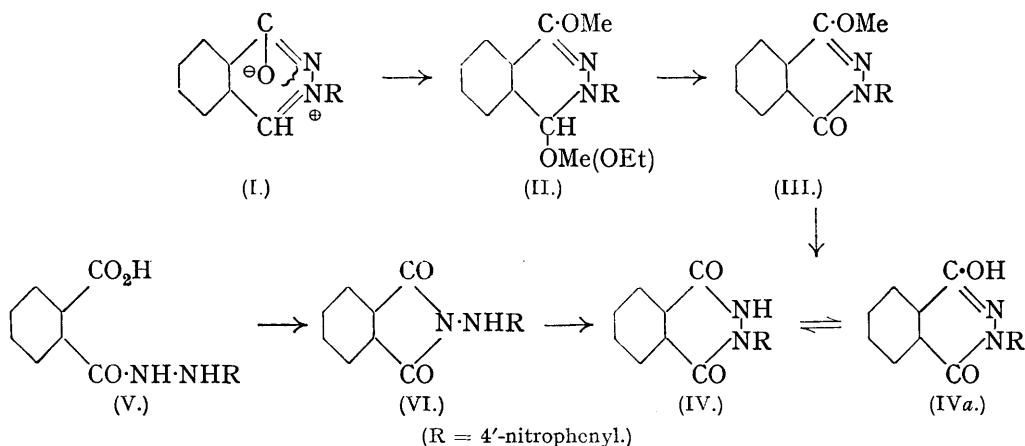


421. *A Reaction of Certain Diazosulphonates derived from β -Naphthol-1-sulphonic Acid. Part XIV. Preparation of 1 : 4-Diketo-3-(nitroaryl)tetrahydrophthalazines or 4-Keto-1-hydroxy-3-(nitroaryl)-3 : 4-dihydrophthalazines and Related Compounds.*

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THE methylated base formed by the interaction of 4'-nitro-3-phenylphthalaz-1-one (I) with methyl sulphate in nitrobenzene solution combines with alcohols, and the resulting compounds (II), heated at 110° and then at 140°, are converted into 4-keto-1-methoxy-3-(4'-nitrophenyl)-3 : 4-dihydrophthalazine (III), which is readily demethylated with form-

ation of 1 : 4-diketo-3-(4'-nitrophenyl)tetrahydrophthalazine (IV) (J., 1928, 2552). The same series of reactions occurs with 3'-nitro- and 4'-nitro-2'-methyl-3-phenylphthalaz-1-one (J., 1928, 2557; 1932, 474), but 2' : 6'-dichloro- and 2' : 6'-dibromo-4'-nitro-, 2'-chloro- and 2'-bromo-4'-nitro-, and 2'-nitro-3-phenylphthalaz-1-one do not give the corresponding 4-keto-1-methoxy-3-(nitroaryl)-3 : 4-dihydrophthalazines (J., 1931, 1076; 1932, 13; this vol., pp. 1135, 1807). As only three 1 : 4-diketo-3-(nitroaryl)tetrahydrophthalazines were obtained in the above way and as the course of the reactions leading to their formation was rather complicated, we have synthesised some of these compounds.



p-Nitrophenylhydrazine and phthalic anhydride in equimolecular proportion react in cold chloroform to form *o*-carboxybenzo-4'-nitrophenylhydrazide (V) almost quantitatively. It is converted by boiling nitrobenzene into phthalyl-4'-nitrophenylhydrazide (" α -phthalyl-*p*-nitrophenylhydrazine ") (VI), prepared by Bülow and Deseniss (*Ber.*, 1906, 39, 2281) from *p*-nitrophenylhydrazine (2 mols.) and phthalylacetylacetone (1 mol.) in glacial acetic acid solution. The same compound is also obtained directly in good yield by melting an intimate mixture of *p*-nitrophenylhydrazine (2 mols.) and phthalic anhydride (1 mol.). Phthalyl-4'-nitrophenylhydrazide dissolves immediately in cold ethyl-alcoholic sodium ethoxide and when this deep red solution of the sodium salt of *o*-carboxybenzo-4'-nitrophenylhydrazide is refluxed for 18 hours (cf. Chattaway and Tesh, J., 1920, 117, 719), conversion into 1 : 4-diketo-3-(4'-nitrophenyl)tetrahydrophthalazine (" β -phthalyl-*p*-nitrophenylhydrazine ") (IV), identical with that obtained from 4'-nitro-3-phenylphthalaz-1-one, occurs to the extent of about 30%.

Attempts to prepare (IV) by the oxidation of the closely related 4'-nitro-3-phenylphthalaz-4-one (J., 1928, 2555) with a variety of oxidising agents, and by the interaction of benzoyl- or acetyl-*p*-nitrophenylhydrazine and phthalic anhydride, were unsuccessful, although Hötte (*J. pr. Chem.*, 1886, 33, 99) obtained 1 : 4-diketo-3-phenyltetrahydrophthalazine from benzoylphenylhydrazine in the latter way.

1 : 4-Diketo-3-(4'-nitrophenyl)tetrahydrophthalazine, being similar in structure to phthalaz-1 : 4-dione or 1 : 4-dihydroxyphthalazine (J., 1933, 1331), may exist in the two tautomeric forms (IV) and (IVa). It appears probable from all its properties, however, that it actually reacts only as 4-keto-1-hydroxy-3-(4'-nitrophenyl)-3 : 4-dihydrophthalazine (IVa), but the nomenclature of (IV) is retained in the present communication to avoid confusion with previous papers in this series. We have prepared the *acetyl* derivative by the action of acetic anhydride on 1 : 4-diketo-3-(4'-nitrophenyl)tetrahydrophthalazine, and of acetyl chloride on its *silver* salt in dry benzene. It is readily hydrolysed and is undoubtedly 4-keto-1-acetoxy-3-(4'-nitrophenyl)-3 : 4-dihydrophthalazine. Unlike 4'-nitro-3-phenylphthalaz-1-one, 1 : 4-diketo-3-(4'-nitrophenyl)tetrahydrophthalazine does not react with methyl sulphate in dry nitrobenzene, and, although it forms a red sodium salt, a methyl ether is not obtained from this salt, aqueous methyl-alcoholic sodium hydroxide and methyl

iodide, either by refluxing or by heating in a sealed tube at 140—145°. On the other hand, refluxing the silver salt with methyl-alcoholic methyl iodide gives 4-keto-1-methoxy-3-(4'-nitrophenyl)-3 : 4-dihydrophthalazine, identical with that obtained from 4'-nitro-3-phenylphthalaz-1-one. This method of preparation and the ease of demethylation confirm that the compound is actually the *O*-ether.

As we were unable to prepare an *N*-ether in the above case or from any other 1 : 4-diketo-3-(nitroaryl)tetrahydrophthalazine that we have now made, we re-examined the alkylation of 1 : 4-diketo-3-phenyltetrahydrophthalazine, because Meyer and Hötte (*J. pr. Chem.*, 1887, **35**, 287) described a "β-phthalylphenylhydrazine ethyl ether," m. p. 105—106°, which they regarded as the *N*-ether, as did also Chattaway and Tesh (*loc. cit.*, p. 713), who gave m. p. 109°. We prepared this compound by refluxing 1 : 4-diketo-3-phenyltetrahydrophthalazine with alcoholic potassium hydroxide and ethyl iodide, and also by refluxing the silver salt with ethyl-alcoholic ethyl iodide. It is readily de-ethylated and there is no doubt that it is actually the *O*-ether, 4-keto-1-ethoxy-3-phenyl-3 : 4-dihydrophthalazine. Consequently, an aryl residue in position 3 has the same effect as an alkyl group in preventing the formation of an *N*-ether subsequently, for 1-hydroxy-3-methylphthalaz-4-one also only forms an *O*-ether (*J.*, 1933, 1333).

The synthetic method described above for the preparation of 1 : 4-diketo-3-(nitroaryl)-tetrahydrophthalazines has limitations: although the use of *m*- and *o*-nitro-, 4-nitro-2-methyl-, 2-chloro- and 2-bromo-4-nitro-, and 2 : 6-dichloro- and 2 : 6-dibromo-4-nitro-phenylhydrazine in place of *p*-nitrophenylhydrazine gave in all cases the corresponding *o*-carboxybenzonitroarylhydrazides, from which the phthalylnitroarylhydrazides were obtained similarly, only in the first three of these cases could the latter be converted into the 1 : 4-diketo-3-(nitroaryl)tetrahydrophthalazines. Under no conditions were we able to prepare any of the halogeno-4'-nitro-analogues by this method, for refluxing the phthalylhalogeno-4'-nitrophenylhydrazides with alcoholic sodium ethoxide or amyloxide for 60 hours merely gave the corresponding *o*-carboxybenzophenylhydrazides, and heating with an alcoholic sodium alkoxide and an alkyl iodide in a sealed tube at 170° was also ineffective. The influence of substituents on the ease of formation of such 1 : 4-diketo-3-(nitroaryl)tetrahydrophthalazines as could be prepared by this method is in the order 3-nitro- > 4-nitro- > 4-nitro-2-methyl- > 2-nitro-compounds. In fact, 1 : 4-diketo-3-(2'-nitrophenyl)-tetrahydrophthalazine is obtained only in traces, whereas the 3'-nitro-analogue is the only nitro-compound of those examined that is formed to some extent directly by refluxing the *o*-carboxybenzonitrophenylhydrazide with nitrobenzene, and the yield obtained from phthalyl-3'-nitrophenylhydrazide by refluxing with alcoholic sodium ethoxide approaches the theoretical. These observations are in agreement with those made during the preparation of mononitro-3-phenyl-1-methylphthalaz-4-ones from acetophenone-*o*-carboxylic acid and *o*-, *m*-, and *p*-nitrophenylhydrazine, where again the order of the ease of ring closure is *m*- > *p*- > *o*- > (*J.*, 1931, 1920); other cases of the influence of substituents on the formation of six-membered rings are being investigated.

Finally, a simple and almost generally applicable method permitted the preparation of 1 : 4-diketo-3-(nitroaryl)tetrahydrophthalazines that we could not obtain in any other way. It had already been found that 1-hydroxy-3-(nitroaryl)-3 : 4-dihydrophthalazine-4-acetic acids are converted by boiling dilute sulphuric acid into nitro-3-arylphthalaz-1-ones (*J.*, 1928, 2250), whereas they are converted by cold acid dichromate into nitro-3-aryl-4-methylphthalaz-1-ones, one of which was also obtained by the use of a warm solution of potassium permanganate in commercial pyridine (*J.*, 1931, 1070). The new reaction consists in the vigorous oxidation of hot aqueous suspensions of the hydroxy-compounds with excess of potassium permanganate, whereby 1 : 4-diketo-3-(nitroaryl)tetrahydrophthalazines are obtained, usually in good yield. The only exception noted was that of the 2' : 6'-dibromo-4'-nitro-compound, with which the reaction could not be controlled and there was always considerable elimination of bromine, so that only a little 1 : 4-diketo-3-(2' : 6'-dibromo-4'-nitrophenyl)tetrahydrophthalazine was isolated. On the other hand, the reaction proceeded normally with the 2'-bromo-4'-nitro-analogue without elimination of bromine. Methylation did not occur when the silver salts of the 1 : 4-diketo-3-(halogeno-4'-nitrophenyl)tetrahydrophthalazines were refluxed with methyl-alcoholic methyl iodide,

but the 4-keto-1-methoxy-3-(halogeno-4'-nitrophenyl)-3:4-dihydrophthalazines were obtained by using dry benzene in place of methyl alcohol.

EXPERIMENTAL.

Details of the quantities and procedure used in the preparation of the 4'-nitro-compounds, and their properties, apply also to the corresponding compounds described subsequently, unless otherwise stated.

o-Carboxybenzo-4'-nitrophenylhydrazide (V).—Solutions of *p*-nitrophenylhydrazine (5 g. in 500 c.c.) and of phthalic anhydride (5 g. in 150 c.c.) in chloroform were mixed and the pale yellow solid formed was filtered off after 12 hours. *o*-Carboxybenzo-4'-nitrophenylhydrazide crystallised from glacial acetic acid in almost colourless needles, m. p. 241—245° (yield, 8.5 g.; 86.4%, calculated on the *p*-nitrophenylhydrazine) (Found: C, 55.5; H, 3.9; N, 14.0. $C_{14}H_{11}O_5N_3$ requires C, 55.8; H, 3.65; N, 13.95%), which became light brown on keeping. It is unnecessary to dissolve the reactants separately, and in a second experiment in which the solids were added to the above chloroform filtrate and left over-night, the yield was almost quantitative. The hydrazide is sparingly soluble in benzene, chloroform, or alcohol, but soluble in cold dilute sodium carbonate solution with a deep red colour, and is reprecipitated unaltered on acidification.

Phthalyl-4'-nitrophenylhydrazide (VI).—(1) An intimate mixture of *p*-nitrophenylhydrazine (10 g.) and phthalic anhydride (5 g.) was melted by heating to 150° during 10 minutes. After cooling, the mass was powdered and extracted with warm alcohol, and the residue crystallised (yield, 7 g.; 73.2%, calculated on the phthalic anhydride). (2) *o*-Carboxybenzo-4'-nitrophenylhydrazide (25 g.) was refluxed with nitrobenzene (150 c.c.) for 1 hour (yield, 20.2 g.; 85.9%). Phthalyl-4'-nitrophenylhydrazide crystallised from glacial acetic acid in very pale yellow, transparent plates, m. p. 248° (Found: C, 59.5; H, 3.0; N, 14.8. Calc. for $C_{14}H_9O_4N_3$: C, 59.35; H, 3.2; N, 14.8%), sparingly soluble in benzene or chloroform, but more soluble in alcohol. It is insoluble in dilute mineral acids, but dissolves gradually in boiling dilute sodium carbonate solution with a red colour and the *o*-carboxybenzo-hydrazide is precipitated on acidification.

1:4-Diketo-3-(4'-nitrophenyl)tetrahydrophthalazine (IV).—(a) Phthalyl-4'-nitrophenylhydrazide (20 g.) was warmed with sodium (2 g.) in dry alcohol (100 c.c.) and the deep red solution was refluxed for 18 hours, poured on ice (500 g.), and acidified with hydrochloric acid. The precipitate was collected and extracted with cold dilute sodium carbonate solution, and the extract acidified (yield, 6.1 g.; 30.5%). (b) Powdered potassium permanganate (15 g.) was added in small portions during 10 minutes to a suspension of 1-hydroxy-3-(4'-nitrophenyl)-3:4-dihydrophthalazine-4-acetic acid (10 g.) in water (100 c.c.) at 70°; the reaction was vigorous. The mixture was finally boiled and filtered, and the yellow filtrate diluted with water (100 c.c.), cooled, and acidified with hydrochloric acid (yield, 6.2 g.; 71.6%). 1:4-Diketo-3-(4'-nitrophenyl)tetrahydrophthalazine crystallised from glacial acetic acid in almost colourless needles, m. p. 307° (Found: C, 59.4; H, 3.3; N, 15.0. Calc. for $C_{14}H_9O_4N_3$: C, 59.35; H, 3.2; N, 14.8%), identical with the compound obtained from 4'-nitro-3-phenylphthalaz-1-one (J., 1928, 2554). Attempts to prepare the 2'-bromo-derivative (p. 1813) by the action of bromine on a glacial acetic acid or chloroform solution of 1:4-diketo-3-(4'-nitrophenyl)tetrahydrophthalazine in presence of anhydrous aluminium bromide were unsuccessful. The silver salt, prepared *via* the ammonium salt, crystallised in small yellow needles (yield, 94.3%) (Found: Ag, 27.9. $C_{14}H_8O_4N_3Ag$ requires Ag, 27.7%).

4-Keto-1-acetoxy-3-(4'-nitrophenyl)-3:4-dihydrophthalazine. (i) The preceding silver salt (1 g.) was refluxed with acetyl chloride (0.4 c.c.) and dry benzene (20 c.c.) for $\frac{1}{2}$ hour, and then part of the benzene was removed (yield, 0.7 g.; 84%). (ii) 1:4-Diketo-3-(4'-nitrophenyl)-tetrahydrophthalazine (1 g.) was boiled with acetic anhydride (10 c.c.) for 3 minutes and then cooled (yield, 0.8 g.; 69.7%). 4-Keto-1-acetoxy-3-(4'-nitrophenyl)-3:4-dihydrophthalazine crystallised from benzene in pale yellow prisms, m.p. 222° (Found: C, 59.3; H, 3.5. $C_{16}H_{11}O_5N_3$ requires C, 59.1; H, 3.4%), insoluble in alkalis, and hydrolysed readily by boiling aqueous alcohol containing a little hydrochloric acid to 1:4-diketo-3-(4'-nitrophenyl)tetrahydrophthalazine.

4-Keto-1-methoxy-3-(4'-nitrophenyl)-3:4-dihydrophthalazine (III).—The above silver salt (2 g.) was refluxed with methyl iodide (0.6 c.c.) and dry methyl alcohol (20 c.c.) for $\frac{1}{4}$ hour, the hot mixture filtered, the residue extracted with boiling methyl alcohol, and the combined filtrates concentrated. The methoxy-compound crystallised in almost colourless needles, m. p.

199° (yield, 1.2 g.; 78.8%), identical with the compound obtained from 4'-nitro-3-phenylphthalaz-1-one (*loc. cit.*).

o-Carboxybenzo-3'-nitrophenylhydrazide separated from the chloroform solution in small, pale yellow prisms, m. p. 193—194° with ring closure, resolidifying, and melting again at 217—219° (yield, 9.75 g.; 99.1%) (Found : C, 55.3; H, 3.8; N, 14.0%), soluble in dilute sodium carbonate solution with a yellow colour.

Phthalyl-3'-nitrophenylhydrazide.—The preceding hydrazide (20 g.) was refluxed with nitrobenzene (75 c.c.) for 1 hour; the crystals which separated on cooling consisted of two portions, one insoluble and the other soluble in cold dilute sodium carbonate solution.

Phthalyl-3'-nitrophenylhydrazide (the former) crystallised from glacial acetic acid in pale yellow prisms, m.p. 227—228° (yield, 11.1 g.; 59%) (Found : C, 59.2; H, 3.4; N, 15.0%). The soluble portion was 1 : 4-diketo-3-(3'-nitrophenyl)tetrahydrophthalazine, m. p. 280° (yield, 3 g.; 16%), which is not formed by boiling phthalyl-3'-nitrophenylhydrazide with nitrobenzene, but is formed directly from the *o*-carboxybenzohydrazide.

1 : 4-Diketo-3-(3'-nitrophenyl)tetrahydrophthalazine [Method (a), 5 hours (yield, 18 g.; 90%). Method (b) (yield, 5.8 g.; 67%)] crystallised from alcohol in colourless needles, m. p. 280° (Found : C, 59.2; H, 3.3; N, 15.0. Calc. : C, 59.35; H, 3.2; N, 14.8%), identical with the compound obtained from 3'-nitro-3-phenylphthalaz-1-one [J., 1928, 2563]. The silver salt crystallised in small, pale yellow prisms (Found : Ag, 28.0%).

4-Keto-1-acetoxy-3-(3'-nitrophenyl)-3 : 4-dihydrophthalazine [Method (i) (yield, 0.6 g.; 72.2%). Method (ii) (yield, 0.7 g.; 61%)] crystallised from dry benzene in colourless needles, m.p. 164° (Found : N, 13.1. C₁₆H₁₁O₅N₃ requires N, 12.9%).

4-Keto-1-methoxy-3-(3'-nitrophenyl)-3 : 4-dihydrophthalazine crystallised from alcohol in long, colourless, prismatic needles, m. p. 182° (yield, 1.1 g.; 72.2%), identical with the compound obtained from 3'-nitro-3-phenylphthalaz-1-one (*loc. cit.*).

o-Carboxybenzo-2'-nitrophenylhydrazide separated from the chloroform (400 c.c.) solution in orange-yellow needles, m. p. 290—294° (yield, 9.75 g.; 99.1%) (Found : C, 55.9; H, 3.8; N, 14.1%). It can be recrystallised from chloroform without ring closure and dissolves in cold dilute sodium carbonate solution with a bluish-violet colour.

Phthalyl-2'-nitrophenylhydrazide.—Method (1) (yield, 6.5 g.; 68%). The yield obtained when *o*-carboxybenzo-2'-nitrophenylhydrazide (3 g.) was dissolved in boiling glacial acetic acid was 2.7 g. (95.7%). *Phthalyl-2'-nitrophenylhydrazide* crystallised from glacial acetic acid in pale yellow prisms, m. p. 293—294° (Found : C, 59.3; H, 3.2; N, 15.1%), soluble in boiling dilute sodium carbonate solution with a violet colour owing to regeneration of the original hydrazide.

1 : 4-Diketo-3-(2'-nitrophenyl)tetrahydrophthalazine.—(a) *Phthalyl-2'-nitrophenylhydrazide* (15 g.) was refluxed with sodium (1.5 g.) in dry alcohol (200 c.c.) for 40 hours (yield, 0.1 g.; 0.7%). Method (b) (yield, 4 g.; 46.2%). 1 : 4-Diketo-3-(2'-nitrophenyl)tetrahydrophthalazine crystallised from glacial acetic acid in pale yellow prisms, m. p. 293—294° (Found : C, 59.4; H, 3.3; N, 14.4%), soluble in dilute sodium carbonate solution with a yellow colour. The silver salt crystallised in yellow needles.

4-Keto-1-methoxy-3-(2'-nitrophenyl)-3 : 4-dihydrophthalazine.—Dry benzene (20 c.c.) was used in place of methyl alcohol, and the mixture refluxed for ½ hour. The crystals which separated from the cold filtrate were ground with dilute aqueous ammonia. 4-Keto-1-methoxy-3-(2'-nitrophenyl)-3 : 4-dihydrophthalazine crystallised from benzene or methyl alcohol in almost colourless, prismatic needles, m.p. 176—177° (yield, 0.3 g.; 19.7%) (Found : C, 60.5; H, 4.0; N, 13.8; OMe, 10.9. C₁₅H₁₁O₄N₃ requires C, 60.6; H, 3.7; N, 14.1; OMe, 10.4%), demethylated by heating with hydrobromic acid and a little glacial acetic acid in an open tube. It could not be obtained from 2'-nitro-3-phenylphthalaz-1-one (this vol., p. 1807).

o-Carboxybenzo-4'-nitro-2'-methylphenylhydrazide.—5-Nitro-*o*-tolylhydrazine (10 g.), phthalic anhydride (9.5 g.), and cold chloroform (400 c.c.) were used. The hydrazide separated in small, pale yellow needles, m.p. 219° (yield, 18.5 g.; 98.1%) (Found : C, 56.9; H, 4.3; N, 13.1. C₁₅H₁₃O₅N₃ requires C, 57.15; H, 4.1; N, 13.3%).

Phthalyl-4'-nitro-2'-methylphenylhydrazide.—The preceding hydrazide (20 g.) was refluxed with glacial acetic acid (200 c.c.) until it dissolved; the solution was boiled for ½ hour and cooled. *Phthalyl-4'-nitro-2'-methylphenylhydrazide* crystallised in almost colourless needles, m.p. 228° (yield, 15 g.; 79.5%) (Found : C, 60.3; H, 3.6; N, 13.9. C₁₅H₁₁O₄N₃ requires C, 60.6; H, 3.7; N, 14.1%).

1 : 4-Diketo-3-(4'-nitro-2'-methylphenyl)tetrahydrophthalazine.—(a) *Phthalyl-4'-nitro-2'-methylphenylhydrazide* (15 g.) was refluxed with sodium (1.5 g.) in dry alcohol (150 c.c.) for

26 hours, poured on ice (200 g.), and acidified. The precipitate was boiled with glacial acetic acid to convert any *o*-carboxybenzo-hydrazide into phthalyl-4'-nitro-2'-methylphenylhydrazide, cooled, the crystals ground with cold dilute sodium carbonate, and the filtered solution acidified (yield, 4 g.; 26.7%). Method (b) (yield, 5.5 g.; 63.2%). 1 : 4-Diketo-3-(4'-nitro-2'-methylphenyl)tetrahydrophthalazine crystallised from alcohol in colourless hexagonal prisms, m. p. 271° (Found : C, 60.6; H, 3.9; N, 14.3. Calc. for $C_{15}H_{11}O_4N_3$: C, 60.6; H, 3.7; N, 14.1%), identical with the compound obtained from 4'-nitro-3-phenyl-2'-methylphthalaz-1-one (J., 1932, 480). The silver salt crystallised in small yellow needles (Found : Ag, 27.0. $C_{15}H_{10}O_4N_3Ag$ requires Ag, 26.7%).

4-Keto-1-methoxy-3-(4'-nitro-2'-methylphenyl)-3 : 4-dihydrophthalazine crystallised from glacial acetic acid in colourless needles, m.p. 185° (yield, 0.9 g.; 58.4%), identical with the compound obtained from 4'-nitro-3-phenyl-2'-methylphthalaz-1-one (*loc. cit.*).

o-Carboxybenzo-2'-chloro-4'-nitrophenylhydrazide.—2-Chloro-4-nitrophenylhydrazine, m. p. 143° (4.7 g.) (Votoček and Rys, *Coll. Czech. Chem. Comm.*, 1929, 1, 346), phthalic anhydride (4 g.), and cold chloroform (250 c.c.) were used. This gave a precipitate (3.5 g.), but by using the filtrate for a second preparation the yield was increased (7.5 g.; 89.2%). The hydrazide separated in colourless needles, m. p. 270—275° (Found : C, 50.0; H, 3.2. $C_{14}H_{10}O_5N_3Cl$ requires C, 50.1; H, 3.0%).

Phthalyl-2'-chloro-4'-nitrophenylhydrazide.—The preceding hydrazide (7 g.) was refluxed with nitrobenzene (50 c.c.) for 1 hour. Phthalyl-2'-chloro-4'-nitrophenylhydrazide crystallised from glacial acetic acid in colourless silky needles, m. p. 267° (yield, 6 g.; 90.6%) (Found : C, 52.9; H, 2.7; Cl, 10.9. $C_{14}H_8O_4N_3Cl$ requires C, 52.9; H, 2.5; Cl, 11.2%).

1 : 4-Diketo-3-(2'-chloro-4'-nitrophenyl)tetrahydrophthalazine, prepared only by method (b), crystallised from glacial acetic acid in colourless needles, m. p. 271—272° (yield, 2.1 g.; 23.9%) (Found : C, 52.5; H, 2.5; Cl, 11.5. $C_{14}H_8O_4N_3Cl$ requires C, 52.9; H, 2.5; Cl, 11.2%). The silver salt crystallised in small yellow needles.

4-Keto-1-methoxy-3-(2'-chloro-4'-nitrophenyl)-3 : 4-dihydrophthalazine.—Dry benzene (20 c.c.) was used in place of methyl alcohol, and the mixture refluxed with methyl iodide (1 c.c.) for $\frac{1}{2}$ hour. The filtrate was concentrated and the solid which separated was washed with dilute aqueous ammonia. The dihydrophthalazine crystallised from benzene in pale yellow prisms, m. p. 193—194° (yield, 0.6 g.; 38.4%) (Found : C, 54.5; H, 3.0. $C_{15}H_{10}O_4N_3Cl$ requires C, 54.3; H, 3.0%). It could not be obtained from 2'-chloro-4'-nitro-3-phenylphthalaz-1-one (J., 1932, 17).

o-Carboxybenzo-2'-bromo-4'-nitrophenylhydrazide.—2-Bromo-4-nitrophenylhydrazine, m. p. 144° (5.8 g.) (Ciusa and Mega, *Gazzetta*, 1928, 58, 83), phthalic anhydride (4 g.) and cold chloroform (250 c.c.) were used. This gave a precipitate (3 g.), but by using the filtrate for a second preparation the yield was theoretical (9.5 g.). The hydrazide separated in colourless needles, m. p. 232° with ring closure, resolidifying, and melting again at 280—282° (Found : C, 43.95; H, 2.9; Br, 20.75. $C_{14}H_{10}O_5N_3Br$ requires C, 44.2; H, 2.6; Br, 21.05%).

Phthalyl-2'-bromo-4'-nitrophenylhydrazide.—The preceding hydrazide (9.5 g.) was refluxed with nitrobenzene (40 c.c.) for 1 hour (yield 8 g.; 88.4%), or was boiled (2 g.) with acetic anhydride (2 c.c.) for 2 hours (yield, 1.2 g.; 63%); boiling with acetic anhydride for only 1 minute gave a yellow modification of the same m. p. (cf. Chattaway and Wünsch, J., 1911, 99, 2256). Phthalyl-2'-bromo-4'-nitrophenylhydrazide crystallised from glacial acetic acid in colourless needles, m. p. 282—283° (Found : C, 46.5; H, 2.4; Br, 22.0. $C_{14}H_8O_4N_3Br$ requires C, 46.4; H, 2.2; Br, 22.1%).

1 : 4-Diketo-3-(2'-bromo-4'-nitrophenyl)tetrahydrophthalazine, prepared only by method (b), crystallised from glacial acetic acid in almost colourless needles, m. p. 273—274° (yield, 5.3 g.; 59.4%) (Found : C, 46.4; H, 2.5; N, 11.1; Br, 22.0. $C_{14}H_8O_4N_3Br$ requires C, 46.4; H, 2.2; N, 11.6; Br, 22.1%).

4-Keto-1-methoxy-3-(2'-bromo-4'-nitrophenyl)-3 : 4-dihydrophthalazine, prepared as described for the chloro-analogue (methyl iodide 1.5 c.c.), crystallised from benzene in small, pale yellow prisms, m. p. 167—168° (yield, 0.7 g.; 43.7%) (Found : C, 48.1; H, 2.8. $C_{15}H_{10}O_4N_3Br$ requires C, 47.9; H, 2.7%). It could not be obtained from 2'-bromo-4'-nitro-3-phenylphthalaz-1-one (this vol., p. 1137).

2 : 6-Dichloro-4-nitrophenylhydrazine.—A cold solution of 2 : 6-dichloro-4-nitroaniline (21 g.) in concentrated sulphuric acid (150 c.c.) was diazotised by rapid addition to a mixture of sodium nitrite (9 g.) and ice (400 g.) and the excess of nitrous acid was destroyed with urea. In the preparation of the four halogeno-4-nitrophenylhydrazines used in this work, it is advantageous to add the diazo-solution to the acid stannous chloride, because, if the order is reversed, the precipitate of the stannichloride soon becomes resinous and intractable. The cold diazo-solution,

therefore, was added during 1 hour with good agitation to a solution of stannous chloride (45 g.) in concentrated hydrochloric acid (60 c.c.) at -10° , the precipitate filtered off and dissolved in boiling water (300 c.c.) (charcoal), and tin removed with hydrogen sulphide. After boiling, sodium chloride was added until the hydrochloride began to separate in colourless crystals, which were collected and dissolved in water, and the base liberated at 60° by addition of sodium acetate. 2 : 6-Dichloro-4-nitrophenylhydrazine crystallised from alcohol in yellow needles, m. p. 133° (yield, 8 g.; 35.5%) (Found: C, 32.5; H, 2.4; N, 18.8; Cl, 31.8. $C_6H_5O_2N_3Cl_2$ requires C, 32.4; H, 2.25; N, 18.9; Cl, 32.0%). The benzaldehyde derivative crystallised from alcohol in orange needles, m. p. 153° (Found: C, 50.45; H, 3.0; Cl, 23.1. $C_{13}H_9O_2N_3Cl_2$ requires C, 50.3; H, 2.9; Cl, 22.9%).

o-Carboxybenzo-2' : 6'-dichloro-4'-nitrophenylhydrazide.—2 : 6-Dichloro-4-nitrophenylhydrazine (5.5 g.), phthalic anhydride (4 g.), and cold chloroform (250 c.c.) were used. The hydrazide crystallised from alcohol in colourless needles, m. p. 192° (yield, 9 g.; 98.2%) (Found: C, 45.4; H, 2.3. $C_{14}H_9O_5N_3Cl_2$ requires C, 45.4; H, 2.4%).

Phthalyl-2' : 6'-dichloro-4'-nitrophenylhydrazide, prepared by refluxing the preceding hydrazide (5 g.) with nitrobenzene (30 c.c.) for 1 hour, crystallised from glacial acetic acid in almost colourless needles, m. p. 202° (yield, 4 g.; 84.1%) (Found: C, 47.7; H, 2.2; Cl, 20.5. $C_{14}H_7O_4N_3Cl_2$ requires C, 47.7; H, 2.0; Cl, 20.2%).

1 : 4-Diketo-3-(2' : 6'-dichloro-4'-nitrophenyl)tetrahydrophthalazine, prepared only by method (b), crystallised from glacial acetic acid in colourless needles, m. p. $309-310^{\circ}$ (yield, 4.5 g.; 50.6%) (Found: C, 47.6; H, 2.2; N, 11.6; Cl, 20.6. $C_{14}H_7O_4N_3Cl_2$ requires C, 47.7; H, 2.0; N, 11.9; Cl, 20.2%).

4-Keto-1-methoxy-3-(2' : 6'-dichloro-4'-nitrophenyl)-3 : 4-dihydrophthalazine, prepared as described for the monochloro-analogue, crystallised from methyl alcohol in almost colourless prisms, m. p. $178-179^{\circ}$ (yield, 0.5 g.; 31.3%) (Found: C, 49.3; H, 2.8; Cl, 19.5. $C_{15}H_9O_4N_3Cl_2$ requires C, 49.2; H, 2.5; Cl, 19.4%). It could not be obtained from 2' : 6'-dichloro-4'-nitro-3-phenylphthalaz-1-one (J., 1931, 1076).

2 : 6-Dibromo-4-nitrophenylhydrazine, prepared from 2 : 6-dibromo-4-nitroaniline (30 g.) as described above for the 2 : 6-dichloro-analogue (yield, 10 g.; 31.7%), crystallised from alcohol in two modifications, both m. p. $135-136^{\circ}$: cooling a hot solution rapidly gave pale yellow needles, turning red at 110° , and gradually converted into deep red prisms by heating at 80° or by leaving in alcohol for several weeks (Found in yellow needles: C, 23.4; H, 1.7; Br, 51.8. $C_6H_5O_2N_3Br_2$ requires C, 23.15; H, 1.6; Br, 51.4%). The benzaldehyde derivative crystallised from alcohol in orange needles, m. p. $168-169^{\circ}$ (Found: C, 39.4; H, 2.3; Br, 39.8. $C_{13}H_9O_2N_3Br_2$ requires C, 39.1; H, 2.25; Br, 40.1%).

o-Carboxybenzo-2' : 6'-dibromo-4'-nitrophenylhydrazide.—2 : 6-Dibromo-4-nitrophenylhydrazine (6 g.), phthalic anhydride (3 g.), and cold chloroform (200 c.c.) were used. The hydrazide crystallised from alcohol in colourless needles, m. p. 200° with ring closure, resolidifying, and melting again at 227° (yield, 8.5 g.; 96%) (Found: C, 36.7; H, 2.0; Br, 34.7. $C_{14}H_9O_5N_3Br_2$ requires C, 36.6; H, 2.0; Br, 34.85%).

Phthalyl-2' : 6'-dibromo-4'-nitrophenylhydrazide, prepared as described for the dichloro-analogue, crystallised from glacial acetic acid in very pale yellow prisms, m. p. 230° (yield, 3.7 g.; 77%) (Found: C, 38.05; H, 1.8; Br, 35.9. $C_{14}H_7O_4N_3Br_2$ requires C, 38.1; H, 1.6; Br, 36.3%).

1 : 4-Diketo-3-(2' : 6'-dibromo-4'-nitrophenyl)tetrahydrophthalazine was prepared only by method (b), accompanied by considerable elimination of bromine. The product crystallised from alcohol or glacial acetic acid in pale yellow needles, m. p. $235-260^{\circ}$ (Found: Br, 19.8%). Repeated fractional crystallisation from alcohol and glacial acetic acid in one experiment gave a small quantity of very pale yellow needles, m. p. $327-329^{\circ}$ (Found: C, 38.0; H, 1.7; Br, 36.0. $C_{14}H_7O_4N_3Br_2$ requires C, 38.1; H, 1.6; Br, 36.3%), soluble in dilute sodium carbonate solution with a yellow colour.

1 : 4-Diketo-3-phenyltetrahydrophthalazine.—*o*-Carboxybenzophenylhydrazide (30 g.), prepared from phenylhydrazine (16.5 g.), phthalic anhydride (30 g.), and cold chloroform (650 c.c.) (yield, 34.5 g.; 88.2%), was refluxed with nitrobenzene (100 c.c.) for 2 hours. The crystals obtained on cooling were separated by extraction with dilute sodium carbonate solution into the insoluble phthalylphenylhydrazide ("α-phthalylphenylhydrazine"), m. p. $178-179^{\circ}$ (yield, 9 g.; 32.3%), and the soluble 1 : 4-diketo-3-phenyltetrahydrophthalazine ("β-phthalylphenylhydrazine"), which crystallised from glacial acetic acid in a mixture of colourless, transparent, rectangular prisms and straw-coloured, opaque, irregular prisms, m. p. and mixed m. p. $212-213^{\circ}$ (yield, 12 g.; 43%).

4-Keto-1-ethoxy-3-phenyl-3 : 4-dihydrophthalazine.—(a) The silver salt of 1 : 4-diketo-3-phenyltetrahydrophthalazine (3.5 g.) was refluxed with ethyl iodide (4 g.) and dry ethyl alcohol (50 c.c.) for 1 hour. The product (yield, 0.9 g.; 33.3%) after crystallisation successively from benzene, light petroleum, and ether six times, formed colourless needles, m. p. 108—109° (Found : C, 72.2; H, 5.3; N, 10.5. $C_{16}H_{14}O_2N_2$ requires C, 72.2; H, 5.25; N, 10.5%). (b) 1 : 4-Diketo-3-phenyltetrahydrophthalazine (5 g.), dissolved in 5% alcoholic potassium hydroxide (100 c.c.), was refluxed with ethyl iodide (10 g.) for 2 hours; the solution was concentrated (30 c.c.), diluted with water (50 c.c.), and extracted with ether; the product (yield, 2.9 g.; 51.9%) isolated from the extract was crystallised as above. Method (b) was used by Meyer and Hötte (*loc. cit.*), who described the compound as the *N*-ethyl ether, m. p. 105—106°. Both specimens, however, are identical in all respects, are equally readily de-ethylated by heating with hydrobromic acid and a little acetic acid at 100° in an open tube, and the de-ethylated product, m. p. 212—213°, is in each case completely soluble in dilute sodium carbonate solution. The compound, therefore, is the *O*-ethyl ether.

4-Keto-1-methoxy-3-phenyl-3 : 4-dihydrophthalazine, prepared by both methods (a) and (b) above, crystallised in colourless needles, m. p. 109—111° (Found : C, 71.4; H, 4.8. $C_{15}H_{12}O_2N_2$ requires C, 71.4; H, 4.75%), and was readily demethylated.

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