

93. *A Reaction of Certain Diazosulphonates derived from β -Naphthol-1-sulphonic Acid. Part XX. The Stabilities of Acrylic Acid Derivatives from Sodium 1-Arylazo- β -naphthaquinone-1-sulphonate and its Derivatives, and an Investigation of derived isoIndolinones.*

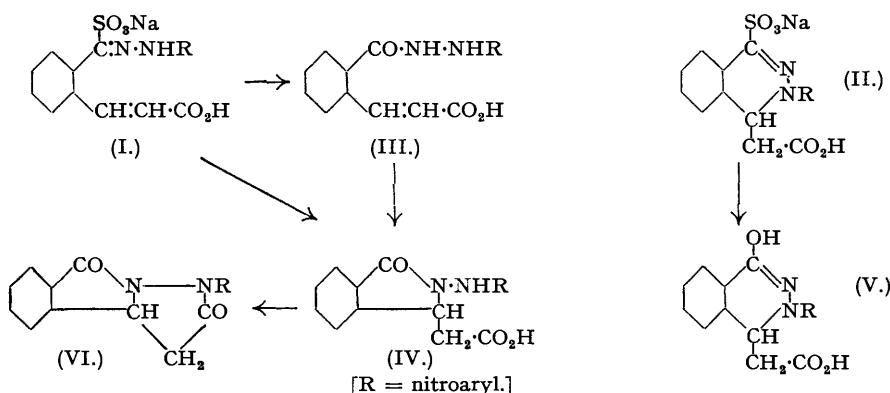
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Following the work of Rowe and Cross (preceding paper), it is shown that restricted action of sodium hydroxide on sodium 1-(4'-nitroarylazo)- β -naphthaquinone-1-sulphonate affords some sodium benzaldehyde 4'-nitroarylhydrazone- ω -sulphonate-2- β -acrylic acid (I). The amount of the latter formed is determined by hydrolysis to 2-(4'-nitroarylamino)isoindolinone-3-acetic acid (IV). The ease of opening of the sodium 1-(nitroarylazo)- β -naphthaquinone-1-sulphonates to give (I) is in the order R = 3'-nitro- > 4'-nitro- > 4'-nitro-2'-methyl > 2'-halogeno-4'-nitro- > 2': 6'-dibromo-4'-nitro- > 2': 6'-dichloro-4'-nitro-phenyl. Once formed, (I) is most stable when R = 2': 6'-dihalogeno-4'-nitrophenyl, and the stability decreases in the reverse order to that given above; finally where R = 3'-nitrophenyl, there is immediate formation of sodium hydrogen 3-(3'-nitrophenyl)-3:4-dihydrophthalazine-1-sulphonate-4-acetate [as (II)] and no trace of the isomeride.

IN Part XIII of this series (*J.*, 1935, 1796), it was shown that limited action of aqueous sodium hydroxide on sodium 1-(2'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate gave sodium benzaldehyde 2'-nitrophenylhydrazone- ω -sulphonate-2- β -acrylic acid (I; R = 2'-nitrophenyl), whereas further action of sodium hydroxide gave sodium hydrogen 3-(2'-nitrophenyl)-3:4-dihydrophthalazine-1-sulphonate-4-acetate (II, R = 2'-nitrophenyl). Boiling dilute hydrochloric acid hydrolyses these sodium salts, (I) giving a mixture of benzo-2'-nitrophenylhydrazide-2- β -acrylic acid (III; R = 2-nitrophenyl) and 2-(2'-nitrophenylamino)isoindolinone-3-acetic acid (IV; R = 2'-nitrophenyl), whereas (II) gives 1-hydroxy-3-(2'-nitrophenyl)-3:4-dihydrophthalazine-4-acetic acid (V; R = 2'-nitrophenyl) (see p. 469).

Compounds of type (II) and (V) had been obtained previously where R = 4'- and 3'-nitrophenyl, 4'-nitro-2'-methylphenyl, and 2'-halogeno- and 2': 6'-dihalogeno-4'-nitrophenyl (*J.*, 1926, 699; 1928, 2558; 1931, 1078; 1932, 13, 476; 1935, 1135), but the existence of an intermediate compound of type (I) had only been postulated. The actual isolation of such a compound therefore was limited to derivatives from *o*-nitroaniline and its homologues (see also *J.*, 1936,

1098). An observation by Rowe and Cross (preceding paper), however, that it is possible to isolate 3-(4'-nitro-2'-methoxyphenylamino)isoindolinone-3-acetic acid (IV; R = 4'-nitro-2'-



methoxyphenyl) as one of the hydrolysis products of the mixture of sulphonic acids obtained by restricted action of aqueous sodium hydroxide on sodium 1-(4'-nitro-2'-methoxybenzeneazo)- β -naphthaquinone-1-sulphonate, led to an investigation of compounds (I), where R did not contain an *o*-nitro-substituent. It has now been found that compounds (I) are more stable than was anticipated. A point of interest is the influence of the substituents in the phenyl ring on the ease of opening of the β -naphthaquinone derivative and the stability of the resulting acrylic acid compound (I) to sodium hydroxide. Conditions of reaction in each case were kept as strictly comparable as possible.

Sodium 1-(4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate reacts with sodium hydroxide after several hours to give sodium hydrogen 3-(4'-nitrophenyl)-3:4-dihydrophthalazine-1-sulphonate-4-acetate (II; R = 4'-nitrophenyl), together with a little 4'-nitrobenzeneazo- β -naphthol (*loc. cit.*). When the action in sodium hydroxide was limited to 15 seconds, however, there was an increase in the yield of azo- β -naphthol derivative corresponding to the stability of the above β -naphthaquinone compound. The resultant mixture of sodium sulphonates was hydrolysed and examined. Comparable results were obtained whether or not the sodium salts were isolated before hydrolysis. Fractional crystallisation of the hydrolysis product from ethyl acetate showed that it was mainly (V; R = 4'-nitrophenyl), with some (IV; R = 4'-nitrophenyl). No derivative of type (III) was detected either in this case or in any other described in this paper.

2-(4'-Nitrophenylamino)isoindolinone-3-acetic acid (IV; R = 4'-nitrophenyl) was isolated most readily from the more soluble fractions by conversion into 2:5-diketo-3-(4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 4'-nitrophenyl) by refluxing with acetic anhydride and a little pyridine for 5 minutes, followed by hydrolysis with warm concentrated sulphuric acid, boiling aqueous-alcoholic sodium hydroxide, or, preferably, boiling hydrochloric and acetic acids. The maximum yield of (IV; R = 4'-nitrophenyl) (13%) was obtained after interaction of sodium 1-(4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate and sodium hydroxide for 15 seconds.

Derivatives from 2-chloro-4-nitroaniline were studied in detail because the chlorine atom in the 2'-position increased the stability of (I; R = 2'-chloro-4'-nitrophenyl) to sodium hydroxide, and enabled it to be isolated without any (II; R = 2'-chloro-4'-nitrophenyl). When a mixture of sodium sulphonates was obtained, its composition was determined by hydrolysis to compounds (IV and V; R = 2'-chloro-4'-nitrophenyl) and separation of the latter. The maximum yield of (IV) (*viz.* 61%), was obtained after interaction of the β -naphthaquinone compound in sodium hydroxide for 45 seconds. It was converted into 2:5-diketo-3-(2'-chloro-4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 2'-chloro-4'-nitrophenyl) similarly to the 4'-nitro-analogue. Compound (VI; R = 2'-chloro-4'-nitrophenyl) was reduced to the corresponding amino-compound by iron and aqueous acetic acid.

2-(2'-Chloro-4'-aminophenylamino)isoindolinone-3-acetic acid (IV; R = 2'-chloro-4'-aminophenyl) was obtained by reducing the nitro-compound (IV) in various ways and was also prepared from (VI; R = 2'-chloro-4'-aminophenyl) by the rapid action of aqueous-alcoholic potassium hydroxide at 80°. It was reconverted into the anhydro-derivative (VI; R = 2'-chloro-4'-aminophenyl) by refluxing with phosphorus trichloride and toluene, but was

unchanged by refluxing with concentrated hydrochloric acid or aqueous sulphuric acid, or by heating with concentrated hydrochloric acid at 200°.

Sodium 1-(2': 6'-dichloro-4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate was relatively very stable to aqueous sodium hydroxide, being unchanged after 15 seconds reaction, and, even after 2 hours, only about half of it was attacked. It is the most stable of the analogues examined. The chlorine atoms in the 2': 6'-positions also resulted in increased stability of (I; R = 2': 6'-dichloro-4'-nitrophenyl), which was obtained in maximum amount after interaction of the above naphthaquinone derivative with aqueous sodium hydroxide for 10 minutes. The sodium sulphonate was hydrolysed to give (IV; R = 2': 6'-dichloro-4'-nitrophenyl) (39%). Compound (II; R = 2': 6'-dichloro-4'-nitrophenyl) was present in the mixed sodium sulphonates after reaction in the sodium hydroxide for 20 minutes, and with more prolonged reaction the proportion of it increased rapidly, with consequent diminution in amount of the isomeride (I).

Sodium 1-(2'-bromo-4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate possessed similar stability in aqueous sodium hydroxide to the 2'-chloro-4'-nitro-compound, but was much less stable than the 2': 6'-dichloro-4'-nitro-analogue. After reacting for 15 seconds in sodium hydroxide, the β -naphthaquinone compound gave a mixture of (I and II; R = 2'-bromo-4'-nitrophenyl) in the approximate proportions of 1 : 2.

Bromine atoms in the 2': 6'-positions rendered sodium 1-(2': 6'-dibromo-4'-nitrophenyl)- β -naphthaquinone-1-sulphonate almost as stable to sodium hydroxide as the 2': 6'-dichloro-analogue, and the resultant compound (I; R = 2': 6'-dibromo-4'-nitrophenyl) was somewhat less stable than the 2': 6'-dichloro-compound.

Sodium 1-(4'-nitro-2'-methylphenyl)- β -naphthaquinone-1-sulphonate approximated in stability in sodium hydroxide to the 2'-chloro-4'-nitro-analogue, but the resultant compound (I; R = 4'-nitro-2'-methylphenyl) was less stable than the 2'-bromo-4'-nitro-analogue, although much more stable than the 4'-nitro-derivative.

The behaviour of sodium 1-(3'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate was exceptional. The ring was opened extremely readily and even after the minimum time for mixing with the sodium hydroxide (15 seconds), very little 3'-nitrobenzeneazo- β -naphthol was formed. There was immediate formation of (II; R = 3'-nitrophenyl) with no trace of the isomeride (I) as was proved by hydrolysis and fractional crystallisation of the product, which consisted of (V; R = 3'-nitrophenyl) only.

EXPERIMENTAL.

2-(4'-Nitrophenylamino)isoindolinone-3-acetic Acid (IV; R = 4'-nitrophenyl).—*p*-Nitroaniline (55 g.) was converted into sodium 1-(4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate (Rowe *et al.*, *J.*, 1926, 699). An ice-cold suspension of the latter compound was stirred for 15 minutes and then added to a solution of sodium hydroxide (80 g.) in water (160 c.c.). The deep crimson solution was well stirred and, after 15 seconds, was rapidly acidified with concentrated hydrochloric acid, ethyl acetate being used to control frothing. The mixture was made alkaline with sodium carbonate, boiled, and filtered from 4'-nitrobenzeneazo- β -naphthol (20 g.; 17.2%), and hydrochloric acid (300 c.c.) was added gradually to the boiling filtrate until the evolution of sulphur dioxide had ceased and reddish-brown crystals had formed (99 g.; 75.9%). The product was washed with hot water, dried, and fractionally crystallised from ethyl acetate. Compound (V; R = 4'-nitrophenyl) predominated. Each successive crop of crystals was tested by mixed m. p. determinations; the more soluble fractions consisted of (IV; R = 4'-nitrophenyl), which crystallised from ethyl acetate in pale yellow prisms, m. p. 254° (17 g.; 13%) (Found: C, 58.3; H, 4.0; N, 12.6. C₁₆H₁₃O₅N₃ requires C, 58.7; H, 4.0; N, 12.8%).

2-(4'-Nitrophenylamino)isoindolinone-3-acetic acid dissolves in cold aqueous sodium carbonate and hydroxide with orange and orange-red colours, respectively.

The proportions of the compounds isolated under varied conditions and calculated as percentages on the weight of *p*-nitroaniline are tabulated below:

Time in sodium hydroxide (seconds).	Weight of sodium hydroxide used (g.).	4'-Nitrobenzeneazo- β -naphthol.	Compound (IV). (R = 4'-Nitrophenyl.)	Compound (V).
8	80	25	12	54
15	80	17	13	63
15	40	65	10	21

The methyl ester of compound (IV; R = 4'-nitrophenyl) crystallised from methyl alcohol in pale yellow needles, m. p. 166° (Found: C, 60.2; H, 4.55; N, 11.9. C₁₇H₁₅O₅N₃ requires C, 59.8; H, 4.4; N, 12.3%).

2: 5-Diketo-3-(4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 4'-nitrophenyl).—Finely powdered 2-(4'-nitrophenylamino)isoindolinone-3-acetic acid (10 g.) was boiled gently for 5 minutes with acetic anhydride (40 c.c.) and pyridine (2 c.c.) and cooled. The crystalline precipitate crystallised from acetic acid in almost colourless, prismatic needles, m. p. 250° (9.1 g.; 96.3%) (Found: C, 61.9; H, 3.6; N, 13.4. C₁₆H₁₁O₄N₃ requires C, 62.1; H, 3.55; N, 13.6%), insoluble in cold aqueous alkalis and dilute

mineral acids. Conversion of (IV; R = 4'-nitrophenyl) into the above *anhydro*-derivative (VI) was utilised as a means of separating it from the isomeride (V; R = 4'-nitrophenyl); the latter remains in acetic anhydride as the soluble acetyl derivative, and (VI) is deposited, indicating the amount of (IV) present in the mixture. The *anhydro*-compound is hydrolysed to (IV; R = 4'-nitrophenyl) by three methods.

(a) Concentrated hydrochloric acid (50 c.c.) was added to a boiling solution of (VI; R = 4'-nitrophenyl) (10 g.) in acetic acid (200 c.c.) during 15 minutes. After refluxing for a further 15 minutes, the mixture was concentrated to 100 c.c. and diluted with water (100 c.c.), and the precipitate was collected (9.7 g.; 91.7%).

(b) (VI; R = 4'-nitrophenyl) (10 g.) was added to a solution of potassium hydroxide (2.5 g.) in water (5 c.c.) and alcohol (25 c.c.), and the mixture was boiled until completely dissolved (3 min.), then cooled, diluted, and acidified (8.8 g.; 83.2%).

(c) (VI; R = 4'-nitrophenyl) (10 g.) was warmed with concentrated sulphuric acid (50 c.c.) at 70° for 3 minutes and the red solution poured on ice (400 g.). The precipitate was collected and extracted with aqueous sodium carbonate, and the solution acidified (7.4 g.; 70%).

2:5-Diketo-3-(4'-aminophenyl)isoindolinopyrazolidocoline.—Iron powder (2 g.) was added gradually to a boiling solution of finely powdered 2:5-diketo-3-(4'-nitrophenyl)isoindolinopyrazolidocoline (2.5 g.) in acetic acid (100 c.c.) and water (25 c.c.). After boiling until dilution with water gave no precipitate (10 minutes), the mixture was filtered (charcoal), cooled, partially neutralised with aqueous sodium carbonate, and shaken with excess of sodium chloride, and the liquid decanted and allowed to stand. Straw-coloured prisms of the amino-compound separated progressively and were filtered off after 0.5 hour, as subsequently a dark tar formed which hindered purification. This procedure was necessary in order to obtain the pure *base*, which crystallised from ethyl acetate in almost colourless prisms, m. p. 213—215° (1.6 g.; 70.9%) (Found: C, 68.95; H, 4.8; N, 15.1. $C_{16}H_{18}O_5N_3$ requires C, 68.8; H, 4.65; N, 15.05%). The *acetyl* derivative crystallised from alcohol in almost colourless needles, m. p. 263—264° (Found: C, 66.95; H, 5.0; N, 12.9. $C_{18}H_{20}O_5N_3$ requires C, 67.3; H, 4.7; N, 13.1%).

2-(2'-Chloro-4'-nitrophenylamino)isoindolinone-3-acetic Acid (IV; R = 2'-chloro-4'-nitrophenyl).—An aqueous suspension of sodium 1-(2'-chloro-4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate was prepared from 2-chloro-4-nitroaniline (52 g.) (Rowe and Dunbar, *J.*, 1932, 13), stirred, ice-cold, for 20 minutes, then added to sodium hydroxide (60 g.) in water (120 c.c.), stirred vigorously, and acidified after 45 seconds. After being made alkaline with sodium carbonate and filtered from 2'-chloro-4'-nitrobenzeneazo- β -naphthol (32 g.; 32.4%), the filtrate (charcoal) was cooled and carefully acidified with hydrochloric acid. Salt was added and, by next day, orange-yellow needles had formed (87 g.; 64.6%), consisting of sodium benzaldehyde 2'-chloro-4'-nitrophenylhydrazone- ω -sulphonate-2- β -acrylic acid, together with a little free sulphonic acid which could not be removed. The sodium sulphonate crystallised from ethyl acetate in golden-yellow needles, m. p. 225—227°, and the barium salt separated from hot water in similar coloured leaflets, m. p. 247°, but neither gave satisfactory analytical results, this being probably partially due to association of water. Hydrolysis of the sodium salt (25 g.) with boiling dilute hydrochloric acid (10 hours) gave 2-(2'-chloro-4'-nitrophenylamino)isoindolinone-3-acetic acid, which crystallised from ethyl acetate or aqueous acetic acid in pale orange prisms, m. p. 254° (18.5 g.; 91.6%) (Found: C, 52.9; H, 3.6; N, 11.05; Cl, 9.5. $C_{15}H_{15}O_5N_3Cl$ requires C, 53.1; H, 3.3; N, 11.6; Cl, 9.8%), soluble in aqueous sodium carbonate and hydroxide with orange and orange-red colours, respectively. Microscopical examination of these crystals, sprinkling on filter paper moistened with aqueous sodium carbonate, or fractional crystallisation from acetic acid (cf. Rowe *et al.*, *J.*, 1935, 1800), failed to reveal the presence of any benzo-2'-chloro-4'-nitrophenylhydrazone-2- β -acrylic acid (III; R = 2'-chloro-4'-nitrophenyl). When the time of reaction in the sodium hydroxide was varied, the following percentage yields were isolated:

Time in sodium hydroxide.	2'-Chloro-4'-nitrobenzeneazo- β -naphthol.	Compound (IV). (R = 2'-Chloro-4'-nitrophenyl.)	Compound (V).
15 seconds	66	23	nil
30 seconds	48	47	nil
45 seconds	32	61	nil
1 minute	28	59	6
2.5 minutes	24	43	18
10 minutes	27	7	54

The *methyl* ester of (IV; R = 2'-chloro-4'-nitrophenyl) crystallised from methyl alcohol in pale yellow needles, m. p. 144° (2.3 g.; 88.6%) (Found: C, 54.8; H, 4.25; N, 11.0; Cl, 9.4. $C_{17}H_{14}O_5N_3Cl$ requires C, 54.3; H, 3.7; N, 11.2; Cl, 9.45%).

2:5-Diketo-3-(2'-chloro-4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 2'-chloro-4'-nitrophenyl).—(i) Prepared similarly to the 4'-nitro-analogue, this *base* crystallised from acetic acid in pale yellow, prismatic needles, m. p. 244° (9 g. from 10 g. of acid) (Found: C, 56.5; H, 3.2; Cl, 10.0. $C_{15}H_{10}O_4N_3Cl$ requires C, 55.9; H, 2.9; Cl, 10.3%), insoluble in cold aqueous alkalis, but soluble in hot sodium hydroxide with a deep crimson colour. It is hydrolysed best by method (c) used for the 4'-nitro-analogue (see above) (9.5 g. from 10 g.; 90.4%). (ii) 2-(2'-Chloro-4'-nitrophenylamino)isoindolinone-3-acetic acid (2 g.) was refluxed with phosphorus trichloride (3 c.c.) and dry toluene (400 c.c.) for 1 hour, and the mixture filtered and concentrated (1.5 g.; 78.9%).

2:5-Diketo-3-(2'-chloro-4'-aminophenyl)isoindolinopyrazolidocoline (VI; R = 2'-chloro-4'-aminophenyl).—Iron powder (4 g.) was added to a solution of (VI; R = 2'-chloro-4'-nitrophenyl) (5 g.) in acetic acid (160 c.c.) and water (40 c.c.), and the mixture boiled for 15 minutes, water (20 c.c.) being added during the reduction. The mixture was filtered (charcoal); the *amino*-compound which separated on standing crystallised from aqueous acetic acid in almost colourless, prismatic needles, m. p. 240° (3.9 g.; 85.5%) (Found: C, 61.0; H, 3.9; N, 13.0; Cl, 11.7. $C_{16}H_{12}O_5N_3Cl$ requires C, 61.2; H, 3.8; N, 13.4; Cl, 11.3%), or from aqueous alcohol in similar crystals containing 1 mol. of H_2O (Found: C, 59.6; H, 3.7; N, 12.8; Cl, 11.2. $C_{16}H_{12}O_6N_3Cl$ requires C, 59.7; H, 4.0; N, 13.1; Cl, 11.0%).

It was stable to a hot solution of chromium trioxide in acetic acid. The *acetyl* derivative crystallised from alcohol in straw-coloured plates, m. p. 245° (Found: C, 60.5; H, 4.0; N, 11.8; Cl, 10.1. $C_{16}H_{14}O_3N_3Cl$ requires C, 60.8; H, 3.9; N, 11.8; Cl, 10.0%).

2-(2'-Chloro-4'-aminophenylamino)isoindolinone-3-acetic Acid (IV; R = 2'-chloro-4'-aminophenyl).—(a) Sodium hydrosulphite (20 g.) was added to a solution of 2-(2'-chloro-4'-nitrophenylamino)isoindolinone-3-acetic acid (10 g.) in sodium hydroxide (10 g.), water (300 c.c.) and alcohol (10 c.c.) at 80°, until the solution became pale yellow (alkaline). The mixture was filtered (charcoal), cooled, and carefully acidified with acetic acid until a precipitate began to form. The first deposits were rejected and the filtered solution allowed to stand; the amino-compound separated as an almost colourless amorphous precipitate (7.2 g.; 78.5%).

(b) Finely divided (IV; R = 2'-chloro-4'-nitrophenyl) (10 g.) was added rapidly to a boiling solution of stannous chloride (50 g.) in concentrated hydrochloric acid (125 c.c.). After boiling for 3 minutes, crystals began to separate. Concentrated hydrochloric acid (150 c.c.) was added and the mixture left over-night. The precipitate was filtered off, washed with cold concentrated hydrochloric acid and extracted with aqueous sodium carbonate, and the alkaline filtrate was neutralised with acetic acid (6.7 g.; 73.1%).

(c) Iron powder (6 g.) was added in portions, during 10 minutes, to a boiling solution of (IV; R = 2'-chloro-4'-nitrophenyl) (10 g.) in acetic acid (100 c.c.) and water (25 c.c.). The mixture was filtered (charcoal) and added to hot water (1 l.) to precipitate the base (4.8 g.; 52.3%).

(d) 2:5-Diketo-3-(2'-chloro-4'-aminophenyl)isoindolinopyrazolidocoline (VI; R = 2'-chloro-4'-aminophenyl) (10 g.) was dissolved in potassium hydroxide (7.5 g.), water (15 c.c.), and alcohol (75 c.c.) at 80° and the solution neutralised immediately with acetic acid (9 g.; 85%).

2-(2'-Chloro-4'-aminophenylamino)isoindolinone-3-acetic acid crystallised from aqueous alcohol in straw-coloured needles, m. p. 156–157° (decomp.), containing 1 mol. of H_2O (Found: C, 54.6; H, 4.9; N, 11.7; Cl, 10.1. $C_{16}H_{14}O_3N_3Cl \cdot H_2O$ requires C, 54.95; H, 4.6; N, 12.0; Cl, 10.2%), removed by heating at 80° (Found: C, 57.2; H, 4.5; Cl, 10.2. $C_{16}H_{14}O_3N_3Cl$ requires C, 57.9; H, 4.2; Cl, 10.7%). It decomposes on prolonged boiling with organic solvents. On refluxing (5 g.) with boiling acetic anhydride (20 c.c.) and pyridine (1 c.c.), it was converted into 2:5-diketo-3-(2'-chloro-4'-acetamido)isoindolinopyrazolidocoline, m. p. and mixed m. p. 245° (5.1 g.; 95.1%).

When a finely divided suspension of the base (IV; R = 2'-chloro-4'-aminophenyl) (2.5 g.) in cold dry toluene (150 c.c.) was refluxed, with stirring, and phosphorus trichloride (3 c.c.) added slowly, the suspension became gradually crystalline. After 10 minutes it was filtered off and extracted with cold aqueous sodium carbonate, and the residue crystallised from aqueous acetic acid in almost colourless, prismatic needles, m. p. and mixed m. p. 240°, of 2:5-diketo-3-(2'-chloro-4'-aminophenyl)isoindolinopyrazolidocoline.

2-(2'-Chloro-4'-aminophenylamino)isoindolinone-3-acetic acid was unchanged after refluxing with concentrated hydrochloric acid for 5 hours, by heating with the same reagent at 200° for 5 hours, or by refluxing with aqueous sulphuric acid, b. p. 140°, for 2 hours.

2-(2':6'-Dichloro-4'-nitrophenylamino)isoindolinone-3-acetic Acid (IV; R = 2':6'-dichloro-4'-nitrophenyl).—2:6-Dichloroaniline (51.5 g.) was converted into sodium 1-(2':6'-dichloro-4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate (Rowe, Dunbar, and Williams, *J.*, 1931, 1078), but excess of sodium β -naphthol-1-sulphonate was avoided, whereby subsequent filtration of the diazosulphonate, hitherto unduly slow with derivatives of dihalogeno-substituted anilines, was made easier.

The suspension of the β -naphthaquinone compound in sodium carbonate was stirred at 0° for 15 minutes, then added to sodium hydroxide (50 g.) in water (100 c.c.) and the deep crimson solution acidified after 10 minutes. 2':6'-Dichloro-4'-nitrobenzeneazo- β -naphthol (45 g.; 50%) was filtered off and the sodium sulphate in the filtrate was hydrolysed by boiling with hydrochloric acid. 2-(2':6'-Dichloro-4'-nitrophenylamino)isoindolinone-3-acetic acid crystallised from acetic acid or ethyl acetate in pale yellow prisms, m. p. 203° (39 g.; 39.6%) (Found: C, 48.95; H, 3.1; N, 10.6; Cl, 18.45. $C_{16}H_{11}O_3N_3Cl_2$ requires C, 48.5; H, 2.8; N, 10.6; Cl, 17.9%), soluble in cold aqueous alkalis with a crimson colour.

Fractional crystallisation from ethyl acetate revealed no trace of 1-hydroxy-3-(2':6'-dichloro-4'-nitrophenyl)-3:4-dihydrophthalazine-4-acetic acid (V; R = 2':6'-dichloro-4'-nitrophenyl), which was detected only after reaction of the β -naphthaquinone compound with sodium hydroxide for 20 minutes or longer, followed by hydrolysis in the usual manner. The following percentage yields were isolated after various periods of reaction in the sodium hydroxide:

Time in sodium hydroxide.	2':6'-Dichloro-4'-nitrobenzeneazo- β -naphthol.	Compound (IV). (R = 2':6'-Dichloro-4'-nitrophenyl.)	Compound (V).
15 seconds	96	nil	nil
1 minute	70	21	nil
10 minutes	50	39	nil
20 minutes	52	35	7
2 hours	48	9	30

The *methyl* ester of (IV; R = 2':6'-dichloro-4'-nitrophenyl) crystallised from methyl alcohol in pale yellow needles, m. p. 180° (Found: Cl, 16.85. $C_{17}H_{13}O_3N_3Cl_2$ requires Cl, 17.3%).

2:5-Diketo-3-(2':6'-dichloro-4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 2':6'-dichloro-4'-nitrophenyl).—Compound (IV; R = 2':6'-dichloro-4'-nitrophenyl) (10 g.) was boiled gently with acetic anhydride (40 c.c.) and pyridine (2 c.c.) for 5 minutes. The *anhydro*-derivative crystallised from acetic acid in pale-yellow prismatic needles, m. p. 256° (9 g.; 94.3%) (Found: C, 50.8; H, 2.7; N, 11.2; Cl, 18.5. $C_{16}H_9O_4N_3Cl_2$ requires C, 50.8; H, 2.4; N, 11.1; Cl, 18.8%), insoluble in cold aqueous alkalis, but soluble in hot aqueous sodium hydroxide with a crimson colour. It (10 g.) was hydrolysed by boiling with hydrochloric acid (50 c.c.) and acetic acid (200 c.c.) for 15 minutes, concentrating, and diluting (9.5 g.; 90.8%).

2-(2'-Bromo-4'-nitrophenylamino)isoindolinone-3-acetic Acid (IV; R = 2'-bromo-4'-nitrophenyl).—

2-Bromo-4-nitroaniline (54 g.) was converted into the β -naphthaquinone compound (Rowe, Jambuserwala, and Partridge, *J.*, 1935, 1135). The suspension of the latter was added to sodium hydroxide (50 g.) in water (100 c.c.), and the crimson solution acidified after 15 seconds. After removal of 2'-bromo-4'-nitrobenzeneazo- β -naphthol (66 g.; 71.3%), the filtrate was hydrolysed (22 g.; 21.8%). Fractional crystallisation from ethyl acetate gave 1-hydroxy-3-(2'-bromo-4'-nitrophenyl)-3:4-dihydrophthalazine-4-acetic acid (7 g.) and 2-(2'-bromo-4'-nitrophenylamino)isoindolinone-3-acetic acid (14 g.; 13.9%), the latter crystallising in almost colourless prisms, m. p. 259° (Found: C, 47.2; H, 3.2; N, 10.05. $C_{16}H_{13}O_5N_3Br$ requires C, 47.3; H, 3.0; N, 10.4%), soluble in aqueous sodium carbonate with an orange-red colour, becoming crimson on addition of sodium hydroxide. The methyl ester crystallised from methyl alcohol in pale yellow needles, m. p. 170° (Found: C, 48.6; H, 3.6; N, 10.5; Br, 19.3. $C_{17}H_{14}O_5N_3Br$ requires C, 48.6; H, 3.3; N, 10.0; Br, 19.05%).

2:5-Diketo-3-(2'-bromo-4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 2'-bromo-4'-nitrophenyl).—Compound (IV; R = 2'-bromo-4'-nitrophenyl) (10 g.) gave, in the usual manner, almost colourless, prismatic needles of the anhydro-derivative, m. p. 272–273° (acetic acid) (9.2 g.; 96.2%) (Found: C, 49.5; H, 2.65; N, 10.95; Br, 20.25. $C_{18}H_{10}O_4N_3Br$ requires C, 49.5; H, 2.6; N, 10.8; Br, 20.6%), best hydrolysed to the acid by refluxing (10 g.) with concentrated hydrochloric acid (50 c.c.) and acetic acid (200 c.c.) for 15 minutes (9.4 g.; 89.7%).

2-(2':6'-Dibromo-4'-nitrophenylamino)isoindolinone-3-acetic Acid (IV; R = 2':6'-dibromo-4'-nitrophenyl).—2:6-Dibromoaniline (59 g.) was converted into sodium 1-(2':6'-dibromo-4'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate (Rowe, Dunbar, and Williams, *loc. cit.*). After being kept ice-cold, with stirring, for 20 minutes, the suspension of the latter was added to sodium hydroxide (40 g.) in water (80 c.c.) and the deep crimson solution acidified after 1 minute. 2':6'-Dibromo-4'-nitrobenzeneazo- β -naphthol (61 g.; 67.8%) was removed and hydrolysis of the sodium sulphonate gave almost pure 2-(2':6'-dibromo-4'-nitrophenylamino)isoindolinone-3-acetic acid. It crystallised from ethyl acetate or aqueous acetic acid in pale yellow prisms, m. p. 232° (26 g.; 26.8%) (Found: C, 40.4; H, 2.3; N, 8.8; Br, 32.6. $C_{16}H_{11}O_5N_3Br_2$ requires C, 39.6; H, 2.5; N, 8.7; Br, 33.0%), soluble in aqueous alkalis with a crimson colour. Compound (V; R = 2':6'-dibromo-4'-nitrophenyl) was not formed until after the reaction with sodium hydroxide had proceeded for 2–3 minutes. The following percentage yields were isolated after various periods of reaction in the sodium hydroxide:

Time in sodium hydroxide.	2':6'-Dibromo-4'-nitrobenzeneazo- β -naphthol.	Compound (IV). (R = 2':6'-Dibromo-4'-nitrophenyl).	Compound (V).
15 seconds	88	8	nil
1 minute	68	27	nil
2.5 minutes	50	31	7
10 minutes	54	12	23
2 hours	55	3	32

The methyl ester of (IV; R = 2':6'-dibromo-4'-nitrophenyl) crystallised from methyl alcohol in pale-yellow needles, m. p. 168° (Found: C, 41.25; H, 2.8; N, 7.9; Br, 32.5. $C_{17}H_{13}O_5N_3Br_2$ requires C, 40.9; H, 2.6; N, 8.4; Br, 32.1%).

2:5-Diketo-3-(2':6'-dibromo-4'-nitrophenyl)isoindolinopyrazolidocoline (VI; R = 2':6'-dibromo-4'-nitrophenyl).—Compound (IV; R = 2':6'-dibromo-4'-nitrophenyl) (10 g.) gave the anhydro-compound (VI), which crystallised from acetic acid in pale yellow, prismatic needles, m. p. 290° (9 g.; 93.4%) (Found: C, 41.25; H, 2.0; N, 9.1. $C_{18}H_{10}O_4N_3Br_2$ requires C, 41.1; H, 1.9; N, 9.0%). It was hydrolysed similarly to the 2'-bromo-4'-nitro-analogue (89.2%).

2-(4'-Nitro-2'-methylphenylamino)isoindolinone-3-acetic Acid (IV; R = 4'-nitro-2'-methylphenyl).—3-Nitro-*o*-toluidine (50 g.) was converted into sodium 1-(4'-nitro-2'-methylbenzeneazo)- β -naphthaquinone-1-sulphonate (Rowe and Siddle, *J.*, 1932, 476); this by interaction in the usual manner with sodium hydroxide (66 g.) in water (140 c.c.) for 15 seconds, gave 4'-nitro-2'-methylbenzeneazo- β -naphthol (64 g.; 63.5%) and a mixture of compounds (I and II; R = 4'-nitro-2'-methylphenyl). Hydrolysis of this mixture and fractional crystallisation of the product from ethyl acetate gave 2-(4'-nitro-2'-methylphenylamino)isoindolinone-3-acetic acid, which crystallised in pale yellow prisms, m. p. 238° (16 g.; 14.3%) (Found: C, 60.2; H, 4.7; N, 12.15. $C_{17}H_{15}O_5N_3$ requires C, 59.8; H, 4.4; N, 12.3%), soluble in aqueous sodium carbonate and hydroxide with orange-red and crimson colours, respectively. The methyl ester crystallised from methyl alcohol in pale yellow needles, m. p. 147° (Found: C, 60.6; H, 5.0; N, 12.15. $C_{18}H_{17}O_5N_3$ requires C, 60.85; H, 4.8; N, 11.8%).

2:5-Diketo-3-(4'-nitro-2'-methylphenyl)isoindolinopyrazolidocoline (VI; R = 4'-nitro-2'-methylphenyl) crystallised from acetic acid in pale yellow, prismatic needles, m. p. 213–214° (9 g. from 10 g. acid; 95%) (Found: C, 63.1; H, 4.1; N, 12.5. $C_{17}H_{13}O_5N_3$ requires C, 63.2; H, 4.0; N, 13.0%), hydrolysed best (89%) by a mixture of hydrochloric and acetic acids.

Derivatives of *m*-Nitroaniline.—*m*-Nitroaniline (55 g.) was converted into sodium 1-(3'-nitrobenzeneazo)- β -naphthaquinone-1-sulphonate (Rowe, Himmat, and Levin, *J.*, 1928, 2558). When the latter reacted with sodium hydroxide (80 g.) in water (160 c.c.) for 15 seconds, two products only were formed, *viz.*, 3'-nitrobenzeneazo- β -naphthol (11 g.; 9.4%) and sodium hydrogen 3-(3'-nitrophenyl)-3:4-dihydrophthalazine-1-sulphonate-4-acetate (130 g.; 78.9%), the latter being hydrolysed to (V; R = 3'-nitrophenyl). No trace of the isomeride (IV) was detected. The acetyl derivative of compound (V; R = 3'-nitrophenyl) crystallised from aqueous acetic acid or aqueous alcohol in pale yellow prisms, m. p. 175° (Found: C, 58.5; H, 4.3; N, 11.5. $C_{18}H_{15}O_5N_3$ requires C, 58.5; H, 4.1; N, 11.4%), soluble in aqueous sodium carbonate and hydroxide with golden-yellow and crimson colours, respectively.

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