247. *A Reaction of Certain Diazosulphonates derived from* β-*Naphthol-*1-*sulphonic Acid. Part XXVI. Phthalazine and* iso*Indolinone Compounds derived from Aniline.*

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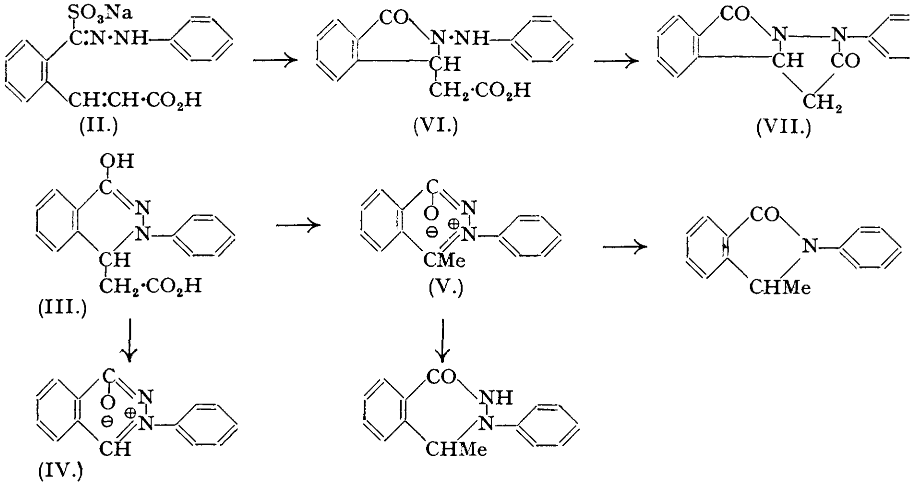
The parent compounds in this series are now prepared. Fission of the naphthalene ring in sodium 1-benzeneazo-β-naphthaquinone-1-sulphonate (I) occurs rapidly in presence of aqueous sodium hydroxide at 0°, but the sodium benzaldehydephenylhydrazone-ω-sulphonate-2-β-acrylic acid (II) formed is quickly converted into sodium hydrogen 3-phenyl-3 : 4-dihydrophthalazine-1-sulphonate-4-acetate. New technique is essential in order to ensure smooth hydrolysis to 1-*hydroxy*-3-*phenyl*-3 : 4-*dihydrophthalazine*-4-*acetic acid* (III). With restricted action of alkali hydroxide, (I) affords a little (II), hydrolysed to 2-anilino*iso*indolinone-3-acetic acid, the presence of which is confirmed by conversion into 2 : 5-*diketo*-3-*phenyl*iso*indolinopyrazolidocoline* (VII). [3-*Phenylphthalaz*-1-*one* (IV) and its 4-*methyl* derivative (V), unlike other analogues in this series, are water-soluble, and special methods are required for their preparation from compound (III).]

SODIUM hydrogen 3-phenyl-3 : 4-dihydrophthalazine-1-sulphonate-4-acetate was hydrolysed by adding a dilute ammonia solution to boiling dilute hydrochloric acid at such a rate as to ensure constant evolution of sulphur dioxide and minimum tar formation. The resulting 1-*hydroxy*-3-*phenyl*-3 : 4-*dihydrophthalazine*-4-*acetic acid* (III) is the most water-soluble of all such analogues prepared, and can be isolated only after concentration of the aqueous solution to a small volume. With boiling acetic anhydride, (III) gave the O-*acetate*, but on prolonged boiling (50 hours) with acetic anhydride and pyridine, the main product of *O*-acetate was accompanied by a little of the internal *anhydride* of (III). Sulphonation first occurs when compound (III) is heated with aqueous sulphuric acid, with probable subsequent formation of the sulphonic acid of (IV); the water-soluble 3-*phenylphthalaz*-1-*one* (IV) was, however, obtained in excellent yield by heating (III) with fuming hydrochloric acid (*d* 1·19) in a sealed tube at 180°, and it is not readily sulphonated. Further evidence for the constitution of (III) was afforded by (*a*) Clemmensen reduction to give *N*-phenylphthalimidine, which is also formed from 4′-amino-*N*-phenylphthalimidine by the diazo-reaction (cf. *J.*, 1926, 690), and (*b*) conversion of (III) by nitric acid (*d* 1·5) into the known 4′-nitro-3-phenyl-4-methylphthalaz-1-one. The phthalazone (IV) was not isomerized by heating it with aqueous hydrochloric acid (1 : 8) in a sealed tube at 180° for 50 hours, whereas when a nitro-group is present in the *p*-position in the 3-phenyl side-chain, transformation into the corresponding 4′-nitro-3-phenylphthalaz-4-one occurs (cf. *J.*, 1937, 90). Oxidation of (III) by sodium dichromate in aqueous sulphuric acid was accompanied by sulphonation, but the water-soluble 3-*phenyl*-4-*methylphthalaz*-1-*one* (V) was formed in 36% yield from (III) and chromic acid in acetic acid at 20°. Alkaline dithionite (hydrosulphite) reduction of (V) gave 1-*keto*-3-*phenyl*-4-*methyltetrahydrophthalazine*, whereas Clemmensen reduction yielded N-*phenyl*-3-*methylphthalimidine*.

When sodium 1-benzeneazo-β-naphthaquinone-1-sulphonate and aqueous sodium hydroxide were kept at 0° for 5 minutes, and the resulting sodium salt hydrolysed, the hydroxy-compound (III) was formed mainly, but about 5% of the isomeric 2-anilino*iso*indolinone-3-acetic acid (VI) was also present. Fractional crystallisation failed to effect a separation, but as (III) is acetylated by acetic anhydride to the soluble *O*-acetate, whereas (VI) loses water to yield the sparingly soluble 2 : 5-*diketo*-3-*phenyl*iso*indolinopyrazolidocoline* (VII), this reaction was used to show the presence of (VI). That compound (VII) possessed the constitution assigned to it was confirmed by nitration to give the known 2′ : 4′-analogue of (VII), which is also derived from a similar reaction to that described above, using 2 : 4-dinitroaniline in place of aniline (cf. *J.*, 1947, 829).



EXPERIMENTAL.

1-*Hydroxy*-3-*phenyl*-3 : 4-*dihydrophthalazine*-4-*acetic Acid* (III).—Benzenediazonium chloride (from 100 g. of aniline), added to an ice-cold solution of 50% sodium β-naphthol-1-sulphonate (400 g.) in water (1200 c.c.), gave 2-naphthol-1-benzenediazosulphonate, which was salted out (sodium chloride), washed with brine, and converted by sodium carbonate (100 g.) in water (400 c.c.) at 0° into sodium 1-benzeneazo-β-naphthaquinone-1-sulphonate. After 15 minutes, sodium hydroxide (100 g.) in water (300 c.c.) at 5° was added to the mixture, and after 15 minutes, it was acidified by hydrochloric acid at below 10° to yield a black tar which did not solidify even after several days at 0°. The tar dissolved readily in aqueous ammonia (only a trace of benzeneazo-β-naphthol was formed), and careful addition to boiling dilute hydrochloric acid by means of a dropping-funnel during 6 hours, the mixture being kept acid to Congo-red, caused liberation of sulphur dioxide and gave an almost clear solution. Too rapid addition of the ammonia solution gave much black insoluble tar. Concentration of the resulting dilute hydrochloric acid solution gave successive crops of product, and final evaporation of the mother liquor to dryness, followed by extraction with ethyl acetate, afforded a further amount of 1-*hydroxy*-3-*phenyl*-3 : 4-*dihydrophthalazine*-4-*acetic acid* (III), which crystallised from acetic acid or ethyl acetate in colourless prismatic needles, m. p. 264° (decomp.) (191 g.; 63%) (Found : C, 68·2; H, 5·2; N, 10·25. $C_{16}H_{14}O_3N_2$ requires C, 68·1; H, 5·0; N, 9·9%).

The *ethyl* ester crystallised from alcohol in colourless rectangular prisms, m. p. 91—92° (Found : N, 8·8. $C_{18}H_{18}O_3N_2$ requires N, 9·0%). On being boiled with acetic anhydride for 3 hours, (III) gave the O-*acetate*, which crystallised from acetic acid in colourless plates, m. p. 183° (Found : N, 8·75. $C_{18}H_{16}O_4N_2$ requires N, 8·6%); when the boiling with acetic anhydride (and a little pyridine) was extended to 50 hours, the *O*-acetate was accompanied by *ca.* 4% of the internal *anhydride* of (III), m. p. > 320° (Found : N, 10·6. $C_{16}H_{12}O_2N_2$ requires N, 10·6%).

1-*Keto*-3-*phenyl*-2-*methyltetrahydrophthalazine*-4-*acetic acid* crystallised from ethyl acetate in colourless, prismatic needles, m. p. 184—186° (Found : C, 69·2; H, 5·35; N, 9·6. $C_{17}H_{16}O_3N_2$ requires C, 68·9; H, 5·4; N, 9·5%.)

3-*Phenylphthalaz*-1-*one* (IV).—1-Hydroxy-3-phenyl-3 : 4-dihydrophthalazine-4-acetic acid (7 g.) and fuming hydrochloric acid (*d* 1·19; 15 c.c.) in a sealed tube at 180° for 1 hour, followed by heating the resulting product with 15% aqueous sodium carbonate for 10 minutes, gave the *phthalazone* (IV), which crystallised from benzene–pyridine (1 : 1) in almost colourless needles, m. p. 208° (5·4 g.; 97%), which became green on keeping (Found : C, 76·0; H, 4·5; N, 12·5. $C_{14}H_{10}ON_2$ requires C, 75·8; H, 4·5; N, 12·6%). It formed a hydrochloride, which separated from water in long, colourless needles, m. p. 162—164°, and a *picrate*, which crystallised from alcohol in yellow prismatic needles, m. p. 226° (Found : N, 15·65. $C_{20}H_{13}O_8N_5$ requires N, 15·5%).

Methylation of (IV) with methyl sulphate at 80° gave a resin which combined with alcohol on boiling a solution for 5 minutes, when almost colourless prisms, m. p. 86—87°, separated (Found : C, 72·5; H, 6·3; N, 10·3. $C_{17}H_{18}O_2N_2$ requires C, 72·3; H, 6·4; N, 9·9%); this methylated *compound* lost alcohol when heated at 140° for 4 hours, and a *compound* was formed which crystallised from ethyl acetate in yellow needles, m. p. 234° (decomp.) [Found : N, 11·45. $(C_{15}H_{12}ON_2)_2$ requires N, 11·9%], probably resulting from the joining of two mols. (after loss of C_2H_6O) at the C_4 position. It differed from compound (V).

N-*Phenylphthalimidine*.—3-Phenylphthalaz-1-one (2 g.) was heated with hydrochloric acid (140 c.c.), water (80 c.c.), alcohol (40 c.c.), and zinc amalgam (200 g.) at 70—80° for 4 hours. The phthalimidine (1·6 g.; 85%) crystallised from alcohol in colourless plates, identical with an authentic specimen.

3-*Phenyl*-4-*methylphthalaz*-1-*one* (V).—Chromium trioxide (4 g.) in acetic acid (20 c.c.) and water (10 c.c.) was added slowly (during 2 hours) to a stirred suspension of finely-divided 1-hydroxy-3-phenyl-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) in acetic acid (70 c.c.) at 20°. After standing overnight, the precipitate was heated with 15% aqueous sodium carbonate and the residue of *phthalazone* (V) crystallised from benzene–pyridine in colourless rhombs, m. p. 235° (3·1 g.; 35·9%) (Found: C, 76·0; H, 5·0; N, 11·8. $C_{15}H_{12}ON_2$ requires C, 76·3; H, 5·1; N, 11·9%). 3-Phenyl-4-methylphthalaz-1-one gave a *picrate*, which crystallised from alcohol in yellow rhombs, m. p. 197° (Found: C, 54·6; H, 3·6; N, 14·8. $C_{21}H_{15}O_8N_5$ requires C, 54·2; H, 3·2; N, 15·05%).

1-*Keto*-3-*phenyl*-4-*methyltetrahydrophthalazine*.—Compound (V) (2 g.) was boiled with sodium dithionite (hydrosulphite) (4 g.) in dilute aqueous sodium hydroxide for 10 minutes, and the precipitate which separated on cooling was crystallised from aqueous alcohol. The *tetrahydrophthalazine* separated in colourless prisms, m. p. 171° (0·45 g.; 44·7%) (Found: C, 75·9; H, 5·8; N, 11·7. $C_{15}H_{14}ON_2$ requires C, 75·6; H, 5·9; N, 11·8%).

N-*Phenyl*-3-*methylphthalimidine*.—When 3-phenyl-4-methylphthalaz-1-one (3 g.), hydrochloric acid (70 c.c.), water (50 c.c.), and zinc amalgam (90 g.) were boiled for 4 hours, a resinous product was formed. On extracting with light petroleum, and cooling, long, colourless needles, m. p. 80°, of the *phthalimidine* separated (Found: C, 80·8; H, 5·6; N, 6·3. $C_{15}H_{13}ON$ requires C, 80·7; H, 5·8; N, 6·3%).

4′-*Nitro*-3-*phenyl*-4-*methylphthalaz*-1-*one*.—1-Hydroxy-3-phenyl-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) was added during 30 minutes to nitric acid (*d* 1·5; 70 c.c.) at below 10°, and the mixture poured on ice, neutralised with aqueous ammonia, and kept overnight. The precipitate of 4′-nitro-3-phenyl-4-methylphthalaz-1-one nitrate (7·8 g.; 73·6%) was basified with warm aqueous ammonia, and the free base crystallised from methyl alcohol in yellow prismatic needles, m. p. 248° (decomp.), identical with an authentic specimen.

3-*Phenylphthalaz*-1-*one*-x-*sulphonic Acid*.—On being refluxed with aqueous sulphuric acid, b. p. 140°, or with equal volumes of sulphuric and acetic acid, for 40 minutes, and poured on ice, the hydroxy-compound (III) yielded a colourless precipitate of a *sulphonic acid* (Found: C, 52·8; H, 4·0; N, 8·7; S, 8·9. $C_{14}H_{10}O_4N_2S,H_2O$ requires C, 52·5; H, 3·75; N, 8·75; S, 10·0%). 3-Phenylphthalaz-1-one (IV) is not readily sulphonated under the above conditions, and thus sulphonation probably precedes phthalazone formation. The sulphonic acid, which does not melt, is probably a derivative of (IV).

3-*Phenyl*-4-*methylphthalaz*-1-*one*-x-*sulphonic Acid*.—1-Hydroxy-3-phenyl-3 : 4-dihydrophthalazine-4-acetic acid (10 g.) was added to concentrated sulphuric acid (100 c.c.) and the mixture poured on ice (250 g.); potassium dichromate (8 g.) was added during 30 minutes, with stirring, and, after 3 hours at room temperature, the resulting precipitate of *sulphonic acid* was collected (9·4 g.). It crystallised from a large volume of water in colourless, prismatic needles, which did not melt (Found: C, 56·9; H, 3·95; S, 9·6. $C_{15}H_{12}O_4N_2S$ requires C, 57·0; H, 3·8; S, 10·1%).

2 : 5-*Diketo*-3-*phenyl*iso*indolinopyrazolidocoline* (VII).—A suspension of sodium 1-benzeneazo-β-naphthaquinone-1-sulphonate (from 50 g. of aniline) in aqueous sodium carbonate at 0° was added to sodium hydroxide (50 g.) in water (180 c.c.) at 0°, with vigorous stirring; the temperature was kept at 5°, and, after 5 minutes, the mixture was acidified quickly (hydrochloric acid and defrothing agent) without cooling. The resulting black mass of sodium salt was hydrolysed as described above, tar removed, and the acid solution evaporated to dryness. Extraction of the residue with ethyl acetate gave colourless prisms, m. p. 200° (softening at 180°) (22 g.). Fractionation from ethyl acetate afforded 1-hydroxy-3-phenyl-3 : 4-dihydrophthalazine-4-acetic acid (6·6 g.), m. p. and mixed m. p. 263—264°; the most soluble fraction (7·2 g.) was boiled with acetic anhydride (80 c.c.) for 5 minutes, and, on cooling, large colourless prisms (1·3 g.), m. p. 219°, separated. 2 : 5-*Diketo*-3-*phenyl*iso*indolinopyrazolidocoline* (VII) crystallised from acetic anhydride or ethyl acetate in colourless prisms, m. p. 220—221° (Found: C, 72·5; H, 4·3; N, 10·1. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·55; N, 10·6%).

Nitration of (VII).—Compound (VII) (0·5 g.) and nitric acid (*d* 1·5; 5 g.) were kept at room temperature for 10 minutes and then gradually warmed to 60° and poured on ice. The yellow solid crystallised from acetic acid in pale yellow prismatic needles, m. p. 238—239° (0·5 g.), not depressed on admixture with an authentic specimen of 2 : 5-diketo-3-(2′ : 4′-dinitrophenyl)*iso*indolinopyrazolidocoline (*J.*, 1947, 829).

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