ACTA CHEMICA SCANDINAVICA 24 (1970) 1867–1877

Electroörganic Preparations

XXX. Reduction of Phthalazine and Some of its Alkyl Derivatives

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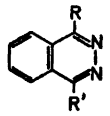
Phthalazine is in acid solution reduced to a mixture of *o*-xylene-α,α′-diamine and isoindoline; the composition of this mixture depends primarily on pH. In alkaline medium the reduction may yield dimeric products, 1,2-dihydrophthalazine or 1,2,3,4-tetrahydrophthalazine, depending primarily on the cathode potential. The first two-electron polarographic reduction of 1,2-dihydrophthalazine in acid solution produces isoindole, the second one isoindoline. 1-Methylphthalazine can in acid solution be reduced to 1-methylisoindole or, at a more negative potential, to 1-methylisoindoline; in alkaline medium the reduction yields 1,2-dihydro-4-methylphthalazine. 2-Methylphthalazinium iodide is in weakly alkaline solution reduced in a one-electron reaction to a mixture of two compounds, both dimerized at C-1; they are suggested to be the D,L- and *meso*-forms.

Phthalazine has previously been investigated polarographically and coulometrically [1] and a preliminary communication on the electrolysis of phthalazine has appeared.[2] In the present paper the polarographic behaviour of some derivatives of phthalazine and the controlled potential electrolysis of the compounds are discussed.

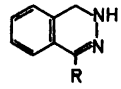
In the investigation are included phthalazine (Ia), 1,2-dihydrophthalazine (IIa), 1,2,3,4-tetrahydrophthalazine (III), 2-methyl-(IVa) and 2-isopropylphthalazinium iodide (IVb), 1-methylphthalazine (Ib), 1,2-dihydro-4-methylphthalazine (IIb), isoindole (Va), 1-methylisoindole (Vb), isoindoline (VIa), 1-methylisoindoline (VIb), *o*-xylene-α,α′-diamine (VII), and benzaldehyde benzylhydrazone (VIII).

POLAROGRAPHIC INVESTIGATION

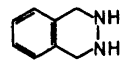
In Fig. 1 are shown the half-wave potentials of 1,2-dihydrophthalazine (IIa), prepared by controlled potential reduction of phthalazine (Ia); in the figure are also included the half-wave potentials of the anodic wave of 1,2,3,4-tetrahydrophthalazine (III).



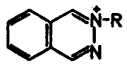
I a R = R′=H′
b R = CH_3 R′=H
c R = CH_3 R′=I
d R = CH_3 R′=Cl



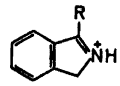
II a R = H
b R = CH_3



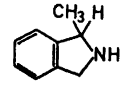
III



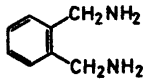
IV a R = CH_3
b R = $CH(CH_3)_2$



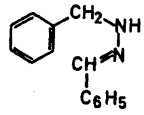
V a R = H
b R = CH_3



VI a R = H
b R = CH_3



VII



VIII

At pH<9 the half-wave potentials of the IIa are less negative than those of Ia, so IIa is reduced preferentially to Ia. IIa is structurally similar to benzaldehyde benzylhydrazone (VIII), and its polarographic behaviour is in accordance with that.[3] Like VIII, IIa is reduced in two two-electron waves at pH<1; these waves merge at pH 1.5 and the four-electron wave disappears between pH 9 and 11, as only the protonated species is reducible. At very negative potentials a two-electron wave is found in alkaline solution; it is

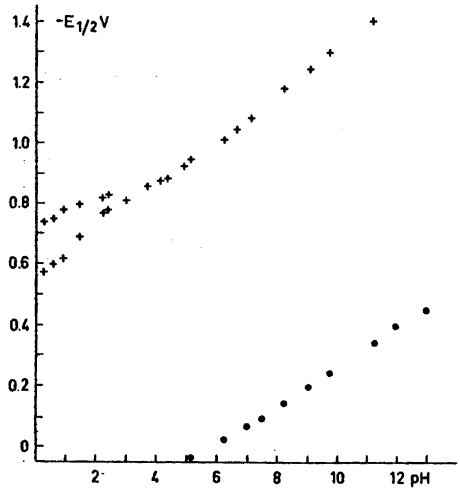


Fig. 1. Cathodic half-wave potentials (V *vs.* SCE) of 1,2-dihydrophthalazine (IIa)+ and anodic half-wave potentials of 1,2,3,4-tetrahydrophthalazine (III) ●.

not well-developed in media containing sodium or potassium ions; in a solution of LiCl the half-wave potential is −1.95 V (SCE); this wave corresponds to the second wave of phthalazine found in this medium.

1,2,3,4-Tetrahydrophthalazine (III) shows no cathodic wave but only an anodic one; III behaves thus as ordinary hydrazines, the oxidation is a two-electron reaction; IIa shows no well-developed anodic wave.

1-Methylphthalazine (Ib) is in acid solution reduced in two steps, a four-electron wave followed by a two-electron wave; in alkaline solution a single two-electron wave is found. 1,2-Dihydro-4-methylphthalazine (IIb) is in acid solution reduced in two two-electron reductions. The half-wave potentials of Ib are given in Fig. 2; included in Fig. 2 are also the half-wave potentials of 1-methylisoindole (Vb).

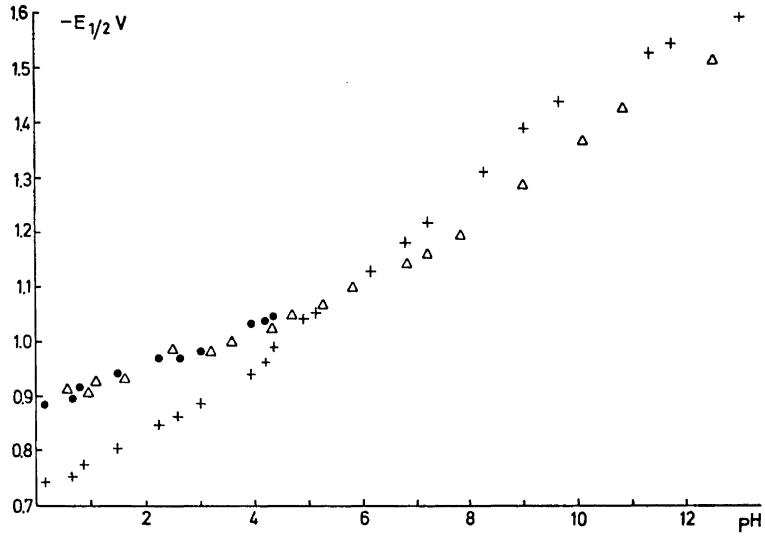


Fig. 2. Cathodic half-wave potentials (V *vs.* SCE) of 1-methylphthalazine (Ib; 1. wave +; 2. wave ●) and of 1-methylisoindole (Vb) △.

The half-wave potentials of Vb are in acid solution close to those of the second wave of Ib; the wave of Vb does not, however, exhibit a pronounced maximum as does the second wave of Ib which might indicate that Vb is not an intermediate in the reduction of Ib.

PREPARATIVE ELECTROLYSIS

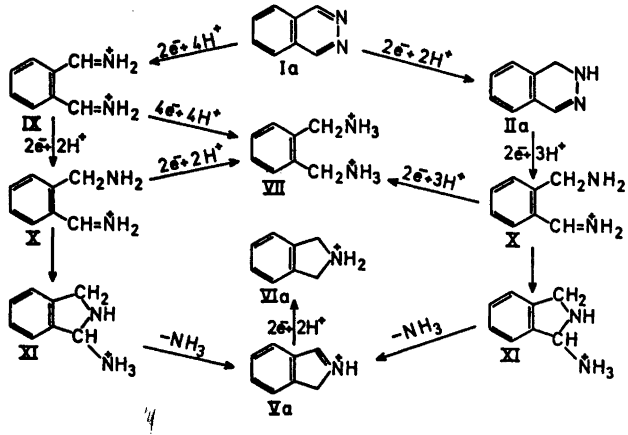
Electrolytic reduction of phthalazine in hydrochloric acid solutions produces a mixture of isoindoline (VIa) and *o*-xylene-α-α′-diamine (VII); the composition of the reaction mixture is dependent on the acidity and to some degree on the temperature, but the potential on the limiting current at which the reduction proceeds seems not to influence the composition of the reac-

Table 1. Yield of isoindoline in the reduction of phthalazine at different acid concentrations and temperatures.

Concentration of HCl	0.2 N	1 N	2 N	2 N	6 N
Temperature °C	25–30	25–30	25–30	0–5	25–30
Yield of isoindoline	85	55	45	35	22

tion mixture. In less acid solution coloured compounds are formed. In Table 1 some of these results are summarized.

The polarographic data and the products isolated from the preparative electrolysis suggest that the following reactions may occur:



From the available data it cannot be decided whether 1,2-dihydrophthalazine (IIa) or the dialdimine (IX) is the primary reduction product. The polarographic data of IIa indicate that the first two-electron reduction of IIa produces the aldimine (X), as the alternative product, 1,2,3,4-tetrahydrophthalazine (III), is not further reducible. The amino group of X attacks the aldimine with formation of XI which loses ammonia to isoindole (Va); Va is further reduced to VIa. *o*-Xylene-α,α'-diamine (VII) may be formed either by a reduction of the dialdimine IX or of X.

The influence of the acidity on the product distribution may be caused by the participation of protons at at least two points in the scheme. The branching may occur in the primary reduction; for instance might the doubly protonated phthalazine be reduced to IX, whereas the singly protonated molecule primarily forms IIa. Alternatively, the branching could occur after the formation of X; a protonation of the amino group would hinder its nucleophilic attack on the aldimine, whereas a protonation of the azomethine group

would facilitate both the reduction and the nucleophilic attack; the effect of higher acidity would be expected to be a greater proportion of VII in the reaction mixture. The finding that the yield of isoindoline in 2 N HCl decreased somewhat by lowering the temperature is in accordance with the suggestion that the branching occurs after the formation of X.

In alkaline solution dimeric products, 1,2-dihydrophthalazine (IIa) or 1,2,3,4-tetrahydrophthalazine (III) are obtained on electrolysis, the most deciding factor being the cathode potential. A reduction performed at a potential of the lower half of the polarographic wave combined with a rapid stirring of the electrode results in a good yield of dimerized products; these are rather insoluble and are contaminated with very finely divided mercury which is observed when the precipitate is dissolved in DMF. Mercury-organic compounds have not been isolated although it seems plausible that the primarily formed radicals are stabilized by some kind of bonding to the mercury electrode; the rapid stirring of the electrode will expose fresh mercury and disrupt any film of radicals stabilized at the electrode; this might favour the dimerization reaction.

The dimeric product is probably a mixture of the *meso*- and the D,L-form where the dimerization has taken place at C-1. The presence of an N–H-absorption in the IR-spectrum supports this formulation; an alternative structure dimerized at N-1 and having an N–H-bond must be formulated with an *ortho*-quinoid structure in both rings; the light yellowish colour of the dimer is not in accordance with the *ortho*-quinoid formulation. The compound is insoluble in solvents commonly used for NMR-spectroscopy so a proof of the structure is lacking; however, as the corresponding dimers from the reduction of 2-methylphthalazinium iodide are shown (see below) to be dimerized at C-1, a similar dimerization for Ia is reasonable.

When the reduction is performed at −1.65 V (SCE) which is on the limiting current of Ia but not sufficiently negative for the formation of III, a high yield of IIa is obtained.

The two-electron reduction product from phthalazine (m.p. 84–85°C) has been formulated as 1,2-dihydrophthalazine (IIa) on the following grounds: The empirical formula is $C_8H_8N_2$; the NMR-spectrum ($CDCl_3$: $\delta = 4.18$ (singlet) $\sum H = 2$; $\delta = 6.1$ (broad signal) $\sum H = 1$; $\delta = 6.9 - 7.6$ (multiplet) $\sum H = 5$) is analogous to that of benzaldehyde benzylhydrazone (VIII) ($CDCl_3$: $\delta = 4.39$ (singlet) $\sum H = 2$; $\delta = 5.7$ (broad signal) $\sum H = 1$; $\delta = 7.0 - 7.7$ (multiplet) $\sum H = 11$) and so is its polarographic behaviour. It forms a thiourea derivative on reaction with phenylisothiocyanate (m.p. 130–131°C) with an NMR-spectrum (see Experimental) analogous to that of the corresponding thiourea derivative of VIII. IIa can further be reduced to the known 1,2,3,4-tetrahydrophthalazine (III) and formed on anodic oxidation of III. This indicates that no ring contraction has taken place during the reduction of Ia to IIa.

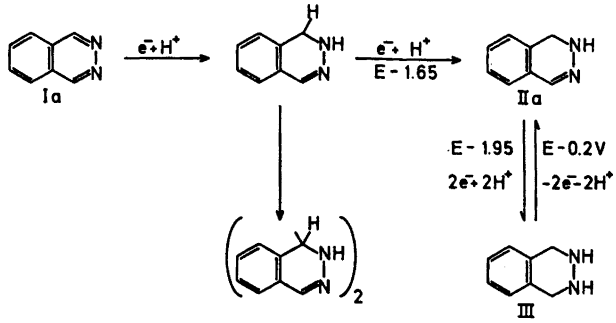
A compound, m.p. 47–48°C, prepared by reduction of phthalazinone with lithium aluminium hydride,[4] has previously been assigned the structure IIa; the thiourea derivative of this compound had m.p. 212–213°C. The reason for this discrepancy is not known.

The further reduction of IIa is analogous to the reduction of other azomethine derivatives of benzaldehyde in alkaline solution;[5] the anodic

oxidation of III probably first produces 1,4-dihydrophthalazine which tautomerizes into 1,2-dihydrophthalazine.

The possibility of reducing Ia to IIa and to oxidize III to IIa makes the electrolytic method an attractive one for the preparation of IIa. If a too negative potential has been chosen in order to minimize the formation of dimeric products, one can reverse the current and reoxidize the III formed to IIa at an anode potential of -0.2 V.

The electrode reactions of phthalazine in alkaline solution can thus be formulated:



The reduction of 2-methylphthalazinium iodide (IVa) in acid solution resembles that of phthalazine; at high pH the nucleus is attacked by hydroxide ions [6] and this attack competes with the reduction. In slightly alkaline solution the reaction with hydroxide ions is so slow that it does not interfere with the reduction.

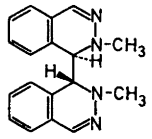
In slightly alkaline solution a pH-independent one-electron reduction is found followed by further reduction; here only the one-electron reduction products have been investigated. The reaction mixture contains two products in the approximate ratio 1:1 (53:47).

The two compounds, A, m.p. 175°C, and B, m.p. 155 – 156°C, both analyzed $C_{18}H_{18}N_4$; they had the same R_F-value in TLC on alumina using several solvent systems. Chromatography was useless in separating the mixture and the compounds were partly oxidized to 2-methylphthalazinone on chromatography on alumina. By repeated crystallization from ethanol, benzene-petrol ether, and cyclohexane the mixture was finally separated.

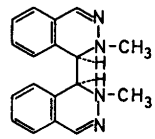
The IR-spectra of the two compounds were very much alike (see Experimental), but the NMR-spectra (compound A, $CDCl_3$: $\delta = 2.80$ (singlet) $\sum H = 6$; $\delta = 4.50$ (singlet) $\sum H = 2$; $\delta = 6.8 - 7.4$ (multiplet) $\sum H = 10$. Compound B: $\delta = 3.39$ (singlet) $\sum H = 6$; $\delta = 4.29$ (singlet) $\sum H = 2$; $\delta = 5.98$ (broadened doublet), $J_0 = 7$ Hz, $\sum H = 2$; $\delta = 6.8 - 7.3$ (multiplet) $\sum H = 6$; $\delta = 7.32$ (singlet) $\sum H = 2$) showed interesting differences.

The NMR-spectrum of compound A is in accordance with what would be expected from a molecule consisting of two 1,2-dihydrophthalazine nuclei dimerized at C-1. The NMR-spectrum of compound B differs from that of A in that the *N*-methyl signal is shifted down-field (0.59 ppm), one of the aro-

matic protons (in each benzene ring) is shifted up-field (~0.9 ppm) and the proton at C-4 gives a signal which is not buried in the phenyl multiplet. The signal at $\delta = 5.98$ was identified as being caused by one of the phenyl protons by its coupling constants and by the fact that irradiation of part of the phenyl multiplet (at $\delta = 6.9$) produced a collapse of the large coupling. This also indicates that the proton adjacent to the "abnormal" proton is found in that part of the multiplet which resonate at the highest field.



A



B

These facts have been interpreted as indicating that both compounds A and B are dimers, dimerized at C-1, and that one of them is the *meso*-form and the other one the D,L-form. The "abnormal" signal of compound B at $\delta = 5.98$ is that from the proton at C-8 (and C-8′) and the large anisotropy effect is caused by the influence of the ring current in one phenyl ring on the proton at C-8 of the phenyl ring of the other half of the molecule. Such an influence requires that the "abnormal" proton passes above the center of the other phenyl ring in a suitable distance during the rotation.

The question of which compound is the D,L- and which is the *meso*-form, is more difficult. Inspection of different models suggests that it is the *meso*-form which behaves abnormally, and that thus B, m.p. 154–155°C, is the *meso*-form. Steric hindrance seems to prevent the proton (C-8) of the D,L-form to attain the required position, whereas that of the *meso*-form passes directly above the center of the other phenyl ring. The assignment can only be taken as a suggestion as the consequences on the possible conformations of having two nitrogen atoms in the ring is not easy to imitate faithfully in the models. A resolution of the D,L-mixture with an optically active acid as, *e.g.*, camphoric acid, seems to be necessary in order to obtain an unequivocal assignment.

From the reduction of 3-isopropyl phthalazinium iodide (IVb) in a borate buffer a similar mixture of dimeric compounds, A′ and B′, was obtained; one of the isomers, B′, showed a similar "abnormal" signal from an aromatic proton ($\delta = 6.02$) in the NMR-spectrum as found for the methyl analog. (NMR-spectrum af A′, $CDCl_3$: $\delta = 0.57$ (doublet, $J = 6.5$ Hz) $\sum H = 6$; $\delta = 0.98$ (doublet, $J = 6.5$ Hz) $\sum H = 6$; $\delta = 2.68$ (septuplet, $J = 6.5$ Hz) $\sum H = 2$; $\delta = 4.37$ (singlet) $\sum H = 2$; $\delta = 6.8 - 7.5$ (multiplet) $\sum H = 10$. B′, $CDCl_3$: $\delta = 1.01$ (doublet, $J = 6.5$ Hz) $\sum H = 6$; $\delta = 1.38$ (doublet, $J = 6.5$ Hz) $\sum H = 6$; $\delta = 3.86$ (septuplet, $J = 6.5$ Hz) $\sum H = 2$; $\delta = 4.43$ (singlet) $\sum H = 2$; $\delta = 6.02$ (broadened doublet, $J_0 = 2$; $\sum H = 2$; $\delta = 6.8 - 7.5$ (multiplet) $\sum H = 8$). The difference in chemical shift of the methine protons of the isopropyl groups in A′ and B′ was greater than the difference of the methyl signals of A and B (1.18 ppm compared to 0.59 ppm).

A similar, but smaller difference (about 0.4 ppm) is found in the chemical shifts of the pairs of methyl groups of A′ and B′. Furthermore, the methyl protons of the isopropyl groups both in A′ and B′ show a rather large magnetic nonequivalence caused by the asymmetric centre at C-1; the difference in chemical shift of the two methyl groups in each isopropyl group is also about 0.4 ppm. A similar effect of magnetic nonequivalence of isopropyl methyl protons has previously been described.[7] All these effects must be caused by the special geometry of the system.

The ratio, A:B or A′:B′, is nearly 1:1 and is not much dependent on the medium; the same ratio is found in aqueous solution at pH 9 and 13 and in acetonitrile.

1-Methylphthalazine (Ib) can in acid solution be reduced in two steps; a reduction at the potential of the first wave yields 1-methylisoindole (Vb). The reduction of Ib to Vb is critically dependent on a control of the cathode potential as the difference between the reduction potential of Ib and that of the further reduction of Vb is only about 0.25 V.

The four-electron reduction product was shown to be 3-methyl-1H-isoindolium chloride from the elementary analysis, its two-electron reduction to 1-methylisoindoline and its NMR-spectrum (CF_3COOH: $\delta = 3.10$ (deformed triplet, $J = 2$ Hz) $\sum H = 3$; $\delta = 5.77$ (multiplet) $\sum H = 2$; $\delta = 7.6 - 8.3$ (multiplet) $\sum H = 4$). This spectrum is similar to that of 1,3,4,7-tetramethylisoindole in acidic solvents.[8]

1-Methylisoindole (Vb) has previously been reported to have been prepared by reduction of 1-chloro-4-methylphthalazine [9] by zinc and hydrochloric acid; later it was claimed [10] that the product obtained was 1-methylisoindoline. In view of the easy further reduction of Vb to VIb and the instability of Vb in solutions not containing excess of acid it would be difficult to obtain and purify Vb by the chemical reduction of 1-chloro-4-methylphthalazine.

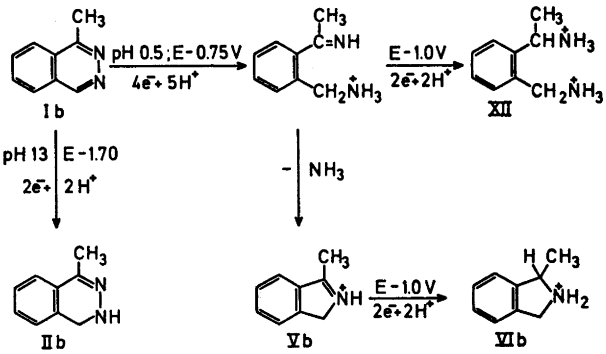
It is, of course, difficult now to prove whether Gabriel and Neumann [9] had methylisoindole in their hands or whether it was methylisoindoline, as claimed by Linstead and Noble [10] as no physical data, except elementary analysis, were reported. One observation, however, suggests that the product was methylisoindole or at least contained some of the compound; it is mentioned [9] that the free base dyed the skin brown to black which in this investigation has been found to be a true statement! Methylisoindoline does not do that to any noticeable extent.

1-Methylisoindole is reasonably stable in aqueous hydrochloric acid at room temperature and has been kept at 0° for some days without any appreciable deterioration. The hydrochloric acid can be removed *in vacuo* without destruction of Vb, but if the residue is dissolved in ethanol the solution becomes coloured. The reason is that the isoindole is a rather weak base which is only protonated in the presence of an excess of hydrochloric acid, and the free base deteriorates rapidly to coloured products. The product can be purified by dissolving the residue in ethanol or chloroform containing hydrogen chloride and precipitating with ether. The hydrochloride of Vb is obtained as a yellowish product which is stable.

1-Methylisoindole is the simplest derivative of isoindole, not substituted at nitrogen, so far prepared as a stable compound;[11,12] isoindole is the expected

product from the first two-electron reduction of 1,2-dihydrophthalazine under polarographic conditions, but when preparative useful concentrations (5×10^{-2} mol/l) are reduced, the separation of the waves disappears; further experiments are necessary for obtaining conditions for the preparation of isoindole by this method.

The product obtained from the reduction of Ib at a potential of the second wave is methylisoindoline. Under polarographic conditions a product is obtained in the first reduction which produces a pronounced maximum on the second wave not found in the polarographic wave of Vb; under these conditions the first reduction product is rather XII than VIb. These reactions are given in the following scheme.



In alkaline solution 1-methylphthalazine is reduced to 1,2-dihydro-4-methylphthalazine (IIb).

1-Methylphthalazine is very conveniently prepared by controlled potential reduction of 1-methyl-4-iodophthalazine (Ic) at −0.5 V (SCE); Ic is obtained from 1-methyl-4-chlorophthalazine (Id) on boiling with hydriodic acid. The detour over Ic is preferable to a direct reduction of Id, for although the polarographic wave of Id in acid solution shows a reduction of the carbon-chlorine bond at a potential 0.2 V less negative than the reduction of the phthalazine ring, the reduction potentials of the two reductions come so close together at higher concentrations that it so far has been impossible to carry out a selective reduction of Id to Ib.

EXPERIMENTAL

For the control of the potential was used a fully transistorized potentiostat from Tage Juul Electronics, Copenhagen; the polarograph was a Radiometer PO 4d Polariter. The NMR-spectra were recorded at 60 MHz on a Varian Associates A-60 spectrometer.

Reduction of phthalazine in acid solution (1). Phthalazine (1 g) was reduced in 8 N hydrochloric acid at −0.85 V (SCE), $n=6$ F/mol. The catholyte was cooled in an ice-bath; during the reduction the catholyte became yellowish, but turned colourless at the end and a white precipitate was formed. It was filtered off (800 mg) and the filtrate evaporated *in vacuo*. The precipitate was identified as *o*-xylene-α,α′-diamine (VII) from the IR-spectrum (identical with the spectrum of an authentic sample) and the m.p.

147°C of the diacetyl derivative (146°C).[13] The residue was extracted with alcohol which left further 350 mg of *o*-xylene-α,α′-diamine.

On addition of dry ether another precipitate, 300 mg, was obtained which contained some VII but after one more recrystallization was identified as isoindoline hydrochloride from the m.p. 254–256°C (255–256°C),[14] and its ability to form an *N*-nitroso derivative.

Reduction of phthalazine in acid solution (2). Phthalazine (0.5 g) was reduced at −1.0 V (SCE) in 0.2 N HCl, $n=6$. The solution became brownish, possibly due to condensation reactions of the intermediate isoindole; the reduction completed, the catholyte was evaporated *in vacuo*; the residue was treated with ethanol which did not dissolve appreciable amounts of the ammonium chloride and *o*-xylene-α,α′-diamine dihydrochloride. Addition of ether to the ethanolic solution precipitated a slightly coloured product, isoindoline hydrochloride, which was purified by further recrystallization, m.p. 253–255°C (255–256°C).[14] The yield of isoindoline was determined polarographically in the reaction mixture after nitrosation.[15]

Reduction of phthalazine in alkaline solution (1). Phthalazine (1 g) was reduced at −1.65 V (SCE) in 0.05 N potassium hydroxide containing 30 % ethanol; only the solution and not the electrode was stirred; $n=2$ *F*/mol. A small amount of dimer was formed; the catholyte was filtered under CO_2 into a flask containing solid CO_2. Chloroform, deaerated with CO_2, was added and the layers separated; the chloroform was dried with molecular sieves and evaporated, leaving 840 mg of 1,2-dihydrophthalazine, m.p. 82–83°C. It was dissolved in a small amount of chloroform and precipitated with light petrol, m.p. 84–85°C. (Found: C 72.65; H 5.91. Calc. for $C_8H_8N_2$: C 72.70; H 6.10). NMR-spectrum, see above; IR-spectrum (KBr; cm^{-1}): 3370(m), 1422(s), 1315(m), 1115(w), 1090(m), 940(w), 912(s), 845(m), 798(s), 750–730(s).

1,2-Dihydrophthalazine was boiled with an ethanolic solution of phenylisothiocyanate; the thiourea derivative thus obtained was recrystallized from acetone-petrol ether, m.p. 130–131°C. (Found: C 67.25; H 4.93; N 15.45; S 11.91. Calc. for $C_{15}H_{13}N_3S$: C 67.39; H 4.90; N 15.72; S 11.99). NMR-spectrum ($CDCl_3$): $\delta=5.52$ (singlet) $\sum H=2$; $\delta=7.0-7.75$ (multiplet) $\sum H=10$; $\delta=9.75$ (broad singlet) $\sum H=1$.

Similarly *1-methylphthalazine* was reduced in alkaline solution; the 1,2-dihydro-4-methylphthalazine was not obtained pure, due to its easy reoxidation. The thiourea derivative had m.p. 170–172°C. (Found: C 68.79; H 5.37. Calc. for $C_{16}H_{15}N_3S$: C 68.32; H 5.37). NMR-spectrum ($CDCl_3$): $\delta=2.42$ (singlet) $\sum H=3$; $\delta=5.50$ (singlet) $\sum H=2$; $\delta=7.1$ (multiplet) $\sum H=9$; $\delta=9.85$ (broad singlet) $\sum H=1$.

Reduction of phthalazine in alkaline solution (2). Phthalazine (1 g) was reduced at −1.55 V (SCE) in 0.2 N potassium hydroxide containing 10 % alcohol with stirring of the electrode surface, $n=1.4$ *F*/mol. The precipitate formed was filtered off (0.55 g) and treated with 10 ml of alcohol which removed 1,2-dihydrophthalazine. The remaining material (0.40 g) was dissolved in 50 ml DMF and precipitated by dilution with water, m.p. 214°C. The m.p. is a poor criterion for the identity of the product, probably because it is a mixture of a D,L- and *meso*-form which has not been separated. (Found: C 72.68; H 5.37; N 20.82. Calc. for $C_{16}H_{14}N_4$: C 73.26; H 5.38; N 21.26). IR-spectrum (KBr: cm^{-1}): 3340(m), 1485(m), 1420(s), 1308(w), 1270(w), 1092(s), 915(s), 838(m), 792(s), 747(s).

Reduction of phthalazine (to 1,2,3,4-tetrahydrophthalazine). Phthalazine (0.5 g) was reduced to 1,2-dihydrophthalazine as described above; the cathode potential was then lowered to −1.95 V (SCE) and two more electrons per molecule were consumed. An anodic wave grew during the reduction; if the current was reversed and the reduction product (III) oxidized at −0.2 V (SCE), 1,2-dihydrophthalazine was formed. The reduced solution was treated with excess of benzoyl chloride, and 1,2,3,4-tetrahydrophthalazine dibenzoate, m.p. 204°C (202–203°C)[14] was obtained.

Reduction of 1-methylphthalazine in acid solution. 1. Methylphthalazine hydrochloride (0.5 g) was reduced in 2 N hydrochloric acid at −0.75 V (SCE) at 0–5°C; it is essential that the potential does not become more negative than corresponding to the first polarographic wave of Ia in the medium; it is advisable to record polarograms several times during the reduction directly in the catholyte in order to check the value of the reduction potential. The reaction completed, $n=4$, the catholyte was evaporated *in vacuo* at a bath temperature <35°C and the residue treated with anhydrous ethanol containing hydrogen chloride (about N HCl) which dissolved the methylisoindole, but only traces of the contaminating ammonium chloride. If ethanol without hydrogen chloride is used, the methylisoindole hydrochloride loses part of its hydrogen chloride as it is a rather

weak base; the unprotonated methylisoindole rapidly forms coloured products. The ammonium chloride was filtered off and the ethanol removed *in vacuo*; the residue was dissolved in chloroform containing hydrogen chloride, filtered, and the 1-methylisoindole hydrochloride precipitated with dry ether, m.p. 157—160°C. The NMR-spectrum has been discussed above. IR-spectrum (KBr, cm^{-1}): 2500—3100(s), 1610(m), 1560(w), 1437(m), 1385(m), 1283(w), 1215(w), 763(m), 711(m).

Reduction of 2-methylphthalazinium iodide. 2-Methylphthalazinium iodide (2 g) was reduced at −1.2 V in a borate buffer. $n=1$ *F*/mol. A yellow precipitate was formed which was dissolved in chloroform, filtered, and dried. Evaporation of the solvent left 940 mg of a 47:53-mixture of two dimeric compounds. The residue was dissolved in a small amount of benzene and a small portion of light petrol added. A precipitate was obtained which by NMR-analysis was shown to be pure isomer A. After recrystallization from cyclohexane it had m.p. 175°C. (Found: C 74.45; H 6.31; N 19.22. Calc. for $C_{18}H_{18}N_4$: C 74.45; H 6.25; N 19.30). The NMR-spectrum of A has been discussed above. IR-spectrum (KBr, cm^{-1}): 2900(w), 1505(w), 1470(w), 1440(m), 1355(m), 1315(w), 1245(w), 1157(ms), 1103(m), 1017(ms), 940(w), 923(s), 843(w), 823(s), 761(s), 747(s), 730(w). The filtrate from A was precipitated with increasing amounts of petrol ether; the fractions contained a mixture of A and B with increasing contents of B. The last fractions were crystallized from cyclohexane (twice) and pure isomer B, m.p. 155—156°C, was obtained. (Found: C 74.17; H 6.34; N 19.00. Calc. for $C_{18}H_{18}N_4$: C 74.45; H 6.25; N 19.30). The NMR-spectrum of B has been discussed above. IR-spectrum (KBr, cm^{-1}): 2910(m), 1510(w), 1468(w), 1437(m), 1361(m), 1315(m), 1240(w), 1158(ms), 1098(w), 1015(ms), 940(m), 928(m), 872(w), 830(s), 757(s), 743(s), 732(w), 720(w). Useful differences in the IR-spectra of A and B are the ratios of the intensities of the two peaks at 920—940 cm^{-1}, the peaks at 830—845 cm^{-1}, and the small peak at 720 cm^{-1}. The compounds are not stable to long heating, and heating during the recrystallizations has to be kept at a minimum.

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Received December 11, 1969.