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Electroörganic Preparations

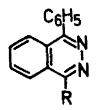
XXXIII. Polarography and Reduction of Some Substituted Phthalazines

HENNING LUND and ERIK TH. JENSEN

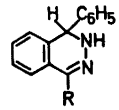
Department of Chemistry, University of Aarhus, DK-8000 Aarhus C, Denmark

The polarography and electrolysis of some substituted phthalazines and the corresponding dihydrophthalazines have been investigated. In alkaline solution, the phthalazines are reduced to the 1,2-dihydrophthalazines which are reducible in acid solution. 4-Dimethylamino-1-phenylphthalazine forms in acid solution in a four-electron reduction 2-(1′-amino-1′-phenylmethyl)-*N*,*N*-dimethylbenzamidine, which at higher pH forms 1-phenyl-3-iminoisoindoline on ring closure; at pH < 7, this compound is reduced in a four-electron reduction to 1-phenylisoindoline. 4-Methoxy-1-phenylphthalazine is in acid solution through an imidic ester in two four-electron steps reduced to the same compound, whereas 4-mercapto-1-phenylphthalazine is reduced similarly, but without any isolable intermediates. In alkaline medium, 4-mercapto-1-phenylphthalazine is reduced to 1,2-dihydro-1-phenylphthalazine.

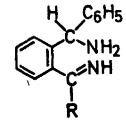
The polarographic and controlled potential reduction of phthalazine and some methyl-substituted phthalazines has previously been investigated;[1] a similar work on some substituted phthalazines is reported below. The present investigation includes the following compounds: 4-dimethylamino-1-phenylphthalazine (Ia), 1,2-dihydro-4-dimethylamino-1-phenylphthalazine (IIa), 2-(1′-amino-1′-phenylmethyl)-*N*,*N*-dimethylbenzamidine (IIIa), 1-phenyl-3-iminoisoindoline (IV), 4-methoxy-1-phenylphthalazine (Ib), 1,2-dihydro-4-methoxy-1-phenylphthalazine (IIb), methyl 2-(1′-amino-1′-phenylmethyl)-benzimidate (IIIb), 1-phenylisoindoline (V), 3-methoxy-1-phenylisoindole, 4-mercapto-1-phenylphthalazine (Ic), 4-dimethylamino-1-methylphthalazine, its 1,2-dihydroderivative, 4-methoxy-1-methylphthalazine, and its 1,2-dihydroderivative.



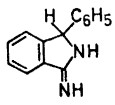
Ia R = $N(CH_3)_2$
b R = OCH_3
c R = SH



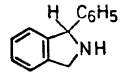
IIa R = $N(CH_3)_2$
b R = OCH_3
c R = SH



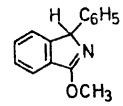
IIIa R = $N(CH_3)_2$
b R = OCH_3



IV



V



VI

RESULTS

In Fig. 1 are given the half-wave potentials in dependence of pH of 4-dimethylamino-1-phenylphthalazine (Ia) and its 1,2-dihydroderivative (IIa). At pH < 2, Ia gives a single four-electron wave; between pH 2 and 5 the height of this wave diminishes to the height of a two-electron wave, and at the same time a second wave at a more negative potential, corresponding to that of IIa, appears in such a manner that the sum of the two waves corresponds to a four-electron wave. At pH > 5, evidence of some further reduction is found, in that the limiting current increases with decreasing potential, but no well-

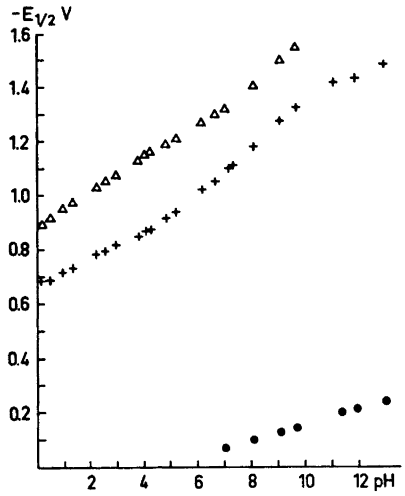


Fig. 1. Half-wave potentials (V *vs.* SCE) of 4-dimethylamino-1-phenylphthalazine (Ia) and 1,2-dihydro-4-dimethylamino-1-phenylphthalazine (IIa). +, 1st wave of Ia; △, cathodic wave of IIa; ●, anodic wave of IIa.

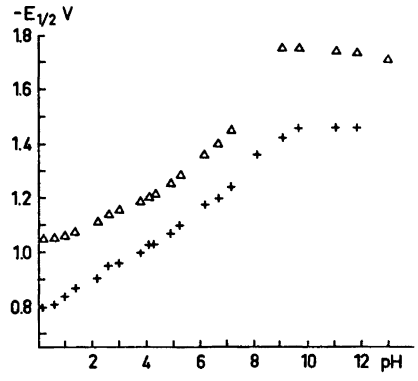


Fig. 2. Half-wave potentials (V *vs.* SCE) of 4-methoxy-1-phenylphthalazine (Ib). +, 1st wave of Ib; △, 2nd wave of Ib.

defined reduction wave is observed. At pH > 9, the second wave gradually disappears, so only the first two-electron wave remains.

The wave of IIa corresponds to the second wave found for Ia at pH > 2; in alkaline solution a two-electron anodic wave is observed.

Controlled potential reduction of Ia in N hydrochloric acid produced 2-(1′-amino-1′-phenylmethyl)-*N*,*N*-dimethylbenzamidine dihydrochloride (IIIa) in a four-electron reaction. The structure was assigned on the basis of the elementary analysis, the NMR-spectrum (D_2O: $\delta = 2.48$ (singlet) $\sum H = 3$; $\delta = 3.46$ (singlet) $\sum H = 3$; $\delta = 6.28$ (singlet) $\sum H = 1$; $\delta = 7.7 - 8.4$ (multiplet) $\sum H = 9$), and its ring closure reaction to 1-phenyl-3-iminoisoindoline (IV). In the interpretation of the NMR-spectrum of IIIa it is assumed that the amidino group is planar, and there is a highly hindered rotation around the C–N bonds in the protonated form; this would be expected from simple resonance considerations; the two methyl groups are thus predominantly in the plane determined by the carbon and the two nitrogen atoms; the bulky substituent on the benzene ring in the *ortho* position to the amidino group makes it unfavourable for the plane of the amidino group to coincide with that of the phenyl ring; these planes are more likely to be at right angles to each other. Such an arrangement would bring the protons of one of the methyl groups into the shielding part of the field produced by the ring current of the phenyl ring and thus induce a resonance at a higher field; the difference in chemical shift between the two methyl groups in the dimethylamino group is 1 ppm.

IIIa possesses a reasonable stability at low pH and low temperatures; at higher pH, the amino group attacks the amidino group under ring closure and elimination of dimethylamine with formation of 1-phenyl-3-iminoisoindoline (IV); this reaction makes it impossible to investigate the polarographic behaviour of IIIa at higher pH.

The reduction wave of 1-phenyl-3-iminoisoindoline (IV) is masked by the hydrogen wave at pH < 4; between pH 4 and 9, the wave-height corresponds to a four-electron wave; between pH 9 and 12, the height diminishes and reaches the height of a two-electron wave at pH > 12; a pronounced maximum in the interval pH 9 – 11 makes the polarograms difficult to interpret with regard to the transition between reduction of the protonated and unprotonated molecule. Some values of $E_{\frac{1}{2}}$ are given in Table 1.

Table 1. Half-wave potentials (*vs.* SCE) of 3-iminoisoindoline (IV) at some pH-values.

pH	4.5 – 8.5	9.0	10.0	11.0	12.3
$-E_{\frac{1}{2}}$ V	1.53	1.57	1.63	1.72	1.80

In alkaline solution pH 13, Ia is reduced at – 1.65 V (SCE) to 1,2-dihydro-4-dimethylamino-1-phenylphthalazine (IIa) in a two-electron reduction; the structure IIa was assigned to the reduction product from the elementary analysis, the NMR-spectrum ($CDCl_3$: $\delta = 2.75$ (singlet) $\sum H = 6$; $\delta = 5.03$ (singlet) $\sum H = 1$; $\delta = 5.28$ (broad singlet) $\sum H = 1$; $\delta = 6.6 - 6.78$ (multiplet) $\sum H = 1$; $\delta = 7.1 - 7.65$ (multiplet) $\sum H = 8$), and its ability to form a thiourea derivative

on reaction with phenylisothiocyanate and a monoacetyl derivative on reaction with acetic anhydride.

Reduction of Ia in a phosphate buffer (pH 6.5) at the potential of the first wave also produces IIa; anodic oxidation of IIa in alkaline solution at the potential of the anodic wave forms Ia.

The polarographic behaviour of 4-methoxy-1-phenylphthalazine (Ib) is shown in Fig. 2; at most pH-values, two waves are observed. At pH < 1.5, two four-electron waves are found; between pH 1.5 and 3.5, the height of the first wave diminishes, and that of the second one grows, making at pH > 3.5 the first wave a two-electron wave and the second wave a six-electron wave. At pH > 6.5, a minimum on the limiting current of the second wave is observed; the minimum becomes broader with increasing alkalinity, and at pH > 9, the second wave has disappeared. Between pH 10 and 12, the first wave disappears, and another two-electron wave appears at more negative potentials in the usual way.

1,2-Dihydro-4-methoxy-1-phenylphthalazine (IIb) is at pH < 2 reduced in a two-electron wave, followed by a four-electron wave; at pH 0, the half-wave potential of the first wave of IIb is about 0.06 V more negative than that of the first wave of Ib. Between pH 2 and 4.5, the first wave of IIb merges with the second wave, and the combined wave becomes a six-electron wave. This wave disappears between pH 6.5 and 9 in the same manner as the second wave of Ib. Ib does not give a well-defined anodic wave.

Controlled potential reduction of Ib in alkaline solution pH 13 produced a dihydro derivative in a two-electron reaction; the structure IIb was assigned to the product from the analysis, the NMR-spectrum ($CDCl_3$: $\delta = 3.80$ (singlet) $\sum H = 3$; $\delta = 5.16 - 5.32$ (broad signal, NH + CH) $\sum H = 2$; $\delta = 6.50 - 6.75$ (multiplet) $\sum H = 1$; $\delta = 7.1 - 7.7$ (multiplet) $\sum H = 8$) and its ability to form a thiourea derivative on reaction with phenylisothiocyanate and a monoacetyl derivative on reaction with acetic anhydride.

Reduction at 0°C of Ib in aqueous hydrochloric acid at the potential of the first wave (−0.80 to −0.85 V (SCE)) gave the further reducible methyl 2-(1′-amino-1′-phenylmethyl)-benzimidate (IIIb). A temperature and potential control is essential for the preparation of IIIb. At 25°C, an appreciable hydrolysis of IIIb to methyl 2-(1′-amino-1′-phenylmethyl)-benzoate or even to 3-phenylphthalimidine takes place. If the potential becomes more negative than 0.90 V (SCE), the reduction of IIIb to V lowers the yield of IIIb, whereas a potential more positive than −0.80 V (SCE) makes the reduction go so slowly that a hydrolysis of IIIb becomes a problem even at low temperatures. At higher pH, IIIb forms the cyclic imidic ester 3-methoxy-1-phenylisoindole (VI).

VI was isolated from the catholyte by extraction of the free imidic ester with chloroform after neutralization. The structure of the product was assumed to be VI from the analysis and the NMR-spectrum ($CDCl_3$: $\delta = 4.12$ (singlet) $\sum H = 3$; $\delta = 5.79$ (singlet) $\sum H = 1$; $\delta = 7.2 - 7.7$ (multiplet) $\sum H = 9$). The IR-spectrum contained an absorption band at 1626 cm^{-1} and no appreciable absorption between this band and 2800 cm^{-1} or N-H-absorption, which is consistent with the formulation VI.

The imidic esters IIIb and VI are polarographically reducible as other imidic esters;[2] their half-wave potentials in acid solution correspond closely to those of the second wave of Ib, which corroborates the assumption that IIIb or VI are the four-electron reduction product of Ib in strongly acid solution.

Attempts to isolate the reducible benzimidate IIIb analogously to the isolation of IIIa were unsuccessful. The compound apparently partly survived evaporation of the solvent from the catholyte ($t < 35°C$, 1 mmHg) as the residue gave a cathodic wave corresponding to the second wave of Ib. Treatment of the residue with acetonitrile or methylene chloride yielded a crystalline product which was not polarographically reducible. The compound was assumed to be the hydrochloride of methyl-2-(1′-amino-1′-phenylmethyl)-benzoate from the analysis, $C_{15}H_{15}ClNO_2$, and the IR-spectrum, which showed a carbonyl absorption at 1725 cm^{-1}.

Reduction in acid solution at a potential on the plateau of the second wave resulted in the formation of 1-phenylisoindoline (V); the yield (90–100 %) was determined polarographically after nitrosation of the secondary amine V.[3]

4-Mercapto-1-phenylphthalazine shows in acid solution a large wave closely followed by a smaller wave; the waves are complicated by an adsorption prewave and a maximum. In alkaline solution (pH 12), a four-electron wave is found, which at pH 14 becomes somewhat smaller, $2 < n < 4$. In a small pH-interval, 7–9, two four-electron waves are observed.

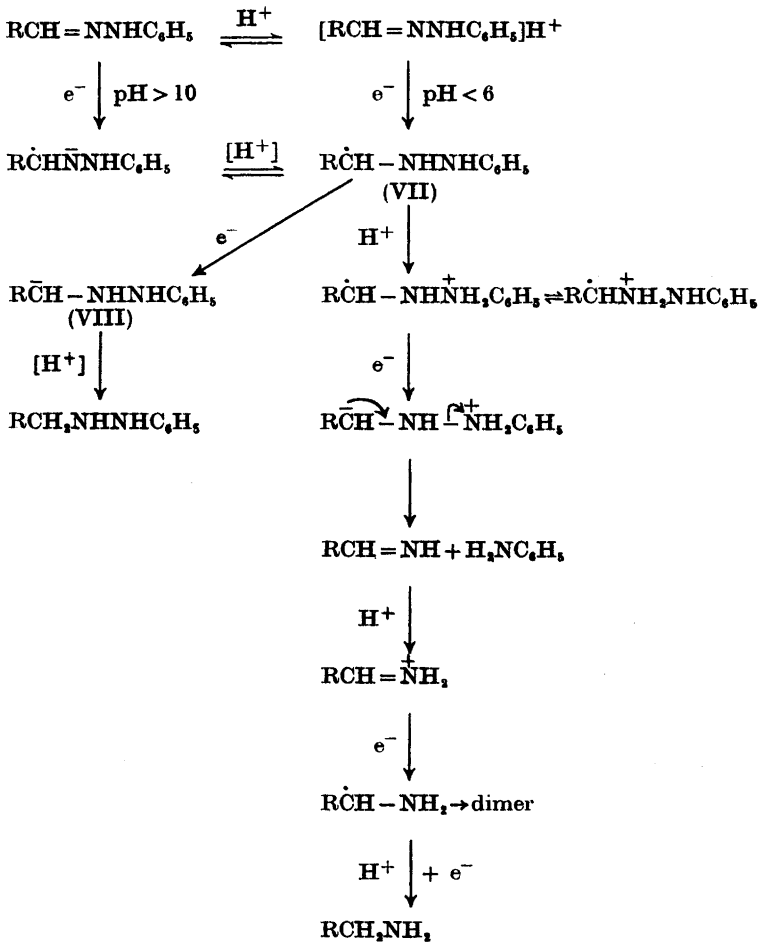
Reduction of Ic in acid solution at −1.1 V (SCE) gives hydrogen sulphide and 1-phenylisoindoline in an eight-electron reduction, whereas in alkaline solution, 1,2-dihydro-1-phenylphthalazine is the product, unless the potential is so negative (−1.90 V *vs.* SCE) that 1-phenyl-1,2,3,4-tetrahydrophthalazine is formed.

DISCUSSION

The reduction of phthalazine and several other diaza heterocyclic compounds has previously been discussed [4–6] in terms of the analogy to the reduction of hydrazones. A scheme for the reduction of an aromatic phenylhydrazone is given below.

Many types of azomethine derivatives fit into such a scheme, in which a cleavage of the bond between the nitrogen atom and a hetero atom precedes the saturation of the carbon–nitrogen bond.[6,7]

According to the scheme, the branching leading to the formation of different products occurs after one proton and one electron are accepted by the substrate. The radical VII may then either accept an electron or a proton; if an electron is transferred to the radical, the carbanion (VIII) may acquire a proton from any weak acid ($=[H^+]$) present, *e.g.* water, with the formation of a hydrazine. In acid solution, the radical may be protonated, and then accept an electron; the zwitter ion thus formed may then react as suggested by the arrows, resulting in a cleavage of the nitrogen–nitrogen bond, as the protonated nitrogen is part of a good leaving group, aniline. It seems unlikely that the carbanion VIII would expel an aniline anion; the carbanion VIII

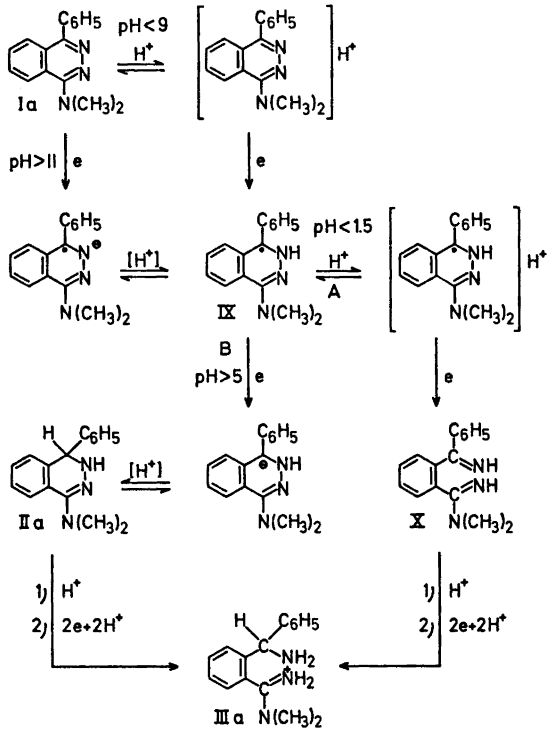


could conceivably accept a proton at nitrogen with resulting cleavage, but it might be expected to give at least some hydrazine from protonation at the carbon atom, and this is generally not observed at low pH; at high pH, the carbanion VIII is generally protonated to a hydrazine.

The only type of compounds which clearly have been demonstrated to be exceptions from the otherwise apparently general rule is 1(2H)-phthalazinones;[8] such compounds may formally be regarded as 1-hydroxyphthalazines, which makes them closely related to the compounds studied here.

The following scheme for the reduction of 4-dimethylamino-1-phenylphthalazine based on the available evidence may be suggested.

The protonated molecule of Ia is the reducible species at the dropping mercury electrode at pH < 9; this is substantiated by the fact that 4-dimethylamino-2-methyl-1-phenylphthalazinium iodide is reduced at potentials near



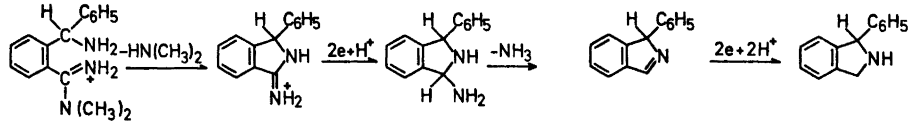
those of Ia up to pH 9. The radical (IX) may either accept a proton or an electron, following either the pathway A or B. The protonated radical (path A) accepts an electron which results in cleavage of the nitrogen – nitrogen bond with the amidino group as leaving group; the benzophenone imine derivative (X) is then protonated and reduced in an over-all two-electron reaction.

If an electron is transferred to the radical IX (path B), the 1,2-dihydro-derivative (IIa) is formed; IIa contains a $>C=N-NHR$ group, and the protonated form is reducible; IIIa is formed with cleavage of the nitrogen – nitrogen bond through steps analogous to those discussed for the reduction of a phenylhydrazone.

The polarographic behaviour of Ia suggests that below pH 1.5, path A is predominantly followed, whereas at pH > 5, path B is the most important one. Between pH 1.5 and 5, both paths are competing, A the dominant one in the acid part of the interval, with B becoming more and more important with increasing pH.

In neutral and alkaline solution, IIIa reacts further to IV; the polarograms of Ia show at pH 6 – 9 only a slight indication of a further reduction, although IV is reducible in this region. The ring closure reaction IIIa→IV is thus comparatively slow, so most of the molecules diffuse away from the electrode before the reducible IV is formed.

The four-electron reduction of the cyclic amidine, 1-phenyl-3-iminoisoindoline IV, may be formulated as follows



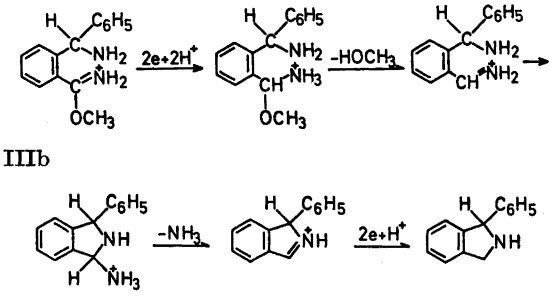
IIIa IV V

In strongly alkaline solution, the wave-height of IV corresponds to a two-electron reduction; this might be due to a slow elimination of ammonia.

The reduction of 4-methoxy-1-phenylphthalazine (Ib) follows a similar scheme as that of Ia; a further reduction, however, is found at pH < 10. The half-wave potential of IIb is only 0.06 V more negative than that of Ib at pH 0, and the evidence that the reduction of Ib at that pH proceeds through the imine (part A) rather than through IIb (path B) is less clear-cut than in the reduction of Ia, where the wave of IIa is 0.2 V more negative than that of Ia. Besides the observed difference in half-wave potential between Ib and IIb, two pieces of evidence favour path A; a maximum is found on the first wave of Ib, but not on that of IIb; a logarithmic analysis of the first wave of Ib failed to show the presence of two consecutive waves, whereas a polarographic curve obtained from a mixture of Ib and IIb directly showed the presence of two consecutive waves.

The benzimidic esters (IIIb or VI) are reducible even at low pH in contradistinction to the amidines (IIIa, IV). This is in accordance with the half-wave potential of benzimidic ester in acid solution [2,6] and the reduction of amidines in neutral solution.[9]

A route for the reduction of IIIb in acid solution could be



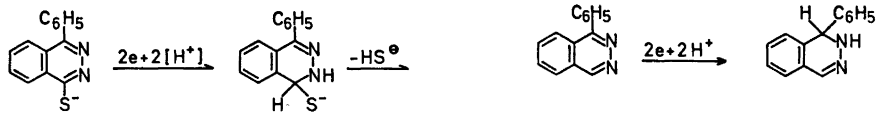
IIIb V

It is difficult to distinguish unequivocally between this reaction route, where IIIb accepts electrons, or one analogous to that suggested above for the transformation of IIIa through IV to V, in which VI would be formed prior to the reduction. The polarographic behaviour of VI shows that, based on this criterion, VI could be the reducible intermediate in the reduction of Ib, as both the half-wave potential of VI and the presence of a maximum is

similar to that of the second wave of Ib. The polarographic criterion is not conclusive, as other imidic esters, *e.g.* methyl benzimidate,[2] are reduced in the same potential region and also show pronounced maxima. The isolation of methyl 2-(1′-amino-1′-phenylmethyl)benzoate as a hydrolysis product of the primarily formed four-electron reduction product suggests, however, that IIIb rather than VI is the intermediate in acid solution, and that VI is formed during the work-up by the neutralization of the catholyte. In the proposed reduction route is suggested a ring closure by attack of the amino group on the aldimine, which in acid solution would be expected to occur more readily than an attack on an imidic ester.

The reduction of 4-mercapto-1-phenylphthalazine (Ic) may in acid solution proceed along at least two routes. The reaction could start with a reduction of the carbon – sulphur bond, followed by elimination of hydrogen sulfide and reduction of the 1-phenylphthalazine thus formed. Alternatively, the reaction could run analogously to those of Ia and Ib (path A and/or B), followed by reduction of the thiobenzamide derivative thus formed.[10] The latter alternative seems the more attractive in view of the occurrence of two waves, which is difficult to explain if 1-phenylphthalazine were an intermediate, and the similarity in structure of Ic and benzaldehyde thiobenzoylhydrazone.[4]

In alkaline solution (pH 13), however, the reduction takes place by reduction of the carbon-sulfur double bond, followed by elimination of hydrogen sulfide (or its anion) and a two-electron reduction of 1-phenylphthalazine. 1,2-Dihydro-1-phenylphthalazine has in alkaline solution a half-wave potential of -1.88 V (SCE) and Ic at -1.67 V (SCE), so a potential control is essential if a reduction to the 1,2-dihydro derivative is desired. The half-wave potential of 1-phenylphthalazine is -1.52 V (SCE) at pH 13, and is thus reducible at the potential used for the reduction of Ic.



EXPERIMENTAL

The polarograph was a pen-recording instrument Radiometer Polariter PO4d, the potentiostat was obtained from Tage Juul Electronics, Copenhagen; a Varian A60 and a Beckman IR 18 were used for the NMR- and IR-spectra, respectively.

Materials. 4-Chloro-1-phenylphthalazine was prepared according to Lieck;[11] the crude product was passed through a short, thick column of alumina with chloroform as eluent; this treatment removes acid impurities, which catalyze the self-quaternization of the active chloro compound. Treatment of the chloro compound with dimethylamine in ethanol or sodium methoxide in methanol yielded Ia or 1b, respectively.

Reduction of 4-dimethylamino-1-phenylphthalazine (Ia). Ia (2 g) was reduced at -1.0 V (SCE) in N hydrochloric acid at $t = 0$°C. The reduction completed ($n = 4$ F/mol), the catholyte was evaporated *in vacuo* (0.2 mmHg) at a bath temperature below 40°C; the residue was treated with acetonitrile which dissolved any dimethylamine hydrochloride present, but left the product largely undissolved. The viscous product crystallized slowly on contact with acetonitrile during a week, 2.35 g. The crystals were dissolved in anhydrous ethyl alcohol, containing hydrogen chloride, and dry ether was added; addition of some crystals induced a slow crystallization of 2-(1′-amino-1′-phenylmethyl)-*N*,*N*-

dimethylbenzamidine dihydrochloride (IIIa). (Found: C 57.60; H 6.54; N 12.68; Cl 21.71. Calc. for $C_{16}H_{21}N_3Cl_2$: C 58.91; H 6.49; N 12.97; Cl 21.74.)

The NMR-spectrum has been discussed above; IR-spectrum (KBr, cm^{-1}): 3500–2700 (broad, s), 2590 (m), 2070 (w), 1670 (s), 1630 (s), 1523 (m), 1450 (w), 1425 (w), 1055 (w), 785 (w), 709 (m), 688 (m). R_F-value (TLC, SiO_2, ethanol containing hydrogen chloride) = 0.55.

Treatment of a solution of IIIa with ammonia to pH 8 precipitated a viscous oil which crystallized in the course of some minutes; the viscous product was soluble in chloroform, whereas the crystals were rather insoluble in common solvents. During recrystallizations, temperatures above 120°C should be avoided, as a blue compound is then formed; such a colour also developed when solutions of IIIa are allowed to stand. The product was assumed to be 1-phenyl-3-iminoisoindoline (IV) from the spectra and the elementary analysis of the hydrochloride. (Found: C 68.60; H 5.40; N 11.41; Cl 14.52. Calc. for $C_{14}H_{13}N_3Cl$: C 68.69; H 5.35; N 11.45; Cl 14.49.) NMR-spectrum (CF_3COOH): $\delta = 6.10$ (singlet) $\sum H = 1$; $\delta = 7.1 - 8.3$ (multiplet). IR-spectrum of IV hydrochloride (KBr, cm^{-1}): 3400–2600 (broad, s), 1695 (s), 1630 (m), 1614 (m), 1590 (m), 1492 (m), 1450 (m), 1370 (m), 1182 (mw), 772 (m), 731 (s), 688 (ms). IR-spectrum of IV (KBr, cm^{-1}): 3455 (s), 3345 (s), 3300–3150 (m), 3100–2900 (m), 2820–2700 (m), 1642 (s), 1612 (w), 1568 (s), 1482 (w), 1436 (m), 1221 (m), 1188 (m), 1055 (ms), 1000 (m), 940 (m), 751 (s), 690 (ms). R_F-value (TLC, SiO_2, ethanol containing hydrogen chloride) = 0.85.

Reduction of 4-dimethylamino-1-phenylphthalazine (Ia). A suspension of Ia (1 g) in 0.5 N potassium hydroxide containing ethanol (20 %) was reduced at −1.6 V (SCE); $n = 2$ F/mol. The reduction completed, the suspension of the white reduction product was filtered under nitrogen, 910 mg. After washing with deoxygenated water it was dried *in vacuo* and the 1,2-dihydro-4-dimethylamino-1-phenylphthalazine (IIa) recrystallized from cyclohexane, m.p. 143–144°C. (Found: C 76.24; H 6.81; N 16.78. Calc. for $C_{16}H_{17}N_3$: C 76.46; H 6.82; N 16.72.) NMR-spectrum has been discussed above. IR-spectrum (KBr, cm^{-1}): 3280 (s), 1596 (w), 1497 (w), 1453 (w), 1430 (w), 1372 (s), 1080 (w), 1060 (w), 1025 (w), 935 (w), 750 (ms), 700 (ms).

On boiling of IIa with phenylisothiocyanate in ethanol, a thiourea derivative, m.p. 198–199°C, was formed. (Found: C 71.98; H 5.69; N 14.31. Calc. for $C_{23}H_{22}N_4S$: C 71.42; H 5.74; N 14.50.) Treatment of IIa with acetic anhydride left an acetate, m.p. 109–110°. NMR-spectrum ($CDCl_3$): $\delta = 2.33$ (singlet) $\sum H = 3$; $\delta = 2.80$ (singlet) $\sum H = 6$; $\delta = 7.07$ (singlet) $\sum H = 1$; $\delta = 7.18$ (singlet) $\sum H = 5$; $\delta = 7.25 - 7.7$ (multiplet) $\sum H = 4$.

Reduction of 4-dimethylamino-1-phenylphthalazine (Ia) (reduction of 1-phenyl-3-iminoisoindoline (IV)). Ia (0.5 g) was reduced at −1.0 V (SCE) in 0.5 N hydrochloric acid containing 40 % ethanol, $n = 4$ F/mol; the reduction completed, concentrated ammonia was added to pH 9, which resulted in the formation of IV; the potential was lowered to −1.70 V (SCE), and the reduction consumed further 4 F/mol. The yield of 1-phenylisoindoline (V) and dimethylamine was determined polarographically after nitrosation;[3] the difference in half-wave potential between the two N-nitrosamines ($E_{\frac{1}{2}}$ (V−NO) = −0.57 V; $E_{\frac{1}{2}}$ (Me_2NNO) = −0.93 V (SCE)) allowed a simultaneous determination; yield of V 90–95 %.

Reduction of 4-dimethylamino-1-methylphthalazine (XI). XI (1 g) was reduced in 0.5 N potassium hydroxide containing 20 % ethanol at −1.75 V (SCE); $n = 2$ F/mol. The reduction completed, the catholyte was extracted with deaerated chloroform, the organic layer washed with deaerated water and dried over molecular sieves. Evaporation of the chloroform left 1,2-dihydro-4-dimethylamino-1-methylphthalazine. NMR-spectrum (CCl_4): $\delta = 1.40$ (doublet) $\sum H = 3$, $J = 6.5$ Hz; $\delta = 2.69$ (singlet) $\sum H = 6$; $\delta = 3.96$ (quartet) $\sum H = 1$, $J = 6.5$ Hz; $\delta = 5.4$ (broad signal) $\sum H = 1$; $\delta = 7.1 - 7.8$ (multiplet) $\sum H = 4$. The compound is easily reoxidized to XI, and attempts to recrystallize the crude product failed.

Reduction of 4-methoxy-1-phenylphthalazine (Ib). Ib (2 g) was reduced at 0°C at −0.82 V (SCE) in N hydrochloric acid containing 30 % ethanol; a potential control is essential, as the further reduction corresponding to the second polarographic wave becomes appreciable at potentials more negative than −0.9 V (SCE). After the reduction was completed ($n = 4$ F/mol), two procedures were attempted to isolate the product. *Procedure A.* To the catholyte was added chloroform and then solid potassium carbonate, until pH was 8 to 9. The chloroform layer was separated, dried (molecular sieves A3), and evaporated. The residue was treated with benzene, which left 550 mg of 1-phenyl-

phthalimidine; evaporation of the benzene filtrate left a crystalline residue, 1250 mg; this was dissolved in methanol and precipitated with water and the product recrystallized from petrolether. The polarographically reducible product, m.p. 109 – 110°C, has been assumed to be 3-methoxy-1-phenylisoindole (VI). (Found: C 79.75; H 5.84; N 6.25. Calc. for $C_{15}H_{13}NO$: C 80.69; H 5.87; N 6.27.) The NMR-spectrum has been discussed above; IR-spectrum (KBr, cm^{-1}): 3100 – 2840 (several weak bands), 1626 (ms), 1600 (m), 1576 (ms), 1491 (w), 1451 (m), 1438 (ms), 1365 (s), 1132 (m), 1029 (w), 1008 (m), 978 (m), 757 (ms), 736 (s), 697 (ms). *Procedure B.* The solvent of the catholyte was removed *in vacuo* (< 1 mmHg) at bath temperature < 40°C. Polarography of the residue showed that the reducible compound responsible for the second wave of Ib at least partly survived the evaporation of the solvent. Two approaches to isolate the reducible product were tried. (B1) The residue was treated with acetonitrile, which resulted in a mixture of ammonium chloride and methyl 2-(1′-amino-1′-phenylmethyl)-benzoate (XII); these compounds were separated by treatment with 4 N hydrochloric acid, which largely left the ester undissolved. (B2) The residue was treated with chloroform, which after drying with molecular sieves was diluted with dry ether; after filtration, the filtrate was evaporated *in vacuo*. Neither the chloroform-insoluble part, which contained ammonium chloride and ester (XII), the ether-precipitated compound (XII), nor the residue from the filtrate (1-phenylphthalimidine) contained any compounds reducible in acid solution at the required potential. The methyl ester hydrochloride (XII) was recrystallized from methanol containing hydrochloric acid and ether. (Found: C 64.76; H 5.72; N 5.06; Cl 12.77. Calc. for $C_{15}H_{16}ClNO_2$: C 64.87; H 5.78; N 5.05; Cl 12.77.) IR-spectrum (KBr, cm^{-1}): 3200 – 2700 (br, s), 2620 (m), 2050 (w), 1725 (s), 1600 (m), 1522 (ms), 1502 (m), 1455 (m), 1444 (m), 1273 (s), 1262 (s), 1207 (m), 1190 (m), 756 (m), 737 (ms), 698 (ms). NMR-spectrum (CF_3COOH): $\delta = 4.00$ (singlet) $\sum H = 3$; $\delta = 6.35$ (quartet) $\sum H = 1$, $J = 6$ Hz; $\delta = 7.3 - 8.3$ (multiplet) $\sum H = 11 - 12$.

Reduction of 4-methoxy-1-phenylphthalazine (Ib). Ib (150 mg) was reduced in N hydrochloric acid at the potential of the second wave – 1.15 V (SCE), $n = 8$ *F*/mol. The concentration of the secondary amine 1-phenylisoindoline (V) was determined polarographically after nitrosation (85 – 100 % yield). The identity of the product was secured by evaporation of the catholyte *in vacuo* and taking an IR-spectrum of the residue, which showed the presence of ammonium chloride and V.

Reduction of 4-methoxy-1-phenylphthalazine (Ib). A suspension of Ib (1 g) was reduced at – 1.70 V (SCE) in 0.5 N potassium hydroxide containing 20 % ethanol. The reduction completed, $n = 2$ *F*/mol, the suspension of the reduction product, 1,2-dihydro-4-methoxy-1-phenylphthalazine (IIb), was filtered under nitrogen, washed with deaerated water, and dried *in vacuo*, 880 mg. It was recrystallized from cyclohexane, m.p. 125 – 126°C. (Found: C 75.35; H 5.85; N 11.74. Calc. for $C_{15}H_{14}N_2O$: C 75.60; H 5.92; N 11.76.) The NMR-spectrum was discussed above. IR-spectrum (KBr, cm^{-1}): 3285 (s), 1630 (m), 1605 (w), 1495 (w), 1453 (w), 1435 (ms), 1357 (ms), 1335 (s), 1083 (ms), 1025 (m), 895 (w), 832 (w), 800 (m), 760 (ms), 750 (s).

On boiling with an ethanolic solution of phenylisothiocyanate, IIb yielded a thiourea derivative, m.p. 167 – 168°C. (Found: C 70.89; H 5.69; N 11.29. Calc. for $C_{22}H_{15}N_3OS$: C 70.75; H 5.13; N 11.26.) Treatment of IIb with acetic anhydride yielded an acetate, m.p. 104 – 105°C. NMR-spectrum ($CDCl_3$): $\delta = 2.32$ (singlet) $\sum H = 3$; $\delta = 3.91$ (singlet) $\sum H = 3$; $\delta = 7.02$ (singlet) $\sum H = 1$; $\delta = 7.19$ (singlet) $\sum H = 5$; $\delta = 7.2 - 7.8$ (multiplet) $\sum H = 4$.

Reduction of 4-methoxy-1-methylphthalazine (XIII). XIII (1 g) was reduced in 0.2 N potassium hydroxide containing 20 % ethanol, at – 1.80 V (SCE), $n = 2$ *F*/mol. The reduction completed, the catholyte was extracted with deaerated chloroform, which was then dried over molecular sieves and evaporated. The residue consisted mainly of 1,2-dihydro-4-methoxy-1-methylphthalazine. NMR-spectrum ($CDCl_3$): $\delta = 1.42$ (doublet) $\sum H = 3$, $J = 6.5$; $\delta = 3.85$ (singlet) $\sum H = 3$; $\delta = 4.25$ (quartet) $\sum H = 1$, $J = 6.5$; $\delta = 4.88$ (singlet) $\sum H = 1$; $\delta = 7.0 - 7.7$ (multiplet) $\sum H = 4$. Treatment of the residue with an ethanolic solution of phenylisothiocyanate gave a thiourea derivative, m.p. 68 – 69°C.

Reduction of 4-mercapto-1-phenylphthalazine (Ic). A. Acid solution. Ic (0.5 g) was reduced in N hydrochloric acid, containing 40 % ethanol, at – 0.85 V (SCE). During the reduction, hydrogen sulphide was evolved; the reduction consumed 8 *F*/mol. In the reduced solution, the yield (70 – 80 % in different runs) of 1-phenylisoindoline (V) was determined by polarography after nitrosation.

B. Alkaline solution. Ic (0.5 g) was reduced in N potassium hydroxide at −1.70 V (SCE); an ether layer was covering the catholyte. The reduction consumed 4 *F*/mol, and an anodic wave due to the presence of sulfide became visible on polarograms in the catholyte. The reaction completed, the layer of ether was separated, dried (potassium carbonate), and evaporated. The product was shown to be 1,2-dihydro-1-phenylphthalazine from the NMR-spectrum ($CDCl_3$): $\delta = 5.33$ (singlet) $\sum H = 1$; $\delta = 5.7$ (broad singlet) $\sum H = 1$; $\delta = 6.6 - 6.9$ (multiplet) $\sum H = 1$; $\delta = 7.1 - 7.6$ (multiplet) $\sum H = 9$.

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