

Electroorganic Preparations

XXIII. Polarography and Reduction of Cinnoline and Related Compounds*

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The polarographic behaviour of several substituted cinnolines and their reduction products has been investigated. The electrode reactions have been elucidated using controlled potential electrolysis. Alkyl- and arylcinnolines are primarily reduced to 1,4-dihydroderivatives; the further reduction is a hydrogenolysis of the nitrogen-nitrogen bond with the formation of an indole or a diamine; only the reduction of benzo[c]cinnoline leads to a hydrazine derivative. 3- and 4-Hydroxycinnoline are reduced to the keto-1,2,3,4-tetrahydrocinnoline. The derivatives of 1,2,3,4-tetrahydrocinnoline can be oxidized anodically; the reduction product from 4-keto-1,2,3,4-tetrahydrocinnoline, 4-hydroxy-1,2,3,4-tetrahydrocinnoline, can be oxidized, and the product loses water and forms cinnoline. 4-Mercaptocinnoline is reduced to 1,4-dihydrocinnoline, and 4-chlorocinnoline yields in alkaline solution 4,4'-bis-cinnolyl.

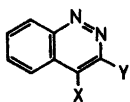
In the current polarographic investigation of nitrogen-containing heterocyclic compounds the polarographic behaviour of some cinnolines has been studied. The investigation includes cinnoline (Ia), 4-methylcinnoline (Ib), 3-phenylcinnoline (Ic), 4-carboxy-3-phenylcinnoline (Id), 8-methyl-3-phenylcinnoline, benzo[c]cinnoline (II), the quaternization products of these compounds, the N-1 and N-2-oxides of Ib and the N-oxide of II, 4-methyl-1,4-dihydrocinnoline (IIIb), 3-phenyl-1,4-dihydrocinnoline (IIIc), 3-hydroxycinnoline (Ie), 4-hydroxycinnoline (If), the N-1 and N-2-methyl derivatives of If, 4-methoxycinnoline (Ig), 3-keto-1,2,3,4-tetrahydrocinnoline (IV), 4-keto-1,2,3,4-tetrahydrocinnoline (Va), 4-hydroxy-1,2,3,4-tetrahydrocinnoline, 4-mercaptocinnoline (Ih), and 4-chlorocinnoline (Ii).

Controlled potential reductions have been used to elucidate the electrode reactions.

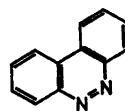
POLAROGRAPHIC INVESTIGATION

In Fig. 1 is shown the dependence on pH of the half-wave potentials of the first cathodic wave of 4-methylcinnoline, the two cathodic waves of 4-

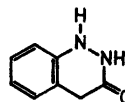
* Part of it presented at the 4th International Congress on Polarography, Praha, July 1966.



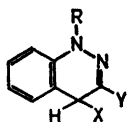
- I a X = H Y = H
 b X = CH₃ Y = H
 c X = H Y = C₆H₅
 d X = COOH Y = C₆H₅
 e X = H Y = OH
 f X = OH Y = H
 g X = OCH₃ Y = H
 h X = SH Y = H
 i X = Cl Y = H



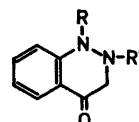
II



IV



- III a X = H Y = H R = H
 b X = CH₃ Y = H R = H
 c X = H Y = C₆H₅ R = H
 d X = H Y = C₆H₅ R = CH₃



- V a R = H R' = H
 b R = CH₃ R' = H
 c R = H R' = CH₃

methyl-1,4-dihydrocinnoline, and the anodic wave of 2,4-dimethyl-1,2-dihydrocinnoline; the latter wave is ill-defined below pH 8.

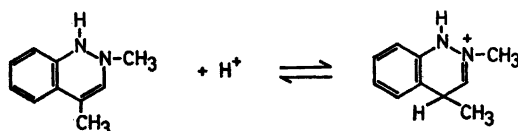
4-Methylcinnoline shows in 6 N hydrochloric acid a single two-electron reduction wave; about pH 0 a second cathodic wave grows up and reaches about pH 3 the height of a two-electron wave; at this pH a small third wave is visible. The half-wave potentials of the second and the third waves are found at the same potentials as those of 1,4-dihydro-4-methylcinnoline.

The occurrence of a single wave of 4-methylcinnoline in strongly acid solution may be explained in at least two ways: 1) A slow step may occur after the uptake of two electrons; the primary product formed in this solution may be a 1,2-dihydrocinnoline, which would be a derivative of phenylhydrazine and would not be expected to be reducible as such, and the transformation of the protonated hydrazine derivative into the reducible hydrazone, the 1,4-dihydrocinnoline, may be a slow step at the dropping mercury electrode; another possibility, 2), is that the protonated dihydrocinnoline rearranges rapidly into the non-reducible 1-aminoskatole.^{1,2}

1,4-Dihydro-4-methylcinnoline shows in acid solution two waves which merge about pH 4 and the combined wave diminishes in height from pH 6 to 8, where it disappears. The second wave is smaller than the first one; the combined wave reaches nearly the height of a four electron wave, before it diminishes in height. 1,4-Dihydro-4-methylcinnoline may be regarded as a hydrazone of an aldehyde, and its polarographic behaviour is in accordance with that.³ Only the protonated molecule is reducible, and in slightly acid solution the protonation takes place at the surface of the electrode; in alkaline solution neither a cathodic nor an anodic wave is found.

The polarographic behaviour of *2,4-dimethylcinnolinium iodide* resembles in acid solution very much that of *4-methylcinnoline*, and the reduction occurs at nearly the same potentials; in neutral and alkaline solution the difference between the half-wave potentials of the two compounds gradually grows, and at pH 12 the quaternary compound is reduced at a potential 0.25 V less negative than that of the parent compound. In strongly alkaline solution the compound slowly loses the *N*-methyl group.

The product of the first two-electron reduction of *2,4-dimethylcinnolinium perchlorate* has been formulated as *1,2-dihydro-2,4-dimethylcinnoline*. In acid solution it behaves polarographically in the same way as *4-methyl-1,4-dihydrocinnoline*, and the protonated species may be formulated as a *1,4-dihydrocinnoline*.



In alkaline solution the behaviour of the free base is better explained by the formulation as a *1,2-dihydrocinnoline*, as it shows an anodic wave at rather negative potentials; neither *1,4-dihydrocinnolines* nor *1-aminoskatole* show an anodic wave in alkaline solution.

The polarographic behaviour of *4-methylcinnoline-N-1-oxide* is similar to that of *4-methylcinnoline-N-2-oxide*. Both show in acid solution a two-electron wave followed by the reduction waves of *4-methylcinnoline*, and this first

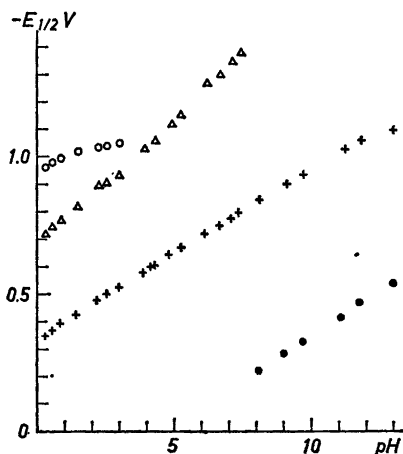


Fig. 1. pH-Dependence of the half-wave potentials (*vs.* SCE) of the first wave of *4-methylcinnoline* +, the two cathodic waves of *1,4-dihydro-4-methylcinnoline* Δ, O, and the anodic wave of *2,4-dimethyl-dihydrocinnoline* ●. Concentration 40 mg/l.

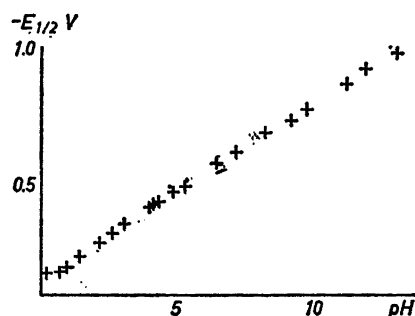


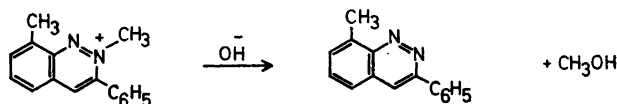
Fig. 2. pH-Dependence of the half-wave potentials (*vs.* SCE) of *benzo[c]cinnoline* in 20% aqueous ethanol. Concentration 40 mg/l.

wave thus corresponds to a reduction of the *N*-oxide to the parent compound. At higher pH this first wave and the two-electron wave of 4-methylcinnoline merge to a single four-electron wave. This wave was observed by Suzuki *et al.*⁴ who polarographed the compounds only at pH 7.

3-Phenylcinnoline (Ic) yields between pH 0 and 10 two one-electron waves which merge to one two-electron wave at pH below 0 and above pH 10. The one-electron waves are followed by a four-electron wave at pH below 8; the four-electron wave disappears at pH >8. The separation of the two one-electron waves are greatest about pH 5 where it is approximately 0.2 V; at pH 4 (citric acid buffer) the half-wave potentials of the three waves are 0.43, 0.60, and 1.10 V (SCE). In slightly alkaline solution the two one-electron waves are drawn out.

1-Methyl-3-phenylcinnolinium iodide is in acid solution reduced as the unmethylated compound, but the potential of the first wave is pH-independent; in strongly alkaline solution the compound adds water with the formation of a non-reducible pseudo-base.

8-Methyl-3-phenylcinnoline is reduced polarographically in a similar way as Ic, and *2,8-dimethyl-3-phenylcinnolinium iodide* is in acid solution reduced more like Id. In strongly alkaline solution the quaternary compound loses the *N*-methyl group according to:



The polarographic behaviour of *3-phenyl-4-carboxycinnoline* (Id) differs from that of Ic in that the separation of the two one-electron steps is very small and hardly noticeable at most pH's. The polarographic behaviour suggests that the carboxyl group is not reduced as in, *e.g.*, the pyridine carboxylic acids.⁵

The pH-dependence of the half-wave potentials of *benzo[c]-cinnoline* (II) is shown in Fig. 2; the oxidation wave of 5,6-dihydrobenzo[c]cinnoline is found at the same potentials as those of the reduction wave of II. A polarogram of a solution containing equal concentrations of II and its reduction product consists of a single wave; a logarithmic analysis (E vs. $\log[i/(i_d - i)]$) of such a wave yields at pH 5 (40 % ethanol) a straight line with the slope 0.034 instead of 0.029 required for a reversible wave. The slope of the line obtained in the logarithmic analysis varies with pH and the alcohol content and approaches the value of the reversible wave at low pH and alcohol content. In solutions containing 40 % ethanol a small adsorption prewave is seen; if the medium contains no alcohol further adsorption phenomena complicate the polarographic curve. The slope of the $E_{1/2}$ -pH curve is 0.063.

Benzo[c]cinnoline (II) and its reduction product behave polarographically very nearly reversibly, whereas this is not the case for other of the cinnolines studied. II is also the only cinnoline which is reduced to a hydrazine derivative rather than to a hydrazone; II can be regarded as an azobenzene and the 5,6-dihydro derivative as a hydrazobenzene. The azobenzene-hydrazobenzene system is potentiometrically reversible, but not polarographically;^{6,7} the

system benzo[*c*]cinnoline — 5,6-dihydrobenzocinnoline approaches polarographic reversibility more than the azobenzene-hydrazobenzene system. The transformation of the 1,2-dihydrocinnolines into the more stable 1,4-dihydrocinnolines prevents the other cinnoline-dihydrocinnoline systems from behaving as a reversible redox system.

The polarographic behaviour of 5-methylbenzo[*c*]cinnolinium iodide resembles in acid and neutral solution that of II. In alkaline solution the quaternary compound is reduced at a less negative potential than II, but the compound is instable in this medium and loses the methyl group with the formation of II. At pH 13 the loss of the methyl group occurs so fast that no wave of the quaternary compound is visible.

5-Methylbenzo[*c*]cinnolinium iodide is in acid solution reduced to the 5,6-dihydro derivative which can be oxidized anodically to the quaternary compound. The anodic wave of the reduction product occurs in this medium at the same potentials as the reduction wave of the quaternary compound.

The behaviour of the 1-methyl and 2-methylcinnolinium compounds in alkaline solution differs in the few cases studied. The 1-methyl derivative forms a pseudo-base probably by attack at C-4, whereas the 2-methyl compound loses the methyl group more or less readily in alkaline solution. A pseudo-base derived from a 2-methylcinnolinium compound would formally require the benzene ring in the *o*-quinoid form. 5-Methylbenzo[*c*]cinnolinium iodide which has no possibility of forming a pseudo-base loses the *N*-methyl group very easily in alkaline solution. The difference in behaviour of the 1- and 2-methylcinnolinium compounds can easily be detected polarographically as the former gives the nonreducible pseudo-base in alkaline solution whereas the 2-methyl derivative forms the reducible demethylated compound. If further examples substantiate these findings, this method may be used for the determination of the site of the quaternization in similar compounds where the quaternization reaction produces mainly one of the two possible isomers.

Benzo[*c*]cinnoline-*N*-oxide gives below pH 2 two two-electron waves; the second wave occurs at the same potential as that of benzocinnoline. About pH 2 the waves merge to a four-electron wave. Ross *et al.*⁸ who polarographed II and its *N*-oxide at pH 1.9, 5.2, and 13 observed the four-electron wave of the *N*-oxide; the high alcohol content (80 %) of their solutions may be responsible for the observation of a single wave in acid solution.

3-Hydroxycinnoline (Ie) is reduced in a single wave from pH 0 to 11; at pH >11 the wave splits into two poorly separated waves of which the more negative wave grows and the other one disappears at higher pH. 3-Hydroxycinnoline shows both basic and acid properties; $pK_1 = 0.21$ and $pK_2 = 8.61$.⁹ The polarographic data suggest that the protonated form is reduced up to pH about 6 where a change into the reduction of the unprotonated molecule takes place. About pH 11 a change into the reduction of the anion of Ie occurs.

The reduction product obtained in slightly acid solution, which has been formulated as 3-keto-1,2,3,4-tetrahydrocinnoline, shows an anodic, but no cathodic wave. In Fig. 3 is plotted the pH-dependence of the half-wave potentials of the cathodic wave of Ie and of the anodic wave of the reduction product.

A compound with a structure as 3-keto-1,2,3,4-tetrahydrocinnoline would be expected to behave in some ways as a β -acylated phenylhydrazine. 1-Acetyl-

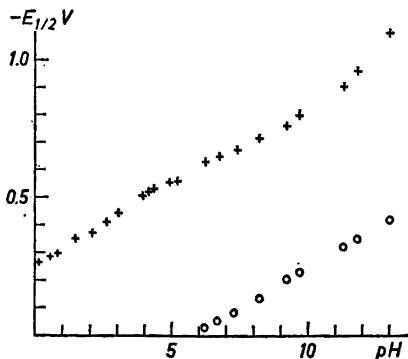


Fig. 3. pH-Dependence of the half-wave potentials (vs. SCE) of the cathodic wave of 3-hydroxycinnoline +, and the anodic wave of 3-keto-1,2,3,4-tetrahydrocinnoline O.

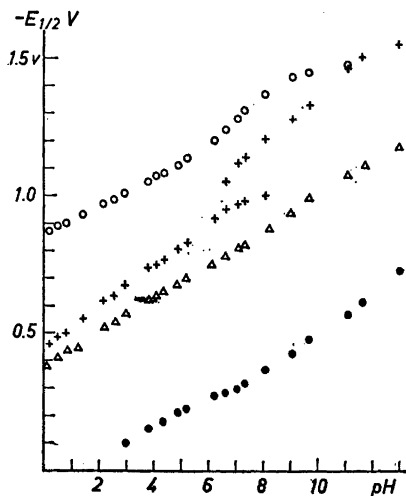
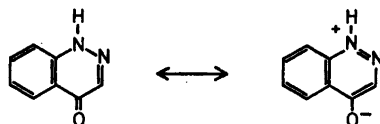


Fig. 4. pH-Dependence of the half-wave potentials (vs. SCE) of the two cathodic waves of 4-hydroxycinnoline, + O, the anodic wave of 4-keto-1,2,3,4-tetrahydrocinnoline ●, and the cathodic wave of 4-methoxycinnoline Δ. Concentration 40 mg/l.

2-phenylhydrazine gives at pH 13 an anodic wave at -0.25 V (SCE) and no cathodic wave at any pH, whereas 1-acetyl-1-phenylhydrazine yields neither a cathodic nor an anodic wave; in accordance with that no well-developed anodic wave was found from 1-aminooxindole.

At Fig. 4 is shown the pH-dependence of the half-wave potentials of 4-hydroxycinnoline (If), 4-keto-1,2,3,4-tetrahydrocinnoline (Va), and 4-methoxycinnoline (Ig). 4-Hydroxycinnoline shows two cathodic waves in acid and slightly alkaline solution; both waves are two-electron waves. They merge about pH 10, and the height of the combined wave corresponds at pH >11 approximately to a three-electron reduction. About pH 8 the first wave diminishes in height and another wave grows up in the way usually found for recombination reactions. 4-Hydroxycinnoline shows both basic and acidic properties, $pK_1 = -0.35$ and $pK_2 = 9.27$.⁹ It is found mainly as the cinnolone which may be formulated as the zwitterion:



4-Keto-1,2,3,4-tetrahydrocinnoline (Va) which can be regarded both as a substituted acetophenone and as a substituted phenylhydrazine shows both a cathodic and an anodic wave. The cathodic wave occurs at the same poten-

tials as the second wave of 4-hydroxycinnoline; in strongly alkaline solution the height of the wave corresponds to a one-electron reduction, at lower pH to a two-electron reaction. The anodic wave occurs at rather negative values and is visible in solutions as acid as pH 3; the free base is very easily oxidized to 4-hydroxycinnoline either electrolytically in a two-electron reaction or by air and should be handled with exclusion of oxygen. The reduction product from Va, formulated as 4-hydroxy-1,2,3,4-tetrahydrocinnoline, shows an anodic wave at nearly the same potential as Va. The occurrence of an anodic wave at such negative potentials seems to indicate the presence of a tetrahydrocinnoline, which has both nitrogen atoms unsubstituted.

4-Methoxycinnoline (Ig) gives a two-electron cathodic wave in the whole pH region; at pH < 0.5 a second wave is visible at the same potentials as that of 4-keto-1,2,3,4-tetrahydrocinnoline. As this compound is the isolated reduction product even at higher pH the primarily formed product which is not electroactive must lose the methoxy group in a slow step. As 4-methoxy-1,4-dihydrocinnoline would be expected to be reducible at about the same potentials as 1,4-dihydrocinnoline, the non-reducible, primarily formed product is probably 1,2-dihydro-4-methoxycinnoline, which can be regarded as an enolic ether.

1-Methyl-4-cinnolone is in acid and neutral solution reduced polarographically in a similar way as 4-hydroxycinnoline. In alkaline solution, however, the two waves do not merge, and here is found a two-electron wave followed by a one-electron wave. A third one-electron wave is found just before the reduction wave of the supporting electrolyte, and this wave is more clearly defined at higher concentrations. The difference in polarographic behaviour in alkaline solution between If and 1-methyl-4-cinnolone is due to the lack of acidic properties of the latter.

The polarographic behaviour of *2-methyl-4-hydroxycinnolinium chloride* resembles in acid and weakly alkaline solution that of 4-hydroxycinnoline. At pH higher than 10, however, two waves are visible, the second wave smaller than the first one. About pH 8 the first wave diminishes in height and another grows up as found for If. As this is found for 2-methyl-4-hydroxycinnolinium chloride and for If, but not for 4-methoxycinnoline, the protonation preceding the reduction most probably is a protonation of the oxygen atom. The polarographic data thus suggest that the zwitterionic structure of 4-hydroxycinnoline is the best representation of the compound to explain its polarographic behaviour.

From the polarographic behaviour of Ig and the 1- and 2-methyl derivatives of If the polarography of If can be explained. The protonated species is the form reduced in acid and neutral solution to about pH 8; the protonation occurs at the surface of the electrode, and between pH 7 and 8 the rate of the protonation determines the height of the wave. The protonation probably takes place at the oxygen atom. Between pH 8 and 10 the unprotonated molecule is the reduced species; above pH 11 the anion of If is the form responsible for the reduction.

Both 1- (Vb) and 2-methyl-4-keto-1,2,3,4-tetrahydrocinnoline (Vc) resemble polarographically the unmethylated compound Va. The cathodic waves of both occur at nearly the same potentials as those of Va. The anodic wave,

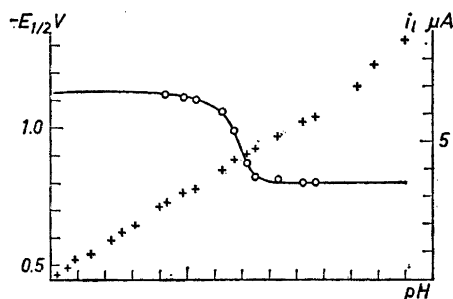


Fig. 5. pH-Dependence of the half-wave potentials (vs. SCE) +, and the limiting current O of 4-mercaptocinnoline. Concentration 40 mg/l.

however, is found at potentials about 0.25 V more positive than those of Va and are close to those of 2,4-dimethyl-1,2-dihydrocinnoline.

3-Bromo-4-hydroxycinnoline and *1-methyl-3-bromo-4-cinnoline* are both reduced at most pH-values in a four-electron reduction followed by a two-electron wave. Both waves occur at about the same potentials as those of the halogen-free compounds. This may be explained by a simultaneous two-electron reduction of the carbon-bromine bond and a two-electron reduction of the nucleus.

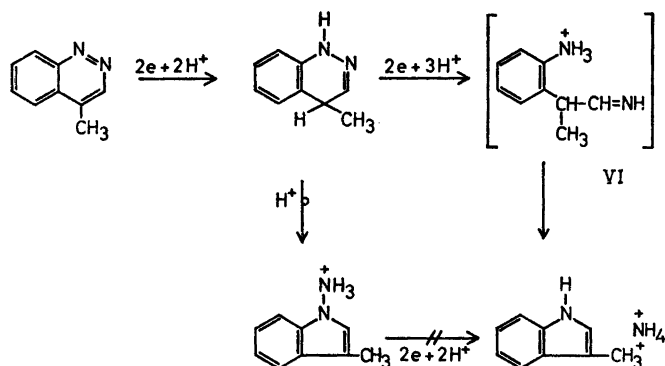
4-Chlorocinnoline is in strongly acid solution reduced in a four electron reduction followed by the reduction of 1,4-dihydrocinnoline. At higher pH a separation of the two-electron waves takes place and in alkaline solution two well separated waves are found; the second wave is found at the same potentials as the wave of cinnoline. The first wave thus corresponds to a reduction of the carbon-chlorine bond.

The dependence on pH of the half-wave potentials and the wave height of the first wave of *4-mercaptocinnoline* is shown in Fig. 5. In a small interval about pH 0 the first wave is split into two poorly separated two-electron waves. The first wave is in the whole pH-region preceded by a small prewave. The four-electron wave found in acid and neutral solution is followed by one or two waves found at potentials slightly more negative than those of the second and third wave of cinnoline. The first wave of cinnoline occurs at less negative potentials than those of 4-mercaptocinnoline.

About pH 7 the four-electron wave diminishes in height and the following waves disappear and at pH > 8 only a single two-electron wave is found. The $E_{1/2}$ -pH curve is approximately linear from pH 0 to pH 11, and no change in the slope is found about pH 7 where the change in wave height occurs. Above pH 11 the slope of the $E_{1/2}$ -pH curve is steeper; in this pH-region the compound is found increasingly as the anion as pH increases. 4-Mercaptocinnoline shows no diffusion controlled anodic wave in alkaline solution.

MACROSCALE REDUCTIONS

The first wave of *4-methylcinnoline* in acid solution was found to be caused by a two-electron reduction to 1,4-dihydro-4-methylcinnoline (IIb). IIb was reduced in acid solution in a two-electron reduction to skatole. The reductions in this medium proceed according to:



In alkaline solution the reduction product from Ib is IIb which is not further reduced in this medium and can not be oxidized at the anode.

4-Methylcinnoline reacts with methyl iodide yielding a mixture of the two isomeric quaternary compounds in the proportions approximately 1:10. The major constituent of the mixture was reduced in acid solution at the potential of the second wave and the product was skatole.

Cinnoline is reduced analogously and the quaternization mixture is not much different from that obtained from Ib.

The reduction of *1,4-dihydro-4-methylcinnoline* to skatole could conceivably follow either of the two routes illustrated on the scheme. 1,4-Dihydrocinnolines are known to rearrange to *N*-aminoindoles under acid catalysis, but as neither *N*-aminoindole nor *N*-aminoskatole was found to be reducible under the conditions employed, the reduction does not follow this route.

1,4-Dihydrocinnolines may be regarded as cyclic phenylhydrazones, and the polarographic behaviour of IIb also resembles that of such compounds. The first step in the reduction of most phenylhydrazones has been shown³ to be a reductive cleavage of the nitrogen-nitrogen bond, and in the present case the aldimine (VI) would be formed. The ring closure which is analogous to that occurring during the Fischer indole syntheses may proceed by addition of the amino group to the aldimine or may be preceded by a hydrolysis to the aldehyde which then is attacked by the amino group.

The reduction route with the aldimine (VI) as the primarily formed product is further substantiated by the presence of a second wave in the polarogram of 1,4-dihydro-4-methylcinnoline. Skatole is not polarographically reducible, but an aldimine as VI would be expected to be reducible at a potential near that of the second wave of 1,4-dihydro-4-methylcinnoline.

During the ring contraction the nitrogen atom originally occurring as N-2 in the cinnoline ring is lost. The isolation of skatole from the reduction of the more abundant isomer in the quaternization mixture shows that the methylation of 4-methylcinnoline takes place preferentially at N-2. This is in accordance with recent results¹⁰ but at variance with the previous assignment.¹¹

By reduction in 2 N hydrochloric acid at -0.5 V (SCE) *3-phenylcinnoline* forms a dihydro derivative that has been formulated as 1,4-dihydro-3-phenylcinnoline from the analysis and the NMR-spectrum. The NMR-spectrum

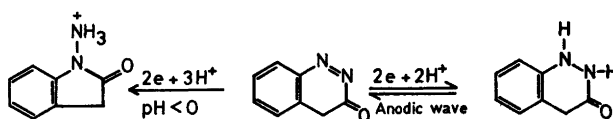
product. A difference in reduction route similar to that between that of Ib and Ic is found in the reduction of 6-phenylpyridazone-3 and 6-methylpyridazone-3. The first step of both reductions is a two-electron reduction to the pyridazinone, but the second reduction of the former is a four-electron reduction to 4-amino-4-phenylbutyric amide, whereas the latter is reduced in a two-electron reaction to a ketimine which is hydrolyzed to the isolated product, levulinic acid.¹²

3-Phenylcinnoline reacts with methyl iodide in acetonitrile yielding a mixture of 78 % of one isomer and 22 % of another. The major isomer was reduced at the potential of the first wave, and the product formulated as 1-methyl-3-phenyl-1,4-dihydrocinnoline (III_d) from the NMR-spectrum (CCl₄) which showed a singlet (3 protons) at $\delta = 3.50$ (N—CH₃) and another singlet at $\delta = 3.68$ (2 protons).

The presence of a methylene group giving a singlet with a chemical shift near that of the methylene group of III_c indicates a 1,4-dihydrocinnoline, and as the compound is soluble in CCl₄, it is non-ionic; the methyl group must then be at N-1 and Ic thus methylated predominantly at N-1.

3-Phenyl-4-carboxycinnoline is in acid solution reduced similarly as Ic in a two-electron reduction followed by a four-electron reduction. From a reduction in acid solution was isolated 1,4-dihydro-3-phenylcinnoline (III_c); the primarily formed product decarboxylated very easily. A reduction in alkaline solution, followed by acidification to pH 3 with phosphoric acid and extraction with chloroform also produced the decarboxylated product III_c.

3-Hydroxycinnoline (Ie) is reduced in a two-electron reduction in the whole pH-region; no further reduction occurs. In strongly acid solution the main product is 1-aminoxindole; in an acetate buffer is obtained a yellowish reduction product which has been formulated as 3-keto-1,2,3,4-tetrahydrocinnoline on the following grounds. The compound has a higher m.p. than 1-aminoxindole and the IR- and NMR-spectra are different from those of that compound. The reduction product shows an anodic wave which suggests the presence of a 1,2-disubstituted hydrazine rather than a 1,1-disubstituted one; it can be oxidized anodically to 3-hydroxycinnoline in a quantitative yield; the IR-spectrum shows a carbonyl absorption at 1640 cm⁻¹ (KBr) which suggests a six-membered rather than a five-membered ring. The reduction product is difficult to isolate pure and it turns rapidly yellow owing to reoxidation.



A compound, formulated as 3-keto-1,2,3,4-tetrahydrocinnoline, has previously¹³ been prepared by reduction of 3-hydroxycinnoline with zinc and sulfuric acid, but the compound prepared by this method has been shown¹⁴ to be 1-aminoxindole, probably formed by hydrolytic cleavage of the primarily formed 3-keto-1,2,3,4-tetrahydrocinnoline, which can be regarded as an acylated phenylhydrazone, followed by ring closure. This ring contraction

in acid solution together with the easy reoxidation in neutral and alkaline solution may account for the fact that IV has not been isolated before. Reduction of Ie with lithium aluminium hydride gives 1,2,3,4-tetrahydrocinnoline.¹⁵

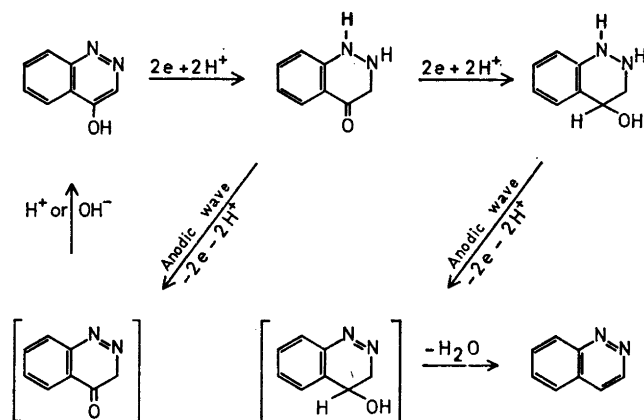
The first wave in acid and neutral solution of 4-hydroxycinnoline corresponds to a two-electron reduction: the reduction product is a compound $C_8H_8N_2O$, which has been formulated as 4-keto-1,2,3,4-tetrahydrocinnoline (Va) on the following grounds: a) It has an anodic polarographic wave at rather positive potentials (Fig. 4) which suggests the presence of a 1,2-disubstituted hydrazine. b) It can be oxidized anodically to 4-hydroxycinnoline thus indicating the presence of a cinnoline nucleus; this is further confirmed by the reactions shown in the reduction scheme below. c) The IR-spectrum exhibits an absorption at 1680 cm^{-1} indicative of a carbonyl group; the polarographic behaviour of the compound is in accordance with its formulation as a substituted acetophenone. d) The NMR-spectrum shows a singlet integrated as two protons at $\delta = 4.62$ (trifluoroacetic acid) corresponding to a methylene group.

Va is in acid and neutral solution reduced in a two-electron reaction. The product has been formulated as 4-hydroxy-1,2,3,4-tetrahydrocinnoline on the following grounds. The compound gives an anodic wave at nearly the same potentials as Va, which is an indication of a hydrazine derivative which has at least one proton at each nitrogen atom. The hetero-ring is six-membered as cinnoline is formed by a two-electron anodic oxidation. On standing, the compound slowly forms 1,4-dihydrocinnoline, which does not give an anodic wave. The compound has not been isolated, and the above mentioned facts could also be explained by the formulation of the compound as 1,2-dihydrocinnoline. The 4-hydroxy-1,2,3,4-tetrahydrocinnoline, however, is the primary product formed by reduction of the substituted acetophenone Va and the loss of water would be expected to be slow compared to the tautomerization of the dehydrated compound to 1,4-dihydrocinnoline.

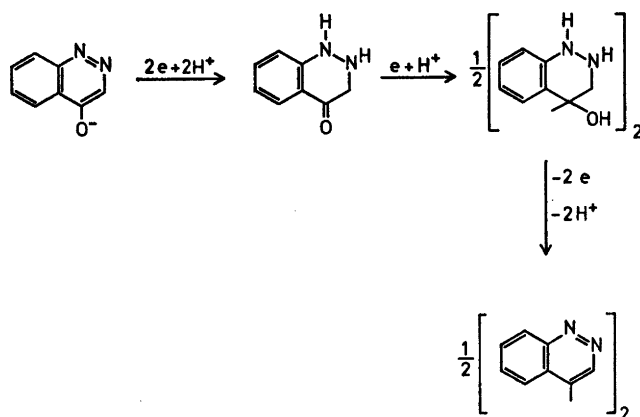
In alkaline solution Va is reduced in a one-electron reaction, the product has been formulated as a pinacol dimerized at C-4. The NMR-spectrum (in trifluoroacetic acid) shows an AB-system with $J_{AB} = 14$ cps. The geminal coupling constant indicates a methylene group containing two non-equivalent protons. This indicates that no loss of water has occurred, and in this case a formulation of the reduction product as a 1,2-dihydrocinnoline is excluded. The signals from both protons are rather broad owing to interaction with the adjacent nitrogen atom. The reactions of 4-hydroxycinnoline can thus be formulated as shown on p. 2537.

As 4-hydroxycinnoline is prepared by diazotization of *o*-aminoacetophenone it is one of the easier obtainable derivatives of cinnoline. Cinnoline may thus be prepared from 4-hydroxycinnoline by reduction in acid solution at the potential of the second wave, making the solution slightly alkaline, and oxidize the product anodically. As no isolation of the intermediates is necessary, and the overall yield is good (70–80 %), the method compares favourably with the usual methods starting with 4-methylcinnoline, going through the styryl derivative and the carboxylic acid,¹⁶ or by dechlorination of 4-chlorocinnoline¹⁷ obtained from 4-hydroxycinnoline.

Acid solution:



Alkaline solution:



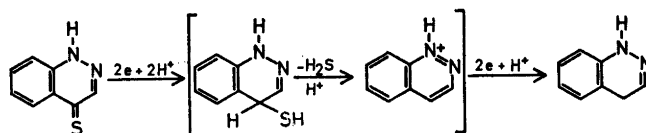
The reaction sequence reminds of that described by Atkinson and Sharpe¹⁸ in which 4-hydroxycinnoline is reduced to 1,2,3,4-tetrahydrocinnoline; this compound is then oxidized to cinnoline by mercuric oxide.

From a reduction of 4-methoxycinnoline in citric acid buffer consuming 2 electrons/molecule, the product was 4-keto-1,2,3,4-tetrahydrocinnoline.

Both 1-methyl-4-cinnolone and the anhydrobase of 2-methyl-4-hydroxycinnolinium hydroxide can be reduced to the corresponding 4-keto-1,2,3,4-tetrahydrocinnolines, and these compounds can be reoxidized anodically in alkaline solution to the starting material. Reduction of 1-methyl-4-cinnolone with lithium aluminium hydride gives mainly 1-methyl-1,2,3,4-tetrahydrocinnoline together with some dimer.¹⁹

The reduction of 4-mercaptocinnoline yielded both in N hydrochloric acid and in a borate buffer 1,4-dihydrocinnoline in a four-electron reaction. During

the reduction in a borate buffer cinnoline could be detected in the catholyte. The reaction may be formulated as:



The four-electron reduction of 4-mercaptocinnoline to 1,4-dihydrocinnoline (IIIa) could conceivably proceed through either 1,2,3,4-tetrahydro-4-thiocinnolone, which would then be reduced further to 4-mercapto-1,2,3,4-tetrahydrocinnoline, and 1,4-dihydrocinnoline would be formed by a loss of hydrogen sulphide from this compound, or the primarily formed compound could be 4-mercapto-1,4-dihydrocinnoline. This compound could either lose hydrogen sulphide to cinnoline as suggested in the scheme above, or it could be reduced further to 4-mercapto-1,2,3,4-tetrahydrocinnoline before the loss of hydrogen sulphide, or reduced directly to IIIa.

In favour of the reaction route suggested in the scheme above the following arguments can be used. The two-electron reduction occurring at the dropping mercury electrode in alkaline solution yields an electroinactive species. This compound can not be 1,2,3,4-tetrahydro-4-thiocinnolone which can be regarded as a derivative of thioacetophenone; this compound would be expected to be reducible at a rather positive potential. A reduction at a macro-mercury electrode yields 1,4-dihydrocinnoline even at pH 9; this means that a slow step occurs after the uptake of the first two electrons and an electroactive species is formed in this slow reaction. The formation of an electroactive species is too slow to influence the polarographic curve at pH > 9, but not the results from the preparative reduction. The slow reaction is suggested to be the loss of hydrogen sulphide, which seems more reasonable than assuming that a slow step is involved in the reduction of the carbon-sulphur bond. The reduction of 4-mercapto-1,4-dihydrocinnoline would require a protonation, which could be slow in alkaline solution, but the reduction of the protonated species would probably result in a cleavage of the nitrogen-nitrogen bond.

A further confirmation of the reduction route suggested in the scheme is found in the results from the preparative reduction of 4-mercaptocinnoline at pH 9. The small prewave which is found in the non-reduced solution at the same potential as the reduction potential of cinnoline grows during the earlier part of the reduction and becomes in the later part of the reaction nearly as high as the wave of the remaining 4-mercaptocinnoline.

The slope of the $E_{\frac{1}{2}}$ -pH curve is the same from pH 0 to 11 suggesting that the same electrode reaction is the primary step both in acid and alkaline solution. The occurrence of a prewave in the whole pH-region at the reduction potential of cinnoline points in the same direction. The explanation of the decrease of the limiting current around pH 7 is thus that the loss of hydrogen sulphide from the primarily formed product is acid catalyzed and becomes a slow step in alkaline solution.

The product isolated from the reduction at the potential of the first wave of 4-chlorocinnoline (Ii) in alkaline solution was 4,4'-bis-cinnolyl rather than cinnoline which would be expected from the polarographic data. Some cinnoline may have been formed, but may have been lost in the mother-liquor from the bis-cinnolyl. Catalytic reduction²⁰ of Ii in methanol (Pd/CaCO₃) yielded some 4,4'-bis-cinnolyl, and this product was also formed on reduction of Ii with lithium aluminium hydride.¹⁵

DISCUSSION

The polarographic reduction of pyridazine, cinnoline, benzo[c]cinnoline, and phthalazine (VII) derivatives is different in some respects. In acid solution phthalazine is reduced in a six-electron reduction²¹ which may start either with a hydrogenolysis of the nitrogen-nitrogen bond followed by a reduction of the diimine or with a formation of the 1,2-dihydrophthalazine²² which is reducible in a four-electron reduction at a potential less negative than that of phthalazine. Cinnoline is first reduced to 1,4-dihydrocinnoline, which at a considerably more negative potential suffers hydrogenolysis of the nitrogen-nitrogen bond. The reduction of a pyridazine as 1-methyl-3,6-diphenyl-5-*t*-butylpyridazinium iodide²³ follows a similar pattern as cinnoline; in the first step a 1,4-dihydropyridazine is formed which at a more negative potential is reduced to a pyrrole. Benzo[c]cinnoline is the only of these compounds in which the dihydro derivative possesses no double bonded nitrogen atoms.

The reduction of the hydroxyl derivatives of pyridazine, cinnoline, and phthalazine also differs. Pyridazines are first reduced to the 4,5-dihydroderivatives²² in which the nitrogen-nitrogen bond is then cleaved reductively. Phthalazinone is reduced to 3,4-dihydro-(2H)-phthalazinone²⁴ which in strongly acid solution can be reduced further to phthalimidine. 3-Hydroxycinnoline is reduced to the 1,2-dihydro derivative; no further reduction is observed. This could be expected to occur in strongly acid solution, but no polarographic evidence of such a reduction is found; a ring contraction of the dihydro derivative should be very fast in order to compete with the further reduction, but must be considered. 4-Hydroxycinnoline differs from the above mentioned hydroxy derivatives in that the carbon carrying the oxygen is not adjacent to a nitrogen atom, and the reduction of If is also different from the others in that a ketone rather than a hydrazide is formed in the first reduction.

The half-wave potentials (in N hydrochloric acid) of benzo[c]cinnoline (II), cinnoline (Ic), pyridazine (VIII), and phthalazine (VII) are -0.17 , -0.29 , -0.51 , and -0.71 (*vs.* SCE), respectively. The sequence of these half-wave potentials is that which would be expected from simple bond number considerations, if it is assumed that a nitrogen-nitrogen double bond is easier reducible than a carbon-nitrogen double bond. The half-wave potential of azobenzene (N HCl) is about $+0.05$ V (SCE)⁶ and that of benzalazine probably about -0.8 V (SCE); the half-wave potential of benzalazine can only be obtained by extrapolation from higher pH-values, as it is rapidly hydrolyzed in N HCl.

The amount of double bond character,²⁵ obtained by considering only Kekulé structures, of the nitrogen-nitrogen bonds in II, Ic, VIII, and VII is 0.80, 0.67, 0.50, and 0.33, respectively. If the half-wave potentials of the four compounds are plotted against the amount of double bond character of the nitrogen-nitrogen bond (B) a straight line is obtained, $E_{\frac{1}{2}} = -1.09 + 0.17 B$.

The observation of a linear relation between $E_{\frac{1}{2}}$ and a parameter as the simple bond number of the nitrogen-nitrogen bond may justify some calculations. By first order perturbation calculation of the lowest unoccupied Hückel-MO of the corresponding hydrocarbons, based upon the parameter values $\alpha_{N^+} = \alpha_C + 2\beta_{CC}$ and $\alpha_{N^*} = \alpha_C + 0.5\beta_{CC}$, were obtained approximations for the corresponding HMO's of the single protonated diaza compounds. From these energies and by means of the correlation between $E_{\frac{1}{2}}$ and the energy of the lowest unoccupied HMO of aromatic hydrocarbons²⁶ was calculated²⁷ the following difference between the half-wave potentials: $\Delta E_{\frac{1}{2}}$ (II, Ia) = 0.111 V (found 0.12 V), $\Delta E_{\frac{1}{2}}$ (Ia, VII) = 0.529 V (found 0.42 V). The calculated results seem sufficiently close to the experimental ones to warrant further investigation along these lines for the compounds mentioned and for other aromatic diazahydrocarbons.

Besides influencing the half-wave potentials of the compounds the position of the benzene ring fused to the hetero-ring is important for the product formation. The benzene ring is not reduced, and one of the double bonds of the hetero-ring of the product remains thus fixed. This fixation of one of the double bonds is essential for an understanding of the differences in reduction route for the compounds mentioned above.

EXPERIMENTAL

The equipment used for polarography and electrolysis at controlled potential was the same as described previously.²⁴ The NMR-spectra were recorded at 60 Mc/s on a Varian Associates A-60 spectrometer.

Materials. 4-Methylcinnoline,¹⁵ 3-phenylcinnoline,²⁸ 3-hydroxycinnoline,²⁹ 4-hydroxycinnoline,³⁰ its 1-¹⁸ and 2-methyl¹⁰ derivatives, 4-chlorocinnoline,³¹ 4-methoxycinnoline,³² and 4-mercaptocinnoline³² were prepared according to known methods.

Analogous to the preparation of 3-phenylcinnoline²⁷ was prepared 8-methyl-3-phenylcinnoline, m.p. 57–58° (light petrol). Intermediates: Benzaldehyde-*o*-tolylhydrazone, m.p. 101–102° (aqueous ethanol), prepared in ethanol containing acetic acid. 1-Benzylideneamino-7-methylisatin, m.p. 162–163° (ethanol). 8-Methyl-3-phenylcinnoline-4-carboxylic acid, decomp. 242–246°.

Reduction of 4-methylcinnoline (1. wave). 4-Methylcinnoline (1 g) was reduced in N hydrochloric acid at –0.4 V (SCE) at 10°. The reduction consumed two electrons per molecule. The solution was then made alkaline with solid sodium carbonate, the precipitate was filtered and dried, 850 mg, m.p. 63–65°. The compound was identified as 1,4-dihydro-4-methylcinnoline from the m.p. (63–65°)¹ and the NMR-spectrum (CDCl₃): $\delta = 1.29$ (doublet, $J_{H,CH_3} = 7.2$ cps), $\sum H = 3$; $\delta = 3.29$ (octet, $J_{H(4),CH_3} = 7.2$ cps, $J_{H(4),H(3)} = 2.8$ cps), $\sum H = 1$; $\delta = 6.5–6.75$ (multiplet), $\sum H = 2$; $\delta = 6.9–7.2$ (multiplet), $\sum H = 3$; $\delta = 7.7$ (broad), $\sum H = 1$.

Cinnoline was reduced similarly. Isolated was 1,4-dihydrocinnoline, m.p. 81–82.5°. NMR-spectrum (CDCl₃): $\delta = 3.25$ (doublet, $J_{H(3),CH_3} = 3$ cps), $\sum H = 2$; $a = 6.5–7.2$ (multiplet), $\sum H = 5$; $\delta = 7.5–7.8$ (broad), $\sum H = 1$.

Reduction of 4-methylcinnoline (2. wave). 4-Methylcinnoline (1 g) was reduced in N hydrochloric acid at –1.0 V (SCE). The reduction consumed four electrons per molecule, and a precipitate was formed during the reduction. This was filtered (825 mg), and identified as skatole from the m.p. 92–94° (95°)³⁴ and the NMR-spectrum (CDCl₃): $\delta = 2.30$

(doublet, $J = 1.1$ cps), $\sum H = 2$; $\delta = 6.80$ (sextet, $J_A = 1.1$, $J_B = 2.2$), $\sum H = 1$; $\delta = 7.0-7.25$ (multiplet), $\sum H = 3$; $\delta = 7.4-7.7$ (multiplet), $\sum H = 2$.

2,4-Dimethylcinnolinium iodide was reduced similarly and *skatole* was the only isolated product.

Reduction of 3-phenylcinnoline (1. wave). 1 g of 3-phenylcinnoline was reduced in 2 N hydrochloric acid containing 50 % ethanol at -0.50 V (SCE). The reduction consumed two electrons per molecule. The reduction completed, half of the solvent was removed by distillation, the remainder made slightly alkaline with sodium carbonate and extracted twice with chloroform. The extract was dried (potassium carbonate) and the solvent evaporated leaving 935 mg of crude 1,4-dihydro-3-phenylcinnoline, m.p. $150-152^\circ$ (benzene). NMR-spectrum (CDCl_3) $\delta = 3.77$ (singlet), $\sum H = 2$; $\delta = 6.5-7.9$ (multiplet), $\sum H = 10$. (Found: C 80.23; H 5.65. Calc. for $\text{C}_{14}\text{H}_{12}\text{N}_2$: C 80.74; H 5.81). The NMR-spectrum in CF_3COOD ($\delta = 4.45$ (singlet), $\sum H = 2$; $\delta = 7.0-7.6$ (multiplet), $\sum H = 4$; $\delta = 7.7-8.1$ (multiplet), $\sum H = 5$; $\delta = 12.78$ (singlet), $\sum H = 1$) did not change during 2 h at 25° , but standing at 60° for 20 h induced a change in the NMR-spectrum. The intensity of the signal at $\delta = 4.45$ diminished to 20 % of its original value, and the signal at $\delta = 12.78$ increased correspondingly.

Reduction of 3-phenylcinnoline (2. wave). 1 g of 3-phenylcinnoline was reduced as described above at -0.5 V (SCE). After this reduction was completed, the potential was lowered to -1.20 V (SCE). This reduction consumed four electrons per molecule. The reduction completed, half of the solvent was removed by distillation, the remainder made strongly alkaline with sodium hydroxide and extracted several times with a mixture of chloroform and 2-propanol (3:1). The solvent was removed by distillation, the residue dissolved in ether, and the solution dried (potassium carbonate). On addition of dry hydrogen chloride a precipitate, 1.1 g, was obtained, m.p. $238-240^\circ$. (Found: C 58.52; H 6.46. Calc. for $\text{C}_{14}\text{H}_{10}\text{Cl}_2\text{N}_2$: C 58.95; H 6.36). NMR-spectrum (CF_3COOH): $\delta = 3.5-4.2$ (multiplet), $\sum H = 2$; $\delta = 4.8-5.2$ (multiplet), $\sum H = 1$; $\delta = 7.1-7.9$ (multiplet with a sharp signal at $\delta = 7.50$), $\sum H = 12-13$. The multiplet at high field is the AB-part of a ABM-system, with the multiplet at $4.8-5.2$ as the M-part. Interpretation of the spectrum gave: $J_{AM} = 6.2$ cps, $J_{BM} = 8.8$ cps, $J_{AB} = 14.5$ cps. $\delta_A = 3.905$, $\delta_B = 3.635$.

4-Carboxy-3-phenylcinnoline was reduced similarly at the potential of the first wave. The only isolated product was 1,4-dihydro-3-phenylcinnoline. The same compound was isolated from a reduction in 0.5 N sodium hydroxide containing 50 % ethanol. The reduced solution was made slightly acid with phosphoric acid and extracted with chloroform. Only the decarboxylated product, IIIc, was isolated.

Reduction of 5-methylbenzo[c]cinnolinium iodide. 200 mg of this compound was reduced at -0.4 V (SCE) in an acetate buffer containing 30 % alcohol. The reduction consumed two electrons per molecule and produced a compound with an anodic wave at the same potential as that of the cathodic wave of the starting material. This 5,6-dihydro derivative was oxidized anodically at -0.2 V with the formation of the starting material. The compound was then reduced again at -0.4 V, and the solution made alkaline with solid potassium hydroxide. An anodic wave was found at -0.7 V together with one at -0.4 V; anodic oxidation at -0.3 V produced a compound with two cathodic waves at -0.75 and -0.98 V. The wave at -0.75 V gradually disappeared and the other one grew up. The product was extracted with chloroform which was then dried and evaporated. The residue was shown to be benzo[c]cinnoline from the IR-spectrum.

In a similar experiment *benzo[c]cinnoline* was reduced at -0.5 V (SCE) with two electrons to 5,6-dihydrobenzo[c]cinnoline. The half-wave potential of II, of the half-reduced solution and of the reduction product was the same. Anodic oxidation of the dihydro derivative produced II.

Reduction of 3-hydroxycinnoline (Ie). 3-Hydroxycinnoline (0.5 g) was dissolved in an emulsion of phosphate buffer pH 6.5 containing potassium chloride (110 ml) and butanol (40 ml). The compound was reduced at -0.80 V (SCE) and the reduction consumed two electrons per molecule; after the reduction no significant polarographic wave, neither cathodic from Ie nor anodic from IV, was found in the aqueous layer. The layers were separated and the butanol evaporated *in vacuo* leaving a nearly quantitative yield of a yellowish product, m.p. $160-164^\circ$. In his paper¹⁸ Neber states that the compound prepared by Bössel, believed to be dihydro-3-hydroxycinnoline, did not have m.p. 166° , as stated in Bössel's dissertation, but 126° ; however, if it was not a misprint in Bössel's dissertation, he might have had the same compound as isolated here. NMR-

spectrum (CF_3COOH): $\delta = 3.98$ (singlet), $\sum \text{H} = 2$; $\delta = 7.2-7.6$ (multiplet with a sharp signal at $\delta = 7.38$), $\sum \text{H} = 4$. The IR-spectrum showed a carbonyl frequency at 1640 cm^{-1} (KBr). If the reduction was performed in the ordinary way and the product extracted afterwards, it was difficult to obtain the reduced product without contamination by 3-hydroxycinnoline formed by reoxydation by oxygen dissolved in the solvents.

Reduction of 3-hydroxycinnoline in 2 N HCl. 3-Hydroxycinnoline (0.5 g) was reduced in 2 N hydrochloric acid at -0.40 V (SCE) with two electrons per molecule. The catholyte was then evaporated *in vacuo*, the residue washed with a little ethanol and neutralized with 40 % aqueous ammonia. The product was filtered and purified by sublimation, white crystals m.p. $126-127^\circ$; N-amino-oxindole has m.p. $127.5-128^\circ$.¹⁴ NMR-spectrum (CF_3COOH): $\delta = 3.83$ (singlet), $\sum \text{H} = 2$; $\delta = 6.8-7.1$ (multiplet), $\sum \text{H} = 1$; $\delta = 7.2-7.5$ (multiplet), $\sum \text{H} = 3$.

Reduction of 4-hydroxycinnoline (1. wave). 4-Hydroxycinnoline (1 g) was suspended in N hydrochloric acid and reduced at -0.5 V (SCE). The compound dissolved during the reduction, $n = 2$. The solvent was removed by distillation *in vacuo* at temperatures below 50° . The residue was dissolved in ethanol and precipitated with ether, 740 mg. A second crop, 300 mg, was obtained from the filtrate by removing the solvent, dissolving the residue in a small amount of ethanol and precipitating the product with ether; m.p. $216-220^\circ$. (Found: C 51.94; H 4.86. Calc. for $\text{C}_8\text{H}_9\text{ClN}_2\text{O}$: C 52.19; H 4.91). The IR-spectrum showed a carbonyl absorption at 1680 cm^{-1} . NMR-spectrum (D_2O): $\delta = 4.23$ (singlet), $\sum \text{H} = 2$; $\delta = 7.0-7.3$ (multiplet), $\sum \text{H} = 2$; $\delta = 7.5-8.0$ (multiplet), $\sum \text{H} = 2$. On addition of NaOD the singlet at $\delta = 4.23$ disappeared. In CF_3COOH the singlet was found at $\delta = 4.62$.

Reduction of 4-hydroxycinnoline (If) (2. wave). 4-Hydroxycinnoline (1.0 g) was reduced in an acetate buffer containing 30 % ethanol at -1.2 V (SCE). When the reduction was completed (4 electrons per molecule), the solution was made alkaline by addition of solid sodium carbonate. The compound was oxidized anodically at -0.05 V (SCE). The mercury electrode was stirred only slowly as a fast stirring disintegrated the electrode into small droplets of mercury. When the anodic wave had disappeared, indicating complete oxidation, the yield of cinnoline was determined by polarography of a sample at pH 4.5. Yield of cinnoline, 71-80 %; the yield may probably be raised by controlling pH and the temperature; the main competing reaction is loss of water from 4-hydroxy-1,2,3,4-tetrahydrocinnoline, and by keeping the temperature low and pH not higher than necessary, the formation of 1,4-dihydrocinnoline may be insignificant. The solution was extracted continuously with ether for 24 h, the ether layer dried (potassium carbonate) and cinnoline hydrochloride precipitated on addition of dry hydrogen chloride. The hydrochloride, m.p. $156-158^\circ$, was purified from ethanol/ether and identified from the NMR-spectrum (CF_3COOH) and m.p. $190-192^\circ$ of the picrate ($190-194^\circ$).¹⁸ The picrate recrystallized at $175-180^\circ$ before it melted.

Reduction of 4-hydroxycinnoline (If) (alkaline solution). 4-Hydroxycinnoline (1.0 g) was dissolved in 0.5 N potassium hydroxide and reduced at -1.6 V (SCE). The reduction consumed 3 electrons per molecule, and a precipitate was formed during the reduction. The precipitate was filtered off, 0.6 g. The compound was soluble in acids, but insoluble in most organic solvents. It was purified from dimethyl sulphoxide/water, m.p. 210° . The compound gave an anodic wave at nearly the same potentials as Va did. NMR-spectrum (CF_3COOH): $\delta = 3.78$ (broad doublet), $\sum \text{H} = 1$, $J = 14$ cps; $\delta = 4.44$ (broad doublet), $\sum \text{H} = 1$, $J = 14$ cps; $\delta = 6.5-7.7$ (multiplet), $\sum \text{H} = 4$.

2-Methyl-4-hydroxycinnoline (anhydro base). The anhydro base (100 mg) was reduced in an acetate buffer at -0.8 V (SCE) with two electrons per molecule. The solution was then made slightly alkaline with sodium carbonate and extracted three times with chloroform which was then dried and evaporated. The residue, contaminated with some reoxidized material, consisted mainly of 2-methyl-4-keto-1,2,3,4-tetrahydrocinnoline. NMR-spectrum (CDCl_3): $\delta = 2.71$ (singlet), $\sum \text{H} = 3$; $\delta = 3.60$ (singlet), $\sum \text{H} = 2$; $\delta = 6.65-7.0$ (multiplet), $\sum \text{H} = 2$; $\delta = 7.2-7.9$ (multiplet), $\sum \text{H} = 2$. In a similar experiment 100 mg of anhydro base was reduced, the solution made alkaline with potassium hydroxide, and the compound reoxidized at -0.4 V (SCE). The oxidation product was the starting material, which was identified from its polarographic behaviour.

1-Methyl-4-cinnolone was reduced and oxidized similarly and in this case, too, was the starting material the final product.

Reduction of 4-mercaptocinnoline. A suspension of 4-mercaptocinnoline (0.5 g) in 150 ml N hydrochloric acid was reduced at -0.55 V (SCE). The reduction consumed four electrons per molecule and the solution smelled of hydrogen sulphide. The reduction completed, the solution was made alkaline with sodium carbonate and extracted three times with carbon tetrachloride (40 + 20 + 20 ml) which was then dried (potassium carbonate) and evaporated leaving 0.36 g of a solid which was identified as 1,4-dihydrocinnoline from the NMR-spectrum.¹

Reduction of 4-mercaptocinnoline at pH 9. 4-Mercaptocinnoline (100 mg) was reduced at -1.2 V (SCE) in a borate buffer pH 9 containing 30 % ethanol. During the reduction a cathodic wave at -0.85 V and an anodic one at -0.65 V grew up. The cathodic wave occurred at the reduction potential of cinnoline and the anodic one at the potential of sulphide. Towards the end of the reduction the cathodic wave at -0.85 V reached nearly the same height as the wave of the remaining 4-mercaptocinnoline before both waves disappeared. The reduction consumed four electrons per molecule, and the product was found to be 1,4-dihydrocinnoline by polarography of the reduced solution at low pH.

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