ELECTROCHEMICAL REDUCTION OF COMPOUNDS WITH A —N=C—C=N— GROUP. I.

QUINOXALINES

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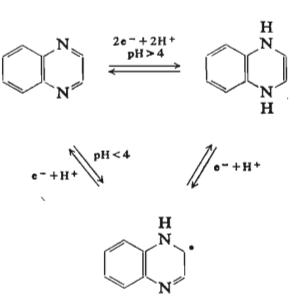
The electrochemical reduction of 2-methyl, 2-phenyl, 2-phenyl 3-methyl, 2,3-diphenyl and 2,3-dimethylquinoxaline leads in alkaline or neutral medium to 1,4-; 1,2- or 3,4-dihydro derivatives or to 1,2,3,4-tetrahydro derivatives. The physicochemical characteristics of these compounds, most of which are new, are given. The mechanism is discussed.

Some quinoxalines have been studied polarographically[1-4] in hydroorganic media. At low pH they evidence two one electron waves. Between pH 4 and pH 10 a single two electrons wave is observed. These waves are generally followed, as in the case of pyrazines[5-8] by a wave corresponding to the catalytic discharge of protons. It has been postulated that the fixation of two electrons leads to the formation of a 1,4-dihydro derivative according to the following Scheme: This process seems to be reversible in the pH range 4–10. The quinoxalines are more easily reduced than the corresponding pyrazines as could be expected from the higher conjugation; for example:



quinoxaline $E_{1/2} = -0{\cdot}55$ V (ref.[2]), pyrazine $E_{1/2} = -0{\cdot}74$ V (ref.[5-8] at pH 4·9. The only quinoxaline in such has been electrochemically reduced in a preparative way to give the 1,4-dihydro derivative and a dimer[8,9].

Preparative electrochemical reductions have been carried out in neutral and alkaline medium with the following compounds[10,11]: quinoxaline(*I*); 2-methylquinoxaline(*II*); 2,3-dimethylquinoxaline(*III*); 2-phenylquinoxaline(*IV*); 2,3-diphenylquinoxaline(*V*); 2-phenyl-3-methylquinoxaline (*VI*).

Polarographic Behavior at pH > 7

In the same way[1-4] as *I*, *II* and *III* the compounds *IV*, *V* and *VI* show a single wave the height of which corresponds to a two-electron reduction. The $E_{1/2}$ values (*vs.* aqueous S.C.E.) are rather insensitive to the nature of the substituents as it can be seen from Table I. The waves of the studied compounds are well defined. Only *II* gives a second wave at pH 7 which disappears when the pH increases.

TABLE I

$E_{1/2}$ Values Compounds *I*— *VI* in 50% Methanol ($c = 10^{-3}$M)

Compounds		*I*	*II*	*III*	*IV*	*V*	*VI*
$E_{1/2}$	pH 7	−0·67	−0·73	−0·77	−0·68	−0·69	−0·72
	pH 13	−1·04	−1·06	−1·11	−1·04	−1·03	−1·06

At pH higher than 7, the slope of the straight line $E_{1/2} = f(pH)$ on one side, and the very close values of the $E_{1/2}$ of the cathodic wave of the starting compound and of the anodic wave of the reduction derivative brought several authors to the conclusion that the simultaneous addition of two protons and electrons is presumed to occur in an essentially reversible manner[2]. In classical polarography we actually observed that the $E_{1/2}$ of the cathodic and anodic waves have the same value. In cyclic voltametry (c 10^{-4}M) triangular voltage sweeps allow to evidence an anodic and a cathodic peak of the same height. The difference between the potentials of the two peaks is very close to the theoretical value for a reversible system when the sweep rate is low. This difference is increased when the sweep rate is higher: $\Delta E = 70$ mV for $v = 0{\cdot}1$ V s^{-1} and $\Delta E = 170$ mV for $v = 1$ V s^{-1}. The quinoxaline-dihydroquinoxaline system thus appears as a quasi reversible system.

Controlled Potential Electrolysis

They are carried out at 25°C, on a mercury pool, in a water–methanol medium, either at pH 13 (NaOH) or at pH 7 (ethylenediamine–acetic acid buffer); the solutions were kept under argon. The potentials are given by reference to the aqueous saturated calomel electrode.

Quinoxaline (*I*). The 1,4-dihydroquinoxaline (yield 20%) precipitates in the course of the reduction in alkaline medium ($E = -1{\cdot}30$ V). This compound has the same melting point and infrared spectrum as the product, of known structure, obtained through the reduction of *I* by sodium in tetrahydrofuran[12].

2-*Methylquinoxaline* (II). The electrolysis in alkaline ($E = -1{\cdot}15$ V) or neutral ($E = -0{\cdot}90$ V) medium leads to 3,4-dihydro-2-methylquinoxaline *VII* (yield 15%). The product is very unstable and decomposes rapidly even under nitrogen. Its structure is demonstrated by its NMR spectrum and by its hydrogenation into 1,2,3,4-tetrahydro 2-methylquinoxaline (ref.[15]) in the presence of palladised charcoal. *VII* is reducible at the dropping mercury electrode at pH 7 ($E_{1/2} = -1{\cdot}25$ V, 2 electrons consumed per mol), but does not show any wave at pH 13. A controlled potential electrolysis at pH 9 ($E = -1{\cdot}36$ V) yields directly the 1,2,3,4-tetrahydro-2-methylquinoxaline.

2,3-*Dimethylquinoxaline* (III). The electrolysis in alkaline ($E = -1{\cdot}50$ V) or neutral ($E = -0{\cdot}80$ V) medium yields the 1,2-dihydro-2,3-dimethylquinoxaline (*VIII*), (yields 64 and 20%, respectively). The structure of *VIII* is proved by its NMR spectrum, its air oxidation into *III* and its hydrogenation (palladised charcoal) into *cis*-1,2,3,4-tetrahydro-2,3-dimethylquinoxaline (*IX*) (ref.[13]). *VIII* is not reducible at the dropping mercury electrode at pH 13 but shows a wave of about two electrons at pH 7 ($E_{1/2} = -1{\cdot}20$ V). An electrolysis at pH 9 allows to obtain only *IX*.

2-*Phenylquinoxaline* (*IV*)The electrolysis in alkaline ($E = -1{\cdot}30$ V) or neutral ($E = -0{\cdot}80$ V) medium furnishes the 1,2-dihydro-2-phenylquinoxaline (*X*), yield 50 and 75%, respectively). The structure of *X* is demonstrated by its NMR and IR spectra, by its air oxidation into *IV*, *X* can be hydrogenated on palladised charcoal into 1,2,3,4-tetrahydro-2-phenylquinoxaline[14]. *X* evidences a two-electron wave at pH 7 ($E_{1/2} = -1{\cdot}08$ V) and at pH 13 ($E_{1/2} = -1{\cdot}47$ V). The electrolysis in alkaline medium ($E = -1{\cdot}60$ V) leads directly to the 1,2,3,4-tetrahydro-2-phenylquinoxaline. The reduction of *IV* at pH 11·9 in a water–dimethylformamide medium ($t = 0°C$, $E = -1{\cdot}30$ V) allows to isolate the 1,4-dihydro-2-phenylquinoxaline identified through its spectroscopic properties.

2,3-*Diphenylquinoxaline* (*V*). In alkaline medium ($E = -1{\cdot}50$ V) the reduction compound precipitates in the course of the electrolysis. It is identified as the *cis*-1,2,3,4-tetrahydro-2,3-diphenylquinoxaline (*XI*) (ref.[15]) (yield 50%). In the course of the electrolysis in neutral medium ($E = -0{\cdot}80$ V) two electrons are consumed. The solid which precipitates is identified as the 1,4-dihydro-2,3-diphenylquinoxaline. Its NMR spectrum shows a multiplet ($\delta = 7{\cdot}0 - 8{\cdot}3$ p.p.m.) the fine structure of which is different from that of *V* and from that of *XII*. In solution it shows an anodic wave ($E_{1/2} = -0{\cdot}66$ V at pH 7·12) and is instantaneously reoxidised by air. In neutral medium ($E = -1{\cdot}00$ V) the 1,2-dihydro-2,3-diphenylquinoxaline (*XII*) prepared according to[16] (condensation of *o*-phenylenediamine with benzoin) shows a polarographic wave the height of which corresponds to a two-electron reduction at pH 7 ($E_{1/2} = -0{\cdot}60$ V) and at pH 13 ($E_{1/2} = -1{\cdot}04$ V). The electrochemical reduction of *XII* in alkaline medium furnishes *XI*.

2-*Phenyl*-3-*methylquinoxaline* (*VI*) The product obtained by electrolysis of *VI* in alkaline medium ($E = -1{\cdot}35$ V) is the 1,2-dihydro-2-phenyl-3-methylquinoxaline (*XIII*), yield (20%). The structure of *XIII* is demonstrated by its NMR and IR spectra, by its air oxidation into *VI*

by its hydrogenation (palladised charcoal) into *cis*-1,2,3,4-tetrahydro-2-phenyl-3-methylquinoxaline (*XIV*). The *cis* configuration of *XIV* is proved by comparison with the spectra of *IX* and *XI* the stereochemistry of which is known[17,18]. The synthesis of *XIII* has also been achieved by condensation under argon, in the presence of sodium acetate[14], of 1-phenyl-1- bromoacetone with *o*-phenylenediamine (yield 16%). Besides, the 3,4-dihydro-2-phenyl-3-methylquinoxaline (*XV*), (yield 40%) is prepared by condensation under argon, in the presence of sodium acetate, of 1-phenyl-2-bromo-1-propanone with *o*-phenylenediamine. If both *XIII* and *XV* show a two electrons wave at pH 7 ($E_{1/2} = -1{\cdot}24$ V and $-1{\cdot}13$ V respectively) the only *XV* evidence a two electrones wave at pH 13 ($E_{1/2} = -1{\cdot}52$ V). This wave corresponds to the reduction into *XIV* as it is proved by a controlled potential electrolysis in alkaline medium ($E = -1{\cdot}80$ V, yield 47%). The results of the electrolysis of the quinoxalines *I*—*VI* are summarised in Table II.

Discussion of the Reduction Mechanism

It will be shown that the following scheme allows to explain the whole set of the obtained results.

A) *Reduction to a* 1,4-*dihydroquinoxaline*: In order to evidence this first step, electrolyses in dilute solutions have been carried out ($c = 10^{-3}$M) in 50% methanol and polarograms have been drawn in the course of the electrolysis. The typical case of 2-phenylquinoxaline (*IV*) will be described. At pH 7, under argon, ($E = -0{\cdot}80$ V) an anodic wave appears the $E_{1/2}$ of which equals that of the cathodic wave of *IV*. Once the electrolysis is achieved (after about 2 F per mol), the starting material is entirely recovered if the solution is left in contact with air. If, on the contrary, the solution is kept under argon after the electrolysis, it appears that the height of the anodic wave decreases slowly; simultaneously a cathodic wave appears which is identical to that of 1,2-dihydro-2-phenylquinoxaline (*X*). If, once the anodic wave has completely disappeared, the solution is left in contact with air

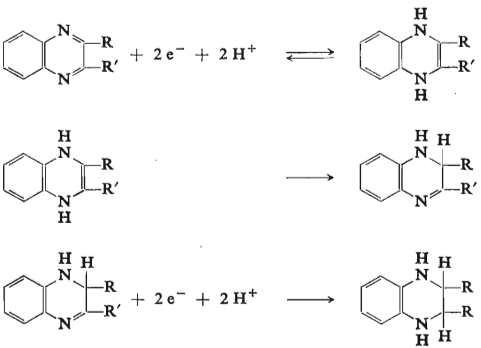


TABLE II

Electrolysis of Quinoxalines *I*— *VI*

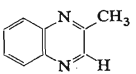
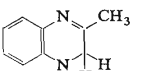
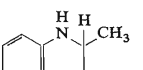
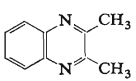
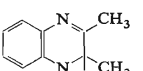
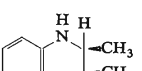
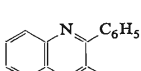
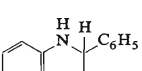
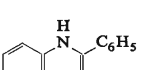
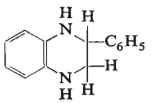
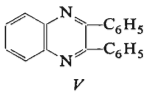
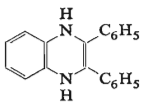
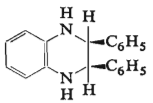
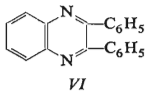
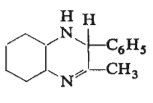
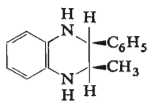
Starting compound	pH; *E*, V	Products	Yield, %	Number of electrons/mol
 *I*	13; −1·30		20	2
 *II*	7; −0·90 13; −1·15	 *VII*	15	2
	9; −1·35		5	4
 *III*	7; −0·80 13; −1·50	 *VIII*	20 65	2
	9; −1·60	 *IX*	45	4
 *IV*	7; −0·80 13; −1·30	 *X*	75 50	2
	11·9; −1·30			2

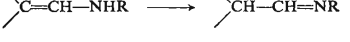
TABLE II
(*Continued*)

Starting compound	pH; *E*, V	Products		Yield, %	Number of electrons/mol
	13; −1·60			13	4
 *V*	7; −0·80			50	2
	13; −1·50		*XI*	50	4
 *VI*	13; −1·35		*XIII*	20	2
	7; −0·90		*XIV*	60	4

for several hours, the wave of 2-phenylquinoxaline is reobtained. The rate at which the anodic wave disappears at the profit of the cathodic wave of *X* varies rapidly with the pH at pH 13·5 for example, this rate is so high that the only cathodic wave of *X* is observed at the end of the electrolysis, while at pH 11·9 in a water–dimethylformamide medium the only anodic wave is observed at the end of the electrolysis. This is why this medium is used to prepare the 1,4-dihydro-2-phenylquinoxaline.

Among the dihydro derivatives obtained by reduction or by synthesis only the 1,4-dihydroquinoxalines give an anodic wave the $E_{1/2}$ of which equals that of the corresponding quinoxalines, as it has been checked. The 1,2- or 3,4-dihydro derivatives do not give any anodic wave. In conclusion, in the 7–13 pH range, the primary reduction process corresponds to the equation (*A*) that is to the formation of a 1,4-dihydro derivative.

B) *Rearrangement of the* 1,4-*dihydro derivatives*: The results of Table II show that all the 1,4-dihydro derivatives can undergo a rearrangement into 1,2- or 3,4-dihydro derivatives with the exception of 1,4-dihydroquinoxaline. In the case of this last compound its extreme insolubility may cause its precipitation before than the rearrangement has occurred. As the 1,4-dihydroquinoxalines have a structure of bi-secondary enediamine their rearrangement may be expected to occur in a way similar to that of primary or secondary enamines. These compounds are known to undergo, in a general way, a rearrangement into the tautomeric imine:



As it can be neatly seen at pH 7, the 2,3-diphenyl-1,4-dihydroquinoxaline shows a much higher stability, towards rearrangement, than the other studied 1,4-dihydro derivatives. This is probably due to the presence of a stilbenic group, this reason having been called for to explain the stability of the $C_6H_5—CH = C(C_6H_5)NH_2$ enamine[19]. An interesting result is that the substituted quinoxalines bearing two different groups give a 1,4-dihydro derivative which rearranges to only one of the two possible 1,2- or 3,4-dihydro derivatives. The rearrangement schemes are the following:

1,4-dihydro-2-methylquinoxaline → 3,4-dihydro-2-methylquinoxaline

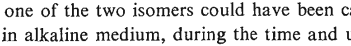
1,4-dihydro-2-phenylquinoxaline → 1,2-dihydro-2-phenylquinoxaline

1,4-dihydro-2-phenyl-3-methylquinoxaline →

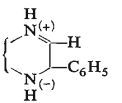
→ 1,2-dihydro-2-phenyl-3-methylquinoxaline

A higher stability of one of the two isomers could have been called for the explain these results. But as in alkaline medium, during the time and under the conditions of the electrolysis, the 3,4-dihydro-2-phenyl-3-methylquinoxaline does not isomerise into the 1,2-dihydro derivative, another explanation must be sought.

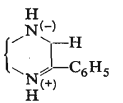
The enamines mesomery allows to explain the univocal formation of 1,2- or 3,4-dihydro derivatives:



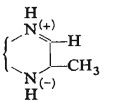
Formulae $a-d$ are the limiting mesomeric formulae of the primary reduction products of 2-phenyl- and 2-methylquinoxaline. The structure *a* will be more stable than the structure *b* as the negative charge on the carbon will be diminished by the inductive effect of the benzene ring and by repartition of this charge (mesomeric effect) on the carbons of the ring. On the contrary the structure *c* will be less stable than the structure *d* as the positive inductive effect of the methyl group increases the negative charge on the carbon atom. This allows to explain the formation of the 1,2-dihydro-2-phenylquinoxaline and of the 3,4-dihydro-2-methylquionxaline. In the case of 2-phenyl-3-methylquinoxaline the two effect are added to lead to 1,2-dihydro-3-methylquinoxaline. The faster rearrangement of 1,4-dihydro-2,3-diphenylquinoxaline in alkaline medium can also be explained by the easier loss of the nitrogen proton in alkaline medium.*



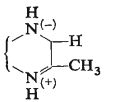
a



b



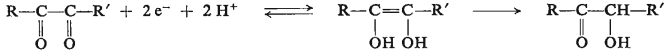
c



d

C) *Preparation of* 1,2,3,4-*tetrahydroquinoxalines*: The preceeding considerations allow to explain the nature of the isolated dihydro derivatives. The reducibility of these compounds must be brought under examination as 1,2,3,4-tetrahydro derivatives are obtained under certain conditions. The 1,4-dihydro derivatives are not reducible at the dropping mercury electrode as shown by the polarograms of the isolated 1,4-dihydroquinoxalines and by that of the quinoxalines itself. Thus, the 1,2,3,4-tetra-

* The set of reactions (*A*) and (*B*) are remindful of what is observed in the course of the electrochemical reduction of α-diketones[20-22].



However, the isolation, in some cases of a single ketol is due to the higher stability of one of the two isomers.

hydro derivatives can only be obtained through the reduction of the 1,2- or 3,4-dihydroquinoxalines.

In the Table III, the values of the half wawe potentials are given for the 1,2- or 3,4-dihydroquinoxalines as well as for the corresponding quinoxalines itself.

It can be seen that at pH 7 the difference between the $E_{1/2}$ of the quinoxalines and that of the 1,2- or 3,4-dihydroquinoxaline is large enough to permit the isolation of these last compounds in the case of *II*, *III*, *IV* and *VI*. On the contrary it is not possible to obtain the 1,2-dihydro-3,4-diphenylquinoxaline (its $E_{1/2}$ is too close from that of the 2,3-diphenylquinoxaline), but only its reduction derivative that is the 1,2,3,4-tetrahydro-2,3-diphenylquinoxaline.

It must be remarked that all the obtained 1,2,3,4-tetrahydroquinoxalines have the *cis* configuration. This can be due, as in the reduction by lithium aluminum hydride, to an attack of the second proton on the least hindered side of the molecule which has already fixed two electrons and one proton.

TABLE III

Half-Wave Potentials for the Reduction of 1,2- and 3,4-Dihydroquinoxalines

Compounds	*II*	*VII*	*III*	*VIII*	*IV*	*X*	*V*	*XII*	*VI*	*XIII*
pH 7	−0·73	−1·25	−0·77	−1·20	−0·68	−1·08	−0·69	−0·60	−0·72	−1·24
pH 13	−1·06	[a]	−1·11	[a]	−1·04	−1·47	−1·03	−1·04	−1·06	[a]

[a] No polarographic wave.

EXPERIMENTAL

Methods

The *polarograms* are drawn on a polarograph Radiometer PO_4. The half wave potentials $E_{1/2}$ are corrected of the ohmic drop and given by reference to the aqueous saturated calomel electrode. The pH are measured with a Radiometer pH meter and a glass calomel electrode. The ***controlled potential electrolysis*** are carried out on a mercury pool, under argon, in a classical device with two concentrical compartments of cylindrical shape. The volume of the solutions for the preparative electrolysis is 200 ml and they generally contain two grams of the compound to be reduced. The anodic solution is identical to the cathodic one but without depolariser. The potential is set at the desired value by a Tacussel ASA 100—1 potentiostat and the number of coulombs is measured with a Tacussel IG4 10 000 integrator.

All the manipulations of dihydroquinoxalines are carried out in a glove box. The NMR spectra are drawn with a Varian A 60 spectrometer with tetramethylsilane as internal reference.

Quinoxaline (*I*)

Quinoxaline (2 g) is dissolved in a mixture of 100 ml of methanol and 100 ml of 10% NaOH (pH = 13·5). The anodic compartment contains 50 ml of the same mixture. The solid precipitates in the course of the reduction ($E = -1{\cdot}30$ V). The precipitate is filtered, washed with water and light petroleum to give a white insoluble compound m.p. 157°C (yield 20%). The IR spectrum is identical to that described in the literature[12]. The reduction at pH 7 does not lead to any defined compound.

2-Methylquinoxaline (*II*)

Alkaline medium: A solution is prepared from 200 ml of methanol and 50 ml of 0·5M-NaOH. 2 g of *II* are dissolved in 200 ml of this solution (pH 13·70). At the end of the reduction ($E = -1{\cdot}15$ V; 2·1 F/mol) 300 ml of water are added. The solution is extracted with ether. The etheral extracts dried and then evaporated to give 300 mg (15%) of a yellow solid *VII*, m.p. 90°C (decomp.) (recrystallised from cyclohexane–light petroleum). This compounds decomposes rapidly at room temperature.

Neutral medium: A solution is prepared from 200 ml of alcohol, 50 ml of water, 6 g ethylene diamine and 10 g acetic acid. 2 g of *II* are dissolved in this solution (pH 7·40). At the end of the electrolysis ($E = -0{\cdot}90$ V; 2·2 F/mol) the solution is worked up as before to give the same compound as in alkaline medium. For $C_9H_{10}N_2$ (146·1) calculated: 73·94% C, 6·90% H, 19·16% N; found: 73·49% C, 6·79% H, 19·60% N. IR spectrum: (KBr pellet) ν(N—H) at 3100 cm^{-1} (s) and ν(C=N) at 1640 cm^{-1} (s). NMR spectrum (deuteriochloroform) $\delta = 2{\cdot}11$ (singulet) $\sum H = 3$ for the 2-methyl group; $\delta = 3{\cdot}98$ (singulet) $\sum H = 2$ for the 3-methylene group; $\delta = 6{\cdot}5-7{\cdot}5$ (multiplet) $\sum H = 4$ for the benzene ring. Dissolved in acetone, it is oxidised into *II* as checked by thin layer chromatography.

Hydrogenation: 100 mg of *VII* are hydrogenated in 20 ml of methanol in the presence of 10% palladised charcoal to give 50 mg of a compound m.p. 70°C identified as 1,2,3,4-tetrahydro-2-methylquinoxaline by comparison with an authentic sample[15]. NMR spectrum: $\delta = 1{\cdot}13$ (doublet $J_{H-CH3} = 6$ Hz) $\sum H = 3$ for the 2-methyl group; $\delta = 2{\cdot}7-3{\cdot}6$ (multiplet) $\sum H = 1$ for the tertiary proton; $\delta = 6{\cdot}3-6{\cdot}6$ (multiplet) for the phenyl group; $\delta = 3{\cdot}4$ displaced by addition of deuterium oxide (singulet) $\sum H = 2$ for the two NH.

Reduction in neutral medium: 2 g of *II* are reduced in 200 ml of 80% ethanol with an ethylenene diamine (10 g)–acetic acid (10 g) buffer: pH 9·20. The reduction ($E = -1{\cdot}35$ V) consumed 4·5 F/mol. The compound which precipitates is filtered and chromatographed on alumina (ether) to give 1,2,3,4-tetrahydro-2-methylquinoxaline in 5% yield.

2,3-Dimethylquinoxaline (*III*)

Alkaline medium: The reduction ($E = -1{\cdot}50$ V, pH 13·7) is carried out in the same way as for *II*. The obtained solution is extracted with ether. Ether is dried and evaporated. The residue (yield 78%) is recrystallised from methanol to give yellow needles *VIII*, m.p. 136°C.

Neutral medium: The same work up as for *II* gives the same compound (70% yield) as in alkaline medium. $E = -0{\cdot}80$ V, pH 7·36, 2·6 F consumed per mol. The same compound is also obtained at pH 9. For $C_{10}H_{12}N_2$ (160·1) calculated: 74·96% C, 7·55% H, 17·49% N; found: 74·80% C, 7·62% H, 17·12% N. IR spectrum (KBr pellet) ν(N—H) 3100 cm^{-1} (m). NMR spectrum deuteriochloroform: $\delta = 1{\cdot}22$ (doublet, $J_{H-CH3} = 6{\cdot}6$ Hz) $\sum H = 3$ for the 2-methyl, $\delta = 2{\cdot}12$ (singulet) $\sum H. = 3$ for the 3-methyl, $\delta = 4{\cdot}00$ (quadruplet) $\sum H = 1$ for the 2-H, δ about 3·6 displaced by addition of deuterium oxide (broad) $\sum H = 1$ for the N—H, $\delta = 6{\cdot}4-7{\cdot}9$ (multiplet) $\sum H = 4$ for the aromatic protons.

The air oxidation of *VIII* is soon completed in solution as checked by thin-layer chromatography.

Hydrogenation: 1 g of *VIII* dissolved in 50 ml of methanol in the presence of 10% palladised charcoal absorbs 150 ml of hydrogen (theory 140 ml for 2 H). To give 0·92 g (yield 90%) of white plates m.p. 112°C (benzene–light petroleum) identical to the *cis*-1,2,3,4-tetrahydro-2,3-dimethylquinoxaline as shown by comparison of NMR spectra[17,18].

Reduction in neutral medium: 2 g of *III* are dissolved in 200 ml of a solution prepared from 150 ml of water, 100 ml of ethanol, 6 g ethylenediamine and 6 g acetic acid (pH 9·20). The reduction ($E = -1{\cdot}70$ V) consumes 4·9 F/mol. The solution is extracted with ether. The etheral extracts are dried and evaporated to dryness, the residue is chromatographed on alumina to give 250 mg (45%) of a white compound m.p. 113°C (cyclohexane) identical with *cis*-1,2,3,4-tetrahydro-2,3-dimethylquinoxaline.

2-Phenylquinoxaline (*IV*)

Preparation[23]. A solution of 1-bromoacetophenone (28 g, 0·14 mol) and *o*-phenylenediamine (15·1 g, 0·14 mol) in 250 ml) of methanol is refluxed for 30 minutes. 300 ml of iced water are added to the cooled solution. 8 g of dark needles are obtained which are chromatographed on alumina (benzene–light petroleum 5 : 1) to give *IV*, m.p. 77°C.

Alkaline medium: In the same way as for *II* (pH 13·45) 0·5 g of *IV* are reduced at $E = -1{\cdot}30$ V; 2·3 F are consumed per mol. 200 ml of water are added to the solution, the precipitate is filtered. A yellow solid X (250 mg, 50%) is obtained m.p. 166°C.

Neutral medium: The same compound *X* is obtained at pH 7·40 ($E = -0{\cdot}80$ V, 2·3 F/mol) in 75% yield. For $C_{14}H_{12}N_2$ (208·2) calculated: 80·74% C, 5·81% H, 13·45% N; found: 80·50% C, 5·83% H, 13·48% N. IR spectrum (KBr pellet) ν(N—H) 3 330 cm^{-1} (w), ν(C=N) 1610 cm^{-1} (s). NMR spectrum deuteriochloroform $\delta = 4{\cdot}40$ (singulet) $\sum H = 1$ for 2-H, $\delta = 9{\cdot}34$ (singulet) $\sum H = 1$ for 3-H, $\delta = 6{\cdot}7 - 8{\cdot}6$ (multiplet) $\sum H = 9$ for the benzenic protons.

The air oxidation of *X* is very easy in solution as checked by thin-layer chromatography.

Hydrogenation: 1 g of *X* is dissolved in 75 ml methanol and hydrogenated with 10% palladised charcoal. 130 ml of hydrogen are absorbed (theory 118 ml for 2 H). The methanol is evaporated and the product recrystallised from cyclohexane m.p. 77°C (yield 85%). This compound is shown to be 1,2,3,4-tetrahydro-2-phenylquinoxaline by comparison with an authentic sample[14].

Reduction in neutral medium: 0·5 g of *IV* are added to 200 ml of a solution prepared from 100 ml of ethanol, 150 ml of water, 6 g ethylenediamine and 10 g acetic acid (pH 7·5). At the beginning of the reduction ($E = -1{\cdot}60$ V) the starting material dissolves slowly then a yellow compound precipitates (probably the dihydroquinoxaline) which is dissolved in its turn after several hours. The solution is extracted with ether. The solid obtained by evaporation of ether and by recrystallisation from cyclohexane is 1,2,3,4-tetrahydro-2-phenylquinoxaline.

Reduction to 1,4-*dihydro-2-phenylquinoxaline*: 800 mg of *IV* are dissolved in 200 ml of an aqueous solution 0·2M in $NaClO_4$ and 0·3M in NH_4OH and containing 80% of dimethylformamide (pH 11·9). At the end of the electrolysis ($t = 0$°C, $E = -1{\cdot}30$ V) 300 ml of water are added. The precipitated compound is filtered and recrystallised from dilute ethanol (80 mg, 10%). But this compound still contains about 10% of starting material which could not be removed, as seen from the NMR spectrum. The NMR spectrum clearly shows the 3-H as a singulet at $\delta = 6{\cdot}60$. This compound is immediatly reoxidised by air.

2,3-Diphenylquinoxaline (*V*)

Alkaline medium: In the same solution as that used for *II*, 2 g of *V* are introduced which are only partially dissolved. During the reduction ($E = -1{\cdot}50$ V) the starting material slowly dissolves and then another compound precipitates. At the end of the reduction 200 ml of water are added to the solution. The precipitate is filtered to give 1·1 g (yield 50%), of a yellow solid which is recrystallised from chloroform–light petroleum m.p. 140—141°C. This compound is identified as *cis*-1,2,3,4-tetrahydro-2,3-diphenylquinoxaline by comparison with an authentic sample[15].

Neutral medium: 2 g of *V* are reduced ($E = -1{\cdot}00$ V) in the same solution as that used for *II* (pH 7·43). At the end of the reduction 300 ml of water are added and the yellow solid is filtered (1 g, 50%) m.p. 101°C. The same compound is obtained at pH 9·20 (1·45 g, 70%). For $C_{20}H_{16}N_2$ (284·2) calculated: 84·48% C, 5·67% H, 9·85% N; found: 84·49% C, 5·58% H, 10·09% N. The IR spectrum: ν(NH) 3 370 cm^{-1} (s); this spectrum is different from that of *V* and *XII* in particular it does not display the strong ν(C=)N band at 1 668 cm^{-1} which is easily seen in the last compound. The NMR spectrum (deuteriochloroform) shows a single multiplet $\delta = 7{\cdot}1-8{\cdot}3$ the fine structure of which is different from that of *V* and *XII*. The air oxidation of the product-1,4-dihydro-2,3-diphenylquinoxaline is instantaneous in solution and gives *V*.

Hydrogenation: 70 ml of 1,4-dihydro-2,3-diphenylquinoxaline in 30 ml methanol are hydrogenated in the presence of 10% palladised charcoal 8 ml of hydrogen are absorbed (theory 5·6 ml for 2 H). The greatest part of methanol is evaporated, water is added and the white solid obtained is recrystallised from dilute methanol, m.p. 141°C. It is identified as *cis*-1,2,3,4-tetrahydro-2,3-diphenylquinoxaline (*XI*).

1,2-Dihydro-2,3-diphenylquinoxaline (*XII*)

Alkaline medium: In 200 ml of the usual solution a methanolic solution of *XII* (1 g in 50 ml) is added dropwise while maintaining a potential $E = -1{\cdot}50$ V. The yellow compound which precipitates (250 mg, 25%) is *cis*-1,2,3,4-tetrahydro-2,3-diphenylquinoxaline.

2-Phenyl-3-methyl quinoxaline (*VI*)

Alkaline medium: 2 g of *VI* (ref.[24]) are reduced in 200 ml of the usual solvent (pH 13·97) ($E = -1{\cdot}35$ V). The solution becomes yellow in the course of the electrolysis. At the end 300 ml of water are added. 400 mg (20%) of yellow needles of *XIII* are filtered and recrystallised from dilute methanol m.p. 161°C.

Neutral medium: 0·6 g (30%) of the compound *XIII* are obtained at pH 7·72 ($E = -0{\cdot}90$ V) (2·6 F/mol). IR spectrum (KBr pellet) ν(N—H) 3 300 cm^{-1} (m) ν(C=N) 1 620 cm^{-1} (s). NMR spectrum (deuteriochloroform): $\delta = 1{\cdot}95$ (singulet) $\sum H = 3$ for the 3-methyl group, $\delta = 4{\cdot}95$ (singulet) for the 2-H, $\delta = 6{\cdot}2-7{\cdot}3$ (multiplet) $\sum H = 9$ for the aromatic protons, $\delta = 4{\cdot}42$ (broad) $\sum H = 1$ displaced by deuterium oxide for NH.

1,2-Dihydro-2-phenyl-3-methylquinoxaline (*XIII*)

The solution of 1-phenyl-1-bromoacetone (21·3 g, 0·10 mol) *o*-phenylenediamine (10·8 g, 0·10 mol) and sodium acetate (10 g) in 100 ml of methanol is left two hours at room temperature under argon; a compound precipitates which is recrystallised from methanol (3·6 g, 15%). The compound is identical to *XIII* obtained by reduction. For $C_{15}H_{14}H_2$ (222·2) calculated: 81·05% C, 6·35% H, 12·60% N; found: 81·14% C, 6·25% H, 12·70% N.

Hydrogenation: 1 g of *XIII* is dissolved in 75 ml of methanol and hydrogenated in the presence of 10% palladised charcoal to give 800 mg (80%) of *cis*-1,2,3,4-tetrahydro-2-phenyl-3-methylquinoxaline (*XIV*) identified by comparison with an authentic sample.

cis-1,2,3,4-Tetrahydro-2-phenyl-3-methylquinoxaline (*XIV*)

A) 1 g *VI* is reduced in a solution as that used for *II* (pH 7·50). At the end of the reduction ($E = -1{\cdot}35$ V 300 ml of water are added and the solution is extracted. By evaporation of ether 600 mg (60%) of *XIII* are obtained which are identified by comparison with an authentic sample.

B) 2 g of *VI* are dissolved in 30 ml methanol and hydrogenated in the presence of 10% palladised charcoal during 3 h at 20°C and under a pressure of 50 bars. After filtration, the methanol is evaporated under vacuum to give 1·2 g (yield 60%) of a yellow oil b.p. 172°C 15 Torr. For $C_{15}H_{16}N_2$ (224·2) calculated: 80·32% C, 7·19% H, 12·49% N; found: 80·04% C, 7·26% H, 12·37% N. IR spectrum (nead liquid): ν(N—H) 3 390 cm^{-1} (s). NMR spectrum (deuteriochloroform): $\delta = 3{\cdot}60$ (broad) $\sum H = 2$ displaced by addition of deuteriumoxide for the two N—H, $\delta = 0{\cdot}81$ (doublet $J_{H_3-CH_3} = 6{\cdot}4$ Hz) $\sum H = 3$ for the 3-methyl group, $\delta = 4{\cdot}31$ (doublet $J_{H_2-H_3} = 3{\cdot}0$ Hz) $\sum H = 1$ for the 2-H, $\delta = 3{\cdot}53$ (octuplet) $\sum H = 1$ for the 3-H, $\delta = 7{\cdot}15$ (singulet) $\sum H = 5$ for the phenyl protons, $\delta = 6{,}3-6{\cdot}7$ (multiplet) $\sum H = 4$ for the aromatic proton of the quinoxaline ring. This spectrum allows to attribute the *cis* configuration to *XIV* as Archer and Moscher[17] give: *1*. $\delta = 3{\cdot}48$ for the protons on the 2- and 3-carbons of *cis*-1,2,3,4-tetrahydro-2,3-dimethylquinoxaline and $\delta = 2{\cdot}98$ for the *trans* derivative. For *XIV* $\delta = 3{\cdot}53$ (3-H). *2*. $\delta = 4{\cdot}68$ for the protons on the 2- and 3-carbons of *cis*-1,2,3,4-tetrahydro-2,3-diphenylquinoxaline and $\delta = 4{\cdot}16$ for the *trans* derivative. For *XIV* (2-H) $\delta = 4{\cdot}31$. Aquilera and coworkers[18] give $J_{H_2-H_3} = 2{\cdot}6$ — $2{\cdot}7$ Hz for the *cis* derivative and $J_{H_2-H_3} = 7{\cdot}0-8{\cdot}2$ Hz for the *trans* derivative. For *XIV* $J_{H_2-H_3} = 3{\cdot}0$ Hz.

Acetyl derivative: 300 mg of *XIV* are dissolved in 10 ml of acetanhydride and 50 ml of water are added after one hour. The solution is extracted with benzene. The dried benzenic solution is evaporated under vacuum. The obtained compound is chromatographed on alumina (benzene) to give 100 mg (28%) of a white product m.p. 122—123°C. This compound is the monoacetylated derivative with CO—CH_3 on the 4-nitrogen as shown by the analysis and the spectra. For $C_{17}H_{18}N_2O$ (266·2) calculated: 76·66% C, 6·81% H, 10·52% N; found: 76·30% C, 6·75% H, 10·31% N. IR spectrum (KBr pellet): ν(NH) 3 180 cm^{-1} (s), ν(C=O) band at 1 680 cm^{-1} (s). NMR spectrum: $\delta = 4{\cdot}60$ (doublet) $\sum H = 1$ for 2-H, $\delta = 4{\cdot}28$ (multiplet) $\sum H = 1$ for 3-H, $\delta = 2{\cdot}28$ (singulet) $\sum H = 3$ for the CH_3 of the acetyl group, $\delta = 0{\cdot}77$ (doublet) $\sum H = 3$ for the 3-methyl. The fact that the hydrogen and the methyl group on the 3-carbon are displaced by reference to the spectrum of *XIV* allows to place the acetyl group on the 4-nitrogen.

3,4-Dihydro-2-phenyl-3-methylquinoxaline (*XV*)

The solution of 1-phenyl-2-bromo-1-propanone (21·3 g, 0·10 mol), *o*-phenylenediamine (10·8 g, 0·10 mol) and sodium acetate (10 g) in 100 ml methanol is left two hours under argon at room temperature. 300 ml of water are then added. Some gummy material is first filtered and then 9 g (40%) of yellow crystals which are recrystalised from methanol m.p. 128°C. For $C_{15}H_{14}N_2$ (222·2) calculated: 81·05% C, 6·35% H, 12·60% N; found: 80·72% C, 6·52% H, 12·79% N. IR spectrum (KBr pellet): ν(N—H) 3250 cm^{-1} (m), ν(C=N) 1 650 cm^{-1} (s). NMR spectrum (deuteriochloroform): $\delta = 1{\cdot}18$ (doublet $J_{CH_3-H_3} = 6{\cdot}7$ Hz) $\sum H = 3$ for the 3-methyl, $\delta = 4{\cdot}67$ (quadruplet) $\sum H = 1$ for the 3-H, $\delta = 6{\cdot}3-8{\cdot}1$ (multiplet) $\sum H = 9$ for the aromatic protons.

Hydrogenation: 2 g of *XV* are dissolved in 75 ml of methanol and hydrogenated in the pre-

sence of 10% palladised charcoal. 210 ml of hydrogen are absorbed (theory 210 ml for 2 H). After filtration, the solvent is evaporated under vacuum to give 1·6 g (80%) of *XIV*.

Acetylderivative: 2 g of *XV* are dissolved in 20 ml of acetanhydride and left one hour at room temperature. 100 ml of water are added and the mixture stirred until it crystallises to give 1·2 g (50%) of a white solid recrystallised from hexane m.p. 113°C. For $C_{17}H_{16}N_2O$ (264·2) calculated: 77·25% C, 6·10% H, 10·60% N; found: 77·06% C, 6·73% H, 10·72% N. IR (KBr pellet) ν(C=O) 1 680 cm^{-1} (s), ν(C=N) 1 660 cm^{-1} (s). NMR spectrum (deuteriochloroform): $\delta = 1{\cdot}10$ (doublet, $J_{CH_3-H_3} = 7{\cdot}5$ Hz) $\sum H = 3$ for the 3-methyl, $\delta = 2{\cdot}30$ (singulet) $\sum H = 3$ for the $COCH_3$, $\delta = 6{\cdot}18$ (quadruplet) $\sum H = 1$ for the 3-H, $\delta = 7{\cdot}1 - 8{\cdot}3$ (multiplet) $\sum H = 9$ for the aromatic protons.

Reduction: 2 g of *XV* are reduced in the usual (see *II*) alkaline solution (pH 13·85) at $E = -1{\cdot}80$ V. The solution is extracted with ether to give by evaporation 950 mg (43%) of *XIV*.

Tentative isomerisation: 1 g of *XV* is dissolved in 200 ml of a solution prepared from 200 ml of methanol and 50 ml of 0·5M-NaOH. The product is recovered unchanged after 5 h.

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