ELECTROCHEMICAL OXIDATION OF 3,5-DIFUNCTIONAL 1,4-DIHYDROPYRIDINE DERIVATIVES*

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An oxidizability at a rotated platinum electrode of 1,4-dihydropyridines substituted by CN, $COOC_2H_5$ and $COCH_3$ in positions 3 and 5 has been found. The effect on the half-wave potentials on current- potential curves of the above substituents in position 3 and 5 on the one hand, and of alkyl substituents in positions 1, 2, 4 and 6 on the other hand, was studied. The obtained dependences were compared with quantum chemical calculations by the HMO and EHT methods. In a preparative oxidation at a large-area rotated platinum electrode the course of which was followed by UV spectra it was found that 1,4-dihydropyridines having no alkyl group in position 4 are oxidized to the corresponding pyridine in a two-electron process. In case position 4 is occupied by two alkyl groups the electrode process is stopped after the loss of the first electron and the resulting intermediate undergoes chemical follow-up reactions.

The 3,5-difunctional 1,4-dihydropyridine derivatives, often denoted as Hantzsch's dihydropyridines[1], represent important intermediates, of heterocyclic chemistry on the one hand, and substances with a considerable practical significance[1−4] on the other hand. In the great number of papers studying their chemical transformations[1], only little attention has been paid to their electrochemical behaviour. A group of compounds of this type, including also the derivatives *I*, *III*, *VIII*, *IX*, *XI−XIII* was recently studied by Dubur and coworkers[5]; the investigation was based on their anodic voltammetric waves. The authors found that the substances are oxidized with defined values of half-wave potentials but no data regarding the oxidation mechanism at the platinum electrodes have been presented. In contrast to this, the polarographic reduction at the dropping mercury electrode was studied in more detail. We have demonstrated[6,7] that in the reduction of these depolarizers the heterocyclic nucleus is preferentially reduced, giving rise mostly to unstable products.

In the present paper − a considerable part of which was already finished at the moment when the above publication[5] appeared − we studied in more detail the electrochemical oxidation of the dihydropyridines *I−XVI* at a rotated platinum disk electrode as well as in a simplified preparative arrangement. A mechanism of the

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observed electrochemical transformations was suggested and in some cases the reaction products were isolated.

EXPERIMENTAL

Instrumental and Procedures

The voltammetric measurements were carried out making use of the electronic polarograph OH 102 of the Hungarian firm Radelkis, Budapest; this instrument works with a three-electrode circuit. In a cell according to Hanzlík[8] three electrodes were placed, further a rotated platinum disk as indicator electrode, a working platinum electrode and a reference electrode (an aqueous saturated calomel electrode). The rotated platinum disk electrode and the whole arrangement ensuring its rotation was a construction of the workshop of the Heyrovský Institute. The speed of rotation was measured with the speedmeter H 6, Kombinat Mess- une Regelungstechnik, Beierfeld, German Democratic Republic. The electrode proper is the circular cross-section of a platinum wire mounted in a Teflon rod. The circular disk forming thus the electrode was degreased with chloroform once a week. Each morning the surface was mechanically polished with fine diamond emery paper. Before each measurement the electrode was regenerated after a 6-minute purging of the solution with purest nitrogen by a polarisation cycle in aqueous $0 \cdot 1$M-HClO$_4$ (from 0 V to $+1 \cdot 2$ V, back to $-1 \cdot 0$ V and again to 0 V). Between the measurements — if the interruption was not too long — the electrode was kept in $0 \cdot 1$M-HClO$_4$. The voltammetric measurements were carried out with 10^{-3}M solutions of samples in acetonitrile (in some cases also in dimethylformamide) mixed with an aqueous solution of the supporting electrolyte in a ratio 1 : 1 by volume; the supporting electrolyte was lithium perchlorate, $0 \cdot 05$M in the final solution to be electrolysed. In perchloric acid solutions the studied substances were spontaneously oxidized. In normal voltammetric experiments a platinum disk electrode with a 1 mm diameter was used which was rotated at a speed of 1 230 rev./min. After the regeneration of the electrode the cell was filled with the solution to be investigated which for 6 minutes was purged with a stream of nitrogen led through a wash-bottle filled with a mixture of acetonitrile with water (1 : 1). In contrast to conventional d.c. polarography with a dropping mercury electrode we estimate the accuracy of measuring the half-wave potentials at ± 25 mV and the accuracy of measuring the wave heights at $\pm 10\%$. The log plots in coordinates log $(i_1 - i)/i = f(E)$ were evaluated with the help of a standard program on a Hewlett-Packard calculator. The measurement of the dependence of $E_{1/2}$ of the oxidation waves on pH was performed with 10^{-3}M solutions of dihydropyridines in mixtures of acetonitrile with aqueous buffers according to Britton- and Robinson (1 : 1). The resulting pH was measured with a glass electrode and with the pH-meter Radiometer PHM4. These base electrolytes, however, showed anodic waves which had to be graphically subtracted from the anodic waves of the substances to be studied.

The coulometric measurements were performed with 10^{-3}M solutions of dihydropyridines in $0 \cdot 05$M-LiClO$_4$ in acetonitrile with water (1 : 1) as supporting electrolyte. The electrolysis took place at a constant potential of $+1 \cdot 05$ V vs s.c.e. on a rotated platinum electrode with a geometric area of 1 cm^2 and at 1 230 rev./min. The consumed electrical charge was measured with the current integrator 558 of the Italian firm Amel, Milano. The results were corrected after comparing them with a blank. The concentration of the electrolysed substance was determined by means of ultraviolet spectra.

The preparative electrochemical oxidations of dihydropyridines were performed in a simple cell without diaphragm with a carbon anode and a nickel cathode. The constant current density applied in this experiment was $8 \cdot 5 \cdot 10^{-3}$ A/cm^2. The composition of the base solutions was

the same as in voltammetry, except for the concentration of the studied substances which was $3 . 10^{-3}$M. The decrease in their concentration during electrolysis was followed by means of ultraviolet spectra. The volume of the solution to be electrolysed was here 20 ml. The experimental arrangement differed thus from that used in voltammetry but it was more convenient from the preparative point of view.

Substances

A part of dihydropyridines studied in the present paper were prepared by procedures described in the literature[1]; a list of them with their melting points and the corresponding quotations are shown in Table I. Further substances (IV, V, X and XIV, were prepared by alkylation of the corresponding derivatives I—III, IX and XIII in a procedure described in the literature[14,17]. Substance IV was obtained in a 30% yield, m.p. 133·5—134°C (according to[18] 132·5—133°C); substance V, yield 48%, m.p. 123·5 — 124°C (ref.[18] 123—123·5°C). Substance X resulted with a 24% yield, m.p. 117·5—118·5°C. For $C_{13}H_{19}O_2N$ (m.w. 221·3) we calculated: 70·56% C, 8·65% H, 6·33% N; found: 70·72% C, 8·61% H, 6·22% N. Substance XIV, 37% yield, m.p. 84·5 to 85·5°C; calculated for $C_{15}H_{23}O_4N$ (m.w. 281·4): 64·03% C, 8·29% H, 4·98% N; found: 63·89% C, 8·31% H, 5·00% N.

TABLE I

Formulae and Melting Points of the Studied 1-R^2-2,6-R_2^1-3,5-X_2-4-R^3-4-R^4-1,4-Dihydropyridines I—XVI

Substance	X	R^1	R^2	R^3	R^4	M.p. °C	M.p. °C[a]	References
I	CN	CH_3	H	H	H	224—226	225—228	9
II	CN	CH_3	H	CH_3	H	187·5—188·5	186—187	10
III	CN	CH_3	H	CH_3	CH_3	244·5—245	238—239	11
IV	CN	CH_3	CH_3	H	H			
V	CN	CH_3	CH_3	CH_3	H			
VI	CN	CH_3	CH_3	CH_3	CH_3	169—170	169—170	12
VII	CN	CH_3	H	$(CH_2)_5$		137—137·5	136	13
VIII	$COCH_3$	CH_3	H	H	H	224—224·5	207—208	10
IX	$COCH_3$	CH_3	H	CH_3	H	156·5—157	155—156	10
X	$COCH_3$	CH_3	CH_3	CH_3	H			
XI	$COCH_3$	H	H	H	H	263—263·5	243—245	14
XII	$COOC_2H_5$	CH_3	H	H	H	182—183	184	15
XIII	$COOC_2H_5$	CH_3	H	CH_3	H	131·5—145	131	15
XIV	$COOC_2H_5$	CH_3	CH_3	CH_3	H			
XV	$COOC_2H_5$	CH_3	H	C_2H_5	H	111—112	112	16
XVI	$COOC_2H_5$	CH_3	H	C_6H_5	H	160—161·5	157	15

[a] Melting points according to literature, cf. last column.

Calculations

Calculations of Hückel molecular orbitals (HMO) were performed with the help of a standard program on a Tesla 270 computer. For the methyl groups a heteroatom model has been chosen which led to the best agreement with the experimental half-wave potentials. The parameters used are summarized in Table II. The calculations by the Extended Hückel Method (EHT) were carried out with an IBM 370/145 computer. The ionisation potentials of the s-orbitals (I_s), of the p-orbitals (I_p) and the Slater exponents (SE) used as parameters were as follows: Hydrogen: $I_s = = -13.6$ eV, SE $= 1.3$; carbon: $I_s = -21.4$, $I_p = -11.4$, SE $= 1.625$; nitrogen $I_s = -26.0$, $I_p = -13.4$, SE $= 1.950$.

RESULTS AND DISCUSSION

Voltammetry with a Rotating Platinum Electrode

In the anodic oxidation at a rotated platinum disk electrode all the studied dihydropyridines $I - XVIII$ are active regardless of the fact whether the substituent X is CN, $COCH_3$ or $COOC_2H_5$ (Fig. 1). Particulars about the anodic oxidation waves are presented in Table III. Over the normal range the limiting currents of the anodic waves are a linear function of the dihydropyridine concentration and of the square root of the angular velocity of electrode rotation; this means that the electrochemical process is controlled by diffusion of the substance to the electrode surface[19]. When using buffered base solutions of different pH-values we found $E_{1/2}$ of the dihydropyridines is virtually pH-independent.

TABLE II

Empirical Parameters Applied in the HMO Method[a]

Except for the value of h_x for O and OC_2H_5 which were taken over from[25] all empirical parameters are taken according to Streitwieser.

X	h_x	X—Y	k_{X-Y}
N [b]	1.5	C—N [b]	0.8
N [c]	0.5	C=N [c]	1.5
CH_3	2.0	C—CH_3	0.7
O [d]	2.0	C=O [d]	1.0
OC_2H_5	3.0	C—OC_2H_5	0.9
		C—C [e]	0.9
		C=C [f]	1.1

[a] In other cases $h_x = 0$ and $k_{X-Y} = 1$; [b] for nitrogen in the dihydropyridine nucleus; [c] for the nitrile group; [d] carbonyl group; [e] bond ring — substituent in position 3; [f] bond between positions 2 and 3 or 5 and 6 in the ring.

When correlating the half-wave potential with the structure of $I-XVIII$ one can derive some generalizing rules which express the willingness of the particle to lose the electrons at the electrode:

TABLE III

Half-Wave Potentials and Limiting Currents of Anodic Oxidation Waves of Dihydropyridines
Three-electrode circuit, s.c.e.; concn. of dihydropyridines $1 . 10^{-3}$M; rotated platinum disk electrode, 1 mm diameter, 1230 rot./min. The values in the third column were obtained with base solutions of type[a].

Substance	$E_{1/2}$, V		$i_d . 10^6$, A	s^d
I	$+1\cdot03^a$; $+0\cdot90^b$; $(1\cdot08)^c$		7·68	0·127
II	$+1\cdot16^a$;	$1\cdot07^b$	8·06	
III	$+1\cdot13^a$;	$1\cdot03^b$; $(1\cdot20)^c$	3·55	0·106: 0·140
IV	$+1\cdot03^a$		10·16	0·134
V	$+1\cdot05^a$		9·95	0·134
VI	$+1\cdot27^a$;	$1\cdot20^b$	(7·50)	
VII	$+1\cdot06^a$		3·93	
$VIII$	$+0\cdot81^a$;	$0\cdot72^b$; $(0\cdot86)^c$	8·15	
IX	$+0\cdot92^a$		7·9	0·121; 0·205
X	$+0\cdot87^a$		7·58	
XI	$+0\cdot94^a$;	$0\cdot87^b$; $(1\cdot03)^c$	7·67	0·112; 0·127
XII	$+0\cdot76^a$;	$0\cdot68^b$; $(0\cdot90)^c$	7·86	0·094; 0·111
$XIII$	$+0\cdot90^a$;	$(0\cdot92)^c$	8·02	0·098; 0·131
XIV	$+0\cdot85^a$;		8·15	0·092; 0·146
XV	$+0\cdot92^a$		7·49	
XVI	$+0\cdot95^a$		7·76	0·087; 0·121

[a] 0·1M-LiClO$_4$ in 50% acetonitrile; [b] 0·1M-LiClO$_4$ in 50% dimethylformamide; [c] according to[5] for acetonitrile solutions with 1M-LiClO$_4$; [d] slope of the straight line from log $(i_1 - i)/i = f(E)$.
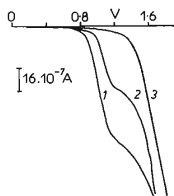

Fig. 1

Anodic Oxidation Waves of Dihydropyridines at a Rotated Disk Platinum Electrode

$1 . 10^{-3}$M Solutions in 0·05M-LiClO$_4$; acetonitrile–water 1 : 1. *1* 2,6-dimethyl-3,5-dicyano-1,4-dihydropyridine (*I*); *2* 2,4,4,6-tetramethyl-3,5-dicyano-1,4-dihydropyridine (*VI*); *3* base solution.

a) Substituent X in positions 3 and 5 shifts $E_{1/2}$ to more positive values in the sequence $COOC_2H_5 < COCH_3 < CN$; this means the ease of oxidation decreases in the same direction. In the Soviet paper[5] a somewhat different sequence $COCH_3 < < COOC_2H_5 < CN$ was found (however, the differences between the half-wave potentials of the derivatives $COCH_3$ and $COOC_2H_5$ are not very large; only the much higher values of $E_{1/2}$ in the derivatives with CN are significant).

b) Substitution by a methyl group on the heterocyclic nitrogen atom 1, i.e. $R^2 = = CH_3$, causes a shift of $E_{1/2}$ to less positive values or, in other words, makes the oxidation easier. This phenomenon can be exemplified with *II* and *V*, *IX* and *X*, *XIII* and *XIV*. A different behaviour was only observed with *III* and *VI* where $E_{1/2}$ of the methylated derivative is 140 mV more positive. The oxidation of these two substances which are in contradistinction to the preceding substances substituted by two methyl groups in position 4, i.e. $R^3 = R^4 = CH_3$, proceeds by a different mechanism; this also follows from the heights of the voltammetric waves.

c) Substitution by methyl groups in position 2, i.e. $R^1 = CH_3$, makes the oxidation easier ($\Delta E_{1/2} = 130$ mV) with *XI* and *VIII*.

d) Substitution by methyl groups in position 4, both by a single one or by two of them, causes a shift of $E_{1/2}$ to more positive values, e.g. for substances *IV*, *V* and *VI* ($E_{1/2}$ are $+1.03$ V, $+1.05$ V and $+1.27$ V, respectively). It is noteworthy to follow the influence of replacement of the substituent R^3 by a different one, the structure remaining otherwise unchanged; if one proceeds in the series *XII*, *XIII*, *XV* and *XVI*, i.e. R^3 becomes gradually H, CH_3, C_2H_5 and C_6H_5, $E_{1/2}$ shifts from $+0.76$ V to $+0.95$ V.

TABLE IV

Coulometric Measurements in Anodic Oxidation of 2,6-Dimethyl-3,5-diacetyl-1,4-dihydropyridine (*VIII*)

Q, C	A^a	Conc. of *VIII* . 10^3, M	
		calculated[b]	measured[b]
0.00	0.62	1.03	1.03
0.23	0.58	0.96	0.96
0.48	0.57	0.90	0.95
0.72	0.51	0.04	0.84
0.94	0.50	0.79	0.83

[a] Measured absorbancy; [b] from the passed current; [c] by means of photometry.

Coulometric Measurements

Coulometric measurements had to elucidate in more detail the oxidation of dihydro-pyridines the mechanism of which — as follows from different wave-heights — is not uniform. Substance *VIII* was chosen as a typical example. A value of n equal to 2 followed from several experiments. The course of electrolysis during coulometry was followed by measuring the UV-spectra of the solution; this indicated a decrease in the concentration of the substance to be electrolysed (absorption at $\lambda_{max} = 375$ nm) and an increase in the concentration of the product, *i.e.* of the substituted pyridine *XVII* (absorption at $\lambda_{max} = 273$ nm). The absorption at $\lambda = 273$ nm gives evidence for the product of the electrode process. The extinctions calculated for a one-electron and a two-electron process were compared with experimental extinctions. The results are summarised in Table IV. This measurements gave thus the primary information about the overall course of the electrodeprocess in substance *VIII*:

$$(1)$$
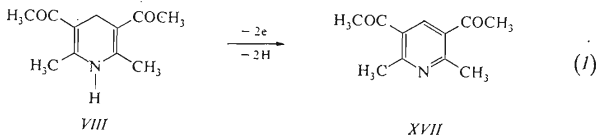
Preparative Electrooxidation

In the electrolytical preparation of the oxidation products of dihydropyridines the substances *I*, *VIII* and *XII* were processed. The final aim was to obtain a picture of how the oxidation products differ as a function of the substituent X, *i.e.* CN, $COCH_3$ and $COOC_2H_5$. With all three substances the corresponding pyridine derivative (Table V) was obtained as the sole product in a rather high yield. The formation of the aromatic products was followed in the ultraviolet spectra (a voltammetric determination is not convenient here). The pyridine derivative was also obtained in the oxidation of *II* but with a lower yield; in addition to this, the starting material was isolated after the electrolysis.

In the electrooxidation of *IV* the corresponding aromatic pyridine was formed, its existence was proved by ultraviolet spectra; we were unable to isolate it, however. The checking of the course of electrolysis by ultraviolet spectra of *II* is shown in Fig. 2.

A distinct difference from the above behaviour was observed in the oxidation of *III* (Fig. 3). The ultraviolet spectra did not point to the formation of an aromatic product. After electrolysis we isolated 37% of the starting material and an oily fraction. The latter was a mixture of substances which — according to their IR and NMR

TABLE V

Results of Electrochemical Oxidation of Dihydropyridine Derivatives *I, II, VIII, XII*

The experiments were performed with constant current at a current density of 8·5 mA cm^{-2} at a graphite electrode without diaphragm.

Starting substance	t, min[a]	Product, %[b]	Yield[c]
I	45	90·5	65
II	45	80·5	45
VIII	15	85	66
XII	15	94	67·8

[a] Duration of electrolysis; [b] weight procent of the product obtained by evaporating the extracts; referred to the weight of the original dihydropyridine; [c] weight procents of the corresponding pyridine obtained by sublimation, referred to the weight of the reacted dihydropyridine.
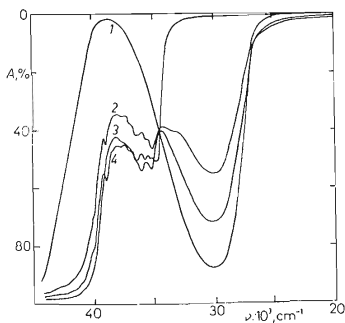

FIG. 2

The Course of Electrolytical Oxidation of 2,4,6-Trimethyl-3,5-dicyano-1,4-dihydropyridine (*II*) at a Platinum Electrode

Measured in acetonitrile. *1* 4 . 10^{-4}M solution of *II* before electrolysis; *2* after 15 minutes of electrolysis; *3* after 30 minutes; *4* 4 . 10^{-4}M solution of 2,4,6-trimethyl-3,5-dicyanopyridine.
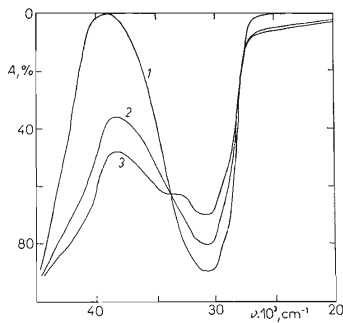
FIG. 3

The Course of Electrolytical Oxidation of 2,4,4,6-Tetramethyl-3,5-dicyano-1,4-dihydropyridine (*III*) at a Platinum Anode

Measured in acetonitrile. *1* 1 . 10^{-3}M solution of *III* before electrolysis; *2* after 30 minutes of electrolysis; *3* after 60 minutes of electrolysis.

spectra — contained aliphatic and olefinic hydrogen atoms and further nitrile, carbo-
nyl, hydroxyl and imine groups. The presence of aliphatic products in the reaction
mixture confirms the validity of the electrode oxidation mechanism of dihydropyridi-
nes given below. The primary oxidation intermediate is probably attacked in a more
complicated radical mechanism. Thus the electrochemical oxidation does not yield
the corresponding substituted pyridine as in chemical oxidation with chromic acid[10].

Mechanism of Dihydropyridine Oxidation

From the voltammetric curves with a rotated platinum disk electrode, from coulo-
metric measurements and, in particular, from preparative electrolyses follows that
the main electrode oxidation mechanism type is a two-electron process. This actually
occurs with all substances studied in this communication as far as at least one hydro-
gen atom is present in position 4. A certain difference in the wave-height which cannot
be only explained by inaccurate measurement was observed in substance *IV* and *V*.
The height of anodic waves where the 2-electron assumption is not fulfilled, *i.e.*
in *III* and *VII*, is one half of that obtained with the above group (Table III) even
though the wave of *VII* almost coincides with the oxidation of the supporting electro-
lyte.

A similarity of the oxidation mechanism in most dihydropyridines is also sup-
ported by the independence of the half-wave potential $E_{1/2}$ on pH for *I, II, VIII, XI*
and *XII*. However, this was also observed with *III*. Hence it follows that under
given conditions no protons participate in the first oxidation step and the mechanism
is rather of the ECEC type, as suggested *e.g.* for 1,4-dihydronicotinamide[20,21].
For this reason we propose the following detailed mechanism which is in accord
with our experiments (see Scheme 1).

This scheme only holds if $R^4 = H$, *i.e.* if in the course of the oxidation a hydrogen
atom is split off in position 4 and the quaternary product *d* is formed. If $R^2 = H$,
however, the product is no quaternary pyridinium cation but a protonated pyridine
which may dissociate:

$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad (2)$$
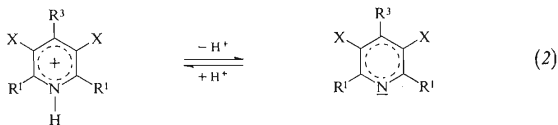
The experimental results of this communication confirm that the first step of the
electrode process is an electron loss which may be followed by the loss of the second
electron or proton. Consequently the above mechanism is — as regards processes
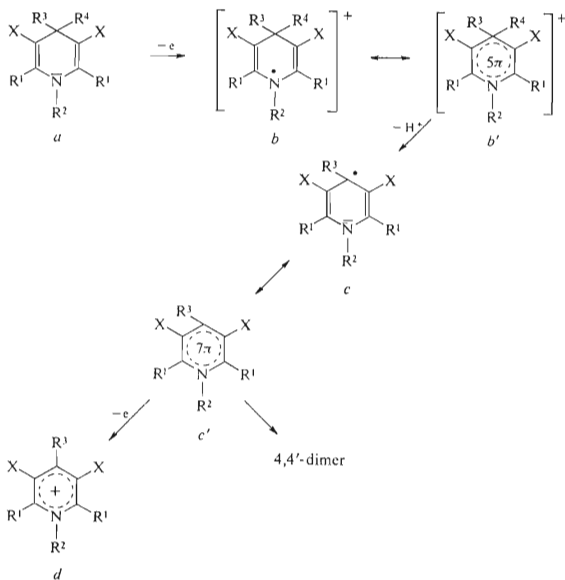
SCHEME 1

after the loss of the first electron — one of the two possible (*cf.* also for the mechanisms proposed in [22]). Neither one of the other possibility changes the overall course of the reaction. The corresponding substituted pyridines actually result as the final product in the electrooxidation of all dihydropyridines with hydrogen atoms in positions 1 and 4 such as *I, II, VIII, IX, XI, XII, XIII, XV* and *XVI*. The substances with an alkyl substituent in position 1 (*IV, V, X, XIV*) gave the corresponding pyridinium salts. If the position 4 is occupied by two alkyl groups (*III* and *VII*) the reaction sequence is probably stopped already in the stage after the loss of the first electron or of the first electron and proton. If working with a separated cathode the particle thus formed cannot be reduced back to the original substance but it can be subject to a radical attack; this means, however, that no aromatisation reaction results. A dimerisation of particle *c'* containing a π-electron septet[22] is not much considered since it is sterically inconvenient with respect to the substitution of the framework by relatively bulky groups. In nitriles this reaction is therefore not probable and

in compounds with $X = COCH_3$ or $X = COOC_2H_5$ it is most probably impossible for sterical reasons.

The literature[8] describes the following equilibrium for substance *XI*:

$$(3)$$
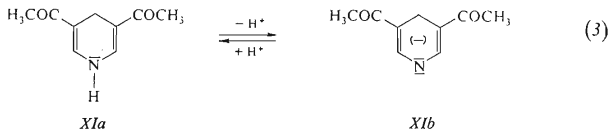
The anion (XIb) differs from *XIa* in a strong coloration. It is probably oxidised at less positive potentials than the non-dissociated substance *XIa*; this is due to a higher electron density on the nitrogen atom. It was found that this dissociation plays a role only at pH > 11. At these pH values, however, the anodic wave coincides with the current of the supporting electrolyte and one is unable to decide whether one or two waves appear on the polarogram. The formation of the anion in non-aqueous media in presence of a strongly basic substance[11] was only successful with *I*, *VIII* and *XII* at high concentrations where the voltammetric curves could not be recorded.

Quantum Chemical Interpretation

An attempt was made to interpret by calculations of the π-electron structure in terms of the simple HMO method the relative reactivity of the dihydro derivatives differing in the substituents in positions 3 and 5. For this interpretation, the energy
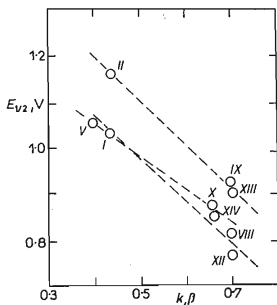

Fig. 4

Plot of Anodic Half-Wave Potential of Some Dihydropyridine Derivatives *vs* the HMO-Energy of Highest Occupied Molecular Orbital HOMO

The studied substances are denoted by Roman numerals at the experimental points.

of the highest occupied molecular orbital (HOMO) were applied on the one hand, and the electron distribution in this orbital on the other hand. Three groups of compounds were chosen (I, $VIII$, XII, further II, IX, $XIII$ and V, X, XIV) differing in the type of substitution by methyl groups. The plot of the half-wave potentials of oxidation waves vs HOMO energies is shown in Fig. 4. One can see that, without exception, a trend exists, and a correlation has been found both for data relating to N-methylated compounds and for compounds lacking the methyl group on the nitrogen atom. Somewhat surprising is the negative slope of the correlation dependence. This sign of the slope holds strictly under the assumption that the electron leaves the molecule reversibly and in a direction towards higher energies; in particular if one admits that the formal energy of the electron at the electrode may be below the HOMO energy level calculated by the HMO method the sign of the slope in the correlation can be interpreted. As far as the electron distribution in HOMO is concerned, use has been made of the positions with maximum electron densities, $i.e.$ of positions 3 (5) (Fig. 5) and 1 (Fig. 6). As follows from both figures two separate lines are obtained for compounds with a methyl group on the nitrogen atom in position 1 on the one hand and for the substances without a methyl group on the other hand. Within the two groups of substances a prominent trend has been found in the dependence between the frontier densities and the half-wave potentials. Only the
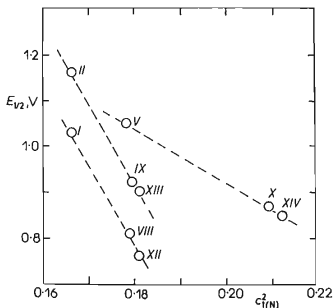

Fig. 5

The Plot of the Anodic Half-Wave Potentials vs Spin Density in the Highest Occupied Molecular Orbital (HOMO) in Position 3 of the Dihydropyridine Ring

The studied substances are denoted by Roman numerals at the experimental points.
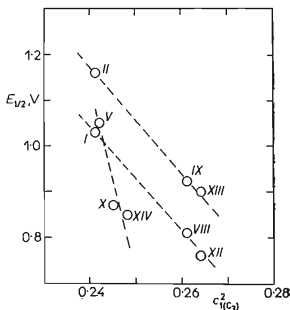
Fig. 6

The Plot of the Half-Wave Potentials vs Spin Density in the Highest Occupied Molecular Orbital (HOMO) for Position 1 of the Dihydropyridine Ring

The studied substances are denoted by Roman numerals at the experimental points.

sensitivity towards substitution in position 1 is different. Whereas in case of density on the nitrogen atom 1 the sensitivity of the quantum chemical interpretation is higher with methylated derivatives it reaches a minimum value for position 3. Accordingly, it can be stated that some aspects of the voltammetric behaviour can be interpreted in connection with HMO data. Since the influence of the methyl group in position 4 which affects the $E_{1/2}$ values has not been respected in the HMO calculations a corresponding disintegration of the correlation field occurs (Figs 4, 5 and 6).

In the series of 4-methylated 1,4-dihydro-3,5-dicyanopyridines the influence of 4-methyl groups was followed by means of the EHT method on the ease of the substituent abstraction from this position. The calculations indicate quite clearly that in substance II, in contrast to substance I, the bond population on the C—H bond increases (0·7924 as compared to 0·7866). The same holds true for the C—C bond between the carbon in position 4 and the carbon of the methyl groups in substances II and III (0·7387 and 0·7453). In a similar manner, the electron densities on atoms bound in position 4 (hydrogen or carbon of the methyl group) are higher if the neighbouring substituent is methyl ($q_H = 0·9832$ for I and 0·9919 for II, $q_{C(CH_3)} = 4·1349$ for II and 4·1407 for III). Basing on these data, it is evident that the splitting off of a group from position 4 as a cation ($cf.$ Scheme 1) will be rendered more difficult in presence of an alkyl in the neighbouring position. Simultaneously, an analysis of the HOMO wave function shows that this orbital which has a π-character results as a linear combination of $2p_z$ orbitals forming the planar framework of the molecule including C_4 and of an antisymmetrical combination of hydrogen $1s$ orbitals in position 4 in case of substance I; in substance II only the $1s$ orbital of the H-atom in position 4 participates in this π-electron system, not the carbon orbitals of the methyl group bound in this position. One can assume that the C—H bond of the methylene bridge in position 4 is, owing to hyperconjugation, a member of the π-electron chain of the molecule; this has been also found in the 1,4- dihydronicotinamide[24] system: the electron abstraction from the HOMO which has a π-character weakens this C—H bond as the only σ-bond in the molecule. It is therefore most probable that after the loss of the electron from the molecule a fission of this C—H bond will occur and the molecule will lose a proton; this agrees with the proposed electrooxidation mechanism.

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