

## POLAROGRAPHIC REDUCTION OF SOME 3,5-DIFUNCTIONAL DIHYDROPYRIDINE DERIVATIVES\*

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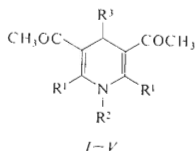
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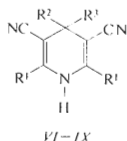
The influence of the structure of studied substances I—XV on their reducibility is discussed and the possibilities of an interpretation of experimental results based on the simple HMO method are considered. In 3,5-diacetyl-1,4-dihydropyridine (I) and its 4-methyl derivative II an influence of prototropic equilibria at higher pH values was found by means of spectrophotometric measurements.

Whereas about two hundred papers have been devoted to the polarographic and electrochemical reduction of various pyridine derivatives one can only find two isolated references referring to the polarography of dihydropyridines<sup>1,2</sup>. When the experimental measurements given in the present paper were approaching their end, two more detailed articles were published, describing an anodic oxidation of some dihydropyridine derivatives<sup>3,4</sup>.

In this paper we describe in detail the results of polarographic reduction of substances I—XVI; in part, we mentioned our results in a preliminary communication<sup>5</sup>. We also paid attention to the possibilities of a quantum chemical interpretation of the polarographic behaviour of the studied substances.

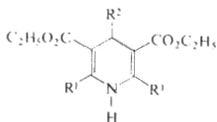


- I, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = H  
 II, R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = CH<sub>3</sub>  
 III, R<sup>1</sup> = R<sup>3</sup> = H, R<sup>2</sup> = CH<sub>3</sub>  
 IV, R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = R<sup>3</sup> = H  
 V, R<sup>1</sup> = R<sup>3</sup> = CH<sub>3</sub>, R<sup>2</sup> = H

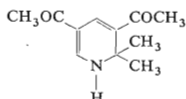


- VI, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = H  
 VII, R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = CH<sub>3</sub>  
 VIII, R<sup>1</sup> = CH<sub>3</sub>, R<sup>2</sup> = R<sup>3</sup> = H  
 IX, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = CH<sub>3</sub>

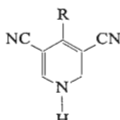
\* Part XXX in the series On Dihydropyridines; Part XXIX: This Journal 39, 854 (1974).



X-VII



XIII



XIV XV

- X,  $R^1 = R^2 = H$   
 XI,  $R^1 = H, R^2 = CH_3$   
 XII,  $R^1 = CH_3, R^2 = H$

- XIV,  $R = H$   
 XV,  $R = CH_3$

## EXPERIMENTAL

### Substances

Substances *I, II, IV, V, VIII, IX* and *XI–XIII* were prepared by a suitably modified Hantzsch synthesis<sup>6–12</sup>, substances *VI* and *X* by a borohydride reduction<sup>13,14</sup> of the corresponding pyridine derivatives. When preparing 3,5-dicyano-1,4-dihydropyridine (*VI*) we had to modify the original procedure<sup>13</sup> by using various solvents. To this purpose 120 mg of sodium borohydride were added in portions to 200 mg of 3,5-dicyanopyridine<sup>15</sup> and 5 ml of the chosen solvent. After 30 minutes the mixture was decomposed with 25 ml water, the precipitated 1,4-dihydro derivative *VI* filtered off and recrystallised from water to a constant m.p. 206–207°C (the data in the literature<sup>13</sup>: m.p. 205–206°C). The yield of crude product (solvent): 63% (acetonitrile), 56% (ethanol), 63% (pyridine), and 47% (dioxane). 3,5-Dicyano-1,2-dihydropyridine (*XIV*) was obtained in mixture with the 1,4-dihydro isomer *VI* by an aluminium hydride reduction. In contradistinction with the procedure<sup>16</sup> the reaction mixture (1.25 g) was separated on a 220 g silufol column; the 1,2-dihydro isomer *XIV* is stable even if exposed to it for a longer period of time. Substances *VII* and *XI* were prepared by reacting methyl magnesium iodide with the corresponding pyridine derivatives<sup>14,16</sup>, substance *III* by alkylation<sup>17</sup> the 1,4-dihydro derivative *I* and substance *XV* by hydrogenation the corresponding 2,6-dichloropyridine derivative<sup>18</sup>.

### Electrochemical Measurements

Polarographic measurements were performed with the Hungarian polarograph Radelkis OH 102 equipped with an electronic compensation recorder. A three-electrode circuit was used with a dropping mercury electrode as indicator and a platinum electrode as working electrode. The reference electrode was either a saturated calomel electrode (when working with buffered solutions) or a saturated calomel electrode containing tetrabutylammonium bromide (for unbuffered solutions with tetrabutylammonium salts as supporting electrolyte). A polarographic cell with a thermostated jacket at  $20 \pm 0.3^\circ\text{C}$  was used. The solutions were deaerated by a stream of nitrogen of highest purity. The following solutions with the 3,5-diacetyl derivatives *I–V* and *XIII* were investigated: 0.05M-NaOH (pH 12.3), borate buffer according to Michaelis (measured pH 10.4), phosphate buffer according to Michaelis (pH 7.9), acetate buffer according to Walpole (pH 5.6) and 0.05M-H<sub>2</sub>SO<sub>4</sub> (pH 1.9). When studying the 3,5-dicyano derivatives *VI–IX, XIV* and *XV*, 0.05M tetrapropylammonium iodide or perchlorate served as supporting electrolytes. Considering the limited water-solubility of the substances the measurements were performed in 50% ethanol the concentration of which was kept constant by leading the stream of nitrogen used in deaeration

through a wash-bottle filled with a 50% solution of ethanol before passing the solution to be investigated. Only freshly prepared solutions of the 3,5-dicyano derivatives *VI*–*IX* and, in particular, of *XIV* and *XV* were used in our measurements. Microcoulometric determinations with a dropping mercury electrode were enabled by placing a Jaissle electronic integrator in series with the polarographic cell.

The preparative electroreduction of 3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridine (*IV*) was carried out at a stirred mercury pool electrode according to Manoušek<sup>19</sup> in a solution of 0.1M acetate buffer in 50% ethanol (measured pH 5.3). To this purpose 193 mg ( $5 \cdot 10^{-3}$ M) of substance *IV* (infrared spectrum:  $1680 \text{ cm}^{-1}$ ,  $\nu(\text{C}=\text{C}-\text{C}=\text{O})$ ) were electrolysed at  $-1.3 \text{ V}$ , until polarographic curves showed that about 99% of the theoretical quantity of *IV* have been reduced. There-

TABLE I  
Half-Wave Potentials of Dihydropyridine Derivatives in Buffered Solutions  
50% Ethanol, pH measured with a glass electrode.

Substance	$E_{1/2}$ , V (SCE) at pH				
	1.9	5.6	7.3	10.4	12.3
<i>I</i>	-0.78	-1.06	-1.26	-1.36	-1.37
				-1.57	-1.56
<i>II</i>	-0.83	-1.09	-1.29	-1.49	-1.50
<i>III</i>	-0.75	-0.98	-1.21	-1.41	-1.44
<i>IV</i>	-0.9 <sup>a</sup>	-1.09	-1.29	-1.51	-1.58
<i>V</i>	-0.87	-1.12	-1.34	-1.55	-1.61
<i>XIII</i>	-0.91	-1.23	-1.39	-1.52	-1.62

<sup>a</sup> Ill-defined wave.

TABLE II  
Half-Wave Potentials and Limiting Currents of Dihydropyridine Derivatives  
50% Aqueous ethanol, 0.05M tetrapropylammonium iodide.

Substance	$c \cdot 10^4$ , M	$E_{1/2}$ , V	$i_1 \cdot 10^6$ , A	Substance	$c \cdot 10^4$ , M	$E_{1/2}$ , V	$i_1 \cdot 10^6$ , A
<i>I</i>	5.6	-1.37	0.5	<i>VI</i>	13.2	-1.86	6.88
		-1.59	0.3	<i>VII</i>	11.9	-1.90	5.28
<i>II</i>	4.2	-1.45	1.30	<i>XIII</i>	5.8	-1.53	1.80
<i>III</i>	5.6	-1.42	1.39	<i>XIV</i>	14.1	-1.64	5.16
<i>IV</i>	5.7	-1.52	1.78	<i>XV</i>	12.3	-1.72	6.84
<i>V</i>	6.2	-1.52	1.83				

after the electrolysed solution was evaporated to dryness *in vacuo* at a temperature not exceeding 35°C. The residue was repeatedly eluted with benzene (75 ml in total), the solution filtered off and evaporated. We obtained 194 mg of a yellow oil which in thin layer chromatography (silica-gel, benzene-acetone 3 : 1, detection by UV-light and iodine vapours) exerted four chromatographic spots over the  $R_F$  region from 0.1 to 0.45. By column chromatography on 35 g of silicagel (benzene-acetone 9 : 1) a mixture of two related compounds in the form of 124 mg of an unstable, partly crystalline oil was obtained. The infrared spectrum (in  $\text{CCl}_4$ ):  $3440\text{ cm}^{-1}$   $\nu(\text{NH})$ , 2960, 2930 and  $2855\text{ cm}^{-1}$   $\nu(\text{CH}_3, \text{CH}_2, \text{CH})$ ,  $1725\text{ cm}^{-1}$   $\nu(\text{C}=\text{O})$ ,  $1660\text{ cm}^{-1}$   $\nu(\text{C}=\text{C}=\text{C}=\text{O})$ ,  $1510\text{ cm}^{-1}$

$\delta(\text{NH})$ . The NMR spectrum (perdeuterioacetone): signals in the regions 7.2–8.0 $\tau$ ( $-\overset{|}{\text{C}}\text{H}-\overset{|}{\text{C}}\text{H}-$   
 $-\overset{|}{\text{C}}\text{O}-$ ;  $-\overset{|}{\text{C}}-\overset{|}{\text{C}}\text{H}_2-\overset{|}{\text{C}}-$ ;  $\text{CH}_3\text{CO}$ ) and 8.7–9.0 $\tau$ ( $\text{CH}_3-\overset{|}{\text{C}}-\text{N}$ ;  $\text{CH}_3-\overset{|}{\text{C}}-\text{O}$ ). The mass  
 spectrum,  $m/e$  (% relative intensity): 213 ( $\sim 2$ ), 207 ( $\sim 2$ ), 195 (24), 191 (40), 180 (7), 176 (70),  
 165(32), 154 (52), 152 (100), 150 (52), 124 (68).

#### Measurement of Optical and Resonance Spectra

Ultraviolet and visible spectra were measured with the NI 4 CF instrument of Optica Milano; the concentrations of the substances to be investigated were  $4 \cdot 10^{-5}\text{ M}$  and the solutions corresponded to those used in polarography both as regards their pH values and the contents of the non-aqueous solvents. The  $\text{p}K_a$  values were calculated from the experimental molar extinction coefficients of the absorption maxima in the usual way. The infrared spectra were measured with a Zeiss UR 10 instrument and NMR spectra with a Tesla 477 apparatus at 60 MHz.

#### Calculations

The HMO calculations were made by means of a standard programme with an Elliot 803b computer. The values of coulomb and exchange integrals were computed according to the usual relationships

$$\alpha_i = \alpha + h_i\beta \quad \text{and} \quad \beta_{ij} = k_{ij}\beta,$$

where  $\alpha$  and  $\beta$  are the corresponding magnitudes for the convention  $\alpha = 0$  and  $\beta = 1$ . The empirical parameters<sup>20,21</sup>: for the heterocyclic nitrogen atom  $h_N = 1.5$  and  $k_{CN} = 0.8$ ; for the nitrile group  $h_N = 0.5$  and  $k_{CN} = 1.4$ ; for the carbonyl group  $h_O = 2.0$  and  $k_{CO} = 1.0$ ; for the methyl group  $h_{\text{CH}_3} = 2.0$  and  $k_{\text{C}-\text{CH}_3} = 0.7$ .

### RESULTS AND DISCUSSION

Polarography with a dropping mercury electrode revealed that the 3,5-diacetyldihydropyridines *I–V* and *XIII* are reduced most easily; the reduction of the 3,5-dicyano derivatives *VI–IX*, *XIV* and *XV* proceeds at more negative potentials whereas no reduction was observed with the 3,5-diester *X–XII* over the studied potential range. The 1,2-dihydro derivatives *XIII–XV* are more easily reducible than the similar 1,4-dihydro derivatives *I–III*, *VI* and *VII*. The polarographic half-wave potentials for selected substances of the studied dihydropyridine type are compiled in Table I and were obtained with buffered solutions. Table II contains  $E_{1/2}$  values for unbuffered

solutions with 50% ethanol and with tetrapropylammonium iodide as supporting electrolyte.

The reduction of substances *I-IX* proceeds irreversibly as can be demonstrated with the  $\alpha n$  values for 3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridine (*IV*) at different pH values:

pH	1.9	5.6	7.9	10.4	12.3
$\alpha n$	1.29	0.74	0.80	0.95	0.89

By comparing the experimental values of  $\Delta E_{1/2}/\Delta \text{pH}$  with the data obtained by log plots of the polarographic curves and making use of the equations  $\Delta E_{1/2}/\Delta \text{pH} = -2.3 pRT/\alpha nF$ , we arrived at the conclusion that the number of protons taking part in the potential-determining step is equal to one: Over the pH-region from 2 to 10 the ratio  $\Delta E_{1/2}/\Delta \text{pH}$  is equal to about  $-0.08\text{V}/\text{pH}$  with substances *I-V*. With respect to the fact that in *IV*  $\alpha n \cong 0.8$ ,  $p = 1$ .

For unbuffered solutions containing 0.05M-N(C<sub>3</sub>H<sub>7</sub>)<sub>4</sub> I the values of  $\alpha n$  of the 3,5-dicyano derivatives are 0.89 with *VI*, 1.20 with *VII* and 1.43 with *XV*. Within the normal range of depolariser concentrations (from  $10^{-4}$  to  $2 \cdot 10^{-3}\text{M}$ ) the heights of the reduction waves are a linear function of the dihydro derivative concentration. The limiting currents of the studied compounds (all of them exhibiting a diffusion-controlled character) are tabulated in Table III, the analogous data for unbuffered solutions are shown in Table II.

More detailed information about the mechanism of the electroreduction of 3,5-diacetyl derivatives *I-V* and that of the 3,5-dicyanoderivatives *VI-IX*, the unlikeliness of which follows from the difference in heights of the polarographic waves, was obtained by microcoulometric measurements with a dropping mercury electrode under conditions of polarographic reduction: 3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridine (*IV*) is reduced by an approximately 4-electron mechanism. With respect to the same wave-heights an analogous process can be expected in the other 3,5-diacetyl derivatives *I-III*, *V* and *XIII* (at pH 5.6). A completely different result was found with 3,5-dicyano-1,4-dihydropyridine (*VI*) where a single electron per molecule is consumed and, because of the same wave-height, also with other 3,5-dicyano derivatives *VII-IX*, *XIV* and *XV*. This last finding is in agreement with our preliminary communication<sup>5</sup>.

### Analytical Aspects

Polarographically active 1,2-dihydro derivatives *XIII-XV* are reduced at less negative potentials than the similar 1,4-dihydro derivatives *IV*, *VI* and *VII*. It can be found in the literature<sup>22</sup> that the presence of two substances in mixture can be determined in different ratios if their half-wave potentials differ at least by 150 or 200 mV.

TABLE III

Limiting Currents of Dihydropyridine Derivatives in Buffered Solutions  
50% Ethanol, pH measured with a glass electrode.

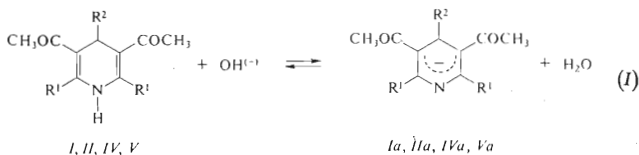
Substance	$c \cdot 10^4 \text{ M}$	$i_l \cdot 10^6, \text{ A at pH}$				
		1.9	5.6	7.9	10.4	12.3
<i>I</i>	5.0	1.85	1.85	1.87	1.08	0.69
					0.41	0.77
<i>II</i>	4.6	1.66	1.63	1.63	1.58	1.71
<i>III</i>	5.5	1.32	1.27	1.37	1.44	1.94
<i>IV</i>	4.5	— <sup>a</sup>	1.83	1.83	1.80	1.42
<i>V</i>	5.3	1.63	1.66	0.91	1.58	1.46
<i>XIII</i>	5.0	1.73	1.77	— <sup>a</sup>	1.75	1.25

<sup>a</sup> Because of an ill-defined wave the value could not be determined.

In our case such an application is possible but it only allows a limited quantitative estimation. Thus one can polarographically determine a small quantity of the 1,2-dihydro derivatives, such as *XIV* and *XV*, in presence of the corresponding 1,4-dihydro derivatives *VI* and *VII*. With larger quantities of the 1,2-dihydro derivatives the simultaneous determination is rendered impossible by the fact that the more negative waves of the 1,4-dihydro isomers coalesce with the current corresponding to the reduction of the cation of the supporting electrolyte, or to the catalytic reduction of hydrogen ions (*cf.* Fig. 1 in our communication<sup>5</sup>). The polarographic determination cannot thus compete here with photometry<sup>23</sup>.

#### Influence of Prototropic Equilibria

At  $\text{pH} > 10$ , 3,5-diacetyl-1,4-dihydropyridine (*I*) is reduced in two waves. The sum of their heights is constant and pH-independent but the mutual ratio of wave-heights depends on hydrogen ion concentration and is time-independent. The phenomenon can be explained by the following equilibrium (*I*):



The anion  $Ia$  ( $R^1 = R^2 = H$ ) is reduced at more negative potentials than the non-ionized form  $I$  (Table I). The same behaviour was found in neutral non-buffered solutions of tetraalkylammonium salts where protons from the water molecules are consumed during reduction and the vicinity of the dropping mercury electrode is made alkaline (Table II). The existence of the equilibrium ( $I$ ) was proved independently by investigating the absorption curves of the 1,4-dihydro derivative  $I$  at different pH-values. It is evident from Fig. 1 that, in accordance with similar data in the literature<sup>24</sup>, the absorption maximum at 490 nm is characteristic of the anion  $Ia$ ; the extinction coefficient increases with pH of the solution. We made an assessment of the ionisation constant under the assumption that in a saturated ethanolic solution of sodium hydroxide substance  $I$  is completely ionised to  $Ia$ : this attempt resulted in the relatively extreme value of  $pK_a$  between 12 and 13 which can be only hardly compared with the scattered data<sup>1,25,26</sup> for different types of dihydropyridine derivatives. The changes in the electron absorption spectrum of the 4-methyl derivative  $II$  ( $R^1 = H, R^2 = CH_3$ ) are analogous to those in substance  $I$  but the ionised form  $IIa$  manifests itself by a maximum at 470 nm; however, we were unable to observe the formation of two polarographic waves (Table I). Since even in strongly alkaline media (0.5M-NaOH) the height of the reduction wave of substance  $II$  does not decrease, the half-wave potentials of  $II$  and  $IIa$  probably only slightly differ so that two waves coalesce. In the 2,6-dimethyl derivatives  $IV$  and  $V$  ( $R^1 = CH_3, R^2 = H$  or  $CH_3$ ),

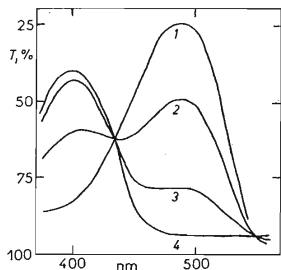


FIG. 1

Ultraviolet Spectra of  $4 \cdot 10^{-5} M$  3,5-Diacetyl-1,4-dihydropyridine ( $I$ )

1 Saturated solution of NaOH in ethanol; 2 0.5M-NaOH in 50% ethanol; 3 0.05M-NaOH in 50% ethanol; 4 0.05M- $H_2SO_4$  in 50% ethanol.

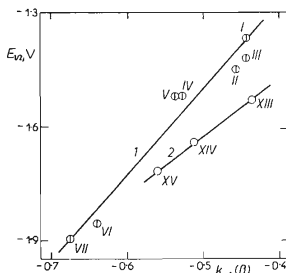


FIG. 2

$E_{1/2}$  of the Dihydropyridine Reduction (0.05M tetrapropylammonium iodide in 50% ethanol) Plotted versus LFMO  $k_{-1}$  Energies Calculated by the Simple HMO Method

and in the other substances to be investigated we did not observe the formation of anions. In substances *IV* and *V* this fact can be explained by steric hindrance of the attack on the nitrogen atom by hydroxyl atoms; this is caused by the methyl groups in the positions 2 and 6 and by a decrease in stability of anions *IVa* and *Va* due to the lower degree of solvation. On the other hand, the fact that prototropic equilibria are not operative in polarography and spectroscopy of the 1-methyl derivative *III*, rules out the alternative that the two observed waves in substance *I* belong to different keto-enol tautomers. With the other compounds *VI*–*IX* the ionisation is not seen under given conditions because of their low acidity so that ionised forms can be observed only in non-aqueous media<sup>17</sup>.

### Effect of Substituents

The most outstanding effect on the polarographic reducibility of the studied compounds is exerted by the character of the functional groups in the positions 3 and 5, and the activation effect decreases in the sequence  $\text{COCH}_3 > \text{CN} \gg \text{COOC}_2\text{H}_5$  (cf. the data in Tables I and II). The introduction of methyl groups into the remaining positions of the 1,4-dihydropyridine nucleus leads in general to a shift of  $E_{1/2}$  to more negative values and the shift depends on the number of the methyl groups. E.g., for solutions of 3,5-diacetyl derivatives *I*–*V* in 0.05M-N(C<sub>3</sub>H<sub>7</sub>)<sub>4</sub>I we found  $E_{1/2}$  in the following sequence: *I* (–1.37 V) < *III* (–1.42 V)  $\approx$  *II* (–1.45 V) < *IV* (–1.52 V) = *V* (–1.52 V). A similar situation exists also in buffered alkaline media; a certain deviation has been only observed with the 1-methyl derivative *III* in strongly acidic media (Table I).

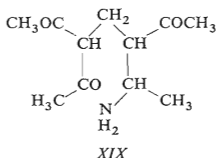
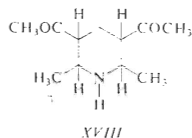
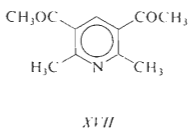
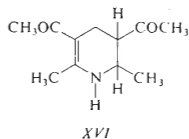
### Structure of the Reduction Products

The primary reduction products are characterized by a considerable instability and their isolation from the diluted solutions is extremely difficult.

In case of 3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridine (*IV*) which is reduced with the uptake of approx. 4 electrons per molecule, we performed a preparative reduction at a large-area stirred mercury pool electrode and isolated a mixture of several reaction products; in most of them a shift of the carbonyl absorption maximum from 1680 cm<sup>–1</sup> for the original substance *IV* to 1725 cm<sup>–1</sup> has been observed in the infrared spectra. The presence of hydroxyl groups cannot be identified in the spectrum by characteristic absorption bands above 3300 cm<sup>–1</sup>. The NMR spectrum exhibits multiplets overlapping with simpler signals in the region 7.2–9.0 $\tau$ ; in comparison with the spectrum of substance *IV* one can see a shift of the methyl signals by 0.2–0.4 p.p.m. to higher field strengths. This is in accord with the assumption that prevalently a reduction of the heterocyclic nucleus occurred and not that of the acetyl groups in substance *IV*. The mass spectrometry of the mixture thus obtained



is not in contradistinction with this conclusion. The ion species  $m/e$  195 corresponds to the presence of a molecular ion resulting from the two-electron reduction of substance *IV* to the tetrahydro derivative *XVI*, i.e.  $IV + 2e + 2H^+ \rightarrow XVI$ , in agreement with the following fragmentation processes:  $XVI^{\ddagger} \rightarrow [m/e 180]^{\ddagger} + CH_3\cdot$ , and  $XVI^{\ddagger} \xrightarrow{-CH_3CO\cdot} [m/e 152]^{\ddagger} \rightarrow [m/e 124]^{\ddagger} + CO\cdot$ , and in particular, to the presence of the aromatised ionic species  $XVII^{\ddagger}$ ,  $m/e$  191, participating in the probable fragmentation process  $XVI^{\ddagger} \xrightarrow{-2H\cdot} XVII^{\ddagger} \rightarrow [m/e 176]^{\ddagger} + CH_3\cdot$ .



The primary formation of the possible product of the four-electron reduction of substance *IV*, i.e. of the hexahydro derivative *XVIII* can be assumed only indirectly basing on our finding the ion species  $m/e$  207 which could correspond to the molecular ion of the product of reaction of *XVIII* with the solvent according to  $XVIII + C_2H_5OH \rightarrow C_{13}H_{21}NO + 2H_2O$ . The found fragmentation  $[m/e 207]^{\ddagger} \xrightarrow{-CH_3\dot{C}NH} [m/e 165]^{\ddagger} \rightarrow [m/e 150]^{\ddagger} + CH_3\cdot$  is not sufficient for suggesting a satisfactory constitution of the probable reaction artefact with a molecular weight of 207. A further probable artefact is evidently also the amino triketone *XIX* formed by hydrolysis ( $XVI + H_2O \rightarrow XIX$ ) and exhibiting itself by the corresponding molecular ion with  $m/e$  213.

### Quantum Chemical Interpretation

Making use of the simple HMO method, two models, *A* and *B*, were used for describing the  $\pi$ -electronic structure of the 1,4-dihydro derivatives *I* and *IX* and that of the 1,2-dihydro derivatives *XIII* – *XIV*. We investigated some characteristics of the LFMO into which – according to all usual assumptions<sup>21</sup> – the electrons enter in the primary

TABLE IV

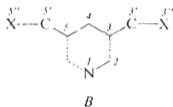
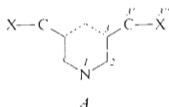
LFMO's of the Studied Substances Calculated by a Simple HMO Method

*I*–*IX* model *A*, positions 2 and 6; *XIII*–*XV* model *B*, positions 2 and 4.

Substance	$k_{-1} (\beta)$	$(c_{-1}^2)_{\max}$	Substance	$k_{-1} (\beta)$	$(c_{-1}^2)_{\max}$
<i>I</i>	–0.444	0.205	<i>VIII</i>	–0.721	0.225
<i>II</i>	–0.460	0.186	<i>IX</i>	–0.760	0.192
<i>III</i>	–0.444	0.205	<i>XIII</i>	–0.433	0.304; 0.225
<i>IV</i>	–0.525	0.204	<i>XIV</i>	–0.524	0.371; 0.204
<i>V</i>	–0.534	0.189	<i>XV</i>	–0.561	0.409; 0.180
<i>VI</i>	–0.639	0.219	AP <sup>a</sup>	–0.483	0.349; 0.159
<i>VII</i>	–0.675	0.194			

<sup>a</sup> For 3-acetylpyridine C=O.

step of the polarographic reduction. In the Table IV we present the corresponding orbital energies  $k_{-1}$ , as well as the maximum found values of squares of AO expansion coefficients  $(c_{-1})_{\max}^2$ . It follows from Fig. 2 that for the individual models A and B there is a satisfactory correlation between the experimental half-wave potentials and the energies  $k_{-1}$  so that the HMO method to a certain degree interprets the effect of substitution on the polarographic reducibility of the individual systems. It should be perhaps mentioned that the high energies of LFMO in 3,5-dinitriles *VIII* and *IX* (–0.721 or –0.760 $\beta$ ) make possible our understanding their polarographic irreducibility within the accessible range of potentials.



On the other hand even with the help of suitable HMO models we did not succeed in elucidating a similar irreducibility of 3,5-diesters *X*–*XII*. The reason is evidently an unsuitable HMO parametrization or a different mechanism of the first step of the electrochemical reduction as compared to the other compounds. It follows also from Table IV that the maximum values of AO expansion coefficients for LFMO,  $(c_{-1})_{\max}^2$  are always obtained for the positions 2 and 6 in the 1,4-dihydro derivatives *I*–*IX* and for the positions 2 and 4 in the 1,2-dihydro derivatives *XIII*–*XV*, i.e. in the

heterocyclic nucleus and not in the carbonyl group. This fact is in accordance with the above mentioned findings concerning the structure of products of electroreduction of substance IV. As an important argument for this kind of HMO interpretation we take the finding that the values of  $(c_{-1})_{\max}^2$  for 3-acetylpyridine are on the atoms of the C=O bond, i.e. in accordance with the mechanism of the polarographic reduction of this compound observed earlier<sup>27</sup>.

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