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Note

Electrochemical Reduction of Intermediates in the Vitamin B_6 Production. III. Reduction of Some Substituted Pyridones

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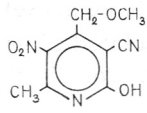
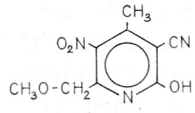
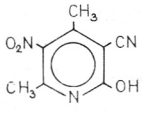
Earlier papers in this series[1,2] treated the selective preparative reduction of substituted pyridines with four reactive functional groups (—NO_2, —CH_2OCH_3, —CN and —Cl). This paper treats the electrochemical reduction of some substituted pyridones with three reactive functional groups (—NO_2, —CH_2OCH_3 and —CN):



I



II



III

Polarograms of 4.5×10^{-4} M solutions of compounds I, II and III in a mixture of glacial acetic acid and 10% hydrochloric acid (pH $\approx$ 0.2, volume ratio 105 : 45) at 25 °C are given in Fig. 1.

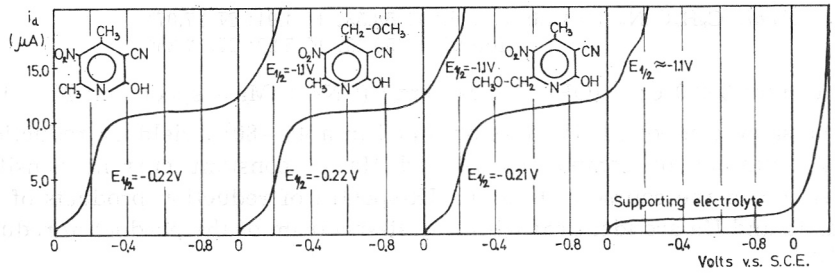


Fig. 1. Polarographic curves of 4.5×10^{-4} M solutions of 3-cyano-4-methoxymethyl-5-nitro-6-methyl-2-pyridone (I), 3-cyano-4-methyl-5-nitro-6-methoxymethyl-2-pyridone (II) and 3-cyano-4,6-dimethyl-5-nitro-2-pyridone (III). Supporting electrolyte (105 ml CH_3COOH + 45 ml 10% HCl).

Compound I exhibits two polarographic waves with half-wave potentials of —0.22 and —1.1 V. Compound II also gave two polarographic waves with half-wave potentials of —0.21 and —1.1 V, whereas compound III exhibits only one wave with half-wave potential of —0.22 V *vs.* S. C. E. The number of electrons calculated from Ilkovič equation for the first waves of compounds

I, II and III were: 5.28, 5.17 and 5.30 (with approximation of the diffusion coefficient $D_{I-III} \simeq D_{benzoate\ ion}$). Temperature coefficients of compounds I, II and III (from 0.74 to 1.4 for the temperature interval from 40 to 60 °C), as well as linear dependences of limiting currents on the concentrations of compounds I, II and III, and also on the square roots of the heights of mercury columns, indicate the diffusional character of limiting currents of the first waves of compounds I, II and III. A logarithmic analysis of these waves points to their irreversible character.

Reductions of 0.03 to 0.12 M solutions of compounds, I, II and III were performed by electrolysis at a controlled cathode potential of —0.5 V *vs.* S. C. E. (Duration of electrolyses was aproximately 60—240 minutes). Electrolytic experiments were performed in a cell with diaphragm, mercury cathode, reference electrode, and platinum wire as anode, as already described.[1] The same catholyte, *i. e.* mixture of acetic and hydrochloric acids, was used. After the reduction of compound I was completed, the product with m. p. = 240—242 °C (lit. m. p. = 240—242 °C)[3] corresponding to 3-cyano-4-methoxymethyl-5-amino--6-methyl-2-pyridone (Ia) was isolated from the catholyte in 70—90% yield depending on the reaction conditions. The number of electrons in the reduction I → Ia, coulometrically determined, amounted to 5.8.

The compound 3-cyano-4-methyl-5-amino-6-methoxymethyl-2-pyridone (IIa) with m. p. = 204—206 °C (lit. m. p. = 206 °C)[3] was isolated after the reduction of compound II in 80—95% yield. The number of electrons in the reduction II→IIa, coulometrically determined, amounted to 5.7.

Reduction of compound III did not result in the expected amino-derivative. As the reduction product 3-cyano-4-methyl-5-hydroxy-6-methyl-2-pyridone (IV) was obtained with 70% of the theoretical yield at 25 °C*. The number of electrons, coulometrically determined amounted to 5.9. M. p. = 283—85 °C (decomp.);

Anal. $C_8H_8O_2N_2$ (164.16) calc'd.: C 58.53; H 4.91; N 17.07%
found: C 58.28; H 5.22; N 17.35%

IR spectrum: 3 400 cm^{-1} (OH--), 2 240 cm^{-1} (CN—). Mass spectrum: M = 164.

The same compound (IV) was obtained in a 40—80% yield by reduction of 0.15 M solutions of compounds Ia and IIa at constant current density of 0.023 A/cm^2 in the course of 6 hours. IR-spectra of reduction products of compounds Ia and IIa are identical with the IR-spectrum of the product of reduction III→IV.

Compound IV is polarographically inactive (Fig. 2).

The first polarographic wave in Fig. 2 represents the reduction of the nitro group to the amino group, the second wave probably represents a reductive cleavage of C—O bonds of the methoxymethyl group of compounds I and Ia[1,2] (Polarograms of compounds II and IIa are almost identical to polarograms I and Ia given in Fig. 2).

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* Controlled potential reduction of III at 10 °C lowered the yield of IV to 40—50%.

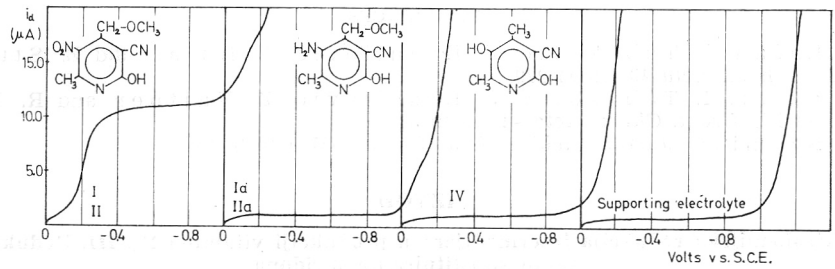
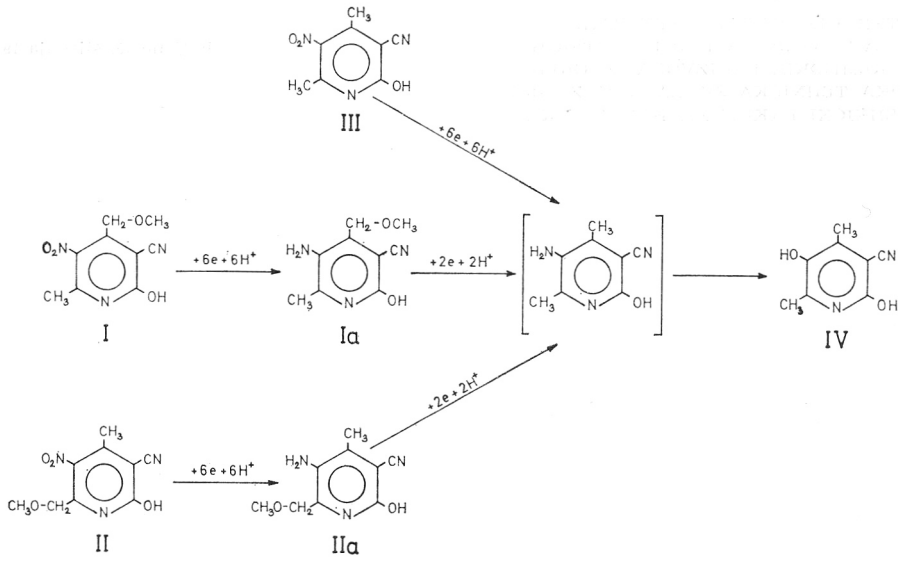


Fig. 2. Polarographic curves of 4.5×10^{-4} *M* solutions of 3-cyano-4-methoxymethyl-5-nitro-6-methyl-2-pyridone (I), 3-cyano-4-methoxymethyl-5-amino-6-methyl-2-pyridone (Ia) and 3-cyano-4-methyl-5-hydroxy-6-methyl-2-pyridone (IV). Supporting electrolyte (105 ml CH_3COOH + 45 ml 40% HCl).

On the basis of the obtained results it is assumed that the electrochemical reduction of substituted pyridones I, II and III occurs according to the following scheme:



The formation of compound IV can be explained by the electrochemical reduction of nitro and methoxymethyl groups of compounds I and II, and by reduction of nitro group of compound III.

After the formation of intermediary 3-cyano-4,6-dimethyl-5-amino-2-pyridone by reductive cleavage of C—O bonds of compounds Ia and IIa, respectively, and by reduction of the nitro group of protonated compound III, a chemical reaction occurs which could be explained by nucleophilic substitution of the amino group by the acetoxy group, and then by hydrolysis of acetoxy derivatives. The decrease in yield of product in reduction III→IV on lowering the temperature from 25 to 10 °C may be explained by the relatively lower rates of the chemical rection.

REFERENCES

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IZVOD

Elektrokemijska redukcija intermedijera u produkciji vitamina B_6. III. Redukcija nekih supstituiranih piridona

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Opisana je elektrokemijska redukcija nekih piridona s tri reaktivne funkcionalne grupe. Elektrolize su izvršene u elektrolitskoj ćeliji s dijafragmom, a kao katolit je upotrebljena smjesa octene i solne kiseline. Diskutiran je mehanizam redukcije slijedećih spojeva: 3-cijano-4-metoksimetil-5-nitro-6-metil-2-piridona (I), 3-cijano-4--metil-5-nitro-6-metoksimetil-2-piridona (II) i 3-cijano-4,6-dimetil-5-nitro-2-piridona (III). Svi navedeni spojevi daju isti konačni produkt, tj. 3-cijano-4-metil-5-hidroksi-6--metil-2-piridon.

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