

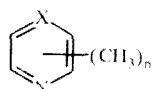
ANODIC OXIDATION OF METHYL-SUBSTITUTED NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS AT THE ACTIVATED NICKEL OXIDE ELECTRODE

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Methyl derivatives of several nitrogen-containing heterocyclic compounds were converted into the corresponding carboxylic acids by means of electrochemical oxidation at the nickel oxohydroxide anode in alkaline medium, using a nondiaphragm electrolyzer. The oxidation of 2,5-dimethylpyrazine was used to demonstrate the effect of adding chromium (III) and cobalt (II) compounds to the reaction mixture. The composition and electronic state of the anode surface were studied using x-ray diffraction and XPS methods.

Mono- and dicarboxylic acids derived from nitrogen-containing heterocyclic compounds are to be found in numerous physiologically active substances and can be used as intermediates in the synthesis of pharmaceuticals and pesticides, or as corrosion inhibitors, etc. [1-3]. The methods described in the literature (principally in patent documentation) for obtaining these acids by oxidation of the corresponding alkyl derivatives can be divided into chemical, catalytic and electrochemical classes (in the citing examples we have limited our choice to what we consider the most representative of each class). Thus, oxidation with potassium permanganate [3, 4], nitric acid (or its salts) under pressure [5-7] and selenium dioxide [8] comprise the most commonly used chemical techniques. Catalytic methods include liquid-phase oxidation in the presence of a homogeneous cobalt-bromide catalyst (under pressure) [9, 10] and vapor-phase oxidation or oxidation ammonolysis using vanadium oxide catalysts that have been modified or promoted by adding other oxides [11-13]. Despite the fact that some of these methods afford the end product in high yield (80% and above), they are not, as a rule, sufficiently versatile. Their use is restricted to the oxidation of just certain alkyl pyridine isomers or they require either high temperature or pressure and, consequently, special apparatus. Chemical oxidation in its turn raises the question of waste utilization. For this reason electrochemical techniques are of particular interest due to their economic and waste-free attributes.

The methods described in the literature for the electrochemical oxidation of some nitrogen-containing heterocyclic derivatives require the use of platinum, lead, lead-silver or lead dioxide anodes. Oxidation generally takes place in 10-60% sulphuric acid solutions using electrolyzers with an ion-exchange membrane or a ceramic diaphragm [14-18]. In this communication we demonstrate that it is possible to perform anodic oxidation in alkaline medium at the activated nickel hydroxide electrode using an electrolytic cell without a barrier between the anodic and cathodic spaces. This electrode first came to prominence thanks to its use in alkaline storage batteries [19-21]. More recently, the nickel oxide electrode has found application in the oxidation of saturated and unsaturated primary and secondary alcohols, and for the selective oxidation of steroid alcohols, 1,ω-diols and vicinal diols, carbohydrate derivatives, γ-lactones, aliphatic and aromatic aldehydes, phenols, and primary, secondary and tertiary amines [22-24]. However, its use in oxidizing the methyl group of certain nitrogen-containing heterocyclic compounds is illustrated here for the first time. The current work involved the oxidation of pyridine and pyrazine methyl derivatives of general formula:



X = CH; n = 1 (2-, 3-, 4- isomers); n = 2 (2,5-, 2,6-, 3,4- isomers);
X = N; n = 1; n = 2 (2,5- isomer)

TABLE 1. Electrochemical Oxidation* of Methyl- and Dimethyl-Substituted Pyridine and Pyrazine at the Activated Nickel Hydroxide Anode

Compound	Oxidation Products	Yield, %
2-Methylpyridine	Picolinic acid	57
3-Methylpyridine	Nicotinic acid	53
4-Methylpyridine	Isonicotinic acid	59
2,6-Dimethylpyridine	Dipicolinic acid	65
2,5-Dimethylpyridine	Isocinchomeronic acid	59* ²
3,4-Dimethylpyridine	Cinchomeronic acid	56* ²
Methylpyrazine* ³	Pyrazine carboxylic acid	60
2,5-Dimethylpyrazine	5-Methyl-2-pyrazine carboxylic acid, 2,5-pyrazine carboxylic acid, pyrazine carboxylic acid	22 5 12

*Current density 1 A/dm², substrate:alkali ratio 1:3, 20°C.

²Product yields quoted from HPLC data.

³Oxidation performed in 0.1 M NaClO₄ with 0.04 M KOH additive.

TABLE 2. Electrochemical Oxidation* of 2,5-Dimethylpyrazine in the Presence of Chromium (III) and Cobalt (II) Compounds

Additive	Substrate conversion, %	Yield, %		
		pyrazine carboxylic acid	2-methyl-5-pyrazine carboxylic acid	2,5-pyrazine dicarboxylic acid
—	55	12	22	5
Cr (III)	60	—	40	20
Co (II)	60	2	42	3

*Current density A/dm², substrate:alkali ratio 1:3, Cr (III) and Co (II) compound concentration 0.05%.

Table 1 shows the results obtained by converting the listed compounds into the corresponding mono- (from monomethyl derivatives) and dicarboxylic acids (from dimethyl derivatives) by means of electrochemical oxidation. As supplementary investigations revealed, the presence of pyrazine carboxylic acid in the reaction mixture results from 2 parallel processes: the partial decarboxylation of 2,5-pyrazine dicarboxylic acid and the splitting-off of one substrate methyl group to yield methyl pyrazine, which is subsequently oxidized to pyrazine carboxylic acid. The oxidation of the substrates shown in Table 1 afforded, in addition to the required end products, CO₂ which combines with alkali in the reaction system to form carbonates.

The anode in question, which consisted of nickel hydroxide deposited on a carrier, was activated so as to obtain the β -crystalline structure of nickel oxohydroxide (β -NiOOH), as described in a previous patent [24]. The crystallographic form of β -NiOOH was maintained during the oxidation of methyl-substituted nitrogen-containing heterocyclic compounds by altering the current in such a way that the electrode potential did not exceed the potential needed for the transition of Ni (III) to a higher oxidation state. Optimum experimental conditions were found by varying the current density, substrate and alkali concentration ratio and temperature. The results shown in Tables 1 and 2 were obtained under these optimum conditions.

Using 2,5-dimethylpyrazine oxidation as a model a study was made of the effect that adding chromium (III) and cobalt (II) to the solution had on reaction rate and oxidation product yield. The influence of these additives on the composition and electronic state of the electrode surface was also investigated. Chromium (III) and cobalt (II) compounds (0.05% concentration) were used in the form of nitrates or their complexes with o-phenanthroline or α , α' -dipyridyl.

It was found (Fig. 1) that the additive type (salt or complex) only influenced the initial oxidation rate, which increased by a factor of 2-2.5 in the presence of nitrates and by a factor of 4.5-5.5 with the complexes. It is evident from Table 2 that the total substrate conversion was virtually unaffected by the presence of the additive in solution, but the latter had a considerable influence on the oxidation product ratio. In the presence of Cr (III) compounds, for example, the greatest selectivity was seen with respect to partial oxidation products. Methyl-5-pyrazine carboxylic acid and 2,5-pyrazine dicarboxylic

acid were formed in a 2:1 ratio; the absence of pyrazine carboxylic acid suggests that chromium (II) compounds inhibit both decarboxylation and demethylation reactions. In the presence of cobalt (II) compounds the oxidation of one methyl group was the preferential reaction, the other two acids only being afforded in insignificant quantities.

In our study we attempted to establish a link between the patterns of behavior which emerged from the findings and the electrode surface changes. X-ray diffraction analysis has revealed [25-28] that, regardless of whether chromium (III) or cobalt (II) compounds are present, the nickel oxohydroxide anode exists in the β -NiOOH crystallographic form (Fig. 2). However, our XPS studies of the electrode surface revealed significant differences in spectra depending on which compound had been added. This spectral data (C1s, O1s, Ni2p, Cr2p and Co2p lines) is shown in Table 3. The C1s line belongs to a carbon with bond energy (E_B) of 284.8 eV and correspond to hydrocarbons deposited as polymers and resins; $E_B = 286$ eV conforms to oxidation products in the form of C—OH or C≡O groups; while $E_B = 288$ eV corresponds to surface carbonates [29-32]. The O1s line with an E_B of 529.6 eV belongs to the simple oxides NiO and CoO, while the energy value differing by ~ 1 eV from the peak maximum corresponds to the phase that contains the OH group. E_B of ~ 532.0 eV can be assigned to carbonates or hydrocarbonates.

The Ni2p line can be assigned to the Ni2p_{3/2} in NiO with an expected bond energy of 854.3 eV. So the energy increase of ~ 1 eV, measured at the peak maximum, suggests that nickel exists in the form of the oxohydroxide or shows that a significant quantity of Ni(3+) is present. Both are high-spin forms, which is reflected in the presence of a strong associate peak at 860 eV. The Co2p line comprises a band without the strong associate peak, which is shifted ~ 5 eV towards the higher E_B values. This provides unambiguous evidence that the cobalt exists mostly in the form of the Co(3+) low-spin octahedral complex, a conclusion supported by the bond energy of the Co2p electrons (780.2 eV, against an expected 781.7 eV for Co(2+)). The Cr2p line is entirely absent in the XPS spectrum [29-32]. Table 3 also shows values of N, which is proportional to the number of atoms of the specific element type (e.g., O²⁻, OH⁻, CO₃²⁻ on the surface have different N). Surface element ratios were calculated from the N values (Table 4). The exclusion of carbon from the surface composition is justified by the fact that it is inactive when deposited. Because of this, corrections to the "catalyst oxygen" were introduced, i.e., the amount of oxygen bound with carbon II (CO) and carbon III (CO₂) was deducted from the total oxygen quantity, and so $N_{(cat)} = N(O_{total}) - N(C-II) - 2N(C-III)$. Data for NiO_{ox} is given in Table 4 for reference purposes. It is clear from the Table that when additive are introduced, the ratio of oxygen to metal(s) on the surface becomes larger than for MeO oxides. This, in turn, suggests that higher oxidation states (+3 or +4 in Ni) may be present and that the electrode surface may have a high concentration of hydroxyl groups or even water molecules.

It is also evident that the presence of cobalt in the anode surface layer gives rise to a substrate methyl group orientation that produces a preferential oxidation of one of these groups. We were not able to establish the reason for the promoting effect of the chromium ions using this method.

EXPERIMENTAL

The reaction course and product purity were monitored using HPLC on a Du Pont Instrument Series 8800 chromatograph with silosorb 600 carrier, 4 \times 100 column, mobile phase comprising 25% MeCN and 75% 0.025 M phosphate buffer (pH 6.9) containing 0.005 M CTMAB, UV detector, $\lambda = 254$ nm. PMR spectra were recorded on a WH-90/DS (Bruker), internal standard TMS. Mass spectra were taken using an MS-50 spectrometer with 70 eV ionizing voltage. The melting points of isolated compounds were measured using a Boetius-type device. Melting points, mass spectra and PMR spectral values did not differ from those in the literature.

Elemental analysis data on C, H, and N were in line with calculated values for the synthesized acids.

The purity of the substrates used in the work, namely pyridine and pyrazine methyl derivatives, measured 93-95%; sodium and potassium oxide hydrates, hydrochloric acid, o-phenanthroline, α , α' -dipyridyl, and cobalt and nickel nitrates were of analytical grade quality.

Experiments were carried out in a thermostatically controlled electrolytic cell similar to one described in a previous report [33]. A stainless-steel electrode was used as the cathode and an Hg/HgO electrode served as the reference electrode.

Nickel Hydroxide Anode Activation Conditions. For an electrode of 20.64 cm² surface area (nickel sintering volume 0.62 cm³, Ni(OH)₂ quantity on electrode 0.87 g) the current did not exceed 0.0136 A, activation time of 18.55 h at room temperature in 0.1 M KOH solution. The activated β -NiOOH anode was stored in 1 M NaOH solution.

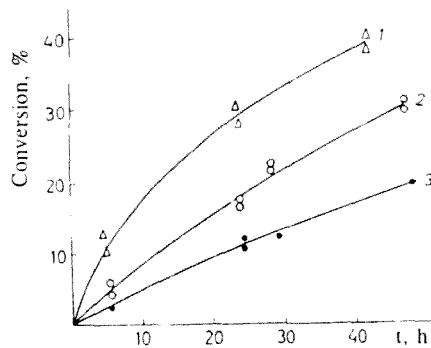


Fig. 1. Kinetic curves illustrating 2,5-dimethylpyrazine conversion under electrochemical oxidation conditions (current density 1 A/dm², substrate:alkali ratio 1:3) in the presence of various additives: 1) 0.05% of Cr(III) or Co(II) complex with o-phenanthroline or α,α' -dipyridyl; 2) 0.05% Cr(NO₃)₂ or Co(NO₃)₃; 3) without additive.

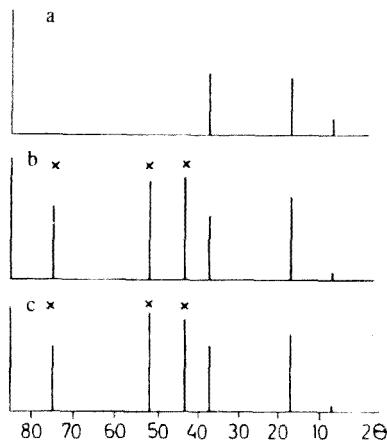


Fig. 2. X-ray diffraction pattern for nickel oxohydroxide anode: a) pure -NiOOH [27, 28]; b) nickel oxohydroxide anode in experiments without additive; c) with chromium (III) and cobalt (II) additives (x is the metallic nickel image, sintered plate).

General Acid Synthesis Technique. The pyridine or pyrazine methyl derivative (5·10⁻³ M), and distilled water (to 50 cm³) were placed in a 50 cm³ electrolyzer, the only exception being methyl pyrazine oxidation experiments, which were performed in 0.1 M NaClO₄ containing 0.04 M KOH (see Table 1). Electrolysis was conducted at room temperature, with a current density of 1 A/dm² and a 2.3 V potential between the cathode and the anode. When the substrate had been completely consumed (chromatographic monitoring), the reaction solution was acidified to a specific pH, equal to the pKa of the particular acid, which was isolated using known methods [34]. Carbon dioxide gas was evolved during acidification. From HPLC data purity of the resultant acids measured ~95%.

XPS spectra were recorded on a VG Scientific ESCA-3 photoelectron spectrometer using an x-ray beam source, AlK $\alpha_{1,2}$ -excitation (1486.6 eV), operating at 13 kV and 10 mA [35]. A working pressure of 2·10⁻⁸ mm Hg was employed. All spectra were recorded with a photoelectron exit angle of 45°. The C1s peak at 284.8 eV for surface-deposited carbon taken as the reference for bond energies. An IBM microcomputer was used for data-retrieval purposes. Data processing operations included smoothing, calibration of peak position relative to the C1s lines and removal of background and K $\alpha_{3,4}$ peaks, together with algorithms for analyzing complex spectra by breakdown into simple peaks or doublets. Spectra were resolved into symmetrical Gauss-20%-Lorentz peaks.

TABLE 3. Bond Energy (E_B) and Relative Element Content (N) from XPS Data

Line	Indices	Sample	
		Ni/Cr	Ni _x O
C1s	E_B	284,8	284,8
	N	126,6	100,94
	E_B	286,8	286,5
	N	445,7	281,9
	E_B	288,9	288,4
	N	179,1	301,1
	E_B	855,4	855,3
	N	380,6	157,4
	E_B	857,0	857,2
	N	398	171
Ni2p _{3/2}	E_B	861,3	861,1
	N	328,2	117,9
	E_B	529,9	529,1
	N	357,6	404,5
	E_B	530,7	530,7
O1s	N	1975,8	1859,4
	E_B	531,9	532,5
	N	538,2	193,3
	E_B	—	—
	Co2p _{3/2}	—	—
Cr2p	E_B	—	780,2
	N	—	256,4
	E_B	—	782
	N	—	586
	E_B	—	784,9
	N	—	478
Co2p _{1/2}	E_B	—	790,3
	N	—	209

TABLE 4. Atomic Ratios of Elements on the Nickel Oxide Anode Surface

Element	Sample		
	Ni(Cr)	Ni(Co)	Ni _x O _x
Ni	0,207	0,133	0,327
Cr	Not determined	—	—
Co	—	0,153	—
O	0,793	0,715	0,673
O/Mc	3,83	2,50	2,06

The relative element content (N) was calculated from a formula advanced in a previous communication [36]:

$$N_n = F I_n E_n^{0,25} \sigma_n^{-1} \exp(-d_C \lambda_{C,n}^{-1}),$$

where F embraces all instrumentation factors and is taken as a constant during measurement;

I_n = measured intensity;

E_n = kinetic energy of the n-level;

σ_n = photoionization diameter (n-level) [37];

$\lambda_{C,n}$ = free inelastic path of photoelectrons (n-level) in the additive carbon deposit [38];

d_C = carbon deposit thickness.

Electrode samples comprised plates measuring 8 × 10 mm. Spectra were recorded for the C1s, Ni2p, O1s, Cr2p and Co2p lines.

X-ray diffraction patterns were recorded on a Dron-2 powder diffractometer using CuK α -emission and a Ni filter at 30 kV and 20 mA. A pulse detector with a reading speed of 4000 pulses/sec and a recording range (2θ) of 8-78° was employed. The electrode sample comprised a 1 × 2 cm plate, which was placed directly in the goniometer.

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