USE OF NAFION MEMBRANES IN LABORATORY ORGANIC ELECTROSYNTHESIS

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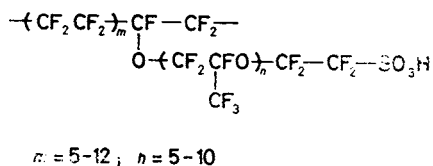Czechoslovak Academy of Sciences, 182 23 Prague 8*

Electrolysis of quaternary ammonium bromides and iodides in a divided cell with a Nafion membrane yields quaternary polyhalogenides at a carbon anode in water–ethanolic anolytes. The electrodialysis of tetrabutylammonium iodide in a cell with a Nafion membrane enables generation of tetrabutylammonium hydroxide. In electrolytic reduction of nitrobezene in presence of 1,3-dibromopropane, N-phenylisooxazolidine results in an approx. 60% yield. This electrosynthesis takes place in dimethylformamide with tetrabutylammonium bromide at a glassy-carbon cathode in a divided cell. In the electroreduction of lobelanine hydrogensulfate in a divided cell in acid water–ethanolic media at a lead cathode prevalently lobelanidine has been obtained.

Energetic and in recent time particularly ecological problems of highly developed industrial countries lead to introducing new and advantageous procedures for synthetizing of organic compounds. Organic electrosynthesis wins through in this field as a progressive technological process. The economic pressure leads even in organic electrosynthesis to looking for the most economical variants. The only way out which results in an innovation as compared with the older procedures, is a transition to the electrolysis in single-compartment cells[1,2] or an introduction of the so-called paired electrolyses[2]. This latter procedure yields required products in both compartments of the divided cell (in a similar manner as in sodium chloride electrolysis).

In small-scale qualified chemical productions, where expensive products are formed, a number of procedures exists or is being developed which apply divided cells. The example most frequently referred to is the cathodic reduction of phthalic acid or the anodic oxidation of butindiol or that of propargyl alcohol[1].

The most difficult problem when working with several-compartment cells is the separation of the compartments by a suitable diaphragma. The application of ionic membranes has made the most pronounced progress in solving this task; among these membranes the catex membranes made from Nafion must be considered the best. Nafion membranes were developed by Du Pont in the U.S.A. They mostly exhibit a composit character and are composed of a support — a teflon net — on which the ionex copolymer proper is placed; the basis of the latter is formed by perfluorinated

polymeric carbon chains containing sulfonic acid groups. The structure of Nafion is schematically depicted in Scheme 1.

$$-\!(CF_2\,CF_2\,)_{\overline{m}}\,CF-CF_2-$$
$$O\!-\!(CF_2\,CFO)_{\overline{n}}\!-CF_2\!-CF_2\!-SO_3H$$
$$CF_3$$

$$m = 5\text{-}12 \; ; \quad n = 5\text{-}10$$

SCHEME 1

The application of cation exchange membranes can be encountered both in electro-dialysis and in electrolysis. Whereas their electrodialytic application enables a careful preparation of expensive and sensitive bases and acids from salts, in electrolysis the selectivity in permeability, the low electric resistivity and the high mechanical and chemical resistance (in particular with those possessing perfluorinated chains) of cationic membranes is made use of. The reactions in which the process is initiated or catalyzed e.g. by electrochemically generated bases, the ion exchange properties of the membrane are simultaneously used.

In the present paper we intend to present our experience obtained in laboratory-scale preparative electrolyses made in divided cells with the cation exchange membrane Nafion 901. This experience includes the preparation of tetrabutylammonium tribro-mide, tetrabutylammonium hydroxide, N-phenylisoxazolidine and lobelanidine. The procedures are based either on electrodialysis or on electrolysis.

EXPERIMENTAL

Analytical grade chemicals were used in laboratory preparations. Nitrobenzene and dimethyl-formamide were purified by vacuum distillation before each experiment.

A divided flange-type cell[1] with parallel disc-shaped electrodes was applied for preparative electrolyses, the solutions in both compartments were stirred.

The potential of the working electrode was measured versus an inserted saturated calomel electrode. The voltage was applied to the electrodes by means of a continually adjustable DC source built in the workshop of this Institute. The electric charge passed through the system was measured with the help of an electronic integrator Amel 554/RM. The potential of the working electrode was controlled manually and measured with an electronic voltmeter Tesla BM 289. The thin-layer analyses of products were performed with commercial Silufol plates (Kavalier, Votice, Czechoslovakia). A Jeol MS-100 mass spectrometer enabled the recording of mass spectra of products.

Tetrabutylammonium Tribromide

A divided cell with a Nafion 901 membrane was provided with carbon rods serving as electrodes in the anodic compartment and with a stainless steel net as a cathode. The anolyte was a solution

of 24·0 g (0·075 mol) tetrabutylammonium bromide in 200 ml ethanol. The cathode chamber was filled with an equally concentrated aqueous solution of the same supporting electrolyte. A potential of − 1·5 V was applied to the cathode; at the beginning a current of 260 mA was passing at laboratory temperature. The solutions in both chambers were stirred. A charge of 1 620 C passed through the cell within the first 2·5 hours, the electrolytic current decreased to 20 mA and from the orange-coloured anolyte a yellow crystalline substance started to deposit. After the electrolysis 14·0 g of a yellow crystalline substance were sucked off from the cooled anolyte, this product displayed a bromine-like smell. It was then recrystallized from ethanol and boiled with charcoal; this led to obtaining 11·0 g of yellow crystals with a melting point of 74°C (30% yield). The results of elemental analysis confirmed a composition corresponding to tetrabutylammoniüm tribromide.

Tetrabutylammonium Hydroxide and Perchlorate

The cathode chamber of the above divided cell with a stainless-steel gauze cathode was filled with distilled water. The anode chamber, in which a glassy-carbon electrode was placed, was filled with 200 ml of a water–ethanol solution (1 : 1 by vol.) containing 0·135 mol of tetrabutylammonium iodide. On applying a potential of − 1·0 V to the cathode a current of 10 mA was passing at first which gradually increased up to 80 mA. The process under investigation which is to be regarded more as electrodialysis than as electrolysis (because of negligible gas evolution) took place at laboratory temperature with stirring the solutions in both chambers. In the catholyte which was gradually acquiring a still more alkaline reaction, tetrabutylammonium hydroxide was accumulated. After about 4 hours the circuit was disconnected and the quaternary hydroxide in the catholyte converted to perchlorate by neutralizing the solution with concentrated perchloric acid; the pH-values were checked with a universal pH-indicator paper. After crystallization, 29·0 g (63%) tetrabutylammonium perchlorate were obtained with a m.p. 211−212°C (cf. ref.[1]).

N-Phenylisoxazolidine

The catholyte contained 0·05 mol of nitrobezene and simultaneously 0·2 mol of 1,3-dibromopropane in 180 ml dimethylformamide. The chambers of the cell were separated by a Nafion 901 membrane. The working electrode (with a total area of 40 cm^2) consisted of glassy carbon, the auxiliary electrode was made of platinum on a titanium support. During electrolysis the electrolytes in both compartments were stirred and bubbled through with nitrogen. At − 1·3 V the average current density at the beginning was 120 mA dm^{-2}. In about 11 hours of electrolysis an electric charge of 19 700 C passed through the solution. The decrease in nitrobenzene concentration was followed by DC-polarography and by analysis of samples by means of thin-layer chromatography. After the electrolysis the orange-coloured catholyte was diluted with an equal volume of distilled water and the resulting yellow suspension was filtered off. The pure filtrate was several times extracted with 50 ml portions of toluene. The combined toluene extracts were dried with calcium chloride and then deprived of the solvent in a vacuum evaporator under nitrogen atmosphere. The remaining red-brown liquid was then subjected to fractional distillation. The main portion − an almost colourless liquid − passed at 54−55°C at a pressure of 2 kPa and weighed 4·5 g. The mass spectrum, m/z (%) : 149 (M^+, 78), 106 (26), 104 (30), 93 (72), 91 (53), and 77 (100). In accord with literature data[3] N-phenylisoxazolidine structure could be ascribed to the isolated substance and the yield was 60% of theory.

Lobelanidine

Lobelanine hydrogensulfate was prepared from the corresponding hydrochloride (Léčiva, Dolní Měcholupy, Czechoslovakia). 50·0 g of this hydrochloride were dissolved in 100 ml of

warm ethanol; under stirring a solution of approx. 24·0 g sodium perchlorate ($NaClO_4 . H_2O$) in 100 ml ethanol was added to the cooled-down solution. The deposited small crystals of lobelanine perchlorate were sucked off and rubbed with a 15—20% ammonia solution. The base thus liberated was filtered off by sucking and neutralized with diluted sulfuric acid (3 : 1) to a slightly acidic reaction. The next day the deposited white lobelanine hydrogensulfate was filtered off from the liquor solution. Its weight was 33·0 g and its m.p. 98—99°C. For $C_{22}H_{27}NO_6S$ (433·5) calculated: 60·35%C, 6·27%H, 3·23%N, 7·39%S; found 60·33%C, 6·54%H, 3·53%N, 7·25%S.

The cathodic chamber of the electrolytic cell was provided with a lead plate cathode (total area 35 cm^2) and a stirrer. This chamber was filled with the catholyte which was obtained by dissolving 3·0 g lobelanine hydrogensulfate in 200 ml ethanol containing 10 ml 0·5M-H_2SO_4. A glassy-carbon rod immersed in aqueous 0·25M-H_2SO_4 served as an auxiliary electrode. At — 1·6 to 1·7 V (vs SCE) a current of approx. 280 to 400 mA passed at 32 to 40°C. On consuming an electric charge equal to 11 350 C (1·6 F mol^{-1}) the irreversible cathodic wave of the substrate at —2·0 V (vs SCE) decreased to less than one half of the original height and the electrolysis was finished. After the electrolysis the catholyte was neutralized with concentrated NH_3. On concentrating this catholyte in a vacuum evaporator the free base was set free by alkalizing the solution with concentrated NH_4OH. It was then carefully neutralized with concentrated HCl and after concentrating the in this way processed solution in a vacuum evaporator the hydrochloride of the base was liberated as a white crystallic substance with a m.p. 140—142°C. The mass spectra, m/z : 218 ($C_{14}H_{20}NO$) 216, 149, 105. Both this result and elemental analysis as well as the melting point confirm that the electroreduction product is lobelanidine whose yield was 1·10 g (42·3%).

DISCUSSION

The main aim of this communication was the use of a cationic membrane — Nafion 901 — in preparative electrolysis. The reaction taking place in the particular compartments (chambers) of the electrolytic cell and the particles passing the membrane for all systems studied in this paper are summarized in Table I.

In a divided cell the behaviour of supporting electrolytes both in aqueous and in non-aqueous solvents was investigated. The use of quaternary halogenides (bromides or iodides) in the anolyte leads to the formation of quaternary polyhalogenides. During the electrolysis elemental halogen is formed in the anodic compartment; this species reacts with non-reacted halogenides under the formation of the above-mentioned polyhalogenides. Owing to the competing electrodialysis the anolyte is depleted of the quaternary ammonium ion; this contributes to the formation of polyhalogenides of quaternary cations. Because of their poor solubility they are easily deposited from the solution. Still present in the solution, they can be used for special halogenations according to Avramoff et al.[4]. An analysis of the catholyte in the same electrolysis revealed a considerable amount of tributylamine as product. This fact confirms the existence of a parasitic reaction in which the tetrabutylammonium cation is reduced to tributylamine. The further fate of the split-off butyl radical has not been investigated. Tributylamine may affect the cathode activity by an electrode reaction and also the follow-up chemical reactions. An electrochemical preparation of tetrabutylammonium hydroxide has been worked out by the Monsanto Company[1]

TABLE I
Reactions and particles in electrode compartments of a divided cell

Experiment No.	Principal and side cathodic reactions	Particles entering the cathodic compartment	Principal and side anodic reactions
1	$(C_4H_9)_4N^+ + 2e + H^+ \rightarrow (C_4H_9)_3N + C_4H_{10}$ $(H_3O^+ + e \rightarrow 1/2 H_2 + H_2O)$	$(C_4H_9)_4N^+$	$2Br^- - 2e \rightarrow Br_2$ $(C_4H_9)_4N^+Br^- + Br_2 \rightarrow$ $\rightarrow (C_4H_9)_4N^+Br_3^-$ $(2 OH^- - e \rightarrow H_2O + 1/2 O_2)$
2	$C_6H_5NO_2 + 2e + 2H^+ \rightarrow C_6H_5NO + H_2O$ $C_6H_5NO + 2e + BrCH_2CH_2CH_2Br \xrightarrow{-2Br^-}$ $\rightarrow C_6H_5-N-(CH_2)_3$ $\diagdown O \diagup$	$(C_4H_9)_4N^+$	$2 OH^- - e \rightarrow H_2O + 1/2 O_2$
3	LOBELANINE $+ 2e + 2H^+ \rightarrow$ LOBELINE LOBELINE $+ 2e + 2H^+ \rightarrow$ LOBELANIDINE	H_3O^+	$2 SO_4^{2-} - 2e \rightarrow S_2O_8^{2-}$ $S_2O_8^{2-} + H_2O \rightarrow 2 SO_4^{2-} +$ $+ 1/2 O_2 + 2 H^+$

when introducing an electrolytic production of adiponitrile in a divided cell. Electro-dialysis of tetrabutylammonium iodide carried out in our cell with a Nafion membrane has pointed to very good possibilities of tetrabutylammonium hydroxide generation.

A determination of the electrochemical yield is somewhat problematic since in addition the passage of a faradaic current in the preparation of tetrabutylammonium tribromide and tetrabutylammonium hydroxide is — to a considerable degree — accompanied by electrodialysis.

The preparative procedure for N-phenylisoxazolidine exemplifies an application of the N—O derivatization of phenylhydroxylamine described by Wagenknecht[5] for different conditions and further studied by Degrand et al.[3]. Our experiments have confirmed, that the raction proceeds in a very favourable way even in an unbuffered solution with DMF as solvent, at laboratory temperature and on a glassy-carbon electrode, with a yield of about 60%. The undesirable excess of tetrabutylammonium ions in strongly alkaline media (resulting from parasitic migration) did not lead to hydrolysis of the solvent, i.e. of dimehtylformamide at laboratory temperature. Our results only confirmed that in dimethylformamide an electrode reaction of nitro-benzene takes place followed by a nucleophilic chemical interaction of the resulting products with dibromopropane, the intermediate thus formed is stabilized by an intramolecular cyclization with the formation of N-phenylisoxazolidine (see Scheme 2).
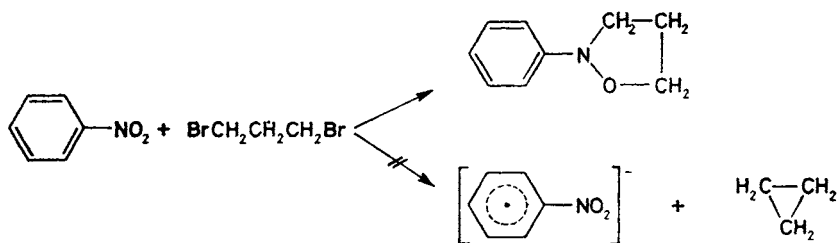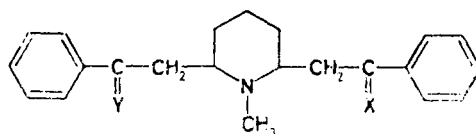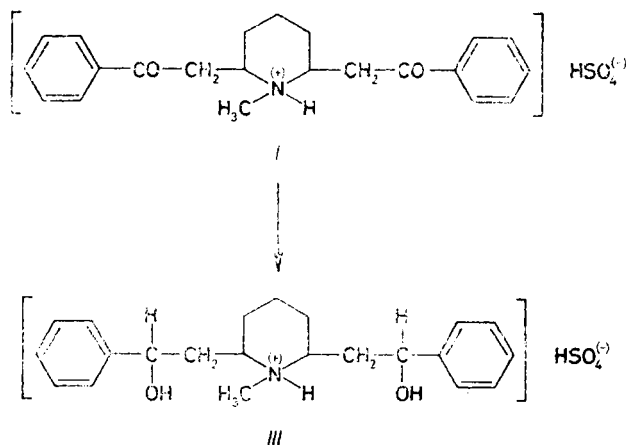

SCHEME 2

This means that the reaction described by Rifi[6], i.e. an elimination of halogen from 1,3-dibromopropane $(E_{1/2} = -1·91$ V vs SCE) which occurs also in presence of water, is not operative here.

Less favourable were the results obtained in the electroreduction of lobelanine. Belluš et al.[7] did not succeed in the partial reduction of lobelanine (I) to the pharma-cologically important lobeline (II) (see Scheme 3).

In their experiments they worked with mercury and lead electrodes in 3 M-HCl, making use of a simple cell. Our reduction of lobelanine hydrogensulfate carried out at $32-40°C$ and at controlled potential with electrodes of different materials (e.g. lead or tin) in ethanolic H_2SO_4 or in acidic aqueous solutions with 50 vol. % co-

I, X = Y = O   lobelanine

II, X = O, Y = OH, H   lobeline

III, X = Y = OH, H   lobelanidine

I

III

SCHEME 3

solvent, such as dimethylformamide or acetonitrile, pointed to a simultaneous reduction of both carbonyl groups. The product isolated after the electrolysis was lobelanidine (III). A quantitative evaluation of the products mixture is rather difficult because of their very similar structure[8].

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