ISSN 1070-4272, Russian Journal of Applied Chemistry, 2009, Vol. 82, No. 7, pp. 1234−1237. © Pleiades Publishing, Ltd., 2009.
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## APPLIED ELECTROCHEMISTRY AND CORROSION PROTECTION OF METALS

# Stereoselectivity of Electroreduction of a Menthone–Isomenthone Mixture

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Received June 23, 2008

**Abstract**—Electroreduction of an equilibrium menthone–isomenthone mixture at a controlled potential in a diaphragm cell on various cathodes was studied. The influence exerted by the nature of a solvent and of an electrode, electrode material, and various additives on the reduction stereoselectivity of ketones was examined. Conditions for a predominant formation of the most stable of the four isomeric alcohols being formed, menthol, were found.

**DOI:** 10.1134/S1070427209070143

The electroreduction of menthone has been rather extensively studied. This reaction was first performed in 1912 [1]. However, early studies are only of a historical interest because no reliable chromatographic analyses had been reported before 1972 in the foreign literature and before 1962 in domestic publications for the reaction mixture composed of six components: two starting ketones (menthone–isomenthone) and four isomeric alcohols being formed (menthol, neomenthol, isomenthol, neoisomenthol). Of these, menthol is widely used in pharmaceutical and food industries. Later, the reaction in which one of the isomeric ketones (specifically, menthone) undergoes electroreduction to give only two isomeric alcohols, menthol and neomenthol, was studied [2, 3]. It was of interest to examine the reduction of an equilibrium menthone–isomenthone mixture to give four isomeric alcohols, and to find conditions in which predominantly one of these, preferably menthol, is formed.

In the industry, menthol is synthesized by catalytic hydrogenation of thymol (over a $Ni/Cr_2O_3$ catalyst). The reaction proceeds in stages via formation of menthones. Therefore, any information on the reduction of menthones is also practically important.

It has been shown [4] that, on the background of tetrasubstituted ammonium salts at an excess of proton donors, menthone gives distinct two-electron diffusion-limited polarographic waves.

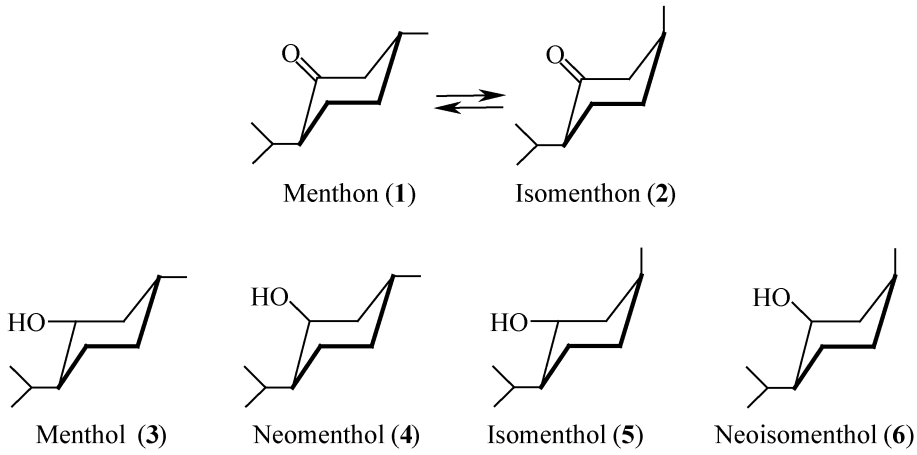
In this study, the stereoselectivity of electroreduction of an equilibrium menthone–isomenthone mixture was examined at a controlled potential in different solvents on electrodes of varied nature.

## EXPERIMENTAL

The electrolysis was performed with a potentiostat developed at the Special Design Bureau of the Institute of General Chemistry, Academy of Sciences of the USSR. The potentiostat had the following technical parameters: potentiostating range at a constant potential, ±3 V; potential sweep range ±3 V; range of polarization currents, ±500 mA; time constant $1.5 \times 10^{-4}$ s; precision of maintaining the potential at polarization currents varied from 1000 mA to 1 μA, 10 mV; precision of maintaining the polarization current, 0.5% of its value; stability of maintaining the potential of the working electrode during 8 h, ±10 mV. The electroreduction was performed at a controlled potential in a cell with a ceramic diaphragm. An Ag/AgCl electrode served as reference. The experiments were carried out at room temperature, with the electrolyte agitated by a flow of argon.

Menthone was produced by oxidation of menthol in the presence of a chromium catalyst. According to GLC data, the mixture contained 70% menthone and 30% isomenthone; bp 207–210°C, $n_D^{20} = 1.45$. The menthone

**Scheme.**




concentration was 5 mM. Twice-distilled water and HCl of special purity were used. Solvents of analytically pure grade were purified and distilled before the experiments. Phenol (PhOH) of analytically pure grade, bp 40–42°C, served as an additive. The reaction products were extracted with ether, distilled in a vacuum, and analyzed by the GLC method (column with 15% LAC-211-446 on W chromosorb, $N_2$, 40 ml min–1, 130°C) under conditions described in [5].

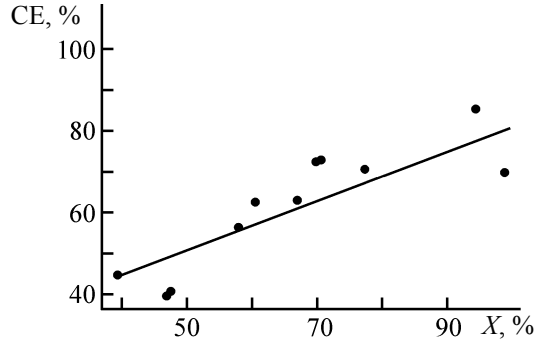
An equilibrium menthone (1)–isomenthone (2) mixture was subjected to electroreduction, which yielded four diastereoalcohols: menthol (3), neomenthol (4), isomenthol (5), and neoisomenthol (6) (see scheme). The experimental results were presented in the table and in the figure, whence it can be seen that the ketones are reduced with a rather high current efficiency by alcohols (76%) at a potential of –2.55 V in an aqueous-alcoholic medium, with a 0.1 M solution of tetrabutylammonium bromide (TBABr) used as an electrolyte. Raising the cathode potential to –3 V results in that a hydrocarbon, menthane, is formed in an amount of up to 1%.

Replacement of the tetrabutylammonium cation in the electrolyte with tetramethylammonium (TMABr) or tetraethylammonium (TEABr) has no effect on the relative amounts of the isomeric alcohols, and, therefore, it is preferable to use TBABr because of its more negative discharging potential.

On acidifying the solution with hydrochloric acid to pH 2 or adding LiCl, the current efficiency and conversion somewhat decrease (to ~40 and ~47%, respectively), but, in the case of HCl, the relative content of neomenthol increases, which is presumably due to an easier protonation of the intermediate anion-radical to give an axial OH group [6] or to inversion of the alcohol anion under the action of the acid [7].

The effect of the solvent on the stereoselectivity of reduction of the (1)–(2) mixture was studied. A slight decrease in the relative content of menthol, observed when the process is performed in an acetonitrile-containing solvent, can be attributed to a shift of the wave of menthone reaction in this solvent toward negative potentials. Electrolysis in the presence of THF and diglyme results in a comparatively high content of menthol. In addition, the dependence of the yield of menthol on the nature of a number of aprotic solvents studied can be presumably attributed to differences in their adsorption on the cathode and to changes in the structure of the electric double layer.

Comparison of the results of electrolyses in DMF in the presence of water or phenol as a proton donor shows that predominantly menthol is formed in the latter case (82%), presumably because of the larger size of the




Current efficiency CE vs. the conversion X of electroreduction of an equilibrium menthone–isomenthone mixture.

Relative amounts of isomeric alcohols in relation to the conditions of electroreduction of a menthone–isomenthone mixture Hg cathode, 0.1 M TBABr as electrolyte

| Run no. | Solvent | Additive | –*E*, V/I, mA | Current efficiency, % | Conversion, % | Composition of the reaction mixture, wt % | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | (3) | (4) | (5) | (6) | total yield | |
| | | | | | | | | | | (3) + (4) | (5) + (6) |
| 1 | EtOH:$H_2O$=3:1 | – | 2.55/0.02 | 76 | 71 | 65 | 8 | 16 | 11 | 73 | 27 |
| 2 | | HCl, pH 2 | 2.45/400 | 41 | 48 | 57 | 19 | 9 | 15 | 76 | 24 |
| 3 | MeCN:$H_2O$=3:1 | – | 2.56/25 | 72 | 70 | 63 | 18 | 8 | 11 | 81 | 19 |
| 4 | DMSO:$H_2O$=4:1 | – | 2.6/20 | 78 | 100 | 75 | 5 | 14 | 6 | 80 | 20 |
| 5 | Dioxane : $H_2O$=5:1 | – | 2.8/9 | 68 | 100 | 77 | 5 | 12 | 6 | 82 | 18 |
| 6 | THF:$H_2O$=5:1 | – | 2.52/17 | 62 | 61 | 80 | 4 | 12 | 4 | 84 | 16 |
| 7 | Diglyme:$H_2O$=4:1 | – | 2.7/– | 83 | 100 | 82 | 2 | 12 | 4 | 84 | 16 |
| 8 | DMF : $H_2O$=5:1 | – | 2.6/10 | 85 | 95 | 68 | 5 | 17 | 10 | 73 | 27 |
| 8 | | PhOH : ketone = 12.5 : 7.7 | 2.55/18 | 96 | 100 | 82 | 6 | 9 | 4 | 88 | 13 |
| 9 | EtOH:$H_2O$:6:1 | 0.01 M ephedrine | 2.1/5 | 45 | 40 | 15 | 77 | 0 | 8 | 92 | 8 |
| 10[a] | 5 : 1 | – | 2.4/6 | 56 | 58 | 14 | 70 | 1 | 15 | 84 | 16 |
| 11[b] | 6 : 1 | – | 2.5/– | 71 | 77 | 73 | 11 | 9 | 5 | 84 | 14 |

[a] (Pd) graphite cathode.
[b] Pb cathode.

phenol molecule. At the same time, the relative content of isomenthols, in which the methyl group is in the axial position (i.e., is the closest to the hydroxy group and shields the latter), is more than twice lower.

It was of interest to find whether or not presence of ephedrine in solution affects the reduction selectivity, because it is known that ephedrine forms a complex with menthone [9]. Indeed, a high content of neomenthol was found in the products, presumably because ephedrine facilitates approach of a proton from the side perpendicular to the ring, i.e., the OH group in the product is in the axial position. It is known that alkaloids [9, 10] facilitate the electroreduction of ketones and favor appearance of chirality in the alcohols obtained. Presumably, the ephedrine cation is discharged, with the subsequent transfer of atomic hydrogen from the radical formed in this process to a menthone molecule, just in such a way that the alcohol formed has an axial OH group.

A study of the influence exerted by the cathode material on the stereoselectivity of reduction of a mixture of ketones (1)–(2) demonstrated that the results obtained on a lead cathode differ from those on mercury only slightly. An electrolysis with the role of cathode played by palladium deposited onto a graphite substrate yielded mostly neomenthol. A similar result was obtained on a graphite cathode. Presumably, the effect of the cathode material on the stereoselectivity depends on the hydrogen overvoltage. For example, it is probable that its high value for mercury and lead facilitates the adsorption and discharge of the protonated ketone. At the same time, the low overvoltage on palladium enables cathodic reduction via electrochemical desorption of atomic hydrogen.

It should be noted that, in electrolysis of an equilibrium mixture of ketones [(1)–(2)], an additional specific feature was revealed in the distribution of alcohols obtained from menthone, menthol + neomenthol [(3) + (4)], and from isomenthone, isomenthol + neoisomenthol [(5) + (6)]. As can be seen in the table, the experimentally obtained distribution of alcohols closely corresponds to the distribution of the starting equilibrium mixture of ketones only in some cases. The total amount of the alcohols (3) + (4) exceeds that of menthone in the starting mixture (70%). Probably, this may be due to the following: menthone is additionally formed from isomenthone as

the former is consumed, so as to restore the equilibrium between these ketones, disturbed by the easier reduction of menthone under the given conditions. This conclusion is confirmed by the ratio between the residual amounts of the starting ketones upon electrolysis: the reaction mixture is to a certain extent enriched with isomenthone.

In catalytic hydrogenation of the (1)–(2) mixture on Ru, Rh, and Pt catalysts, the same phenomenon is observed [11], whereas in the presence of powdered Co, and Ni–Co catalysts, the starting mixture is enriched with menthone [5]. Because the amount of isomenthone, with which the mixture is enriched in electrolysis under the given conditions, is smaller than that of the alcohols (3) + (4) formed, inversion of isomeric alcoholic anion radicals under the action of an exceedingly strong electric field at the electrode–solution interface is also possible [12].

It is known that the reduction of alicyclic ketones occurs via the stage of formation of anion radicals [13, 14]. The most favorable and thermodynamically stable is the conformation in which all the substituents are in the equatorial position, and, under the proton deficiency conditions, the least sterically hindered anion radical will be faster protonated. According to published data, both isomerization of (1) and (2) and inversion of alcohols are possible in strongly acidic and strongly basic media and under the action of acid and alkaline catalysts. In this case, a desired isomer can be predominantly obtained.

Thus, in the previously studied catalytic reduction of an equilibrium menthone–isomenthone mixture on powdered Co and Co–Ni catalysts [5], the reaction proceeds toward formation of neoisomenthol, the least stable alcohol among all the isomeric menthols, whereas for the electrochemical reduction, conditions were found in which the process predominantly occurs toward formation of menthol (see table, run nos. 6–8) or neomenthol (run nos. 9 and 10).

## CONCLUSIONS

(1) The maximum yield of menthol (80–82%) was obtained on the Hg cathode in the following solvents: tetrahydrofuran, diglyme, and dimethylformamide with addition of phenol.

(2) Conditions were found in which neomenthol is predominantly formed: in ethanol on palladium deposited onto a graphite substrate (70%). On a Hg cathode in ethanol with addition of ephedrine, the yield of neomenthol increases to 77%.

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