

ELECTROREDUCTION OF D(-)-PHENYLACETYL CARBINOL

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The present work deals with the polarographic behaviour and preparative electroreduction of D(-)-phenylacetylcarbinol in alkaline medium. The products were phenylacetone and a mixture of D(-)-*threo* and D(-)-*erythro*-1-phenyl-1,2-propanediol, which were separated by means of ion exchange chromatography. The mechanism of the electroreduction is discussed.

The polarographic behaviour of D(-)-phenylacetylcarbinol and its isomer, methylbenzoylcarbinol, was studied¹ mainly for the purpose of their analytical determination in mixtures with benzaldehyde occurring in production of (-)-ephedrine². The possibility of a polarographic determination of phenylacetylcarbinol with the aid of a derivative curve was mentioned³. Colorimetry^{4,5} and chromatography^{6,7} were also used in the determination of this compound. Later we studied the electrochemical behaviour of other α -hydroxycarbonyl compounds in more detail⁸⁻¹¹. The results showed the necessity of studying more carefully the polarographic behaviour of D(-)-phenylacetylcarbinol in order to elucidate not only the reduction mechanism of this optically active substance but also that of other, optically inactive substances with an α -hydroxycarbonyl group.

EXPERIMENTAL

Apparatus. The curves were recorded on an LP 60 type polarograph (Laboratorní přístroje, Prague) with the use of a Kalousek cell with a separated saturated calomel electrode. The capillary had a rate of flow (m) 2.33 mg/s and drop time (t) 5 s at a height of mercury column 50 cm. To obtain products of electroreduction on the dropping electrode (m 3.33 mg/s, t 1.71 s, h 50 cm), a vessel of a similar design as described earlier¹² was used with a small holding capacity of 0.5–1.0 ml of electrolyzed solution. The potential of a large mercury pool electrode⁸ during preparative electrolyses was maintained constant by a PRT 500 LC type potentiostat (Tacussel, France). The pH values of buffers were measured with a compensator of the type E 148c (Metrohm A. G., Herisau, Switzerland). The optical rotation was measured with an automatic polarimeter of the type ETL-MPL 143A (Bembix Ericsson, Nottingham). IR spectra were recorded on a spectrophotometer of the type UR-10 (Zeiss, Jena) and absorption in the UV region was measured on a universal spectrophotometer of the type VSU-1 (Zeiss, Jena). Melting points were measured on a Koffler block.

Chemicals. D(-)-Phenylacetylcarbinol was prepared according to Molnár and Bauer¹³; its boiling point was 100–102°C (0.01 Torr), $[\alpha]_D^{20} -164^\circ$ (c 4, ethanol), n_D^{20} 1.5320. Its methyl ether, D(-)-phenyl-1-methoxypropane-2-one, was prepared according to ref.¹⁴; b.p. 66°C (0.45 Torr), $[\alpha]_D^{20} -115^\circ$ (c 4, ethanol), n_D^{20} 1.5078. Buffers were prepared from reagent grade chemicals, solvents for chromatography were purified by column distillation.

Methods. Electroreduction of D(-)-phenylacetylcarbinol on a preparative scale (0.2 ml) was carried out in 100 ml of 0.05M veronal buffer, pH 7.9, in the presence of 20% ethanol and 0.2M CaCl_2 at -1.8 V (s.c.e.). The products were isolated and determined in two ways: a) By extracting into chloroform or tetrachloromethane, drying by sodium sulphate and concentrating. IR spectrum of the raw product showed the presence of carbonyl or α -diol derivatives. The products were separated on a small column (10×1 cm) of powdered silica heated prior to use, or on a larger plate with the aid of chloroform as a separating agent. An alkaline solution of tetrazolium blue⁷ served as a detecting agent. The more mobile substance contained a carbonyl group, whereas the less mobile one was distinguished by an α -diol group. The pure substances thus obtained were characterized by IR and UV spectra. b) After electroreduction, the inorganic portion was precipitated by methanol, 10 ml of a solution of 0.7 g 2,4-dinitrophenylhydrazine and 2.8 ml concentrated HCl in 28 ml methanol was added to the filtrate and the crystalline precipitate was after 30 min filtered off, washed by water and little ethanol and dried (m.p. $152-153^\circ\text{C}$, ref.¹⁷, found $149-151^\circ\text{C}$). For $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_4$ (314.3) calculated: 57.32% C, 4.48% H, 17.82% N; found: 57.13% C, 4.47% H, 17.67% N. After the product had been separated, the mother liquor was evaporated to a small volume, the unreacted 2,4-dinitrophenylhydrazine was filtered off and the light yellow solution was fractionated on a Dowex 50 WX8 (100-200 mesh) ion exchange column (200×1 cm) in Ba^{2+} cycle. Distilled water served as an elution agent. The course of the separation was followed by paper chromatography in an acetone-n-butanol-water system (8:1:1) (S_1) on a Whatman 1 paper impregnated by a solution of 1% sodium tetraborate. The spots were detected by a saturated aqueous potassium periodate solution and after 5 min reaction the chromatogram was sprayed by a solution of 2.5 g benzidine in 400 ml ethanol and 100 ml acetic acid. The location of spots of two obtained substances was determined with respect to the location of D(-)-phenylacetylcarbinol (R1). Both substances were obtained in crystalline forms from a small amount of absolute ether, m.p. $56-57$ and $90-91^\circ\text{C}$.

Electroreduction of 1.0 ml of 0.001M D(-)-phenylacetylcarbinol was carried out in the mentioned small coulometric cell in the presence of veronal buffer at -1.8 V (s.c.e.); after 24 h the solution was desalted by ion exchangers and the products analyzed by paper chromatography (S_1). The amount of products formed at -1.65 , -1.75 and -1.85 V (s.c.e.) was determined in the form of 2,4-dinitrophenylhydrazone¹⁵ (phenylacetone) and by oxidation with periodate¹⁶ (α -diols).

RESULTS

As noted previously¹, D(-)-phenylacetylcarbinol gives an irreversible polarographic two-electron reduction wave in buffered solutions of $\text{pH} > 7$. Its half-wave potential is practically independent of pH and is shifted to more positive values by addition of certain cations. The mentioned compound gives well-developed polarographic waves in ammoniacal and certain amine buffers.

The product with a carbonyl group obtained by preparative electroreduction of D(-)-phenylacetylcarbinol in veronal buffer in the presence of Ca^{2+} ions (better developed polarographic wave¹) reacted with 2,4-dinitrophenylhydrazine to give phenylacetone hydrazone (m.p. $149-151^\circ\text{C}$). The formation of phenylacetone was also evidenced by elementary analysis, IR and UV spectra ($\bar{\nu}_{\text{C=O}} = 1725 \text{ cm}^{-1}$, ref.¹⁷; $\lambda_{\text{C=O}} = 280 \text{ nm}$) (Fig. 1). The other product of electroreduction isolated by chromatography was shown by IR ($\bar{\nu}_{\text{C-OH}} = 3600-3630 \text{ cm}^{-1}$, ref.¹⁸) and UV spectra (Fig. 1) to contain an α -diol group in an asymmetrical molecule, in our case a mixture of isomers of 1-phenyl-1,2-propanediol with optical rotation $[\alpha]_{\text{D}}^{20} = -26^\circ$ (c 4, etha-

mol). The isomers separated by ion exchange chromatography crystallized from ether and melted at 56–57 and 89–90°C; $[\alpha]_D^{20}$ –36° and –16°, respectively (*c* 4, ethanol). The isomer with the lower melting point has a *threo* configuration, the other one *erythro*^{19–24}. The mass ratio of both electroreduction products, phenylacetone and the mentioned isomeric mixture (approx. 1 : 1) was within experimental errors independent of the reduction potential. Also on the dropping electrode, both reduction products were detected by chromatography and by precipitation with 2,4-dinitrophenylhydrazine.

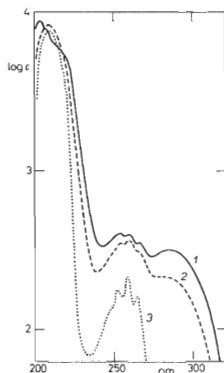
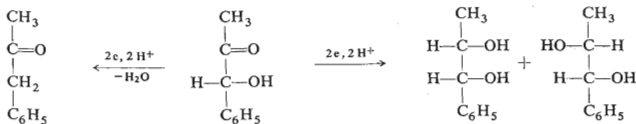


FIG. 1

UV Spectra of D(-)-Phenylacetylcarbinol (1), Phenylacetone (2) and a Mixture of *threo*- and *erythro*-D(-)-Phenyl-1,2-propanediol (3) in Ethanol

DISCUSSION

D(-)-Phenylacetylcarbinol is polarographically similar to compounds containing an α -hydroxycarbonyl group that is polarographically active^{8–11}. During an irreversible two-electron reduction, the studied compound splits off a hydroxyl to form phenylacetone or its CO group is reduced to give an isomeric mixture of *D-erythro* and *D-threo*-1-phenyl-1,2-propanediol. The formation of these optically active diols is an evidence for the absence of a chemical change of the α -hydroxycarbonyl group, since in the opposite case racemization would take place on the optically active C atom of D(-)-phenylacetylcarbinol. The experimental results lead us to assume the following scheme of the electrode process:



(Here the absolute configuration of D(-)-phenylacetylcarbinol found by Freudenberg and coworkers²⁵ is considered.) The polarographic hydrogenolysis of the C—OH group and the reducibility of the CO group of D(-)-phenylacetylcarbinol in the given potential range is made possible by their mutual influencing. It follows from stuart atomic models of D(-)-phenylacetylcarbinol that the proton orbit of the OH group cannot sufficiently overlap with the orbit of the CO group to form an intramolecular hydrogen bond, so that a mutual steric influencing of these groups is not important in facilitating their reduction. Therefore, and since no intermediate is formed in the electroreduction of the studied compound, it is apparent that a mutual polar influencing of the mentioned groups is mainly responsible for enabling their reduction. The fact that under various conditions of the reduction always a mixture of both types of products (about 1 : 1) is obtained is an evidence that the hydrogenolysis of the OH and reduction of the CO group require about the same amount of energy.

It is interesting that reduction of D(-)-phenylacetylcarbinol with aluminium amalgam results also in phenylacetone and a mixture of optically active isomers of 1-phenyl-1,2-propanediol²⁶, a further evidence that in some cases the electroreduction and reduction with a metal follow a similar course⁸. The methyl ether of D(-)-phenylacetylcarbinol (D(-)-phenyl-1-methoxypropane-2-one¹⁸) in a veronal buffer of pH 8 in the presence of Ca²⁺ ions gives a two-electron reduction wave at a potential by 40 mV more negative than the parent compound. Preparative electroreduction of D(-)-1-methoxy-1-phenylacetone takes a similar course as with D(-)-phenylacetylcarbinol and the products, phenylacetone and a mixture of D(-)-1-methoxy-1-phenyl-2-propanols, substantiate the conclusions mentioned above.

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