

# Electroreduction of DL-glyceraldehyde and D-forms of its 2,3-di-O-methyl- and 2,3-O-isopropylidene derivatives

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Polarographic behaviour of DL-glyceraldehyde and its two given derivatives was investigated in buffered and nonbuffered solutions. Two polarographic reduction waves of the studied compounds were found to be dependent on pH of the medium, buffer concentration, reservoir height, and the temperature. Preparative electroreductions of the compounds were carried out under potentiostatic and pH-static conditions. Based upon the products of the preparative reductions performed at the limiting currents of the first and the second wave, mechanisms of the corresponding chemical and electrochemical processes were suggested.

Исследовано полярографическое поведение DL-глицеральдегида и двух его приведенных производных в буферных и небуферных растворах. Обнаружено, что две полярографические волны восстановления изучаемых соединений зависят от pH среды, концентрации буфера, высоты ртутного столба и температуры. Проведено препаративное электровосстановление соединений в потенциостатических и pH-статических условиях. На основании продуктов препаративного восстановления, проводимого при лимитных токах первой и второй волн, делается предположение о механизмах соответствующих химических и электрохимических процессов.

In our previous paper [1] attention was paid to polarographic behaviour of DL-glyceraldehyde and to its preparative electroreduction in a phosphate buffer, pH = 11. Paper chromatography showed besides glycerol as the main product of the electroreduction, the presence of hexoses formed in an aldol condensation of DL-glyceraldehyde with transiently appearing dihydroxyacetone. This is in contrast to electroreduction of glycolaldehyde which leads exclusively to acetaldehyde [2]. The present work is devoted to a more detailed study of the electroreduction of the title compounds plus glycolaldehyde in a wider range of pH values, so that the mechanism of electroreduction of the electrochemically active  $\alpha$ -hydroxycarbonyl arrangement in the studied compounds could be more precisely defined.

## Experimental

### Equipments

Polarographic curves were registered on a LP 7 polarograph (Laboratorní přístroje, Prague) provided with a Kalousek vessel having a separated saturated calomel electrode (SCE). Preparative electroreductions were done in the vessel described in our previous paper [1]. The potential of the mercury cathode referred to SCE was controlled by a potentiostat PRT 40-5X (Tacussel, France). Adjusted pH values were maintained by a TTT 2 Titrator (Radiometer, Copenhagen) as described [3]. Vigorous stirring of the mercury surface was performed by a mechanical stirrer linked to an electromotor. Analysis of the obtained products was done by GCMS system using a 1 m long column packed with Porapac Q, particle size 0.15–0.17 mm, at an initial temperature of 170 °C (15 min) and then using a temperature rise to 220 °C (4 °C min<sup>-1</sup>). The GC apparatus was linked to a JMS-D 100 mass spectrometer (Jeol, Japan). Condensation products with 2,4-dinitrophenylhydrazine were analyzed with a Perkin—Elmer 240 automatic analyzer. Optical rotations were measured with a Perkin—Elmer 141 polarimeter.

### Chemicals

DL-Glyceraldehyde was from Reanal (Budapest) and 2,3-di-*O*-methyl-D-glyceraldehyde was prepared as described earlier [4]. 2,3-*O*-Isopropylidene-D-glyceraldehyde was obtained by periodate oxidation of 1,2:5,6-isopropylidene-D-mannitol, m.p. = 122 °C [5, 6]. A solution of the mannitol derivative (5 g) in water (50 cm<sup>3</sup>) was mixed with 50 cm<sup>3</sup> of aqueous solution of sodium periodate (4.5 g). After 30 min standing at room temperature the solution was saturated with sodium chloride and the product extracted to ether. The ether solution was dried with calcium chloride, filtered and evaporated *in vacuo* (20 °C, 1.0 kPa) to give the desired product (2.5 g, 52 % yield),  $[\alpha]_D(25^\circ\text{C}) = +65.3^\circ$  ( $\rho = 10 \text{ g dm}^{-3}$ , benzene, 24 h),  $[\alpha]_D(25^\circ\text{C}) = +4.6^\circ$  ( $\rho = 10 \text{ g dm}^{-3}$ , H<sub>2</sub>O, 24 h). The corresponding 2,4-dinitrophenylhydrazone, m.p. = 103 °C, was subjected to elemental analysis. For C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>6</sub> ( $M_r = 310.26$ )  $w_i(\text{calc.})$ : 46.45 % C, 4.55 % H, 18.06 % N;  $w_i(\text{found})$ : 46.43 % C, 4.59 % H, 18.46 % N.

Polarographic monitoring of the reduction of the studied compounds was done in Britton—Welford phosphate buffers and in Gottschalk ammonium buffers. All chemicals used in this work were of anal. grade purity.

### Procedures

Polarographic curves were registered after addition of samples to a basic electrolyte and after subsequent removal of oxygen by bubbling with pure nitrogen. In the case of the reaction media containing reactive components, oxygen was removed before sample addition. Preparative electroreductions were done always using 100 cm<sup>3</sup> of  $5 \times 10^{-2} \text{ M}$

solution of compounds in water containing 0.1 M potassium chloride or calcium chloride. During electrolysis the adjusted potential of the working mercury electrode was maintained by a potentiostat and the adjusted pH value of the catholyte was maintained using a pH-stat dosing 1 M hydrochloric acid [3]. A saturated solution of ammonium sulfate diluted with water (volume ratio = 1 : 1) was used as anolyte. Preparative electroreductions were monitored polarographically and, in the case of DL-glyceraldehyde and glycolaldehyde, also by periodate oxidation.

### *Product analysis*

Preparative electroreduction of DL-glyceraldehyde at a potential of the limiting current of the first wave ( $i_l$ ) gave two products. A polarographically active product, 3-hydroxypropanal, was isolated from the reaction medium as 2,4-dinitrophenylhydrazone derivative, m.p. = 134–135 °C. Since 3-hydroxypropanal is very labile [7] the corresponding hydrazone was obtained by reacting 2,4-dinitrophenylhydrazine (200 mg) with one portion of the reduced DL-glyceraldehyde in aqueous solution. The reaction was carried out under stirring at 50 °C for 6 h. The crystalline product was washed with water and analyzed. For  $C_9H_{10}N_4O_5$   $w_i$ (calc.): 42.53 % C, 3.97 % H, 22.04 % N;  $w_i$ (found): 42.54 % C, 3.97 % H, 22.04 % N. The formation of 3-hydroxypropanal was also confirmed by GCMS. Its dehydration in the column afforded 2-propenal [8] characterized by peaks at  $m/z$  56 (M), 55, and 27. A parallel formation of glycerol was demonstrated by paper chromatography [1] and GCMS analysis. After termination of the electrolysis, the solution was evaporated *in vacuo* (40 °C) and the residue treated with methanol to precipitate the salts. The presence of glycerol in the supernatant was confirmed by the characteristic peak at  $m/z$  = 61. The amount of glycerol was determined by periodate oxidation. Since the oxidation of one mole of DL-glyceraldehyde requires similarly as the oxidation of glycerol, two moles of sodium periodate, the periodate consumption, after the reduction of DL-glyceraldehyde was completed, was taken for the measure of the formed glycerol. For this purpose, a new polarographic method of DL-glyceraldehyde and glycerol determination was elaborated that employs periodate oxidation. DL-Glyceraldehyde or glycerol ( $10^{-4}$ – $10^{-3}$  M solution in water) is treated with  $2.5 \times 10^{-4}$ – $2.5 \times 10^{-3}$  M solution of sodium periodate for 30 min. The excess of periodate is precipitated with solid calcium oxide and the resulting supernatant is analyzed polarographically for the formed sodium iodate. Its curve was registered from –0.6 V vs. SCE. This way of determination of periodate consumption is rapid and precise since it employs a six-electron wave of sodium iodate instead of a two-electron wave of sodium periodate. The same principle was used to follow the decrease of DL-glyceraldehyde from its starting concentration  $5 \times 10^{-4}$  mol dm $^{-3}$  due to glycerol formation. Sodium periodate was used at  $12.5 \times 10^{-4}$  mol dm $^{-3}$  concentration. Preparative electroreduction of DL-glyceraldehyde at a potential of the limiting current of its second wave afforded 1,3-propanediol. The product was identified in the concentrated reaction solution (vacuum distillation below 40 °C) from which salts were precipitated with methanol, by GCMS analysis based on the peaks at  $m/z$  58, 57, 43, and 30. Preparative electroreduction of glycolaldehyde at

the potential of the limiting current of the first wave gave, similarly as in the case of DL-glyceraldehyde, two products, acetaldehyde and ethylene glycol. Acetaldehyde was isolated from the reaction medium by precipitation with saturated aqueous solution of 2,4-dinitrophenylhydrazine in 1 M hydrochloric acid. The product was recrystallized from ethanol (m.p. = 161—162 °C) and analyzed. For  $C_8H_8N_4O_4$   $w_i$ (calc.): 42.86 % C, 3.59 % H, 24.99 % N;  $w_i$ (found): 42.88 % C, 3.61 % H, 25.06 % N. Ethylene glycol was determined by the periodate oxidation method described above.

Two products were also obtained in preparative electroreduction of 2,3-di-*O*-methyl-D-glyceraldehyde carried out at the potential of the limiting current of the first wave. Polarographically active product, 3-methoxypropanal, was isolated from the reaction mixture as its 2,4-dinitrophenylhydrazone, m.p. = 115 °C, by the same procedure as that given for the isolation of 3-hydroxypropanal. For  $C_{10}H_{12}N_4O_5$   $w_i$ (calc.): 44.77 % C, 4.51 % H, 20.89 % N;  $w_i$ (found): 44.74 % C, 4.58 % H, 21.12 % N. The formation of 3-methoxypropanal was also demonstrated by GCMS analysis of a sirupy residue of an ether extract ( $m/z$  59, 45, 31, and 29). The same way was used to prove the presence of the second optically active product, 2,3-di-*O*-methyl-D-glycerol ( $m/z$  89, 75, 57, 45, and 31). Its concentration at the end of the electroreduction was determined from the difference of optical rotation of two equal solutions of 2,3-di-*O*-methyl-D-glyceraldehyde, one reduced with  $NaBH_4$ , the other electrochemically.

Preparative electroreduction of 2,3-*O*-isopropylidene-D-glyceraldehyde at the potential of the limiting current of the first wave afforded only one product, optically active 3-hydroxypropanal, which was subsequently reduced to 1,3-propanediol, as shown by GCMS analysis. The electroreduction of the starting compound was accompanied by liberation of acetone, isolated as its 2,4-dinitrophenylhydrazone, m.p. = 122—123 °C. All physicochemical constants of known compounds were in consonance with the published data.

## Results

### *Polarographic behaviour*

DL-Glyceraldehyde (*I*), 2,3-di-*O*-methyl-D-glyceraldehyde (*II*), and 2,3-*O*-isopropylidene-D-glyceraldehyde (*III*) underwent electroreductions characterized by two polarographic waves. The heights of the waves and their ratios depended on reaction conditions. Polarographic behaviour of *II* and *III* in phosphate buffers was similar to that of *I* reported in our previous paper [1]. A typical example of the dependence of the two polarographic waves on pH of ammonium buffers is shown in Fig. 1. Characteristic data of the polarographic waves of the reduction of all three compounds as a function of pH are shown in Table 1. The heights of both waves were enhanced with increasing pH. The increase of the second wave ( $i_2$ ) was relatively greater than that of the first wave ( $i_1$ ) in the case of compounds *I* and *II*. At pH values lower than 7 only the first more positive wave was observed. A similar situation occurred in aqueous

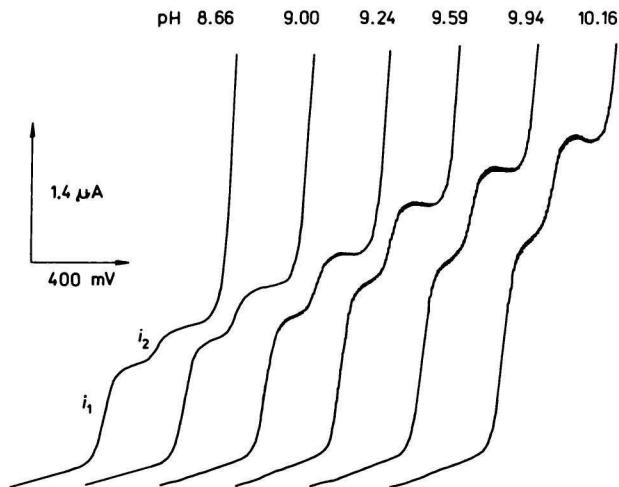


Fig. 1. pH-Dependence of polarographic waves of the reduction of  $1 \times 10^{-3}$  M 2,3-di-O-methyl-D-glyceraldehyde in aqueous ammonium buffers. Curves registered from  $-1.0$  V vs. SCE.

solutions of ammonium chloride only. Height of the more positive wave increased linearly with depolarizator concentration. On the other hand, in aqueous solutions of potassium chloride or calcium chloride both polarographic waves of the studied compounds were observed and their heights showed an exponential increase with concentration. The heights of both polarographic waves of all three compounds also increased with rising concentration of the ammonium buffers. At higher pH values of the medium and, particularly, after longer reaction times, undesired reactions took place. In the case of compounds *I* and *II* these reactions have been already investigated [9–11].

#### *Preparative electroreductions*

All three studied compounds showed two well developed polarographic waves (Table 1). The data characteristic of the two waves could not be applied in the preparative reductions because at higher concentration of the compounds or after longer reaction time, reactions leading to the corresponding imines took place in a considerable extent and complicated the electroreductions. Hence, the preparative reductions were carried out in nonbuffered aqueous solutions of potassium chloride or calcium chloride under potentiostatic and pH-static conditions in pH range 4–9 [3]. At pH values lower than 4 the electroreductions were disturbed by exclusion of hydrogen, while at pH values higher than 9 accompanying chemical reactions occurred [1, 9–11]. A typical time course of



a preparative electroreduction of DL-glyceraldehyde at the potential of the limiting current of the first wave in aqueous solution of calcium chloride is demonstrated in Fig. 2. It can be seen that the decrease in the concentration of the starting compound during electroreduction corresponding to the more positive wave ( $i_1$ ) is accompanied by formation of a polarographically active intermediate evident from the increase of the second wave ( $i_2$ ) at a more negative potential. Simultaneous monitoring of the preparative electroreduction of DL-glyceraldehyde by periodate oxidation pointed to the formation of an oxidizable product in about 25 % yield. The same course of the electroreduction was recorded at pH values 5 and 9 at a constant potential of the working electrode, — 1.6 V *vs.* SCE. Electroreduction of DL-glyceraldehyde proceeded similarly under the same conditions in the presence of potassium chloride. The consumption of periodate, however, indicated that both products were formed in the same ratio. After switching the potential of the working electrode to the value of the limiting current of the second wave, *i.e.* to the value of — 1.8 V *vs.* SCE, the electroreduction was terminated by disappearance of this wave. From the data obtained by polarography, periodate oxidation, and product analysis it follows that electroreduction of DL-glyceraldehyde leads in the first step to glycerol and 3-hydroxypropanal which is subsequently reduced to 1,3-propanediol. Preparative electroreduction of glycolaldehyde in aqueous solutions of potassium chloride and calcium chloride at pH = 7 and at a potential of the working mercury electrode — 1.6 V *vs.* SCE was carried out for comparative

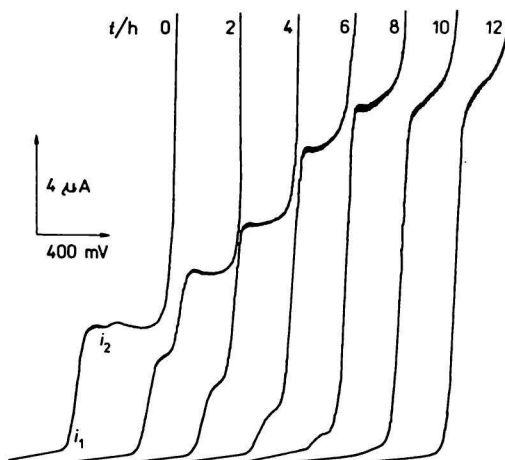


Fig. 2. Preparative electroreduction of  $5 \times 10^{-2}$  M DL-glyceraldehyde in 100 cm<sup>3</sup> of 0.1 M aqueous solution of calcium chloride at pH = 7 and at a potential of the working electrode of — 1.6 V *vs.* SCE. The electroreduction was followed by registration of curves at the given time intervals in ammonium buffer, pH = 7.3, starting from — 1.0 V *vs.* SCE.

purposes. The reaction sequence was found to be analogous to that of DL-glyceraldehyde, however, the first step gave only 20 % of ethylene glycol and 80 % of acetaldehyde which can be further reduced to ethyl alcohol.

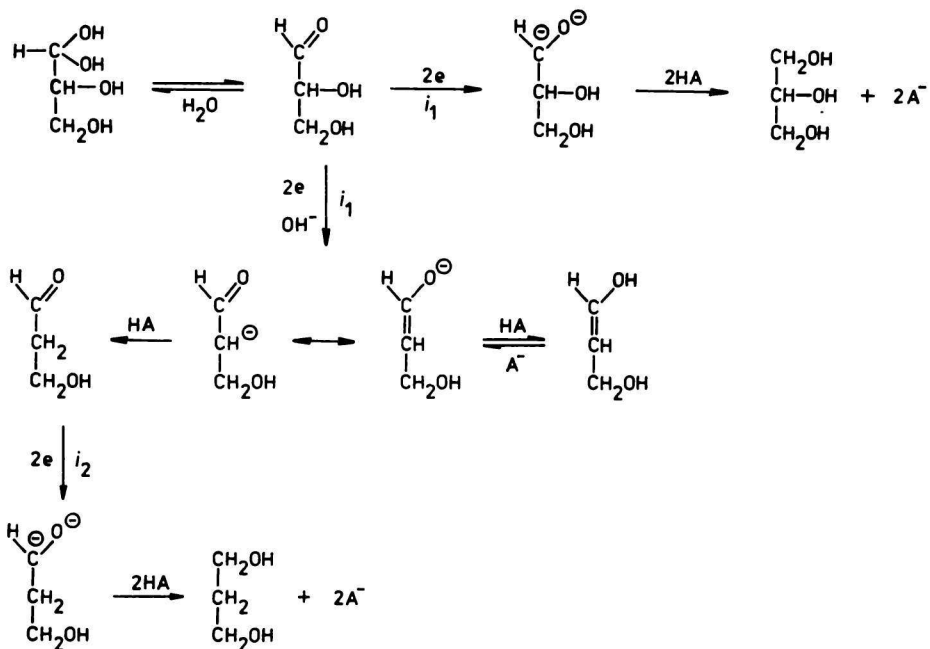
Time course of the preparative electroreduction of 2,3-di-*O*-methyl-D-glyceraldehyde in both electrolytes at a potential of the working electrode — 1.5 V *vs.* SCE and at pH = 7 showed a similar polarographic dependence as that of DL-glyceraldehyde. Product analysis pointed out that the first electroreduction step gave 36 % of 2,3-di-*O*-methyl-D-glycerol and 64 % of 3-methoxypropanal which was reduced to 3-methoxy-1-propanol at a potential of — 1.8 V. Products of the preparative electroreduction of 2,3-*O*-isopropylidene-D-glyceraldehyde at a potential of the working electrode of — 1.6 V and — 1.8 V *vs.* SCE, included 3-hydroxypropanal, 1,3-propanediol, and acetone. Formation of 2,3-*O*-isopropylidene-D-glycerol was excluded because the final electroreduction mixture was optically inactive and did not afford glycerol on acid hydrolysis [12].

### Discussion

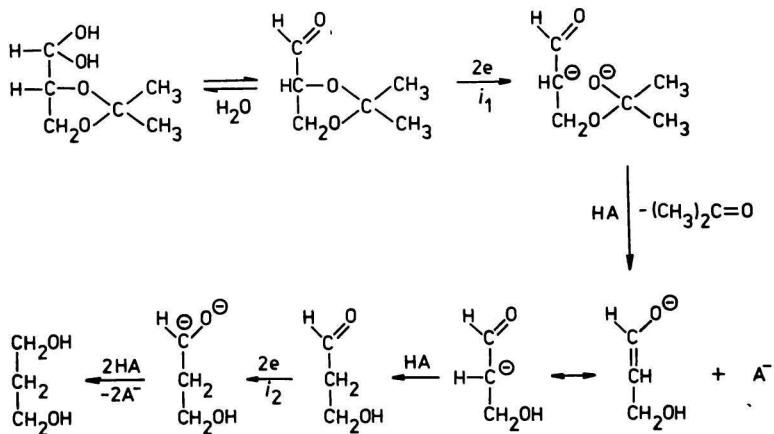
Polarographic behaviour of all three studied compounds pointed out that subjects to electroreduction are only free compounds, the formation of which is limited by generally acid-base catalyzed dehydration of their hydrated forms [1]. More positive values of potentials of their reductions represented by the first wave, in comparison with reduction potentials of analogous aliphatic aldehydes, serve as an evidence that the reduction of the carbonyl group is facilitated by the presence of the C—OH or C—OCH<sub>3</sub> groups in  $\alpha$ -position. The electroreductive cleavage of these groups is attributable only to the polarization effect of the carbonyl group. It is interesting that both types of reduction of glyceraldehyde and its *O*-methyl derivative proceed parallelly giving products, the ratio of which depends not only on the starting compound but also on the quality of the medium. The fact that the heights and ratios of the two polarographic reduction waves depend on pH of the medium, means that a polarographically active product formed in the first wave undergoes a time-dependent chemical transformation to a compound which exhibits polarographic activity in the second wave. Polarographic behaviour, progression of preparative electroreductions, and products formed from DL-glyceraldehyde are apparent from the mechanism of its chemical and electrochemical reactions (Scheme 1).

In the first step a free form of DL-glyceraldehyde is formed by dehydration. The free form undergoes electroreduction. The first wave ( $i_1$ ) corresponds either to reduction of the carbonyl group to give glycerol, or to electroreductive cleavage of its C—OH bond in  $\alpha$ -position to the carbonyl group under the





Scheme 1



Scheme 2

formation of an anion stabilized by resonance. Such an anion is generally in an acid-base catalyzed reaction in an equilibrium with its enol form. In acidic media the equilibrium is shifted more in favour of polarographically nonreducible 3-hydroxy-1-propenol. Therefore, the second polarographic wave ( $i_2$ ) is practically not observed at  $\text{pH} < 7$ . More of the corresponding anion is formed at higher pH values. Already during the life of the mercury drop, certain amount of the anion is transformed into polarographically active 3-hydroxypropanal resulting in a small polarographic wave ( $i_2$ ) at more negative potentials. The same chemical and electrochemical reactions are involved in the electroreduction of 2,3-di-*O*-methyl-D-glyceraldehyde.

Despite the polarographic behaviour of the third studied compound, 2,3-*O*-isopropylidene-D-glyceraldehyde, was analogous to that of the two previous compounds, the formation of 2,3-*O*-isopropylidene-D-glycerol as an anticipated product, was not observed. This means that the electroreduction of the carbonyl group of this compound was not confirmed. 1,3-Propanediol and acetone are the final products of the electroreduction of 2,3-*O*-isopropylidene-D-glyceraldehyde as outlined in Scheme 2.

The first more positive wave ( $i_1$ ) corresponds to electroreductive cleavage of the simple C—O bond in the  $\alpha$ -position to the carbonyl group in 2,3-*O*-isopropylidene-D-glyceraldehyde molecule. The formed dianion is cleaved under the action of general acid to give acetone and an anion stabilized by resonance. Subsequent chemical and electrochemical transformations of the anion follow the pattern discussed with the corresponding compound derived from DL-glyceraldehyde.

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