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Electrosynthesis of 2,3-dimethyltartaric acid from pyruvic acid in acid medium

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Abstract

This study reports the electrohydrodimerization of pyruvic acid to 2,3-dimethyltartaric acid in sulphuric acid medium (0.5 M H_2SO_4) on a lead cathode. The main products detected were lactic acid and 2,3-dimethyltartaric acid. The selectivity towards the formation of 2,3-dimethyltartaric acid was studied vs. pyruvic acid concentration in sulphuric acid solution, at −1.1 V vs. MSE. The best selectivity of 2,3-dimethyltartaric acid reached 69% for an initial concentration of 1.7 M pyruvic acid. The yield of pyruvic acid was 84%.

1. Introduction

The catalytic reduction of organic molecules containing a carbonyl group has been a reaction widely investigated in the preparation of intermediates for the fine chemicals and pharmaceutical industries. The control of selectivity is one of the important problems in organic electrosynthesis. Various electrolytic conditions, such as electrode materials, supporting electrolyte, electrode potential, reagent concentration and pH, affect the product distribution. The electroreduction of carbonyl compounds is complex and can lead to varied products, such as alcohols, hydrocarbons or pinacols (electrohydrodimerization). Many researchers have studied the electroreduction of carbonyl compounds to monomeric and dimeric products using acetophenone and furfural as model molecules. The selectivity of electroreduction of acetophenone to the monomeric product 1-phenylethanol and the dimeric product 2,3-diphenyl-2,3-butanediol in aqueous media have been much studied [1–7] with interesting results. Likewise, in the presence of cyclodextrins, the dimeric product of electroreduction of acetophenone has also been obtained selectively [8–10].

Different methods have been used to selectively produce 2,3-dimethyltartaric acid or lactic acid by the reduction of pyruvic acid and its derivatives. Lactic acid, which is the hydrogenation product of this reduction, is an useful intermediate in the biological sector, food and polymer industries [11, 12]. Electrosynthesis of 2,3-dimethyltartaric acid from pyruvic acid in aqueous medium, which presents two asymmetric carbons, is very interesting in fundamental research to elucidate the distribution of the reaction products by diastereoselectivity. Indeed, in some cases diastereo- and enantioselective pinacol coupling reactions of chiral α-ketoamides mediated by samarium diiodide (SmI_2) have afforded extremely high diastereoselectivities [13, 14]. Some authors have successfully reduced the carbonyl group by redox reaction using sodium borohydride [15], C2 symmetric diamines as chiral ligands [16] and solutions of cation perchlorates (V^{2+}, Eu^{2+}, Cr^{2+}) [17]. Up to 99% enantiomeric excess at 100% conversion were obtained. Lactic acid has also been synthesized from glucose by fermentative manufacture in the presence of externally added pyruvic acid [18, 19]. Elsewhere electroenzymatic route for producing lactic acid from pyruvic acid has been used extensively [20–23].

However, few results in the literature concern the electrochemical reduction of pyruvic acid. The selectivity of lactic acid in electroreduction of pyruvic acid, on lead or copper, in aqueous media was studied [24, 25].

Several methods for synthesizing 2,3-dimethyltartaric acid have been suggested in previous work. One of them was to produce it in one step using pyruvic acid as raw material and an ionizing radiation (γ-rays) as energy source [26]. In these particular experimental conditions, 2,3-dimethyltartaric acid was obtained at 73%. The side-products were carbon dioxide, acetic acid and some polycarboxylic acids. Elsewhere, this carboxylic acid or its corresponding ester was synthesized using various organic substrates such as 2,3-dihydroxy-2,3-dimethylsuccinonitrile/methanol [26], 2,2,2-trimethoxy-4,5-dimethyl-2,5-[1,3,2]dioxaphospholane-4,5-dicarboxylic acid dimethylester [28] or dimethylmaleic acid dimethyl ester/aq.$RuCl_3$/aq.$NaClO_4$ [29]. In 1958 the electrosynthesis of 2,3-dimethyltartaric acid was studied on Cu(Hg) in ammonia. The maximum selectivity obtained was close to 11% [30].

Our previous results showed that two reaction products are obtained from the electroreduction of the carbonyl group of pyruvic acid on lead and in sulphuric acid (Figure 1).

The present work was focused on the optimization of 2,3-dimethyltartaric acid synthesis by the effect of the substrate concentration and that of the electrode potential.

2. Experimental details

2.1. *Reagents*

All the experiments were carried out in aqueous solutions using "ultrapure" water (18 MΩ cm, Millipore system). The analytical grade supporting electrolytes were purchased from Merck. Pyruvic acid (96%), lactic acid (98%), methylpyruvate (94%) and methyllactate (98%) were supplied by Sigma-Aldrich. The solutions were degassed by bubbling nitrogen (U Quality from Air Liquide) and were magnetically stirred under a nitrogen atmosphere during the electrochemical studies.

2.2. *Apparatus*

The electrolysis equipment was composed of a potentiostat (Wenking PGS 77). The current vs. time was followed on a Kipp & Zonen BD 40 X-t recorder, and the quantity of electricity involved (Q_{exp}) was measured directly by a coulometer (Wenking EVI 80). Electrochemical experiments were carried out in a three-electrode Pyrex cell ($V = 50$ cm^3) at room temperature (22 ± 1 °C) (Figure 2). The working electrode consisted of two lead plates with a geometric surface area of 32 cm^2. The current densities are given vs. the geometric area. In order to observe the state of the electrode surface, a voltammogram was recorded before applying the electrolysis potential. A 90% platinum/10% iridium plate and $Hg/Hg_2SO_4/K_2SO_4$sat. (MSE) ($E_{\mathrm{REF}} =$ 0.65 V(RHE) at pH = 0) served as counter and reference electrodes, respectively. This electrode was separated from the solution by a Luggin-Haber capillary tip. The anode was wrapped with an ion exchange membrane (Nafion® 427) in order to avoid oxidation of the organic compounds on its surface. This wrapping of the anode was obtained by carefully heating the sides of two pieces of membrane, which were cut according to the dimensions of the electrode plate.

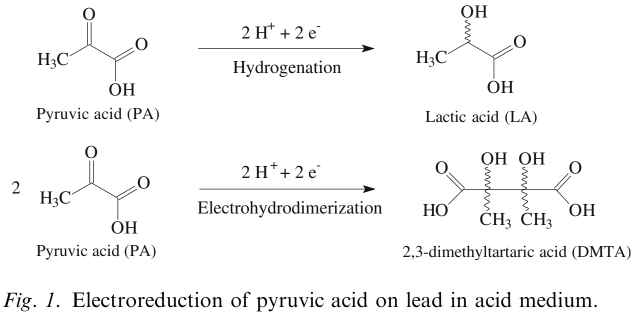

Fig. 1. Electroreduction of pyruvic acid on lead in acid medium.

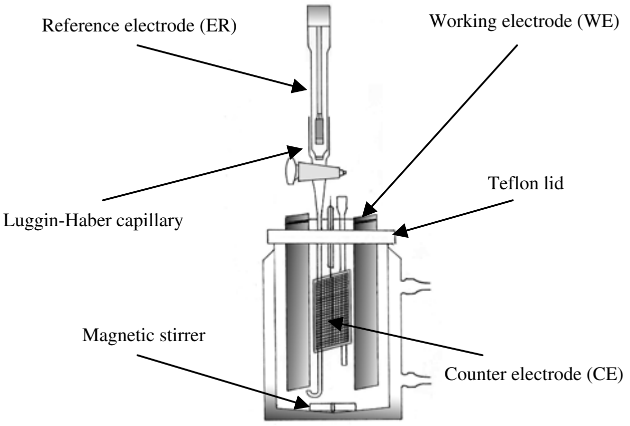

Fig. 2. Three-electrode cell used for electrochemical measurements.

For cyclic voltammetry studies, the lead cathodes were pretreated in nitric solution (HNO_3, 25%), polished with fine emery paper, then polished with successively finer grade alumina powders ranging from 9.5 μm for each new electrode to 0.3 μm and rinsed with ultrapure water by ultrasonication.

2.3. *Analysis*

The HPLC equipment consisted of an isocratic pump (Knauer Pump 64), an ion-exclusion column (HPX-87H 300×7.8 mm, from Bio-Rad). The eluent was a dilute solution of sulphuric acid (3.3 mM H_2SO_4) at a flow rate of 0.6 cm^3 min^{-1}. The column was thermostatized at 25 °C and the reaction products were detected successively by a UV detector (Applied Biosystems 785A) working at 210 nm and a refractometer (Shodex RI-71). Chromatograms were recorded on a two-channel integrator (D-2500 Merck-Hitachi). The nature of the organic compounds (methylpyruvate and methyllactate) was determined by comparing their retention times to those of pure reference products under the same analysis conditions (external calibration). As the dimethylester of 2,3-dimethyltartaric acid is not commercialized, it was necessary to separate it quantitatively. At the end of electrolysis, the reaction products were identified by GC-MS-MS (EI: 70 eV, CI/NH_3 and CI/CH_4: 100 eV, 1200L Varian), ESI-MS (MS ion trap with Spray voltage: 4 kV, Thermo Electron) and ^{1}H- and ^{13}C-NMR (WP 200 SY Bruker spectrometer). However, the electrolyte was first neutralized with an anion exchange resin (Amberlite IRA-900 Cl from Sigma). The aqueous solutions of the electrolyzed products, free from inorganic ions, were removed at 50 °C under vacuum. The dry organic product was then dissolved in 10 cm^3 methanol and esterified using 1 cm^3 of 2,2-dimethoxypropane per mmol of initial substrate. After stirring for

1 day, the solvent was removed under reduced pressure. The esterified products were separated with a Varian capillary gas chromatograph equipped with a DB-5, 95% dimethyl 5% diphenyl polysiloxane bounded capillary column (30 m, 0.25 μm film thickness).

The dimethylester of 2,3-dimethyltartaric acid was isolated by chromatography on silica gel 15–40 μm (Silica Gel 60 from Sigma) with ethylacetate/petroleum ether (60:40) as eluent.

2.4. *Expressions of some determined values*

The various determined quantities are defined as follows:

- Yield of pyruvic acid: $X = \frac{C_0 - C_t}{C_0} \times 100$
- Faradaic yield: $\tau_{F,\mathrm{it}} = \frac{nFVC_{it}}{Q_{\mathrm{exp}}}$
- Selectivity: $S_{it} = \frac{1}{\nu_i} \times \frac{C_{it}}{C_0 - C_t} \times 100$ where C_0 is the initial concentration of pyruvic acid and C_t its concentration at time t. $C_{it}, \tau_{F,\mathrm{it}}$ and S_{it} are the concentration, the Faradaic yield and the selectivity of the reaction product i at time t, respectively. ν_i is stoichiometric number of the reaction product i.

3. Results and discussion

3.1. *Electrochemical behaviour of pyruvic acid on lead cathode in acid medium*

Cyclic voltammetry was used to check the degree of purity of the medium before performing each electrolysis and to follow the state of reduction of the molecule studied. Figure 3 represents the voltammogram at a Pb electrode in the absence and presence of 0.1 M pyruvic acid in sulphuric acid. During the positive variation of potential, an oxidation peak can be seen at $E_a = -0.85$ V vs. MSE. This is followed by a large shoulder of $PbSO_4$ species which start reducing irreversibly from the electrode surface at $E_c = -1.05$ V vs. MSE. During the negative scan, in the presence of the organic substrate, the reduction of 0.1 M pyruvic acid is observed; it consists of a large wave, which reaches −30 mA cm^{-2} at *ca.* −1.9 V vs. MSE.

3.2. *Long-term electrolyses of pyruvic acid on lead electrode in acid medium*

Electrolysis of pyruvic acid was carried out cathodically at −1.1 V vs. MSE in 0.5 M H_2SO_4 and on Pb electrode (32 cm^2). This electrode potential was chosen to minimize hydrogenation (which yields lactic acid) and to optimize the Faradaic yield for dimerizing pyruvic acid according to our previous results [25]. A series of electrolyses were carried out at this potential with various initial concentrations of pyruvic acid (between 0.125 and 1.7 M). Up to 2 M, no reduction of pyruvic acid is observed, which is probably due to the saturation of the lead surface by adsorbed molecules of pyruvic acid. In Table 1, all these electrolyses were stopped at *ca.* 80% conversion of pyruvic acid. Moreover, increase in the initial concentration of pyruvic acid favoured the electrohydrodimerization to 2,3-dimethyltartaric acid. The conversion of pyruvic acid and the selectivity of dimethyltartaric acid reach 84 and 69%, respectively on lead and at −1.1 V vs. MSE.

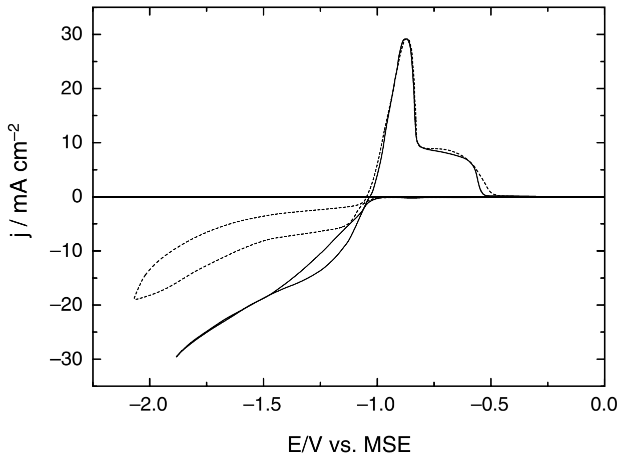

Fig. 3. Voltammograms of lead electrode at 50 mV s^{-1} in supporting electrolyte 0.5 M H_2SO_4 alone (– –) and in the presence of 0.1 M pyruvic acid (—).

To separate the two reaction products, 2,3-dimethyltartaric acid and lactic acid, the final solution of electrolysis was first neutralized on an anion exchange resin. Then the obtained solution was chromatographied again to be sure of the reproducibility of the last analysis. After esterification of the final bulk solution, dimethylester of 2,3-dimethyltartaric acid was separated from the methylester of lactic acid by flash chromatography; the esterified pinacol was finally isolated and identified by GC-MS and NMR. Figure 4 shows the ^{13}C-NMR spectrum of the dimethylester of 2,3-dimethyltartaric acid recorded in $CDCl_3$; the chemical shifts are given in ppm from tetramethylsilane (TMS) as internal reference.

As can be seen on this spectrum, the dimethylester of 2,3-dimethyltartaric acid produced is a mixture. These two diastereoisomeric forms of dimethylester of 2,3-dimethyltartaric acid, Meso-dimethylester of 2,3-dimethyltartaric acid and Racemic-dimethylester of 2,3-dimethyltartaric acid (Figure 5), are represented by twin

Table 1. Effect of the initial concentration of pyruvic acid on the selectivity towards 2,3-dimethyltartaric acid during electrolysis of pyruvic acid at −1.1 V vs. MSE

Initial concentration of pyruvic acid /M	X_{PA} / %	S_{DMTA} / %	$\tau_{F_{DMTA}}$/ %	S_{LA}/ %	$\tau_{F_{LA}}$ / %	Q_{exp} / C
0.125	78	41	14	54	36	1390
0.3	79	54	23	38	33	2510
0.9	76	56	26	35	32	7180
1.7	84	69	33	30	29	14,100

Q_{exp}: total charge involved; X: yield of pyruvic acid; S_{DMTA} and $\tau_{F_{DMTA}}$: Selectivity and Faradaic yield of 2,3-dimethyltartaric acid; S_{LA} and $\tau_{F_{LA}}$: Selectivity and Faradaic yield of lactic acid.

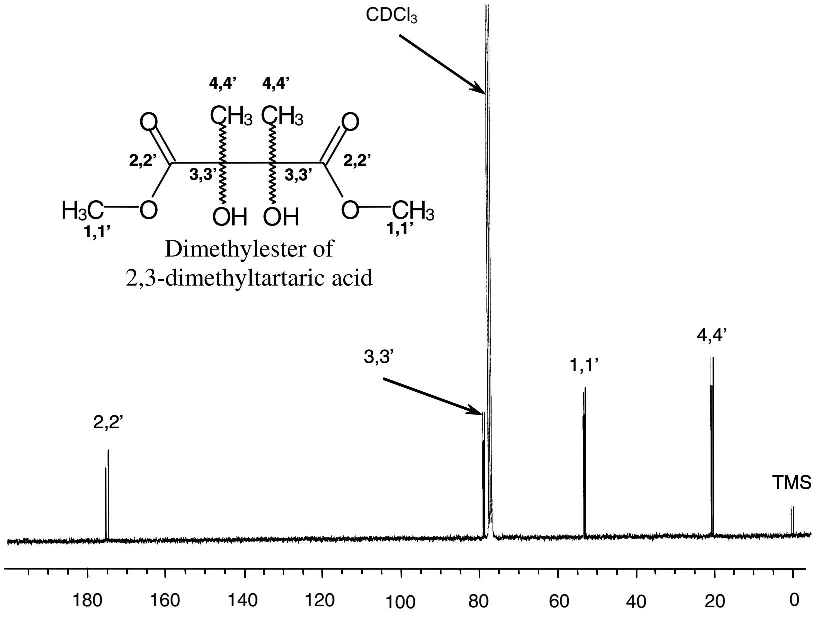

Fig. 4. ^{13}C NMR spectrum of dimethylester of 2,3-dimethyltartaric acid in $CDCl_3$ obtained at the end of electrolysis of 0.1 M pyruvic acid at −1.1 V vs. MSE on lead cathode and after esterification. The internal reference is TMS.

peaks. Although these two configurations of dimethylester of 2,3-dimethyltartaric acid were separated successfully, the different spectra which present low shifts have not yet been assigned.

Under the optimized experimental conditions found in Table 1, electrolysis of 1.7 M of pyruvic acid was performed at −1.1 V vs. MSE to follow the kinetics of the reduction of the substrate over 6 h. Figure 6a shows the quantity of electricity which increases with time. At the end of the electrolysis it reaches 15,300 C. The charge producing 2,3-dimethyltartaric acid increased slowly until *ca.* 5084 C i.e. 33% of the total quantity of electricity involved during the electroreduction. Moreover, the Faradaic yield of 2,3-dimethyltartaric acid passes through a maximum at about 60 min before reaching a plateau.

Figure 6b represents the variation of the yield of pyruvic acid and that of the selectivity of 2,3-dimethyltartaric acid. As described previously, the selectivity decreases but remains favourable i.e. higher than 69%. The electroreduction of 1.7 M pyruvic acid at −1.1 V vs. MSE, shows that the production of lactic acid is minimized because of the low production of hydrogen at this electrode potential.

Table 1, shows that 2,3-dimethyltartaric acid synthesis is favoured when the initial concentration of pyruvic acid is increased. However, the high consumption of this latter competes with both hydrogen evolution and the production of lactic acid (Figure 6).

4. Conclusion

Cyclic voltammetry provided valuable information on the electrochemical behaviour of pyruvic acid, which allowed us to optimize the electrode potential for its

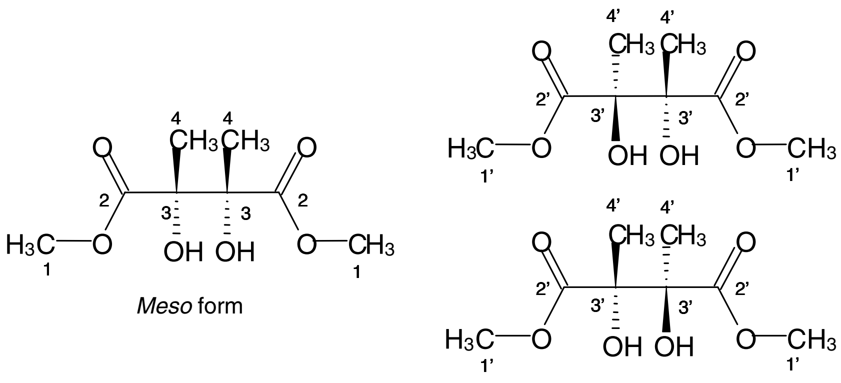

Fig. 5. Different configurations of dimethylester of 2,3-dimethyltartaric acid: Meso-dimethylester of 2,3-dimethyltartaric acid and Racemic-dimethylester of 2,3-dimethyltartaric acid.

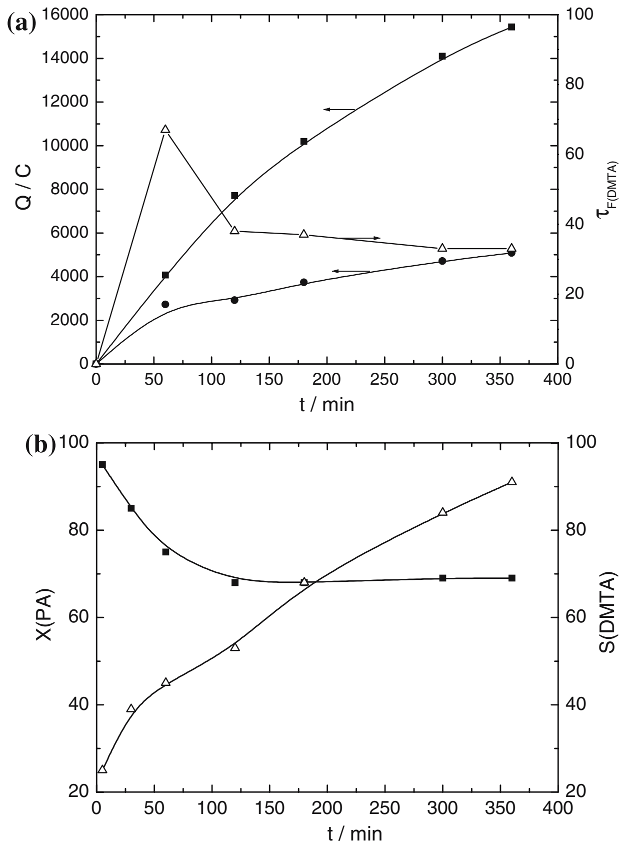

Fig. 6. (a) Variation of the experimental quantity of electricity (■) against the time of electrolysis of 1.7 M pyruvic acid on Pb at −1.1 V vs. MSE; (●) charge due to the production of 2,3-dimethyltartaric acid and (▲) Faradaic yield of 2,3-dimethyltartaric acid. (b) Variation of the conversion yield (△) of pyruvic acid during electroreduction on Pb at −1.1 V vs. MSE in 0.5 M H_2SO_4; (■) selectivity of 2,3-dimethyltartaric acid synthesized during electrolysis.

electroreduction. During electrolysis of pyruvic acid at −1.1 V vs. MSE in sulphuric acid on a lead cathode, various analyses (HPLC, LC-MS) showed that 2,3-dimethyltartaric acid and lactic acid were the main reaction products. The compounds were esterified and isolated after neutralizing the final bulk solution. The dimethylester of 2,3-dimethyltartaric acid was then determined by GC-MS, and NMR (^1H and ^{13}C) spectroscopy. We also demonstrated that pyruvic acid was mainly reduced to 2,3-dimethyltartaric acid at −1.1 V vs. MSE when the initial concentration was 1.7 M. The formation of lactic acid competes with the synthesis of 2,3-dimethyltartaric acid at any electrode potential. But the low hydrogen evolution which gives rise to hydrogenation and the high concentration of pyruvic acid contribute to increase the process of pinacolization at −1.1 V. The selectivity towards 2,3-dimethyltartaric acid reached 69% when the yield of pyruvic acid was close to 84%.

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