

Synthesis of optically pure chirals by the anodic oxidation of tartaric esters

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Abstract The 4-R,5-R-2,2-dimethyl-1,3-dioxolan-4,5-dicarboxylic ester has been anodically oxidized on platinum and graphite anodes. Electrolysis products have been identified using ¹H-NMR, ¹³C-NMR and GC-MS techniques. The reaction mechanism has been proposed according to the product's spectra.

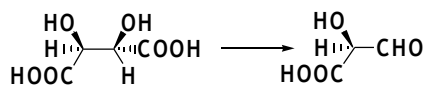
Keywords: anodic oxidation, electrochemical decarboxylation, tartaric esters

1. Introduction

Carboxylic acid anodic oxidation is a well-known way to synthesis different syntons: ethers, amides, alcohols, etc, according to experimental conditions [1,2,3,4].

A new method of anodic oxidations aims to use esters as raw materials in the process of electrochemical decarboxylation [5,6]. This starts from the idea of *in situ* generation of carboxylic ions by means of an ester alkalize reaction. Their further oxidation could lead to valuable compounds.

The general development of the process is represented in *Scheme 1*.



This method was applied to the anodic oxidation of tartaric esters in order to obtain optically pure tartronic semialdehyde with R configuration.

The direct oxidation of tartaric acid has no chance to occur with good yields, as the intermediate tartronic semialdehyde once formed could react further (stronger acid) with the formation of glyoxal, which is a less interesting synton.

In the same time, the synthesis of a tartaric acid half ester that could react to a single carboxylic group is difficult to perform.

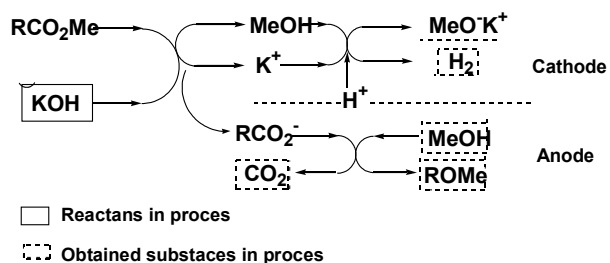
To avoid the formation secondary products, as a result of a possible participation in the carbenium ion stabilization of hydroxyl groups in the tartaric esters, it is advisable to have them in a protected form consequently oxidation of dimethyl ester of 4-R,5-R-2,2-dimethyl-1,3-dioxolan-4,5-dicarboxylic acid were performed.

2. Experimental

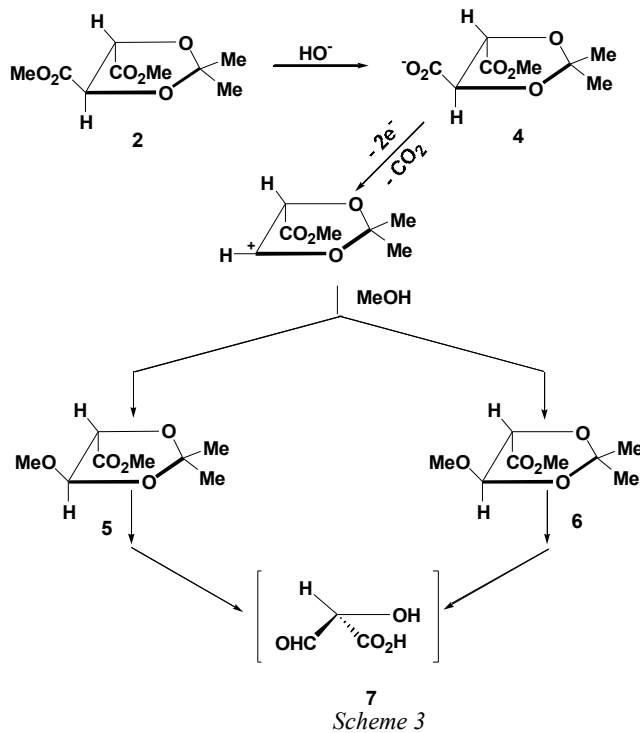
The compounds with 1,3-dioxolan skeleton were synthesized by means of the cetalization of tartaric acid in acid catalysis with methanol as solvent.

The structural characterization was made relying on the ¹H-NMR (300 MHz Varian spectrometer), ¹³C-NMR (Bruker Avance DRX 400 and Varian 300 Gemini) and GC-MS (Varian 3400 Saturn 2 System gas chromatograph-mass spectrometer on a 25 m capillary glass column DBS; Tinj=2500C; 80⁰-250⁰ C with 10⁰ /min.) spectra.

The electrolyses were performed in methanol containing the esters having a concentration of 0.2 mole L⁻¹ and KOH (0.4 mole L⁻¹) at a constant tension (7 V) and initial current densities of 60 – 80 mA/ cm². An undivided cell and graphite anode was used.



Scheme 1



Scheme 3

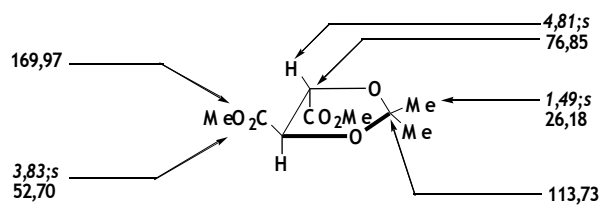


Figure 1

The solution obtained after electrolysis was concentrated at normal pressure up to a volume of about 1 mL, diluted with a buffer solution (pH = 7). The resulted solution was extracted with ethyl ether (3 x 15 mL), concentrated and then analyzed through ¹H-NMR and GC-MS spectroscopy.

3. Results and discussion

The dimethyl ester of the 4-R,5-R-2,2-dimethyl-1,3-dioxolan-4,5 dicarboxylic acid **1**, was obtained by heating at reflux a mixture of tartaric acid and 2,2-dimethoxy-propane in anhydrous methanol, in the presence of p-toluene sulphonic acid as catalyst with 56% efficiency.

The product **2** was isolated as a liquid with b.p. = 120 – 122°C / 10 mmHg with 98% purity (GC-MS) and was characterized by the ¹H-NMR, ¹³C-NMR and GC-MS spectral data.

The main characteristics of ¹H-NMR and ¹³C-NMR are shown in *Figure 1*.

Anodic oxidation of the ester **2**.

The product **5** and **6** indicated in *Scheme 3* were obtained in the undivided cell both on graphite and platinum anodes. The following characteristics of the electrooxidation process were deduced from independent experiments carried out with a reasonable reproducibility:

-the conversion of the initial ester is 50 – 70 % at an amount of electricity representing 2 Q_T (Q_T = the theoretical amount of electricity necessary for non-Kolbe oxidation of a carboxyl group);

-a mixture of diastereoisomers **5** – **6** is formed with 70 – 75 % efficiency (compared to the reacted raw material).

-the intermediate **4** is absent from the electrolysis mixture (the electrolysis was faster then alkalize);
-Kolbe products are not formed even in favorable conditions for this mechanism (on platinum anode);

The configurations of diastereoisomers **5** and **6** were deduced relying on the ¹H-NMR spectrum of the reaction raw electrolysis product.

For instance in the spectrum the characteristic signals of protons in the 4 and 5 position of the dioxolan skeleton appear in the δ=4.5 –5.5 ppm area; they form two systems AM, one characterized by signals at δ =4.69 ppm and δ = 5.26 ppm having

a coupling constant J=5 Hz and the other one having signals at δ= 4.59 ppm and δ= 5.21 ppm with a coupling constant J = 2 Hz.

Taking into account the information on the trans coupling in the dioxolan system, the signals form 4.68 ppm and 5.62 ppm are assigned to the trans diastereoisomer **5**, and the signals form 4.59 ppm and 5.21 ppm to the cis diastereoisomer **6**. The ratio of the integrals of the two types of signals shows that the major diastereoisomer is the one with a trans configuration.

The GC-MS determination shows that the proportion of the two stereoisomers (trans-cis) is 2:1. The relative low value of the diastereoisomeric excess does not influence the synthesis performance because, in fact, both diastereoisomers could be hydrolyzed (in acid catalysis) in order to regenerate the aldehydic function and supply an optically pure compound (*Scheme 3*).

4. Conclusions

A new anodic oxidation reaction of the tartaric acid protected by esterification and a cetilization was performed to obtain optically pure syntons. The anodic oxidation is preceded by the alkalyse that is the rate-determining step of the process.

This reaction could be applied for the synthesis of optically active compound with an enantiomeric excess of 95%. The reaction can be used in preparatory aims, obtaining optically pure compounds with 70-75 % efficiency.

5. References

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