SYNTHESIS OF SOME TARTARIC ACID DERIVATIVES

N. Katsaros[*], E. Vrachnou-Astra, J. Konstantatos, and C.I. Stassinopoulou.

Department of Chemistry, Nuclear Research Center "Demokritos", Aghia Paraskevi Attikis, Athens, Greece.

Summary

The synthesis of dimethyltartaric, diphenyltartaric and dibenzyltartaric acids as products of the reaction of V^{2+} aqueous with pyruvic, phenylglyoxylic and phenylpyruvic acids is described.

Although the derivatives of tartaric acid, dimethyltartaric (4), diphenyltartaric (5), and dibenzyltartaric (6) acids have been known for some time there is no convenient method for their preparation in the literature. Dimethyltartaric[1] and diphenyltartaric acids[2] have been prepared by photolysis of pyruvic and phenylglyoxylic acids in methanol and isopropyl alcohol respectively. Dibenzyltartaric acid has been prepared along with other products by reduction of an aqueous solution of the sodium salt of γ-oxy-α-oxo-β,γ-diphenylbutyric acid with sodium amalgam under an atmosphere of carbon dioxide.[3]
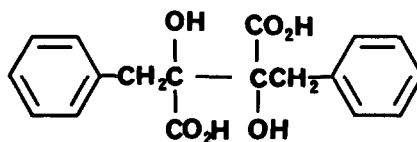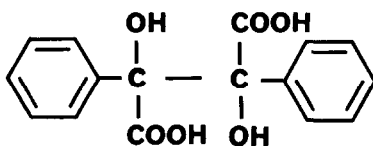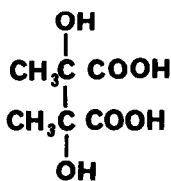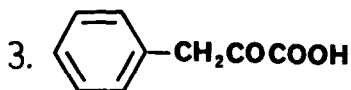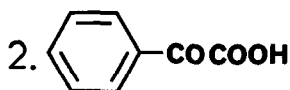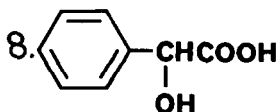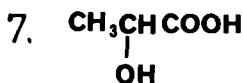
During our studies on the mechanisms of reactions of Cr^{2+}, V^{2+}, and Eu^{2+} cations in acid aqueous solutions with the α-ketoacids pyruvic (1), phenylglyoxylic (2), and phenylpyruvic (3) acid we identified these three derivatives of tartaric acid in the reaction products. Here we wish to describe simple methods for the synthesis of these acids.

Methods. Solutions of chromium (II) perchlorate and europium (II) perchlorate were prepared from the corresponding Cr(III) and Eu(III) solutions electrolytically under an atmosphere of deoxygenated argon.[4,5]

Vanadium(II) perchlorate solutions were prepared by treatment of a suspension of V_2O_5 in aqueous perchloric acid with hydrogen peroxide yielding soluble pervanadic acid, which (after destroying the excess of the peroxide) was electrolyzed to produce $V(ClO_4)_2$. In order to minimize oxidation of V_{aq}^{2+} by $HClO_4$ the deaerated vanadous ion solutions were stored at ~ 0°C, at which temperature they can be preserved for several days.

Triply distilled water was used in all experiments. Dimer-free sodium pyruvate, phenylglyoxylic acid and sodium phenylpyruvate were supplied by Fluka and stored at ~ 0°C. Stock solutions of sodium pyruvate were prepared immediately before use, because sodium pyruvate dimerizes upon prolonged standing. The solutions of the organic acids were deoxygenated prior to mixing by a stream of argon.

Dimethyltartaric Acid. A solution of $V(ClO_4)_2$ in 1 M $HClO_4$ was added to an excess of a solution of sodium pyruvate (3:1 molar ratio organic acid to metal ion) dissolved in 1 M $HClO_4$. The reaction was complete after about 10 hrs., giving dimethyltartaric acid as the only product. The reaction product was isolated as follows:

The reaction mixture was first passed through a Dowex-50W ion exchange column in the H^+ form in order to remove the V_{aq}^{3+} ions from the solution. The eluate was extracted with ether. The ether extract contained only the unreacted pyruvic acid. The aqueous layer was brought to pH ~ 6 with NaOH and concentrated to about 20% of its original volume. An excess of a saturated solution of $BaCl_2$ was added and the barium salt of dimethyltartaric acid was precipitated after heating the solution to 70°C for a few minutes. The precipitate was washed, dried and weighed. The free acid was obtained by addition of the equivalent amount of H_2SO_4 to a suspension of the salt in water. After the removal of the insoluble $BaSO_4$ the solution was evaporated and the dimethyltartaric acid was recrystallized in ethanol. Yield 80%, m.p. 173-175°C. The product was identified by its infrared and proton nmr spectrum (single peak for methyl at 1.54 δ in acid D_2O solution). The product was not optically active, which shows that it has to be either in its dl- or in its meso form. The presence of only one peak in its nmr spectrum, and also the sharp melting point suggest either the dl- or the meso form.

Analysis. Calcd. for $C_6H_{10}O_6$: C, 40.3; H, 5.6; Found: C, 40.1; H, 5.7.

The stoichiometry of the reaction in an excess of pyruvic acid was found to be 1:1 and the reaction kinetics and mechanism will be described elsewhere. When V_{aq}^{2+} was in excess (molar ratio 10:1 metal ion to organic substrate) lactic acid was formed in addition to dimethyltartaric acid.

The reaction of Cr_{aq}^{2+} or Eu_{aq}^{2+} with pyruvic acid had a stoichiometry 2:1 and the product

Table 1.   Products and stoichiometry of the reactions between the low-valent
            metal ions and the α-keto acids.

Metal Ion	α-Keto Acid	Stoichiometry	Product
Cr^{2+}	Pyruvic Acid	2:1	Lactic Acid
Eu^{2+}	" "	2:1	" "
V^{2+}	" "	1:1	Dimethyltartaric Acid
Cr^{2+}	Phenylglyoxylic Acid	<2:1	Mandelic Acid + Diphenyl-tartaric Acid
Eu^{2+}	Phenylglyoxylic Acid	<2:1	Mandelic Acid + Diphenyl-tartaric Acid
V^{2+}	Phenylglyoxylic Acid	1:1	Diphenyltartaric Acid
V^{2+}	Phenylpyruvic Acid	1:1	Dibenzyltartaric Acid

was lactic acid (7). (Table 1). The kinetics and reaction mechanism of this system have been described elsewhere.[4]

Diphenyltartaric Acid.   A solution of $V(ClO_4)_2$ in 1 M $HClO_4$ was added to an excess of a solution of phenylglyoxylic acid (2:1 molar ratio organic acid to metal ion) dissolved in 1 M $HClO_4$. The mixture was left to stand for about 3 days to allow for complete hydrolysis of the V^{3+} complexes formed intermediately. White crystals precipitated then from the reaction mixture. More crystals were formed by condensation to about 50% of the original volume. These were filtered and washed with ether and dried in a vacuum dessicator to afford diphenyltartaric acid. Yield 70%, m.p. 154-155°C. The product was identified by mass spectrometry, infrared and proton nmr spectroscopy (broad peak for phenyl at 7.24 δ in DMSO-d_6 solution). The sharp melting point suggests the formation of either the dl- or the meso form.

Analysis.   Calcd. for $C_{16}H_{14}O_6$: C, 63.6; H, 4.6. Found: C, 63.4; H, 4.7. Molec. wt (Rast): 301.5, theoretical 302.29.

The stoichiometry of the reaction was found to be 1:1. When acid aqueous solutions of Cr^{2+}_{aq} or Eu^{2+}_{aq} were mixed with an excess of acid aqueous solution of phenylglyoxylic acid the stoichiometry was found to be 1.5:1 and the reaction product was a mixture of mandelic (8) and diphenyltartaric acids (Table 1).

Dibenzyltartaric Acid.   Phenylpyruvic acid is sparingly soluble in water. The desirable concentration of the organic acid was reached by using a mixed solvent (isopropanol-water 30:70 by volume). A solution of $V(ClO_4)_2$ in the same solvent was added to the organic acid solution in a 2:1 molar ratio of organic acid to metal ion. Both solutions were 1 M in $HClO_4$. The mixture was left to stand for about 20 hrs. to allow time for the V(III) complexes to be completely dissociated. The reaction mixture was concentrated to 50% of the original volume and then by extraction with ether, dibenzyltartaric acid was isolated as the only product. Yield 80%, m.p. 210-212°C. The dibenzyltartaric acid was further identified by infrared and nmr spectroscopy

(broad peak for aromatic protons at 7.23 δ, AB system for benzylic protons, J_{AB} = 12.5 Hz ,
H_A: 2.80 δ and H_B: 3.06 δ in DMSO-d_6 solution).
<u>Analysis.</u> Calcd. for $C_{18}H_{18}O_6$: C, 65.8; H, 5.5. Found: C, 65.7; H, 5.2.
Molec. wt(Rast): 331, theoretical 330.35.

A comparison of the reactions of the three metal ions with the three α-ketoacids shows
that V^{2+} is exceptional in giving almost exclusively one product. This is the result of an
one-electron reduction and subsequent dimerization of the resulting free radical. A compa-
rison of the kinetic data for the reactions of the three metal ions with pyruvic acid[4,6]
shows that the V_{aq}^{2+} reacts more slowly than either Cr_{aq}^{2+} or Eu_{aq}^{2+}. The rates of V_{aq}^{2+} reactions
are from two to four orders of magnitude slower than the corresponding Cr_{aq}^{2+} or Eu_{aq}^{2+} re-
actions. The free radical formed by one-electron reduction can either dimerize or accept a
second electron and form the reduced monomer. In the case of V_{aq}^{2+} the dimerization reaction
is the prefered path due to the slow reaction rates of this ion, to give dimethyltartaric a-
cid. With Cr_{aq}^{2+} and Eu_{aq}^{2+} though, the free radical formed during the reduction of pyruvic a-
cid reacts exclusively with a second metal ion.

A more stable radical, like the ones formed during the reduction of the phenylglyoxylic
and phenylpyruvic acids, may escape further reduction even with Cr_{aq}^{2+} and Eu_{aq}^{2+} and give rise
to dimerization products.

Acknowledgements

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