OXIDATION OF VALERIC ACID

Thesis

by

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I.

THEORY AND PURPOSE

An obstacle to the electron displacement theory[1] is the fact that the fatty acids when halogenated do not behave as the theory predicts. Because of the proximity of the strongly negative carboxyl group, the electrons on the α carbon atom are the most firmly held, so that the halogen should substitute more easily on some other carbon atom. This, however, has been found not to be the case. The α carbon atom is the one that takes the halogen.

It has been suggested that an enolization might account for the fact that in the case of the halogenation of the fatty acids the theory does not hold. If an equilibrium of the form:

$$CH_3CH_2COOH = CH_3CH{=}C(OH)_2$$

exists, the halogen would be expected to add on to the unsaturated bond

$$CH_3CH{=}C(OH)_2 + X_2 = CH_3CHXCX(OH)_2$$

followed by the elimination of HX

$$CH_3CHXCX(OH)_2 = CH_3CHXCOOH + HX ,$$

yielding an α halogenated acid.

The purpose of this research was to determine whether or not the fatty acids exhibited this phenomenon

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1) Lucas and Jamison, J.Am.Chem.Soc., <u>46</u>, 2475(1924)

of enolization in a reaction other than that of halogenation.

The reaction chosen was the oxidation of valeric acid by chromic acid. This fatty acid was chosen because it is claimed by the Bio-chemists that the fatty acids containing an odd number of carbon atoms are more easily oxidized than the even numbered ones. If butyric acid were used the α oxidation product,propionic acid,is quite soluble in water and would probably,due to its greater concentration in the aqueous phase,be further oxidized,whereas butyric is relatively insoluble so that there would be a lesser probability of the α oxidation product of valeric acid,if formed,being further oxidized. An acid oxidizing agent was used because it has already been found that the enol form does not exist in basic solution.[2]

An oxidation reaction was chosen because it was thought that since the atom adding on in the case of both halogenation and oxidation is a strongly negative one that the reaction should proceed in the same manner. It was also thought that it would be an easy matter to determine how the reaction proceeded by measuring the CO_2 evolved and analyzing the oxidation mixture for fatty acids.

2) Evans and Sefton,J.Am.Chem.Soc.,<u>44</u>,2276,(1922).

II.

PREPARATION OF MATERIALS.

Since no valeric acid could be obtained that was known to be absolutely free from other fatty acids, and since these acids are so strongly associated that fractional distillation will not effect a separation from an impure material, it was decided to synthesize the valeric acid.

The method chosen was the malonic ester synthesis, starting with n-propyl alcohol since this may be obtained quite pure. The reactions are as follows:

$$CH_3CH_2CH_2OH + NaBr + H_2SO_4 = CH_3CH_2CH_2Br + NaHSO_4 + H_2O$$

$$CH_2(COOCH_3)_2 + NaOCH_2CH_3 = CHNa(COOCH_3)_2 + C_2H_5OH$$

$$CH_3CH_2CH_2Br + CHNa(COOCH_3)_2 = CH_3CH_2CH_2CH(COOCH_3)_2 + NaBr$$

$$CH_3CH_2CH_2CH(COOCH_3)_2 + KOH = CH_3CH_2CH_2CH(COOK)_2 + CH_3OH$$

$$CH_3CH_2CH_2CH(COOK)_2 + 2\ HCl \underset{heat}{=} \underline{CH_3CH_2CH_2CH_2COOH} + 2\ KCl + CO_2$$

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PREPARATION OF N-PROPYL BROMIDE

Materials

N-propyl alcohol, E.K.Co., (B.P. 96.5°-97°)	198 g.- 3.3 mol
Sodium bromide (2 H_2O), Kahlbaum	500 g.- 3.6 mol
Sulphuric acid, sp. gr. 1.84	250 cc- 4.4 mol
Water	250 cc.
Propyl bromide (yield 75%)	302 g.- 2.46 mol

The diluted sulphuric acid was added to the propyl alcohol, then the NaBr. The mixture was refluxed 1 1/2 hours and then distilled, the product dried and fractionated. A yield of 302 g. - 2.46 mols - of propyl bromide, B.P., 70.5 - 71.5° (cor.).

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PREPARATION OF VALERIC ACID.

Materials

Methyl Malonate, Kahlbaum	264 g.- 2 mol
Sodium	46 g.- 2 mol
Absolute Alcohol	750 cc.
Propyl Bromide	246 g.-4.5 mol
Hydrochloric Acid (12 N)	500 cc.- 6 mol

Procedure

The absolute alcohol was put in a 3 neck 3 liter balloon flask fitted with a stirrer, dropping funnel, thermometer, and a reflux condenser. The flask was supported in a cooling bath.

The sodium was added in small pieces to the absolute alcohol. When this reaction was complete the methyl malonate was allowed to run in slowly from a dropping funnel, (30 minutes). When this reaction was complete as indicated by a fall in temperature, the propyl bromide was slowly added, maintaining the temperature at about 50°.

The sodium bromide that separated out at this point was filtered off. The filtrate was returned to the reaction flask and heated to boiling. The potassium hydroxide, dissolved in 400 cc. of water, was added to the boiling solution through the top of the reflux condenser.

After refluxing for 1 hour the alcohols were distilled off and the solution evaporated to dryness. The hydrochloric acid was then added. What potassium chloride separated out was filtered off and washed with ether. The filtrate was distilled, the dibasic acid decomposing to valeric acid and coming over as a steam distillate.

The acid layer of the distillate was separated, dried with phosphoric anhydride, and fractionated. All potassium chloride that separated out was washed with ether and the washings distilled. A considerable portion of the yield was recovered in this way.

Yield - 107 g., 51%, B. P., 184.7-186.2°

III.

OXIDATION OF VALERIC ACID.

In order to determine the smallest concentration of H^+ in which sodium dichromate would oxidize valeric acid and also to determine whether or not this same concentration would affect butyric acid, a series of test tube experiments were carried out.

Mixtures of sodium dichromate solution (1 gram per cc. of water) and valeric or butyric acid with various concentrations of sulphuric acid were tried.

Test #1

Valeric Acid	2 cc.
Water	2 cc.
Sodium Dichromate	2 g.

This was heated to 60° and concentrated sulphuric acid (93.5%) added, a drop at a time, from a burette. Gas was evolved with the addition due to local high concentration and temperature. It was evolved steadily in small bubbles after 0.5 cc. had been added.

Test #2

Valeric Acid	1 cc.
Sulphuric Acid (93.5%)	0.5 cc.
Dichromate	2 g.
Water	2 cc.

Since in #1 there was uncertainty as to what the conditions were when the oxidation started, in #2 the sulphuric acid was added to the dichromate and this mixture added to the valeric acid. When this mixture was slowly heated, gas started to be evolved at 50°.

Test #3

Butyric Acid	1 cc.
Sulphuric Acid	0.5 cc.
Dichromate	2 g.
Water	2 cc.

Butyric acid was subjected to the oxidizing conditions of #2. When heated to 50° there was no apparent evolution of gas and it was only after standing for several minutes at this temperature that a green color was apparent.

Test #4

Butyric Acid	1 cc.
Dichromate	2 g.
Sulphuric Acid	0.5 cc.
Water	4 cc.

No oxidation up to 80°.

Test #5

Valeric Acid	1 cc.
Dichromate	2 g.
Sulphuric Acid	0.5 cc.
Water	4 cc.

Oxidation started and continued for some time at 80°.

Test #6

Butyric Acid	1 cc.
Dichromate	2 g.
Sulphuric Acid	0.5 cc.
Water	3 cc.

No oxidation up to 75°.

Test #7

Same as #6 except with valeric acid. Oxidation proceeded slowly at 75°.

From the results of these tests, it is apparent that if butyric acid is an oxidation product of valeric acid that it will not be further oxidized under the above conditions. It was decided that the conditions of test #2 would be best for carrying on the oxidation due to the moderate temperature required.

In order to maintain an approximately constant H^+ concentration throughout the oxidation, it was decided to put the valeric acid and sulphuric acid of the proper concentration in the reaction flask and run in slowly a mixture of equivalent parts of sulphuric acid and sodium dichromate. The acid concentration of test #2 was

$$\frac{1.713}{5} = .342 \text{ g. of } H_2SO_4 \text{ per cc.} = 3.5 \text{ molal}$$

According to the reaction,

$$Na_2Cr_2O_7 + C_4H_9COOH + 5\ H_2SO_4 = 2\ NaHSO_4 + C_3H_7COOH + CO_2 + 5\ H_2O + Cr_2(SO_4)_3$$

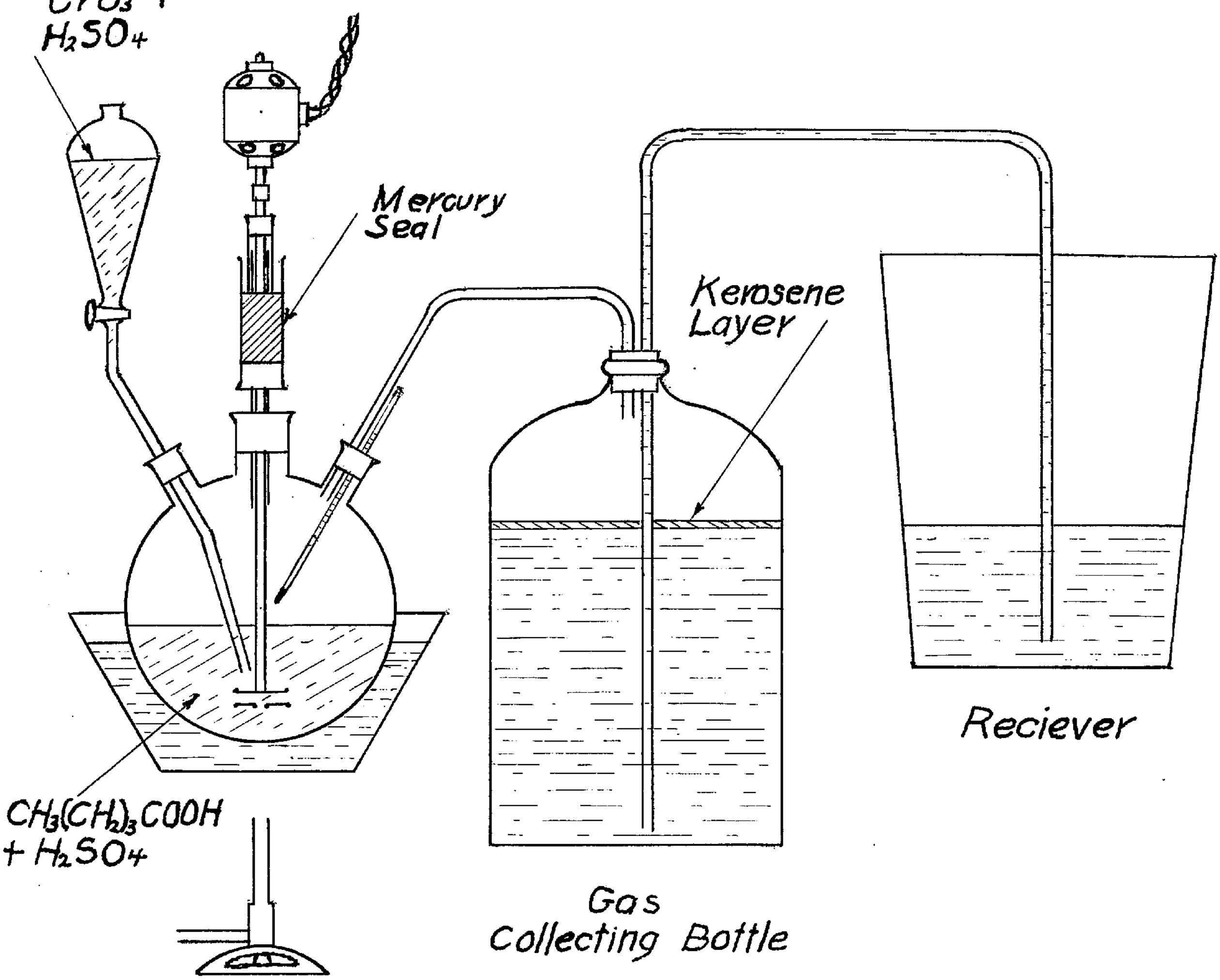
an equivalent mixture of sodium dichromate and sulphuric acid will consist of 1 mol of dichromate to 5 mols of sulphuric.

FIRST RUN

Materials

Valeric Acid (B.P., 184.7-186.2°)	50 g.-.49 mol
Sodium Dichromate (Tech.)	146 g.-.49 mol
Sulphuric Acid (93.5%)	376.5 cc.
Water	400 cc.

OXIDATION APPARATUS



Apparatus

A 5 liter 3 neck reaction flask was fitted with a mercury seal stirrer, a 200 cc. dropping funnel, a thermometer, and an outlet tube and was placed in a water bath over a Bunsen burner. The outlet was carried to a 5 gallon bottle filled with water. The water was covered with a 1 cm. layer of kerosene to prevent absorption of CO_2. A receiving tank of 5 gallons capacity to receive the water displaced from the bottle by the CO_2 evolved during the reaction. This was so arranged that its height could be varied so that the water levels in the receiver and bottle could be maintained the same. It was set up as shown in the accompanying drawing.

Procedure

The valeric acid and a mixture of 100 cc. water and 18.5 cc. sulphuric acid were put in the flask and heated to 60°. The oxidizing mixture, 146 g. sodium dichromate, 140 cc. sulphuric acid, 200 cc. water, was added slowly with vigorous stirring, the temperature being maintained at 60°. The oxidation, as evidenced by the green color of chromium sulphate and the evolution of gas, started when about 25 cc. of the oxidation mixture had been added. This indicates that the oxidizing potential depends on the concentration of the chromic acid as well as on the H^+ concentration.

After all the oxidizing mixture had been added, 200 cc. more of 18 N sulphuric acid (100 cc. of 93.5% H_2SO_4, 100 cc. water) were added and the temperature raised to 80° to insure the complete reduction of the dichromate. The apparatus was allowed to come to room temperature, the water in the receiver brought level with that in the bottle, the water displaced measuured and the gas volume calculated to standard.

In order to prevent any further oxidation in the subsequent steam distillation, the excess of sulphuric acid that had been added was neutralized with NaOH.

The reaction product was distilled with steam at 140° until 800 cc. of distillate had been collected and the distillate was no longer acid.

The distillate was heated to 65 - 70° and Na_2CO_3 added until the solution was neutral to litmus. It was then evaporated to dryness and the powdered residue dried at 110° for 36 hours. To this an excess of methyl sulphate (80 g.) was added in a distilling flask, thoroughly mixed and gradually distilled up to 140° over a period of 6 hours.

$C_4H_9COONa + (CH_3)_2SO_4 = C_4H_9COOCH_3 + CH_3NaSO_4$

(B. P. methyl valerate = 127° ; methyl sulphate = 188°)

The distillate was refractionated until the following portions were obtained:

125°- 128°	(methyl valerate)	31.7 g.
53°- 56°	(methyl acetate)	5.5 g.

Intermediates	0.8 g.

Results

CO_2 evolved	.237 mol
Valerate recovered	.27 mol
Acetate formed	.105 mol
Valeric unaccounted for	.115 mol

SECOND RUN

Since in the first run only a small portion of the valeric acid was oxidized,using equivalent parts of valeric acid and oxidizing agent,it was decided to use double the amount of oxidizing agent. This would give more accurate results due to a greater production of acetic acid and CO_2. In order to keep the number of components in the oxidation mixture as low as possible,it was decided to use chromic oxide rather than sodium dichromate as the oxidizing agent.

Materials

Chromic **Acid** (Kahl. anhydrous)	200 g.- 2 mol 2. mole
Valeric Acid (B. P.,184.7-186.2°)	51 g.- 2 mol .5 mole
Sulphuric Acid (93.5%)	200 cc.
Water	500 cc.

Procedure

This run was made with the same apparatus and under the same conditions as before,special precautions being taken to have the apparatus gas tight.

After all the oxidizing mixture had been added, the temperature was raised to 98°. This was done in place of adding the excess sulphuric acid as in the first run. About 30% of the total CO_2 came over on heating to 98°. When the apparatus had cooled to room temperature, the water displaced was measured and the volume of CO_2 evolved calculated to standard.

In order to prevent further oxidation in the subsequent steam distillation, the remaining chromic acid was reduced by passing sulphur dioxide into the solution until it was no longer absorbed.

The mixture was then steam distilled as in the first run, a total volume of 1200 cc. of distillate being collected. The last 100 cc. of this showed almost no acidity. The acids in this distillate were converted to the methyl esters, as in the first run, and fractionated.

<u>Results</u>

CO_2 evolved (12.6 liters (cor.))	.564 mole
Methyl Acetate (B.P., 55-56°)	17.3 g.-.234 mole
Intermediate (56°- 126.5°)	3 g.
Methyl Valerate (126.5°- 128°)	18.8 g.-.161 mole

Since the temperature range of the 3 g. of intermediate fraction showed no pause, there was no indication of any propionic or butyric acid being present.

Comparison of the Results of Both Runs

I $\frac{CO_2}{\text{Acetate}} = \frac{.237}{.105} = 2.3$

II $\frac{CO_2}{\text{Acetate}} = \frac{.564}{.234} = 2.4$

I $\frac{\text{Acetate}}{\text{Mols oxidized}} = \frac{.105}{.22} = .477$

II $\frac{\text{Acetate}}{\text{Mols oxidized}} = \frac{.234}{.339} = .69$

The results of the two experiments agree as well as could be expected in the case of the amount of CO_2 evolved per mol of acetic acid formed. The agreement is not so good in the case of the number of mols of acetic acid formed per mol of valeric oxidized.

Interpretation of Results.

Since it was found that butyric acid is more difficultly oxidized than valeric acid,none being found in the oxidation product,and furthermore since not more than 2.4 mols of CO_2 were formed for each mol of acetic acid,the oxidation could not have started on the α carbon atom and proceeded down to acetic.

The fact that less than 3 mols of CO_2 are liberated per mol of acetic acid points toward the possibility that part of the oxidation started on the γ carbon atom and proceeded according to the following equation:

$$CH_3CH_3 \vdots CH_2CH_2COOH + 5\ O = CH_3COOH + CH_2(COOH)_2 + H_2O$$

$$CH_2(COOH)_2 \underset{\text{heat}}{=} CH_3COOH + CO_2$$

This reaction yields 2 mols of acetic acid per mol of CO_2. Due to the fact that this would not yield enough CO_2, it is probable that part of the oxidation started on the β carbon atom and proceeded according to the equation:

$$CH_3CH_2CH_2 \vdots CH_2COOH + 5\ O = CH_3CH_2COOH + (COOH)_2 + H_2O$$

Since the propionic is very easily oxidized to acetic acid and the oxalic to CO_2, the final product would not be expected to contain propionic acid.

Since oxidation on the γ carbon atom as indicated would give 2 mols of acetic for each mol of valeric acid oxidized, the total acid recovered should have been greater than the amount before oxidation. As this is far from being the case, it is probable that part of the oxidation, starting on the γ carbon atom, proceeded according to the equation:

$$CH_3 \vdots CH_2CH_2CH_2COOH + 5\ O = CO_2 + COOHCH_2CH_2COOH + 2\ H_2O$$

Succinic acid was tested under the conditions of the experiment and it was found that no oxidation took place, so that any of this formed would remain in the oxidation mixture since it is non-volatile.

It therefore seems probable that the oxidation took place simultaneously in the three ways indicated with possibly some oxidation on the δ carbon atom yielding glutaric acid.

IV.

CONCLUSIONS

It may be concluded therefore that there is no enolization of the fatty acids which takes place in acid solution. However,it might be noted that the oxidation apparently proceeds as the electron displacement theory predicts,if there is no enolization,principally on the γ carbon atom and partially on the β and δ atoms.

This work has been carried out under the direction of Professor H. J. Lucas as a contribution to the work on the electron displacement theory that he is carrying on.

V.

SUMMARY

1.An enolization has been suggested as the explanation of fatty acids halogenating on the α carbon atom. It was therefore desireable to find whether or not this enolization was exhibited in other reactions.

2.Butyric acid is not as easily oxidized as valeric acid.

3.Valeric acid,when oxidized with CrO_3 in H_2SO_4 solution,yields acetic and carbonic acids as the only volatile products.

4. No evidence was found that an enol form exists.