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ON THE MECHANISM OF THE GUERBET REACTION

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Abstract—The reaction between an alcohol and an alkanolate in presence of excess potassium hydroxide (the Guerbet reaction) has been studied, mainly with benzyl alcohol and potassium lactate as reactants, α-hydroxy-γ-phenylbutyric acid being formed in the reaction.

1. It has been confirmed that the reaction proceeds in a series of consecutive steps:
   (a) A dehydrogenation of the hydroxyl compounds to carbonyl compounds.
   (b) Aldol condensation between the carbonyl compounds, followed by elimination of water.
   (c) Hydrogenation of the α,β-unsaturated ketone formed, the orginal hydroxyl compounds reacting as hydrogen donors, thus initiating a chain reaction.
   (d) A disproportionation of aldehyde to alcohol and acid under the influence of potassium hydroxide, this reaction breaking the chain reaction mentioned under (c).
2. The reaction may take place without the addition of a catalyst but it is strongly catalysed by hydrogen-transferring catalysts (Raney-Ni, Pd).
3. At relatively low temperatures (130–140°) the dehydrogenating process is the rate determining process.
4. At higher temperatures (160–180°) the reaction steps (b) or (c) are rate determining, most likely (b), as, if (c) were rate determining, an accumulation of aldol would take place, leading to a polycondensation, and no tendency of polycondensation has been observed.
5. At still higher temperatures other reactions, resulting in the formation of carbon monoxide and other destruction products, become dominating.
6. At the temperature at which the reaction usually has been studied (160–180°) the composition of the reaction mixture is determined by the ratio between the rates of step (b) and step (d).
7. Addition of the α,β-unsaturated ketone presumed as intermediate to the reaction mixture allows the reaction to proceed at considerably lower temperature than without such addition, thus improving the yield as the temperature coefficient of step (d) is higher than that of (b) and (c).

Guerbet[1] discovered in 1899 that when a potassium alkanolate is heated to about 300° with the corresponding alcohol condensation takes place, leading to an alcohol with the double number of carbon atoms. Besides, with evolution of hydrogen, one molecule of the alcohol is dehydrogenated to the corresponding carboxylic acid, the overall reaction being expressed by Guerbet by the stoichiometric equation:

$$CH_3(CH_2)_nCH_2OK + 2\,CH_3(CH_2)_nCH_2OH \rightarrow CH_3(CH_2)_nCH_2\overset{(CH_2)_{n-1}CH_3}{CH}CH_2OH + CH_3(CH_2)_nCOOK + 2\,H_2$$

By prolonged heating alcohols with 3 or 4 times the number of carbon atoms of the original alcohol may be obtained.

Since then the reaction has been studied thoroughly by several authors[2–4] and different suggestions for the mechanism have been put forward. It has been found that the reaction is catalysed by metals usually acting as hydrogenation catalysts (Ni, Pd).

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[1] M. Guerbet, *C.R. Acad. Sci., Paris* **128**, 511; 1002 (1899).

[2] H. Machemer, *Angew. Chem.* **64**, 213 (1952).

[3] Ch. Weizmann, E. Bergmann and M. Sulzbacher, *J. Org. Chem.* **15**, 54 (1950).

[4] J. Bolle, *C.R. Acad. Sci., Paris* **233**, 1628, (1951).

[5] E. F. Pratt and D. G. Kubler, *J. Am. Chem. Soc.* **76**, 52 (1954).

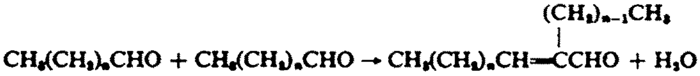
[6] R. E. Miller and G. E. Bennett, *Ind. Eng. Chem.* **53**, 33 (1961).

Common for most of the suggestions is that 3 different stages have to be considered, *viz.* a dehydrogenation of the alcohol to the corresponding carbonyl compound, an aldol condensation followed by crotonization between two molecules of the carbonyl compound, and a hydrogenation of the unsaturated aldehyde to a saturated alcohol. As a side reaction, two molecules of aldehyde may under the influence of potassium hydroxide at the elevated temperature (uncatalysed reaction about 300°, catalysed 150–200°) undergo a Cannizzaro-like dismutation to alcohol and carboxylic acid, but at the lower temperature of the catalysed reaction much less carboxylic acid is found than in the uncatalysed reaction, especially when the water formed in the reaction is removed continuously.

It is thus generally assumed that at least the following 4 consecutive reactions are involved in the overall reaction:

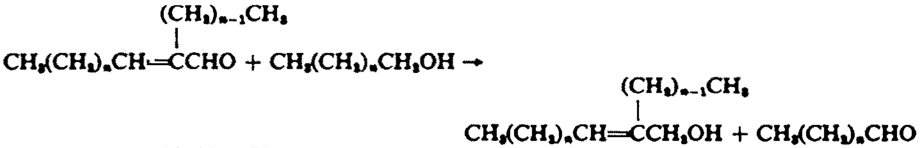
(1) $2\,CH_3(CH_2)_nCH_2OH \rightarrow 2\,CH_3(CH_2)_nCHO + 2\,H_2$

(2)



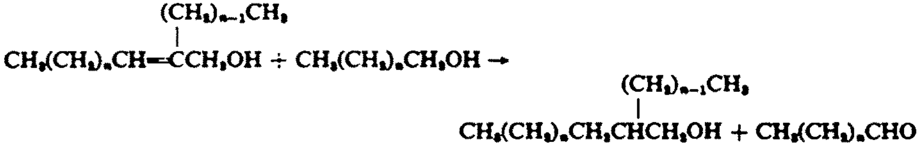
$$CH_3(CH_2)_nCHO + CH_3(CH_2)_nCHO \rightarrow CH_3(CH_2)_nCH{=}\overset{\overset{\textstyle (CH_2)_{n-1}CH_3}{|}}{C}CHO + H_2O$$

(3)



$$CH_3(CH_2)_nCH{=}\overset{\overset{\textstyle (CH_2)_{n-1}CH_3}{|}}{C}CHO + CH_3(CH_2)_nCH_2OH \rightarrow CH_3(CH_2)_nCH{=}\overset{\overset{\textstyle (CH_2)_{n-1}CH_3}{|}}{C}CH_2OH + CH_3(CH_2)_nCHO$$

(4)



$$CH_3(CH_2)_nCH{=}\overset{\overset{\textstyle (CH_2)_{n-1}CH_3}{|}}{C}CH_2OH + CH_3(CH_2)_nCH_2OH \rightarrow CH_3(CH_2)_nCH_2\overset{\overset{\textstyle (CH_2)_{n-1}CH_3}{|}}{C}HCH_2OH + CH_3(CH_2)_nCHO$$

The sequence of these 4 reactions has not, however, been determined but it is seen that once initiated by the dehydrogenation reaction of the alcohol it may proceed as a chain reaction in which the formation of a carboxylic acid will break the chain.

In a long series of papers Haga[7–10] has studied this reaction, using Raney-Ni as catalyst, potassium salts of hydroxycarboxylic acid as one reaction partner and different primary alcohols as the other reaction partner. He found that with active primary alcohols such as benzyl alcohol or *p*-methoxybenzyl alcohol high yields of hydroxysubstituted acids containing the total number of carbon atoms of the two reactants were obtained. He therefore regarded the reaction as an example of the Guerbet reaction.

As we became interested in an investigation of the reactivity of the Me group in lactic acid we repeated some of the experiments of Haga and extended them in different ways. We found that the reaction may proceed without the addition of a catalyst, but the yields are very much improved when Raney-Ni is added as catalyst.

In order to see if the catalytic effect could be due to the surfaceactivity of finely divided particles we compared the catalytic effect of Cu-powder, of norite, of Pa–C and of Raney-Ni. A very great difference in catalytic effect of Cu powder and norite

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[7] T. Haga, Nippon *Kagaku Zasshi* **81**, 272; 274; 277 (1960); *Chem. Abstr.* **55**, 6370 (1961).

[8] T. Haga, *Kagaku Zasshi* **81**, 944; 948 (1960); *Chem. Abstr.* **56**, 311 (1962).

[9] T. Haga, *Kagaku Zasshi* **81**, 1113; 1116 (1960); *Chem. Abstr.* **56**, 5827 (1962).

[10] T. Haga and M. Sato, *Kagaku Zasshi* **83**, 609 (1962); *Chem. Abstr.* **59**, 433 (1963).

on one side and of Pd–C or Raney-Ni on the other side was found, indicating that a catalyst able of transferring hydrogen from one molecule to another is essential for a good yield of the reaction.

The reaction between benzyl alcohol and potassium lactate, catalysed by Raney-Ni, was studied most thoroughly. According to the scheme outlined above, the following part-reactions were presumed:

(5) $2\,C_6H_5CH_2OH + \text{cat} \rightarrow 2\,C_6H_5CHO + (\text{cat}, 4H)$

(6) $CH_3CHOHCOOK + \text{cat} \rightarrow CH_3COCOOK + (\text{cat}, 2H)$

(7) $C_6H_5CHO + CH_3COCOOK \rightarrow C_6H_5CH{=}CHCOCOOK + H_2O$

(8) $C_6H_5CH{=}CHCOCOOK + C_6H_5CH_2OH \xrightarrow{\text{cat}} C_6H_5CH{=}CHCHOHCOOK + C_6H_5CHO$

(8a) $C_6H_5CH{=}CHCOCOOK + CH_3CHOHCOOK \xrightarrow{\text{cat}} C_6H_5CH{=}CHCHOHCOOK + CH_3COCOOK$

(9) $C_6H_5CH{=}CHCHOHCOOK + C_6H_5CH_2OH \xrightarrow{\text{cat}} C_6H_5CH_2CH_2CHOHCOOK + C_6H_5CHO$

(9a) $C_6H_5CH{=}CHCHOHCOOK + CH_3CHOHCOOK \xrightarrow{\text{cat}} C_6H_5CH_2CH_2CHOHCOOK + CH_3COCOOK$

(10) $2\,C_6H_5CHO + KOH \rightarrow C_6H_5CH_2OH + C_6H_5COOK$

(11) $(\text{cat}, 4H) + (\text{cat}, 2H) \rightarrow 2\,\text{cat} + 3\,H_2$

Of these reactions (5) and (6) must be regarded as processes initiating the chain reactions (7) to (9). (10) is a chain-breaking process, the action of which is compensated for by (5) and (6), these reactions not being exclusively restricted to the induction period.

It is seen that the hydrogen-evolving processes are (5) and (6) combined with (11). Reaction (10) is decisive for the scope of the hydrogen formation as it is the only one which uses up aldehyde without regenerating it in a following reaction.

The crotonization reaction (7) is the essential reaction in the whole scheme but, as pointed out,[2,4,6,11] the carbonyl compounds are principally formed in the hydrogen-transferring reactions (8)–(8a) and (9)–(9a). A corroboration of this assumption has been obtained by adding to a system of alcohol and alkanolate the aldehyde corresponding to either the alcohol considered or to the alcohol formed in the Guerbet-reaction at a temperature lower than the one at which the Guerbet reaction can usually be carried out. An increase of the yield of the final alcohol more than equivalent to the amount of aldehyde added was obtained, indicating that the chain reaction may be initiated by addition of aldehyde.

In order to obtain a more thorough understanding of the mechanism of the reaction we in some experiments collected the hydrogen evolved and found that the volume corresponded to about 0·3 moles of hydrogen per mole of α-hydroxy-γ-phenylbutyric acid (2·5–2·8 moles per mole of benzoic acid) formed, when no intermediate product was added.

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[11] J. Bolle and L. Bourgeois, *Mem. serv. chim. état, Paris* 87 (1956); *Chem. Abstr.* 52, 16182 (1958).

As mentioned[4] the yield of the Guerbet reaction improved when one of the intermediate products, the aldehyde, was added to the reaction mixture and the reaction carried out at a temperature lower than that ordinarily used in the non-catalysed Guerbet reaction.

We studied the effect of adding another of the intermediates, *viz.* the crotonization product formed in reaction (7), to the reaction mixture in experiments with Raney-Ni as catalyst. Two series of experiments, with benzyl alcohol and potassium lactate as reactants, were carried out under identical conditions as to temperature, time of heating and amount of catalyst, but in one of the series potassium benzylidenepyruvate was substituted for about 10% of the potassium lactate and an equivalent amount of benzyl alcohol. The volume of hydrogen evolved, the yields of α-hydroxy-γ-phenylbutyric acid and, in some instances, the yield of benzoic acid were determined. A survey of the results obtained is given in table 1.

The results may be summarized as follows.

1. The addition of potassium benzylidenepyruvate in an amount of about 10% of the reactants caused a decrease of about 30% in the volume of hydrogen evolved. The influence of the addition is possibly decreasing with increasing reaction temperature but the figures registered here are not sufficiently significant to be taken as a proof of this effect. A temperature dependence as indicated would mean that the reactions (8), (8a), (9) and (9a) are favoured by the addition of potassium benzylidenepyruvate, thus causing a formation of benzaldehyde and pyruvic acid at a lower temperature than that at which the reactions (5) and (6) take place.

2. The molar ratio between hydrogen evolved and α-hydroxy-γ-phenylbutyric acid formed is very considerably decreased by the addition of potassium benzylidenepyruvate. This ratio is dependent on the reaction temperature, the effect of the addition of the intermediate decreasing with increasing reaction temperature. At 130°, the lowest temperature investigated, the addition of about 10% of the intermediate causes a drop in the molar ratio from about 0·35 to about 0·03.

3. In experiments without addition of the intermediate no significant dependence on the temperature of the ratio mole of hydrogen: mole of α-hydroxy-γ-phenylbutyric acid is found.

4. The molar ratio between benzoic acid and α-hydroxy-γ-phenylbutyric acid formed seems to be 0·10–0·15 at 130°. This ratio seems to be independent of the addition of the intermediate. From the experiments registered here no conclusion as to dependence of the ratios hydrogen evolved: benzoic acid formed or benzoic acid: α-hydroxy-γ-phenylbutyric acid formed on the temperature can be drawn.

5. At 130° and to a lesser degree at 160° the addition of the intermediate causes an absolute increase in the yield of α-hydroxy-γ-phenylbutyric acid. This is seen by comparing the yields after deducting in the experiments with addition of intermediate the amount of α-hydroxy-γ-phenylbutyric acid resulting simply from the hydrogenation of the added intermediate.

In another series of experiments we tried to compare the reactivity of benzyl alcohol and of cyclohexylmethanol. Preliminary experiments had shown that the alicyclic alcohol reacted much more slowly than the aromatic. Therefore we investigated the reaction of a mixture of benzyl alcohol and cyclohexylmethanol with

TABLE 1. REACTION BETWEEN POTASSIUM LACTATE AND BENZYL ALCOHOL WITHOUT (−) AND WITH (+) ADDITION OF POTASSIUM BENZYLIDENEPYRUVATE. CATALYST ABOUT 0·2 g OF RANEY–Ni. IN EACH EXPERIMENT 0·25 MOLE OF POTASSIUM LACTATE, 0·29 MOLE OF BENZYL ALCOHOL AND 0·07 MOLE OF POTASSIUM HYDROXIDE WERE HEATED TO THE TEMP INDICATED. IN SOME EXPERIMENTS 0·025 MOLE OF POTASSIUM BENZYLIDENEPYRUVATE WAS SUBSTITUTED FOR THE EQUIVALENT AMOUNT OF POTASSIUM LACTATE AND BENZYL ALCOHOL BEFORE STARTING THE EXPERIMENT.

Experiment no.	Temperature	Time of heating	Addition of potassium benzylidene-pyruvate	Yield of α-hydroxy-γ-phenylbutyric acid, mole	Yield %	Yield of benzoic acid, mole	Hydrogen evolved, mole	Ratio hydrogen/α-hydroxy-γ-phenylbutyric acid	Ratio hydrogen/benzoic acid	Ratio benzoic acid/α-hydroxy-γ-phenylbutyric acid
A 70	160°	1 hr	−	0·174	69·5	?	0·056	0·322	?	?
A 71	160°	1 hr	+	0·132	53·7	?	0·029	0·216	?	?
A 72	160°	35 min	+	0·175	63·2	?	0·030	0·172	?	?
A 73	160°	35 min		0·122	49	?	0·037	0·302	?	?
A 74	130°	30 min		0·0103	4·1	0·00115	0·0032	0·31	2·78	0·11
A 75	130°	30 min	+	0·057	22·8	0·0092	0·0021	0·037	0·23	0·16
A 76	130°	30 min	−	0·0094	3·8	0·0014	0·0036	0·38	2·56	0·15
A 77	130°	30 min	+	0·059	23·6	0·0066	0·0012	0·02	0·18	0·11

TABLE 2. COMPARISON OF THE REACTIVITY OF BENZYL ALCOHOL AND CYCLOHEXYLMETHANOL TOWARDS POTASSIUM LACTATE

Experiment no.	Temperature	Time of heating	Potassium lactate, mole	Benzyl alcohol, mole	Cyclohexyl-methanol, mole	α-hydroxy-γ-phenylbutyric acid, mole	%	α-hydroxy-γ-cyclohexylbutyric acid, mole	%
A 78	130°	1·5 hr	0·025	0·025	0·025	0·0023	9·1	0	0
A 79	130° 150°	1·5 hr 2·0 hr	0·025	0·025	0·025	0·0087	35	0·0005	2
A 80	160°	1·75 hr	0·05	0·0116	0·0456	0·0089	71	0·0063	14
A 81	170° 180°	0·25 hr 1·33 hr	0·05	0	0·058	0	0	0·025	50
A 39	160°	1·2 hr	0·25	0·29	0	0·1738	69·5	0	0
A 37	180°	0·16 hr	0·25	0·29	0	0·1272	50·9	0	0
A 74	130°	0·5 hr	0·25	0·29	0	0·0103	4·1	0	0
A 70	160°	1·0 hr	0·25	0·29	0	0·1738	69·5	0	0

potassium lactate, catalysed by Raney-Ni, analysing the reaction product for contents of α-hydroxy-γ-phenylbutyric acid and α-hydroxy-γ-cyclohexylbutyric acid. Table 2 gives a survey of the results, showing that the difference in reactivity seems to decrease with increasing temperature.

DISCUSSION

From the experiments described above some information on the mutual relationship between the part reactions of the Guerbet reaction may be deducted.

At 130° the addition of the postulated intermediate potassium benzylidenepyruvate causes a considerable increase in the yield of α-hydroxy-γ-phenylbutyric acid. A possible interpretation of this effect is that the chain reaction (7)–(9) is made independent of the initiating processes (5) and (6) by the addition and proceeds at a higher rate than (5) and (6). This will mean that the dehydrogenation of the alcohol is facilitated when the hydrogen can be transferred to an acceptor instead of being stored on the catalyst (see (5) and (6)). Thus, at the temperature considered here, the dehydrogenation processes seem to be the rate determining processes, the aldol condensation being rapid as compared with the dehydrogenation processes.

In the chain reaction the amount of aldehyde and keto acid produced is the same as the amount used up. A chain-breaking reaction is (10), using up benzaldehyde without reproducing it. The overall result of the reaction will therefore be dependent on the ratio between the rates of the initial processes (5) and (6), the consecutive reactions (7)–(9) and the chain-breaking process (10), at all events in the reactions where the chain-mechanism is not initiated by the addition of the intermediate.

A priori it cannot be excluded that the mechanism followed when the intermediate is added is different from that followed without addition of intermediate. As, however, the ratio α-hydroxy-γ-phenylbutyric acid/benzoic acid is practically the same in the two instances it seems reasonable to conclude that the ratio between the rates of the two overall processes aldehyde → α-hydroxy-γ-phenylbutyric acid and aldehyde → benzoic acid, too, is the same. The rate of the overall reaction aldehyde → benzoic acid cannot be influenced by the addition of the intermediate which thus, according to the just mentioned statement, also is without influence on the overall reaction aldehyde → α-hydroxy-γ-phenylbutyric acid.

At 130° the Guerbet reaction thus follows the same mechanism from (7) to (10), independent of the addition of an intermediate. As the chain reaction proceeds without hydrogen being evolved it is natural that the molar ratios between hydrogen and α-hydroxy-γ-phenylbutyric acid and hydrogen and benzoic acid decrease considerably on addition of the intermediate as most of the aldehyde used up in the chain reaction is formed without evolution of hydrogen.

A comparison of the experiments at 130° and the experiments at 160° shows that at 130° the net yield of α-hydroxy-γ-phenylbutyric acid increases from 4·1% to 13·2% as a result of the addition of the intermediate (the net yield is the total yield minus the amount of acid formed by simple hydrogenation of the intermediate added), at 160° the net yield is increased from 49% to 53%. The absolute increase in yield is thus 9·1% at 130° and 4% at 160°.

These figures allow some conclusions as to the relative temperature coefficients of the dehydrogenation processes (5) and (6) and of the chain reaction (7)–(9). The chain reaction can be maintained only by compensation for the aldehyde used up in reaction (10) through the dehydrogenation reactions (5) and (6). At 130° the rate of these reactions are not sufficient to maintain the chain reaction, and the dehydrogenation reaction is thus the rate determining reaction at this temperature. At 160° the overall reaction proceeds with approximately the same rate with and without the addition of the intermediate. This means that the rates of the dehydrogenation reactions increase more rapidly with increasing temperature than does the rate of the chain reaction.

The reaction (10) uses up aldehyde without formation of α-hydroxy-γ-phenylbutyric acid. This means that if the temperature coefficient of (10) is higher than that of the chain reaction the increase in net yield caused by the addition of the intermediate will decrease with increasing temperature, thus exactly the effect found in the experiments mentioned above.

Extrapolating these considerations to temperatures higher than 160° it is to be expected that the rate determining process is no longer the dehydrogenation process but another step of the overall reaction.

Deciding for the yield of the Guerbet reaction is the ratio between the rates of the main reactions (7)–(9) and the chain-breaking process (10) (and particularly between the aldol condensation (7) and reaction (10) as these two reactions compete for the aldehyde present).

A search of the literature on the Guerbet reaction seems to substantiate this conclusion as it can be seen that alcohols of which the corresponding aldehydes are poor partners in the aldol condensation will give lower yields in the Guerbet reaction than alcohols of which the corresponding aldehydes readily give rise to an aldol condensation.

Apparently contradictory to this we found that the reactivity of benzyl alcohol towards potassium lactate is greater than the reactivity of cyclohexylmethanol, notwithstanding the fact that the deactivating effect of the phenyl group on the carbonyl group in benzaldehyde should make this aldehyde less adapted to an aldol condensation with potassium lactate (or pyruvate) than cyclohexanecarbaldehyde. This is true, however, only at temperatures above the limit where the dehydrogenation reaction is the rate limiting reaction. An explanation of this may be that benzyl alcohol is more readily dehydrogenated than cyclohexylmethanol. This being the case, the difference in reactivity should decrease with increasing temperature, in accordance with the experimentally found results.

Miller and Bonnett[6] studied the Guerbet reaction at temperatures as high as 300°. They found no influence of the addition of intermediates which corroborates the theory that at high temperatures the dehydrogenation processes are not rate determining. They also found that at 300° not only hydrogen but also alkanes and carbon monoxide is formed, thus indicating that several side reactions take place, obscuring the interpretation of the results obtained.

An extension of the investigation to long-chain aliphatic alcohols reacting with potassium lactate failed to give results as potassium lactate is so sparingly soluble in such alcohols that the reaction had to be heterogeneous not only with regard to the catalyst but also with regard to one of the reactants (hexadecyl alcohol selected as an example).

In other experiments we used glycols (from 1,2-ethanediol to 1,6-hexanediol) as reactants together with potassium lactate. The reaction with glycols proved to be very complex as thin-layer chromatography of the mixture of acids obtained showed a considerable number of acids, none of which could be regarded as the main product. These experiments were, therefore, discontinued.

EXPERIMENTAL

Substances used

Potassium lactate was prepared from commercially available lactic acid containing 5–10% water, by neutralizing it with KOH and evaporating the resulting salt soln to dryness at 50 mm Hg and 100°. In order to remove water as completely as possible the salt was dissolved in abs EtOH and the soln again evaporated with stirring 30 min at 50 mm Hg and 100°. Alternatively commercially available ethyl lactate was saponified by refluxing it with KOH for 1 hr and isolating the dry K salt as described.

Benzyl alcohol was a commercially available product of *Purum* quality (Fluka).

Cyclohexylmethanol was prepared[12] and redistilled to a gas chromatographic purity higher than 98%.

Potassium benzylidenepyruvate was prepared from benzaldehyde and pyruvic acid.[13]

General procedure

A Pyrex-glass reaction flask was stoppered with a stopper, equipped with a stirrer and a water separator of Dean-Stark-type connected to a reflux condenser. Lactic acid or ethyl lactate (usually 0·25 mole) and KOH (usually 0·32 mole) were introduced into the flask which was then placed in an electrically heated silicone oil bath equipped with an efficient stirrer. Stirring was started and water (and EtOH) evaporated as mentioned above.

Benzyl alcohol (usually 0·29 mole) was added to the dry amorphous mixture of potassium lactate and excess KOH at 100°. When a homogeneous soln had been obtained the flask was removed from the bath and cooled to room temp. Then Raney-Ni was added and the flask again placed in the silicone oil bath heated to the temp at which the experiment should be carried out. As soon as the viscosity of the reaction mixture made it possible, stirring inside the flask was started. In most experiments the reaction temp (150–190°) was high enough to allow the water–alcohol azeotrope usually formed in the reaction to reach the water separator, thus making it possible to follow the course of the reaction.

When no more water separated out or, in other experiments, after heating for the prescribed time, the reaction mixture was cooled to room temp, water was added and the aqueous soln extracted continuously with ether in order to remove excess alcohol and non-acidic by-products. The aqueous layer was then acidified and the organic acids formed in the reaction isolated by extraction with two portions of ether, most of the unreacted lactic acid remaining in the aqueous phase.

By evaporating the ether soln crude α-hydroxy-γ-phenylbutyric acid was isolated as brownish-white crystals with m.p. about 100°, the m.p. of the pure acid being 104·5–105°[14]. The crude acid is contaminated with a few % of benzoic acid.

The yields obtained were calculated from the weight of crude acid, disregarding its content of benzoic acid. Table 3 summarizes the results.

It is seen that the yield with Raney-Ni or Pd–C as catalyst is about twice as high as when no catalyst, Cu-bronze or norite is used. Experiment 12 shows that at all event Pd–C has lost its catalytic activity when isolated after the reaction. Experiment 17 shows that the yield is the same with sodium lactate as with potassium lactate. The Na salt is, however, much less soluble in alcohols than the K-salt. It is therefore preferable to use the K-salt.

In order to estimate the composition of the mixture of acids formed in the Guerbet reaction the crude acids isolated were converted into Me esters which were then separated gas chromatographically, using a 1 m silicone-coated celite-column.

The Me esters were prepared according to a slight modification of the method.[15] 100 mg of the mixture of acids were refluxed for 1 hr with 4 ml of a 14% soln of BF_3 in abs MeOH, then

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[12] H. Gilman and W. E. Catlin, *Org. Synth.* (2nd Edition) Vol. I, p. 188 (1964).

[13] M. Reimer, *J. Am. Chem. Soc.* **46**, 785 (1924).

[14] R. Fittig and N. Petkow, *Liebigs Ann.* **299**, 32 (1899).

[15] L. D. Metcalfe and A. A. Schmitz, *Analyt. Chem.* **33**, 363 (1961).

TABLE 3. COMPARISON OF CATALYSED AND UNCATALYSED REACTIONS

Exp. No.	Catalyst, g	Reaction time	Temp	Yield %
1	Copperbronze, 0·1	4 hr 20 min	180–185°	26·8
2	Copperbronze, 0·1	4 hr	180–185°	22·4
3	Copperbronze, 0·1	4 hr	180°	29·4
4	Copperbronze, 0·5	4 hr	180°	19·8
5	Raney-Ni 0·5	10 min	180°	50·9
6	Raney-Ni 0·5	20 min	170°	63·4
7	Raney-Ni 0·5	1 hr 12 min	160°	69·5
8	Raney-Ni 0·5	4 hr	150°	68·5
9	No catalyst	4 hr	185°	18·5
10	10% Pd–C, 1 g	40 min	180°	62·5
11	10% Pd–C, 1 g	4 hr	150°	63·8
12	Cat. used 2nd time	4 hr	150°	34·2
13	Norite, 1 g	4 hr	150°	30·8
14	No catalyst	4 hr	150°	34·9
15	No catalyst	5 hr 30 min	190°	21·8
16	No catalyst	5 hr 30 min	190°	24·4
17	(Sodium salt)	6 hr	190°	29·0

20 ml ice-water were added and the Me esters taken up in "hexane" (b.p. 62–82°) by shaking the aqueous soln vigorously with 50 ml hexane for 1 min, washing the hexane-soln with 20 ml 0·2N $NaHCO_3$, separating the non-aqueous phase and finally isolating the esters by distilling off the hexane through a 45 cm Podbielniak column to prevent loss of the most volatile of the esters, the methyl benzoate.

The retention times of methyl benzoate and of methyl α-hydroxy-γ-phenylbutyrate were determined using authentic samples, and the composition of the ester-mixtures isolated were calculated by comparing the chromatograms of these mixtures with chromatograms of mixtures of methyl benzoate and methyl α-hydroxy-γ-phenylbutyrate with known content of methyl benzoate.

The figures for benzoic acid and α-hydroxy-γ-phenylbutyric acid indicated in Table 1 (Experiments no. A 74–A 77) are determined by this method.

Effect of addition of potassium benzylidenepyruvate on the evolution of hydrogen and the formation of hydroxy-γ-phenylbutyric acid

Two parallel series of experiments were run, the one following the general procedure whereas in the other potassium benzylidenepyruvate was substituted for about 10% of potassium lactate and the equivalent amount of benzyl alcohol. In both series the amount of hydrogen evolved, of potassium α-hydroxy-γ-phenylbutyrate, and of potassium benzoate formed were determined. The hydrogen was collected in a gas-burette by equipping the top of the reflux condenser with an outlet tube connected by a rubber-tubing to the gas-burette. The gas-burette was adjusted to zero at room-temp after addition of catalyst and intermediate to the reaction flask, and the system was again cooled to room temp before reading the volume of hydrogen after termination of the heating.

The reaction was interrupted before running to completion in order to facilitate the detection of a possible effect of the addition of the intermediate. Therefore, these experiments were run at a rather low reaction temp and with short reaction times. Consequent upon this the water-alcohol azeotrope did not reach the water separator and thus water was not removed during the reaction.

The ester mixture resulting from the esterification of the crude reaction product from the experiments with addition of potassium benzylidenepyruvate did not contain the ester of the corresponding α,β-unsaturated ketoacid. This might be due to hydrolysis during the conversion of the K salts to acids. We found, however, that treatment of authentic potassium benzylidenepyruvate with the BF_3–MeOH reagent as described above for the methylation of the free acids gave a Me ester which could easily be separated from both methyl benzoate and methyl α-hydroxy-γ-phenylbutyrate gas chromatographically. We found, on the other hand, that Me esters prepared directly from the mixture of salts formed in experiments with addition of potassium benzylidenepyruvate, when gas chromatographed, did not show any trace of methyl benzylidenepyruvate. We, therefore, are confident that the potassium benzylidenepyruvate added has been completely hydrogenated to potassium α-hydroxy-γ-phenylbutyrate during the reaction.

Comparison of the velocity of reaction of cyclohexylmethanol and of benzyl alcohol with potassium lactate

This investigation was complicated by the fact that potassium lactate is only very slightly soluble in cyclohexylmethanol, even at the temp at which the reaction is carried through, whereas it is soluble in benzyl alcohol. We therefore had to carry through the investigation by using a mixture of benzyl alcohol and cyclohexylmethanol with sufficient benzyl alcohol to form a homogeneous solution at the temp of the reaction. The acids formed were isolated, converted to Me esters and analysed gas chromatographically, using a 50 cm reoplex column. It had been found previously that the retention times of methyl-α-hydroxy-γ-phenylbutyrate and of methyl α-hydroxy-γ-cyclohexylbutyrate are sufficiently different to allow a separation when this column is used, whereas nearly identical retention times were found for the two esters when a silicone column is used.

The results are recorded in Table 2.

The acid α-hydroxy-γ-cyclohexylbutyric acid has to our knowledge not been described in the literature and we, therefore, would like to give the following figures.

The acid was isolated in 50% yield from experiment A 81. White, somewhat oily crystals with m.p. 98–100° after 2 recrystallizations from benzene, m.p. 102·5° after recrystallization from water. (Found: C, 63·72; H, 9·43. Calc. for $C_{10}H_{18}O_3$ (286·2): C, 64·49; H, 9·74%.)

IR and NMR spectra showed clearly that the acid is different from α-hydroxy-γ-phenylbutyric acid.

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