XXXIII.—*The Formation of Acids from Aldehydes by the Action of Anhydrides and Salts, and the Formation of Ketones from the Compounds resulting from the Union of Anhydrides and Salts.*

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THE reactions which take place when aldehydes are heated with anhydrides and salts of fatty or bibasic acids, an account of which I had the honour of bringing under the notice of this Society some years since, have caused much work to be done with the object of obtaining a clearer insight into the way in which they take place. Fittig and his pupils, especially, have paid much attention to this subject, and this has resulted in the discovery of many very interesting products, and furnished us with fresh information respecting the reaction itself.

Since I brought this subject before the Society, much knowledge has been obtained in reference to the formation of condensation products, and it has been shown that the first phase of the reaction is, in very many cases at least, analogous to that of the formation of aldol from aldehyde discovered by Würtz in 1873; the splitting off of water being a second result. Fittig has shown that a change of a similar kind takes place in the formation of the unsaturated acids which are produced by this reaction, and that their formation is preceded by that of hydroxy-acids or their derivatives containing acid radicals, or of lactonic acids.

In my experiments, I was led to conclude that, in this reaction, condensation takes place between the aldehyde and anhydride, and Tiemann and Kraaz (*Ber.*, **15**, 2061) who, have worked a good deal on the subject, are of the same opinion. Fittig and others, however, consider that this is not the case, but that the condensation takes place between the aldehyde and the salt. As the evidence they give in support of this view does not appear to me to be conclusive, I have taken up the subject again. My experiments, however, are not yet completed, but as they have led to some new results which I desire to lay before the Society, I have ventured to refer to some of them, and to briefly consider their bearing. A very important point in the discussion of this matter is the double decomposition which may take place on heating the anhydride of one acid with the salt of another acid: results have been obtained in reference to this subject, but the work is still incomplete. I may state, however, that when sodium isobutyrate is boiled with acetic anhydride, the compound of sodium acetate and acetic anhydride I described some years since (*Chem. Soc. J.*, 1868, **21**, 185) is formed, and therefore there can be no doubt about double decomposition taking place in this instance. This is corroborated by Fittig and Otto (*Annalen*, **227**, 79), who show by their experiments that this takes place even at 100°. Sodium succinate when boiled with acetic anhydride was also found to form the compound of sodium acetate and acetic anhydride, and succinic anhydride was obtained from the mother-liquors.

In a former paper on the subject of this reaction, I referred to the fact that benzaldehyde with acetic anhydride yielded *benzylidene diacetate*, and said: "It is possible that the formation of this substance precedes that of the acid," meaning cinnamic acid (*Chem. Soc. J.*, 1877, **i**, 425), and I am still inclined to believe that this is the case, and that in the formation of other acids also, analogous products are first produced from the aldehydes.

There is the remarkable circumstance in connection with the formation of cinnamic acid, that the compound which (judging from Fittig's results) is the first product of the reaction, *i.e.*, acetylphenyllactic acid, has the same composition as benzylidene diacetate, only a slight intramolecular rearrangement of the latter substance being necessary for its formation:—

This acid, as shown by the experiment of Fittig and Slocum (*Annalen*, **227**, 60), splits up when heated, yielding cinnamic and acetic acids,

the reaction taking place more easily in the presence of acetic anhydride.

The succinate of benzylidene does not appear to have yet been isolated, but there is no reason to doubt its existence. Its composition is the same as that of phenylparaconic acid, and its change into this compound may be thus written:—

This acid on being heated also gives up carbonic anhydride, and phenylcrotonic acid is formed.

Why an acetate or other analogous salt should induce this intramolecular change in the benzylidene derivative is difficult to understand. It is possible that the two first form a compound, and the reaction may in some way be connected with the fact that the above salts containing feeble acids are capable of furnishing a base for the new acid. Thus in the formation of cinnamic acid I have shown that the product of the reaction contains a compound of sodium cinnamate and cinnamic acid.

Caro's method of formation of cinnamic acid, which is used technically, also bears upon this subject. It is well known that silver acetate and benzylidene dichloride yield benzylidene diacetate; if, however, sodium acetate is used, this acetate, although undoubtedly formed at first, yet changes directly it comes in contact with the sodium acetate, cinnamic acid being formed as the final result. I hope to make further experiments on the salts of benzylidene in reference to this subject.

These observations point to the condensation taking place between the aldehyde and anhydride, as do several of my older experiments. Thus I found that cinnamic acid could be formed whether the salt used were an acetate, butyrate, or valerate, but on these I would not

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lay much stress, because it may be I was practically working to a large extent with an acetate, the acetic anhydride entering into double decomposition, butyric or valeric anhydrides and the salt being formed. And as the acetic anhydride was somewhat in excess, and the more active body at the temperatures employed, cinnamic acid would be produced, the other anhydrides taking no part in the reaction. But I also made an experiment which is the opposite of this, and has moreover been confirmed by the work of Conrad (*Annalen*, **204**, 188), and on this I do lay stress. I found that isophenylcrotonic acid could be formed from benzaldehyde and propionic anhydride apparently equally well whether sodium acetate or propionate were employed. But, as remarked by Tiemann and Kraaz (*Ber.*, **15**, 2061), anhydrides of acids richer in carbon would be feebler than those containing less carbon; therefore, acetic anhydride would turn out a compound richer in carbon from its sodium salt. It would be very improbable that the converse of this should take place to any considerable extent, and in fact, experiment goes to bear out this view.

I have, however, made some more experiments on this subject. It will be remembered that I found that when isobutyric anhydride was heated with benzaldehyde and an isobutyrate, instead of obtaining an unsaturated acid, carbonic anhydride and butenylbenzene were formed. It appeared to me, therefore, that this anhydride might be used in these experiments, because the carbonic anhydride given off might serve as a measure of the extent of the reaction. Fittig has shown that the first part of this reaction consists in the formation of phenylhydroxypivalic acid (phenylhydroxytrimethacetic acid) or its isobutyl-derivative, which are not very stable compounds, but when heated split up into carbonic anhydride and butenylbenzene. This, of course, does not militate against the following results, because the final products still show the amount of change which has taken place in the above direction. A mixture of benzaldehyde, isobutyric anhydride, and an acetate was therefore experimented with. Now if the salt be the agent with which the condensation takes place, cinnamic acid should be produced, and no carbonic anhydride; but if the anhydride, then carbonic anhydride and butenylbenzene should result. On heating this mixture, carbonic anhydride was evolved freely and in abundance, and butenylbenzene was also formed in quantity. In one experiment, the amount of carbonic anhydride obtained in relation to the aldehyde used was 24.2 per cent., and in a second experiment 22.5. The temperature of the oil-bath used was about 170°, and the time of digestion five and a half hours in one case, and six hours in the other. A small quantity of cinnamic acid was formed. A mixture of isobutyric anhydride, sodium isobutyrate, and benzaldehyde was then taken, to see what amount of carbonic anhydride this would

evolve in comparison with the preceding under similar conditions. The temperature of the oil-bath was 170° , and the heating was continued for six hours. The amount of carbonic anhydride formed amounted to 28 per cent. An operation was also made with isobutyric anhydride, sodium butyrate (normal) and benzaldehyde, a temperature of about 160° being used, and the digestion continued for five hours. This gave 21.6 per cent. carbonic anhydride, and only 17 per cent. phenylangelic acid.

In the above experiments, the proportions of the sodium salts and aldehyde used were molecular, the amount of anhydride being rather in excess of this proportion.

Three experiments were then made the reverse of the foregoing, that is to say, acetic anhydride and an isobutyrate were used with the benzaldehyde, molecular proportions being taken. These were not expected to give any very definite results, because double decomposition would be sure to take place between the anhydride and salt, so that it would be a question as to the rate at which this would take place, compared with that of the combination of the anhydride and aldehyde. The results, however, show that cinnamic acid is produced in considerable quantity, and although carbonic anhydride and butenylbenzene are formed, their amount is comparatively small. The following are the results:—

	I.	II.	III.
Cinnamic acid	44.4	43.6	45.0
CO ₂	10.1	11.0	7.4

The temperature at which the last experiment was made was about 160° , the others nearer 170° .

The largest yield of cinnamic acid I have obtained by heating acetic anhydride, an acetate, and benzaldehyde, was 84 per cent. on the benzaldehyde, so that these experiments have yielded over 50 per cent. of that obtained under the most favourable circumstances.

Fittig and Ott made experiments with a similar mixture, but used a temperature of 100° C., which had been previously shown by Fittig and Slocum (*Annalen*, **227**, 59) was too low to allow of cinnamic acid being formed under any circumstances. The formation of this acid, therefore, being prevented, phenylpivalic compounds, which are produced at this temperature, were gradually formed from the isobutyric anhydride which was slowly produced by double decomposition. This hypothesis is supported by the fact that when Fittig and Ott employed acetic anhydride, the formation of phenylpivalic derivatives took place very slowly, and only a small quantity was produced by heating at 100° for 20 hours, whilst when isobutyric anhydride was used the formation took place very much more quickly (*Annalen*, **227**, 79).

Other experiments are in progress in reference to this subject, but I now wish to refer to some results which have been obtained while studying the nature of this reaction, though they are not intimately connected with it.

While examining into the changes which take place when normal butyric anhydride, a butyrate, and benzaldehyde are heated together, a high temperature being used (the mixture being in fact boiled), it was noticed that carbonic anhydride was very slowly but continuously given off. At first it was thought that this might be due to the decomposition of the phenylangelic acid produced, but not being satisfied on this point, it was determined to make experiments with butyric anhydride and a butyrate, omitting the benzaldehyde, and on doing so it was found that carbonic anhydride was still evolved in a slow but regular manner, and when the volatile products were distilled, the distillate not only contained butyric anhydride, but also a neutral oil possessed of great stability.

Larger operations were then made. At first the proportions of anhydride to salt used were molecular, but afterwards an excess of anhydride was employed. The mixture was heated in a fractioning apparatus with a column about 2 feet long; this was connected with a condenser and a receiver, and this again with a potash bulb filled with sulphuric acid to observe the progress of the operations by the bubbles of gas passing. In one case bromine and water was used, to see if any absorbable gases were formed, but none were found to be produced. The mixture was kept boiling by means of an oil or fusible alloy bath, but only gently; a thermometer with its bulb in the mixture generally indicated a temperature of between 185° and 190° ; this was maintained for about 36 hours, a small quantity of product being distilled over now and then. The temperature was then increased, so that nearly all the volatile products passed over. No appreciable increase in the formation of carbonic anhydride was observed during the extra heating, in fact it nearly ceased towards the end of the distillation.

The product when fractioned showed no definite boiling point, it was therefore treated with aqueous potash to remove butyric anhydride or acid, usually present in the anhydride. This, however, was not found sufficient, and as the oil did not appear to be decomposed by alcoholic potash, it was mixed with this in excess, and, after standing for some time, separated by the addition of water, and dried over potassium carbonate. On being fractioned, it commenced to boil at about 115° , the last parts not coming over until about 170° or 180° . After repeating this operation a few times, a boiling point was indicated between 140° and 150° , and eventually the principal part of the oil was obtained, boiling between 144.3° and 146.3° .

This gave on analysis the following numbers:—

I. Boiling point, 144·3—146·3°.

0·1433 gram substance gave 0·3885 gram CO₂ and 0·1592 gram OH₂.

II. Boiling point, 144—145°.

0·1453 gram substance gave 0·3937 gram CO₂ and 0·1617 gram OH₂.

	I.	II.	Calculated for C ₇ H ₁₄ O.
C	73·92	73·51	73·68
H	12·34	12·31	12·28

This substance is in fact butyrene, or dipropyl ketone.

The density determinations are pretty close to those given by Chancel. He gives 0·8195 at 20°. The above gave—

$$d_{\frac{4}{4}}^{\frac{4}{4}} = 0·83048$$

$$d_{\frac{15}{15}}^{\frac{15}{15}} = 0·82165$$

$$d_{\frac{25}{25}}^{\frac{25}{25}} = 0·81452$$

Having only a limited quantity at my disposal, I do not assume it was quite pure, especially as these substances, having a very low specific heat, are very difficult to purify by fractioning, therefore the density must not be taken as absolutely correct for pure butyrene. This ketone is a very stable compound, and dissolves in concentrated sulphuric acid with heat, apparently combining with it, but on the addition of water it separates unchanged.

Isobutyric anhydride and sodium isobutyrate react in a similar manner, producing a neutral oil consisting of various ketones, but their examination has not yet been completed.

Having obtained the above results, similar experiments were made with propionic anhydride and a propionate. On boiling these products together, carbonic anhydride is given off, but very slowly indeed, the boiling point of the mixture being scarcely sufficient for the reaction. The mixture was therefore heated in sealed tubes at 180—190°. The amount of carbonic anhydride evolved was then sufficient to burst some of the tubes, in fact it was found best to open them after heating for three or four hours, and then to reseal and re-heat them. After the tubes were opened and the carbonic anhydride allowed to escape, condensing tubes were fitted to them, and they were heated in an air-bath up to about 200°, until no more fluid came over. This distillate was heated with aqueous potash, dried, and dis-

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tilled; most of it came over between 99° and 109°, leaving some higher product; this was chiefly propionic anhydride, which had escaped the action of the aqueous potash. On refractioning the product, it again commenced to boil at 99°, but soon rose to 102°, when most of it came over between this and 103°. This substance gave on analysis the following numbers:—

0.1472 gram substance gave 0.3770 gram CO₂ and 0.1564 gram OH₂.

	Found.	Calculated for C ₅ H ₁₀ O.
C	69.84	69.76
H	11.80	11.62

This product was therefore *propione*. This ketone dissolves in concentrated sulphuric acid, and separates unchanged on the addition of water.

On preparing a quantity of propionic anhydride from sodium propionate and propionic chloride, and fractioning the product, a small quantity of oil of low boiling point was obtained. When purified, this boiled at the same temperature as propione, and had all its properties. This would be most probably produced by the action of the anhydride, as it was formed on some of the propionate which had escaped the action of the chloride, though it is just possible it might have been formed by the action of heat on some of the unchanged propionate during the process of distillation; the latter, however, is the less probable of the two.

Acetic anhydride was next heated with sodium acetate. No carbonic anhydride was given off, and on heating strongly acetic anhydride distilled over, leaving acetate of sodium behind. If, however, the mixture is heated in a sealed tube at 190—200° for three or four hours, carbonic anhydride is formed in quantity, and the product becomes brownish in colour. On opening the tubes and distilling off the volatile products, a colourless liquid was obtained, evidently containing acetic anhydride. On fractioning, a good deal passed over between 60° and 120°, and this on being refractioned gave a product boiling chiefly between 56.5° and 59.5°, which was evidently acetone, as it combined with sodium bisulphite, forming the ordinary easily soluble crystalline compound. It was not thought necessary to analyse it.

This reaction therefore appears to be general between the salts and anhydrides of the fatty acids. How can it be explained? Of course it is easy to understand that an anhydride, on losing carbonic anhydride, can yield a ketone, thus:—

but an anhydride at the temperatures which have been used certainly does not undergo this change.

Again, a salt of a fatty acid when heated yields, as is well known, a carbonate and a ketone, but this decomposition requires a much higher temperature than was used in the foregoing experiments, in fact it was found that as soon as the mixture of the anhydride and salt had been heated sufficiently high to distil off all volatile products, no more carbonic anhydride or ketone was formed, so that this reaction does not explain the matter.

In a paper published in this Journal a good many years since (1868, p. 185), I showed that sodium acetate combined with acetic anhydride to form the compound $\text{NaC}_2\text{H}_3\text{O}_2\cdot\text{C}_4\text{H}_6\text{O}_3$, already referred to, and there is no doubt that similar compounds are formed with other anhydrides and salts: in fact, when they are heated together the salts swell up, and a good deal of the anhydride disappears, and it seems to me that the production of the ketones is due to the formation and subsequent decomposition of such products, which are doubtless true chemical compounds.

It is well known that benzaldehyde combines with acetic anhydride to form benzylidene diacetate, which has already been referred to:—

Acetaldehyde also combines with acetic anhydride to form ethylidene diacetate.

If we apply this reaction to sodium acetate, which is simply aldehyde with an atom of hydrogen replaced by NaO, we get the following result:—

That this is the constitution of the compound $\text{NaC}_2\text{H}_3\text{O}\cdot\text{C}_4\text{H}_6\text{O}_3$, there is no reason to doubt, any more than in the case of the compound obtained from oil of bitter almonds and acetic anhydride. Now if this be the case, it is not difficult to see how this compound should yield a ketone and carbonic anhydride—

because it appears quite probable that the weakest part of the compound would be between the oxygen-atoms associated with the one carbon-atom and the acetyl-groups.

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The production of butyrene may be represented in an analogous manner:—

the latter compound breaking up as follows:—

If this explanation be true, and the sodium salt actually takes a definite part in the reaction, it is clear, if a salt were used containing an acid differing from that from which the anhydride was produced, that unsymmetrical ketones should be formed, because the hydrocarbon radical of the acid should go to form part of the ketone. This was put to the test, and sodium acetate was used in conjunction with butyric anhydride, because if it entered into the reaction it would produce a ketone containing methyl, which could be easily separated from other kinds of ketones by acid sodium sulphite; sodium butyrate would also be formed.

The reaction in this case should be—

and then—

On heating this mixture of sodium acetate and butyric anhydride, the reaction went on much in the same way as when sodium butyrate was employed, carbonic anhydride being regularly given off, but the combination of the salt and anhydride took place, apparently, more rapidly, so that it was necessary to add an excess of the latter to keep sufficient fluid present to allow the boiling to take place properly. The crystalline salt gradually changed in appearance, and after about 24 hours the product became perfectly fluid. The volatile products were then distilled off, leaving a mass of fused sodium salt, which was found to consist chiefly of sodium butyrate. By fractioning, the oily distillate was separated into three portions—

I	B. p. =	98—140°
II	„	140—165
III	„	165° and above.

The two first were mixed with sodium bisulphite and allowed to stand a few days. The first fraction gave a considerable quantity of a crystalline compound, the second gave no crystals, but a small quantity of it dissolved. The crystals and solution of bisulphite were separated from the undissolved oil, rendered alkaline, and then distilled until oil ceased to come over. This oil was collected, dried over potassium carbonate, and fractioned; it commenced to boil at about 87°, but soon reached 100°, and nearly all had come over when the temperature had reached 108°; when refractioned, it commenced to boil at about 80°, but soon reached 103°; the fraction boiling between this and 104·5° was selected for analysis. Although the yield of this product was considerable for the size of the operation, yet I did not have enough to fraction the product very thoroughly, and it is probable, judging from the boiling point of the product, that a little acetone was formed in the operation, and that a minute quantity of this was still contained in the product, as the numbers are a little low.

0·1467 gram substance gave 0·3718 CO₂ and 0·1531 OH₂.

	Found.	Calculated for C ₅ H ₁₀ O.
Carbon.....	69·12	69·76
Hydrogen	11·59	11·62

Not having sufficient to refraction, it was combined with sodium bisulphite, with which it soon formed a crystalline compound. On analysis, this product gave the following result:—

0·2958 gram substance gave 0·1066 Na₂SO₄ = 11·68 per cent. Na.

The formula C₅H₁₀O·NaHSO₃· $\frac{1}{2}$ OH₂, which is the formula given for the compound of methyl propyl ketone, requires 11·56 per cent. Na, therefore there can be no doubt that this product was methyl propyl ketone; it could not be its isomeride diethyl ketone, as this only combines with bisulphite with great difficulty.

The oil unacted upon by the acid sulphite consisted chiefly of butyrone; that this substance should be formed is a necessary consequence of the reaction, because as the sodium acetate becomes converted into butyrate, this reacts with the butyric anhydride, and yields butyrone.

These results, therefore, appear to establish the view of the reaction which is given above.

There is one matter worthy of notice in connection with the formation of ketones by this new reaction, that is the formation of com-

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pounds of lower and higher boiling point than the ketone which alone should be produced, and this seems to become more marked as the molecular weight of the compounds used increases. These products, which consist of ketones, I have not as yet been able to separate in a satisfactory condition for analysis, but hope to be able to do so.

The formation of higher and lower ketones also occurs when the calcium or barium salts of the fatty acids are distilled; thus the product obtained from calcium butyrate is said to distil between 100° and 160° ; in the case of barium propionate the variation in temperature is less, viz., $80-108^{\circ}$.

It was thought that by heating a mixture of an anhydride of a fatty acid with a formate, an aldehyde might be formed; it was found, however, that formates decompose very readily under these circumstances, giving off carbonic oxide.

Experiments are in progress with reference to the action of the anhydrides of bibasic acids on salts, but at present the results have been unpromising: thus, when succinic anhydride is heated with an acetate at about 190° , a black product is formed, which dissolves in part in boiling water with a brown caramel colour, leaving a brownish-black insoluble product.