

VIII.—*The Action of Salicylic Aldehyde on Sodium Succinate in presence of Acetic Anhydride.*

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IN order to see if Perkin's reaction is equally applicable to the hydroxyaldehydes, I undertook, at the request of Professor Fittig, to study the action of salicylic aldehyde on sodium succinate.

Jayne (*Annalen*, **216**, 97) has shown that by acting on sodium

succinate with benzaldehyde, at a temperature of 100—120°, phenylparaconic acid is principally formed. It was, therefore, to be expected that by substituting salicylic aldehyde for benzaldehyde, hydroxyphenylparaconic acid would be obtained. This was not found to be the case, however, the product being a neutral substance having the composition $C_{18}H_{10}O_4$, which subsequent investigation proved to be dicoumarin. In 1872, Zwenger (*Annalen*, Sup. 8, 32) showed that when coumarin, in aqueous solution, is treated with sodium amalgam, it gives melilotic acid, $C_9H_{10}O_3$: by acting with sodium amalgam on a saturated alcoholic solution of coumarin, however, the reaction proceeded quite differently; in this case he obtained the sodium salt of a new acid, which he called hydrocoumaric acid, $C_{18}H_{18}O_6$. The characteristic properties of this acid are, that its sodium salt is practically insoluble in alcohol, and that on being heated it gives off 2 mols. H_2O , forming an anhydride melting at 222·6°.

Cohen (*Inaugural Dissertation*, München, 1884), by the reduction of β -methylumbelliferon-paramethyl ether in alcoholic solution with sodium amalgam, obtained a compound, $C_{22}H_{22}O_6$, which he regarded as belonging to the same class of compounds as Zwenger's acid. As the substances above mentioned are the only dicoumarins known, it seemed desirable that the dicoumarin obtained by the action of salicylic aldehyde on sodium succinate should be submitted to a thorough investigation.

Preparation of Dicoumarin.

A mixture of salicylic aldehyde, sodium succinate (dried at 140° C.), and acetic anhydride, in the proportions of their respective molecular weights, was heated for 24 hours on the water-bath in a flask connected with a reflux condenser. It is essential to the success of the experiment that every trace of moisture should be excluded from the apparatus, and that all the material used should be perfectly dry. The contents of the flask, which had darkened in colour, were treated with hot water to remove sodium succinate and the acetic anhydride which still remained unacted on; and the excess of salicylic aldehyde was removed by a current of steam. The dicoumarin, after being washed with ether to remove a tarry substance which is always formed in small quantity, remained as a pale-yellow crystalline powder, insoluble in all the ordinary solvents. It was recrystallised from hot glacial acetic acid, in which it is only sparingly soluble; on cooling, it separated out in needle-shaped crystals.

The analysis of this compound indicated the composition $C_{18}H_{10}O_4$; it is formed by the condensation of 2 mols. of salicylic aldehyde with 1 mol. of succinic acid.

As by the above method the greater part of the aldehyde remained unacted on, the following modification was tried, and the results being more satisfactory, it was adopted for the preparation of all the material used in this research.

A mixture of 10 grams of sodium succinate, 15 grams of salicylic aldehyde, and 13 grams of acetic anhydride, was heated in a sealed tube for 40 hours at 140° . The contents of the tube were then extracted with hot water, and the residue, which consists of dicoumarin and unaltered salicylic aldehyde, was treated in exactly the same manner as previously described. From 10 grams of salicylic aldehyde about 5 grams of dicoumarin were obtained. It was found that an excess of acetic anhydride did not increase the yield of dicoumarin, but gave rise to the formation of various complicated condensation products, which have not been further investigated. The dicoumarin was purified by recrystallisation from hot glacial acetic acid; the product thus obtained was slightly yellow, and it was found impossible by this method of purification to render it colourless. It can, however, be completely decolorised by dissolving it in a hot solution of soda, and then reprecipitating it by the addition of hydrochloric acid.

The melting point of dicoumarin lies above 330° . On fusing it with caustic soda, salicylic acid is formed.

The following are the analytical results obtained:—

I. 0.2012 gram of substance gave 0.5522 gram of CO_2 and 0.0650 gram of H_2O .

	Calculated for $\text{C}_{18}\text{H}_{10}\text{O}_4$.	Found.
C	74.48 per cent.	74.84 per cent.
H	3.45 „	3.54 „

II. Analysis (after being recrystallised). 0.285 gram of substance gave 0.7775 gram of CO_2 and 0.0908 of H_2O .

	Calculated for $\text{C}_{18}\text{H}_{10}\text{O}_4$.	Found.
C	74.48 per cent.	74.40 per cent.
H	3.45 „	3.53 „

Dicoumarin is an extremely stable compound, insoluble in ether, alcohol, and benzene, but slightly soluble in chloroform and glacial acetic acid; it is not acted on at the ordinary temperature by sodium carbonate, ammonia, or caustic soda. On boiling it for some time with a solution of sodium or barium hydrate, it slowly dissolves, forming a yellow solution from which it is reprecipitated unchanged on addition of an acid.

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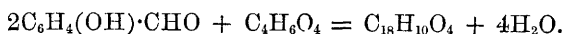
The following is an analysis of the product thus obtained :—

0·220 gram of substance gave 0·6003 gram of CO₂ and 0·0726 gram of H₂O.

	Calculated for C ₁₈ H ₁₀ O ₄ .	Found.
C	74·48 per cent.	74·45 per cent.
H	3·45 „	3·66 „

If, however, hydrochloric acid is gradually added to the alkaline solution, and this is kept cool by means of a freezing mixture, a precipitate is obtained which redissolves on addition of sodium carbonate. On attempting to separate this precipitate by filtration, it is immediately decomposed, dicoumarin being regenerated. It is probable that the compound formed is an unstable oxyacid, similar in fact to that obtained by dissolving dicoumarin in caustic soda.

The formation of dicoumarin from salicylic aldehyde and succinic acid may be represented by the following equation :—



Action of Sodium Amalgam on Dicoumarin.

An alkaline solution of dicoumarin, prepared by dissolving dicoumarin in hot concentrated caustic soda and diluting with water, was treated on the water-bath, with sodium amalgam (containing 5 per cent. of sodium), until the precipitate produced by the addition of hydrochloric acid redissolved completely on adding sodium carbonate.

In order that the reduction may not proceed too slowly, it is necessary to keep the solution as nearly neutral as possible. This is done by the occasional addition of hydrochloric acid. The alkaline liquid was decanted from the mercury, acidified with hydrochloric acid, and the precipitate formed collected on a filter. It is not soluble in chloroform or benzene, and only slightly so in water and ether, but dissolves freely in alcohol; it is also soluble in a solution of sodium carbonate, with evolution of carbon dioxide. It was purified by recrystallisation from dilute alcohol. The product thus obtained was found to have an indefinite composition, and it was, therefore, assumed to be a mixture. Proceeding on this assumption, various methods of separation were tried, and it was finally found that by converting it into the barium salt, and fractionally recrystallising the latter, the pure acid could be obtained. The mixture was accordingly dissolved in a solution of barium hydrate, and the excess of barium precipitated from the hot solution by a current of carbon dioxide. On filtering and allowing the filtrate to cool, a barium salt separated out, having the composition (C₁₈H₁₃O₅)₂Ba + xH₂O, being, in fact,

barium hydrodicoumarate. In the mother-liquor, there still remained a small quantity of the last-named salt, together with a salt much more easily soluble in water. The latter is undoubtedly the barium salt of the acid obtained by further reduction of hydrodicoumaric acid. It was found that when the reduction of the dicoumarin was only continued until it was all decomposed, very little of this more highly-reduced acid was formed.

Hydrodicoumaric Acid, C₁₈H₁₄O₅.

This acid was obtained, as a white precipitate, by adding hydrochloric acid to a solution of the barium salt. It is insoluble in chloroform and benzene, and dissolves only slightly in hot water or ether, but freely in alcohol. By recrystallisation from dilute alcohol, it was obtained in needle-shaped crystals.

When heated at 130°, it loses the elements of water, forming an anhydride, C₁₈H₁₂O₄.

Dried over sulphuric acid (when dried at 100° it lost weight, probably due to the formation of a small quantity of the anhydride) it yielded on analysis the following figures:—

0·0215 gram of substance gave 0·5485 gram of CO₂ and 0·0906 gram of H₂O

	Calculated for C ₁₈ H ₁₄ O ₅ .	Found.
C	69·67 per cent.	69·58 per cent.
H	4·51 „	4·67 „

Barium Salt, (C₁₈H₁₃O₅)₂Ba + xH₂O.

The preparation of this salt has already been described. It is only slightly soluble in cold water, but more readily in hot, from which it separates on cooling in well-defined crystals. These on exposure to the air effloresce and become opaque, rendering it impossible either to determine the water of crystallisation or the crystalline form. The following are the analytical figures obtained:—

I. 0·3861 gram of salt gave on heating at 130° 0·04725 gram of water, and on treatment with sulphuric acid 0·1047 gram of barium sulphate.

	Calculated for the dried salt.	Found.
Ba	18·18 per cent.	18·14 per cent.

The formula (C₁₈H₁₃O₅)₂Ba + 6H₂O requires 12·51 per cent. of water. Found 12·2 per cent.

II. 0.31275 gram of the salt gave 0.05675 gram of water, and on treatment with sulphuric acid 0.0787 gram of barium sulphate.

	Calculated for the dried salt.	Found.
Ba	18.18 per cent.	18.34 per cent.

Calculated for $(C_{18}H_{13}O_5)Ba + 9H_2O = 17.66$ per cent. of water.
Found 18.14.

Silver Salt, $C_{18}H_{13}O_5Ag$.

On adding silver nitrate to a solution of the barium salt, the silver salt was obtained as a white curdy precipitate, which on standing became crystalline. It is almost insoluble in water. The analysis of the salt, dried over sulphuric acid, gave the following figures:—

0.2325 gram of the salt yielded 0.4427 gram of CO_2 , 0.0687 gram of H_2O , and 0.0595 gram of Ag.

	Calculated for $C_{18}H_{13}O_5Ag$.	Found.
C	52.13 per cent.	51.93 per cent.
H	3.12 „	3.28 „
Ag	25.82 „	25.59 „

The calcium salt, obtained by treating the ammonium salt with calcium chloride, is almost insoluble in water.

Hydrodicoumarin, $C_{18}H_{12}O_4$.

Hydrodicoumaric acid, as has already been mentioned, splits up on being treated at 133° , into the anhydride, hydrodicoumarin, and water. In order to prepare hydrodicoumarin, hydrodicoumaric acid, which for the purpose need not be quite pure, is melted between watch-glasses. The melt, on cooling, is first washed with alcohol, in order to remove any unaltered acid, and then dissolved in hot chloroform; on allowing the chloroform to stand, hydrodicoumarin is deposited in small but well-defined crystals. It can also be precipitated directly by the addition of alcohol. Hydrodicoumarin is insoluble in water, alcohol, and ether; it melts at 256° , and when heated above this temperature it sublimes with partial decomposition in needle-shaped crystals; the vapour has an odour resembling that of coumarin.

On analysis, the following numbers were obtained:—

0.2217 gram of the anhydride yielded 0.6028 gram of CO_2 and 0.0833 of H_2O .

	Calculated for $C_{18}H_{12}O_4$.	Found.
C	73.97 per cent.	74.09 per cent.
H	4.11 „	4.17 „

In order to see if it could easily be reconverted into the acid, it was boiled with water for three days; at the end of which time it was found to be unaltered. It is not attacked when boiled with sodium carbonate or dilute caustic soda, but if heated for some time with a concentrated solution of caustic soda it is reconverted into the acid.

The crystals of hydrodicoumarin obtained from its solution in chloroform were not satisfactory, and it was thought that a better product might be obtained by recrystallising it from dilute acetic acid. Hydrodicoumarin was, therefore, dissolved in hot glacial acetic acid, and water, added until the precipitate formed just redissolved on boiling.

After two crystallisations a well-crystallised substance was obtained, which on analysis gave the following results:—

0.2173 gram of substance gave 0.5581 gram of CO_2 and 0.091 gram of H_2O .

Calculated for hydrodicoumaric acid, $\text{C}_{18}\text{H}_4\text{O}_5$.		Found.
C	69.97 per cent.	70.00 per cent.
H	4.51 „	4.65 „

From the above result, it would follow that by boiling hydrodicoumarin with acetic acid hydrodicoumaric acid is reformed. I hope to be able to give more details regarding this reaction in my next paper.

Action of Bromine on Hydrodicoumaric Acid.

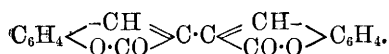
Hydrodicoumaric acid, suspended in chloroform, was treated with the calculated quantity of bromine (2 mols. of Br to 1 mol. of the acid). It is necessary, in order to prevent the formation of substitution products, to keep the mixture cool by surrounding it with ice; if this precaution is taken, no hydrogen bromide is given off. A clear solution was obtained, which after a time deposited a white precipitate; it was impossible, however, to analyse this compound, as on attempting to dry it, it immediately decomposed, giving off hydrogen bromide and leaving a white insoluble substance. This was purified by dissolving it in hot glacial acetic acid, from which on cooling it separates out in crystals. On analysis, the following numbers were obtained:—

0.291 gram of the substance gave 0.1499 gram AgBr.

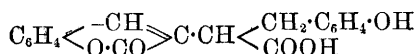
Calculated for $\text{C}_{16}\text{H}_{11}\text{BrO}_4$.		Found.
Br	21.56 per cent.	21.92 per cent.

The compound is consequently monobromohydrodicoumarin. It is insoluble in alcohol and ether, and dissolves only slightly in chloroform. In the original solution there still remained a compound, easily soluble in chloroform, which has not yet been analysed.

As dicoumarin is formed by the condensation of 2 mols. of salicylic aldehyde with 1 mol. of succinic acid, it follows that the simplest constitution that can be assigned to it is



It has further been shown that by limited reduction dicoumarin yields a monobasic acid, to which the constitution



has been given.

From this it would appear as if it were necessary, in order for the oxyacid to be stable, that the COOH group be combined with a saturated carbon-atom. It was therefore to be expected that, by further reduction of hydrodicoumaric acid, a bibasic acid would be formed, which should be identical with Zwenger's acid.

Action of Sodium Amalgam on Hydrodicoumaric Acid.

Hydrodicoumaric acid was dissolved in a solution of sodium carbonate and treated repeatedly on the water-bath with sodium amalgam (containing 5 per cent. of sodium). The reduction must be continued for several days, and the solution kept as nearly neutral as possible. On decanting the alkaline solution from the mercury, and acidifying with hydrochloric acid, the new acid was obtained as a white precipitate. It can be purified by recrystallisation from water or dilute acetic acid. The best method, however, to obtain it perfectly pure, is to convert it into the calcium salt, which can be purified by recrystallisation from hot water. As the calcium salt of hydrodicoumaric acid is nearly insoluble in the last-named solvent, an easy separation of the two acids can be effected.

The new acid, crystallised from dilute acetic acid, forms colourless crystals soluble in alcohol but insoluble in chloroform. When heated above 100°, it is slowly decomposed, without changing its outward appearance, forming an anhydride. The analysis shows it to have the same composition as Zwenger's hydrocoumaric acid, $\text{C}_{18}\text{H}_{18}\text{O}_6$, with which, however, it is not identical. This acid may be named *dihydrocoumaric acid*. It forms an insoluble silver salt, and a sodium salt soluble in alcohol.

0.2216 gram of the acid yielded 0.5333 gram of CO_2 and 0.1101 gram of H_2O .

	Calculated for $\text{C}_{18}\text{H}_{18}\text{O}_6$.	Found.
C	65.45 per cent.	65.63 per cent.
H	5.45 „	5.52 „

Calcium Dihydrocoumarate, $\text{C}_{18}\text{H}_{16}\text{O}_6\text{Ca} + 6\text{H}_2\text{O}$.

This salt was prepared by boiling the acid with water containing calcium carbonate in suspension. On filtering from excess of calcium carbonate and concentrating the filtrate, it separated on cooling in radiating groups of acicular crystals, containing 6 mols. H_2O , which it loses at 140° .

I. 0.3084 gram of the salt gave 0.0710 gram of water, and on addition of sulphuric acid 0.0893 gram of calcium sulphate.

	Calculated for $\text{C}_{18}\text{H}_{16}\text{O}_6\text{Ca} + 6\text{H}_2\text{O}$.	Found.
Ca	8.40 per cent.	8.52 per cent.
H_2O	22.69 „	23.00 „

II. 0.1616 gram of salt gave 0.036 gram of water and 0.0466 gram of calcium sulphate.

	Calculated for $\text{C}_{18}\text{H}_{16}\text{O}_6\text{Ca} + 6\text{H}_2\text{O}$.	Found.
Ca	8.4 per cent.	8.48 per cent.
H_2O	22.69 „	22.27 „

Silver Salt, $\text{C}_{18}\text{H}_{16}\text{O}_6\text{Ag}_2$.

On adding silver nitrate to a solution of the calcium salt (if the ammonium salt be used the product is impure), the silver salt was obtained as a white voluminous precipitate, which on standing became crystalline. The analysis of this salt dried at 100° , gave the following results:—

0.1945 gram of salt yielded 0.2831 gram of CO_2 , 0.0578 gram of H_2O , and 0.0768 gram of Ag.

	Calculated for $\text{C}_{18}\text{H}_{16}\text{O}_8\text{Ag}_2$.	Found.
Ag.....	39.70 per cent.	39.48 per cent.
C	39.70 „	39.76 „
H	2.96 „	3.26 „

Second determination of the silver:

0.2377 gram of salt gave 0.0939 gram of Ag.

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	Calculated.	Found.
Ag.....	39.7 per cent.	39.5 per cent.

Dihydrocoumarin, $C_{18}H_{14}O_4$.

The anhydride was obtained by melting the acid between watch glasses. The melt was then washed with alcohol, in order to remove any undecomposed acid, and dissolved in chloroform; from this solution it separated out on the addition of alcohol, or on standing, in needle-shaped crystals. It melts at $222-224^\circ$, and sublimes, with partial decomposition, when heated above this temperature; the vapours have an odour similar to that of coumarin; on boiling with water or carbonate of soda, it is not altered, but when heated with caustic soda it is slowly dissolved, being reconverted into the acid; when it is fused with solid caustic soda, salicylic acid is formed.

The following are the analytical results obtained:—

0.169 gram of the substance gave 0.4554 gram of CO_2 and 0.0734 gram of H_2O .

	Calculated for $C_{18}H_{14}O_4$.	Found.
C	73.47 per cent.	73.49 per cent.
H	4.76 „	4.81 „

The anhydride seems to be identical with that obtained by heating Zwenger's acid, possessing as it does the same chemical composition and melting point.

As the properties of the acid, from which the anhydride was prepared, do not correspond with those given by Zwenger to his acid, it was thought desirable to prepare a specimen of the acid according to his directions.

Preparation of Hydrocoumaric Acid.

20 grams of coumarin were dissolved in about 50 c.c. of absolute alcohol, and treated repeatedly on the water-bath with sodium amalgam (5 per cent. of sodium). In a short time, the insoluble sodium salt separated, and the quantity was further increased by the addition of more absolute alcohol. The salt, after washing with alcohol in order to remove coumarin, sodium coumarate, and sodium melilotate, was dissolved in water and the solution acidified with hydrochloric acid; on standing for about two days, the acid was deposited in acicular crystals. That this acid is not identical with that obtained by the reduction of hydrodicoumaric acid, is shown by the different solubilities of the sodium salts in alcohol; hydrocoumaric acid is also much more readily soluble in water, and the difference between their calcium salts is most marked.

Calcium Hydrocoumarate, $C_{18}H_{16}O_6Ca + 2H_2O$.

Calcium hydrocoumarate was prepared by boiling a solution of the acid in water with calcium carbonate until no more carbon dioxide was evolved. On filtering off the excess of calcium carbonate and concentrating the filtrate, the salt separated in crystals containing 2 mols. H_2O , which were driven off on heating at $133-140^\circ$.

It dissolves only slightly in either hot or cold water; if anything, it is rather more soluble in cold than hot water.

On analysis, the following results were obtained:—

0.1167 gram of the salt, on heating at 140° , gave 0.0101 gram of water, and on addition of sulphuric acid 0.0422 gram of calcium sulphate.

Calculated for $C_{18}H_{16}O_6Ca + 2H_2O$.		Found.
H_2O	8.00 per cent.	7.97 per cent.
Ca	10.00 „	9.79 „

Hydrocoumarin, $C_{18}H_{14}O_4$.

Hydrocoumaric acid was melted between watch-glasses, and the product after solidifying washed with alcohol till colourless. It was then dissolved in boiling chloroform, and from this solution it separated, on the addition of alcohol, in fine acicular crystals. It melted at 222° , and on analysis gave the following numbers:—

0.2066 gram of the substance gave 0.5596 of CO_2 and 0.09 gram of H_2O .

Calculated for $C_{18}H_{14}O_4$.		Found.
C	73.47 per cent.	73.87 per cent.
H	4.76 „	4.84 „

The existence of two isomeric acids, having the composition $C_{18}H_{16}O_6$, has thus been proved. Both these acids, when heated, yield an anhydride, $C_{18}H_{14}O_4$, melting at $222-224^\circ$. Whether they are identical or not is at present an open question, the identity of the melting points being possibly a mere coincidence. By reconverting the anhydrides into acids and studying the products thus obtained, there is no doubt but that this question could be satisfactorily settled.

If the anhydrides are found to be identical, we have here another case of isomerism similar to that observed by Perkin (*Chem. Soc. J.*, **39**, 409) as existing between α - and β -coumaric acids; on the other hand, should they prove to be different, hydrocoumaric acid must have a constitution different from that generally assigned to it.

The investigation of these compounds is being continued. I take the present opportunity of thanking Professor Fittig for the valuable advice he has given me whilst engaged upon the above work.
