

VI.—*On the Artificial Production of Coumarin and Formation of its Homologues.*

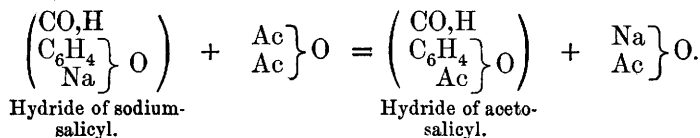
By W. H. PERKIN, F.R.S.

It is well known that coumarin, when fused with hydrate of potassium, yields salicylic and acetic acids. This fact has naturally led chemists to assume that there must exist a close relationship between this body and the salicylic series. No one, however, appears to have studied this subject, and, in fact, when we consider the formula of coumarin and compare it with that of any member of that series, we see that there is but little room for speculation; for example, if we compare the formula of coumarin with that of the hydride of salicyl, it will be seen that there exists only a difference of two equivalents of carbon, but it must be remembered that salicylic acid does not result from the action of hydrate of potassium upon coumarin, but is, in fact, a product of the decomposition of coumaric acid, therefore, speaking correctly, it is coumaric acid, and not coumarin, which is related to the salicylic series.

Under the name of aceto-salicylol, is described a body isomeric with coumaric acid, and this substance, being an acetyl derivative of the hydride of salicyl, should yield, if fused with hydrate of potassium, exactly the same products of decomposition as coumaric acid would, if treated in a similar manner.

In a paper I lately had the honour of reading before this Society, I mentioned that I was unable to obtain aceto-salicylol, or, more correctly, the hydride of aceto-salicyl, by the method of Cahours, and also that my endeavours to prepare it by the action of acetic anhydride upon the hydride of salicyl were unsuccessful.

It then appeared to me probable that if the hydride of salicyl were replaced by its sodium derivative, I might expect a better result, thus,—



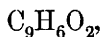
On performing this experiment, the following results were obtained.

The hydride of sodium-salicyl, when submitted to the action of acetic anhydride, rapidly loses its yellow colour, and then dissolves; this change is attended with a very considerable elevation of temperature, the mixture becoming quite hot. After this reaction has moderated, the product, when boiled for a few minutes, and then poured into water, sinks as an oil, acetate of sodium dissolving. On distilling this oil, any acetic anhydride that may have escaped decomposition comes over at first, then hydride of salicyl; the temperature then rises rather quickly, and when it has reached 290°, all the remaining product on being distilled into a separate receiver, solidifies to a crystalline mass on cooling.

This product, when purified by pressure between bibulous paper, and recrystallised two or three times from alcohol, gave the following number on analysis:—

- I. ·2396 of substance gave  
·6508 of CO<sub>2</sub> and  
·0942 of H<sub>2</sub>O.
- II. ·2387 of substance gave  
·6467 of CO<sub>2</sub> and  
·0920 of H<sub>2</sub>O.

These numbers give percentages agreeing with the formula—



as the following comparisons will show :—

	Theory.		Experiment.	
			I.	II.
C <sub>9</sub> . . . . .	108	73·97	74·07	73·87
H <sub>6</sub> . . . . .	6	4·11	4·36	4·28
O <sub>2</sub> . . . . .	32	21·92	—	—
	146	100·00		

It will be seen that this formula is not that of the hydride of aceto-salicyl, being deficient by an equivalent of water. It is, however, the formula of *coumarin*.

To prove that this substance is in reality pure coumarin, and identical with the natural product, the following comparisons of its properties with those of a specimen prepared from the Tonka bean, were made.

I. When crystallised from water, side by side, these two products could not be distinguished the one from the other, the appearance of the crystals and their grouping being identical.

II. Crystallised from alcohol, side by side, they appeared perfectly alike.

III. Their melting points were also the same.

IV. Their boiling points were also the same.

V. When heated with strong aqueous hydrate of potassium, each yielded coumaric acid, and moreover the acid prepared from both specimens possessed the same melting point.

VI. Fused with hydrate of potassium, they yielded salicylic acid.

VII. They also possessed exactly the same odour.

It will be remembered that some time since I made a verbal communication to the Society, upon the artificial formation of this body,\* but stated that I had not had an opportunity of ascertaining whether it was identical, or only isomeric with the natural product; from the foregoing comparisons, however, I think I may safely conclude that this artificial coumarin is the same as that obtained from the Tonka bean.

It will not, perhaps, be out of place to make a few obser-

\* Laboratory, vol. i, p. 136.

vations respecting the properties of coumarin, which I have found to differ somewhat from those described in chemical works. The melting point of this substance is nearly  $20^{\circ}$  higher than that recorded, being between  $67^{\circ}$  and  $67\cdot5^{\circ}$  C. Its boiling point is also much higher, my experiments giving  $290\cdot5$  to  $291^{\circ}$  C. as the temperature, whereas it is generally stated as  $270^{\circ}$  C. It is also mentioned that coumarin is easily soluble in a solution of hydrate of potassium; this remark is perfectly true when applied to boiling, but not to cold solutions of that alkali; the slender crystals obtained by crystallising this substance from water, dissolving only with extreme slowness in a strong, cold, aqueous solution of hydrate of potassium.

The melting point of coumaric acid I have found to be between  $207^{\circ}$  and  $208^{\circ}$  C.,  $190^{\circ}$  C. being the temperature usually given.

The production of coumarin by means of acetic anhydride and the hydride of sodium-salicyl, made it appear probable that if other anhydrides were substituted for the acetic, a whole series of bodies homologous with coumarin, might be produced.

This anticipation has been verified by experiment.

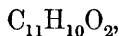
#### *Butyric Coumarin.*

Butyric anhydride acts but slowly upon the hydride of sodium-salicyl, unless heat be applied, the sodium compound then loses its colour, and gradually dissolves; after boiling for a few minutes, the product, if poured into water, separates as an oil, the butyrate of sodium which has been formed dissolving. On rectifying this oil, butyric anhydride and a little hydride of salicyl at first come over, the temperature then rapidly increases, and all the product distilling above  $290^{\circ}$  C. crystallises on cooling. This is rendered perfectly pure by pressure between bibulous paper and two or three crystallisations from alcohol. In one experiment I obtained three grammes of this substance from twelve grammes of the hydride of sodium-salicyl. When submitted to analysis, it gave the following numbers:—

- I.  $\cdot 1976$  of substance gave
- $\cdot 5474$  of  $\text{CO}_2$  and
- $\cdot 1049$  of  $\text{H}_2\text{O}$ .

II. ·2125 of substance gave  
 ·5902 of CO<sub>2</sub> and  
 ·1115 of H<sub>2</sub>O.

These numbers give percentages agreeing with those required by the formula—



as the following comparisons will show :—

	Theory.		Experiment.	
			I.	II.
C <sub>11</sub> .....	132	75·86	75·55	75·74
H <sub>10</sub> ....	10	5·75	5·89	5·82
O <sub>2</sub> .....	32	18·39	—	—
	174	100·00		

The formula of this substance is C<sub>2</sub>H<sub>4</sub> higher than that of coumarin, the difference being the same as that existing between acetic and butyric acids; this body is in fact a *butyric coumarin*, homologous with the natural product.

Butyric coumarin melts at from 70° to 71° C., and on cooling solidifies to a beautiful crystalline mass; at 296° to 297° C. it distils with slight decomposition. It is but little soluble in boiling water, the solution becoming milky as it cools, and after a time depositing a small quantity of crystals in the form of minute needles. In boiling alcohol it dissolves freely, and on standing separates from this solvent in large semi-opaque prisms. It is easily soluble in ether.

This body possesses the odour of ordinary coumarin, and also of fresh honey.

Butyric coumarin is nearly insoluble in cold aqueous hydrate of potassium, and even when gently heated with a saturated solution of that alkali, it only melts and floats as an oil upon its surface; if more strongly heated, however, it dissolves perfectly, forming a pale yellow solution; this, on being further concentrated, becomes opaque, and on standing a few moments an oily fluid rises to the surface, which, upon cooling, changes to a tenacious mass; it can then easily be separated from the excess of hydrate of potassium which remains fluid. This substance is a compound of butyric coumarin and hydrate of potassium; it is deliquescent and very soluble in water; acids

easily decompose it, with separation of butyric coumarin. When heated, this compound dries up to a yellow amorphous mass, and then undergoes decomposition, being converted into the potassium salt of a new acid, apparently homologous with coumaric acid; in fact, the coumaric acid of butyric coumarin. This acid is crystalline and easily soluble in carbonate of sodium and ammonia. For want of sufficient substance I have not been able to analyse this acid.

The addition of bromine to this coumarin causes it to liquefy, and on distilling the product, a tough resinous mass is obtained, giving, when digested with alcoholic hydrate of potassium, an acid which may be separated from the alkaline solution by means of hydrochloric acid. Ordinary coumarin, when treated with bromine, yields a similar product.

Butyric coumarin, when heated with fused hydrate of potassium, decomposes, yielding salicylic acid, together with hydrate of phenyl, and apparently butyric acid; but the odour of this latter compound is much masked by the presence of the hydrate of phenyl.

#### *Valeric Coumarin.*

The hydride of sodium-salicyl appears to be scarcely affected by valeric anhydride in the cold, but upon the application of heat, these two substances gradually react upon each other, forming a clear liquid. In performing this experiment I prefer to add the sodium compound to the boiling anhydride, and then to digest the mixture for a few minutes. The oily product of this reaction, after being agitated with water to remove valerate of sodium, is collected and distilled, the portion boiling above 290° C. being kept separate. This distillate, unlike those obtained in the preceding experiments, does not crystallise, even after standing for days, and it was only by repeated trials, that I succeeded in obtaining a method for its purification.

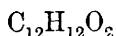
This process is based upon the property of coumarins to dissolve in boiling solutions of hydrate of potassium, and was carried out in the following manner:—

The above oily distillate, after being well agitated with a strong boiling solution of hydrate of potassium, was diluted with

water, and then mixed with ether, to separate all oily products, the clear aqueous solution, when acidified with hydrochloric acid, liberated the new coumarin, which was taken up with ether, and the ethereal solution agitated with carbonate of sodium, to remove any acids that might be present. On evaporating this solution, the new product was obtained as an oil solidifying to a crystalline mass upon cooling. It was then separated from oily impurities by pressure between bibulous paper; two or three crystallisations from alcohol then rendered it perfectly pure. From twelve grammes of the hydride of sodium-salicyl and about 14 grammes of valeric anhydride, I have obtained, by the above method, two grammes of this new coumarin. Two combustions of separate preparations of this body gave the following numbers :—

- I. ·1990 of substance gave  
 ·5600 of CO<sub>2</sub> and  
 ·1153 of H<sub>2</sub>O.
- II. ·2725 of substance gave  
 ·7630 of CO<sub>2</sub> and  
 ·1610 of H<sub>2</sub>O.

These numbers give percentages agreeing with the formula—



as the following comparisons will show.

	Theory.		Experiment.	
			I.	II.
C <sub>12</sub>	144	76·59	76·74	76·36
H <sub>12</sub>	12	6·38	6·43	6·56
O <sub>2</sub>	32	17·03	—	—
	<hr/>	<hr/>		
	188	100·00		

This substance is therefore *valeric coumarin*.

Valeric coumarin melts at 54° C., and on cooling solidifies to a splendid crystalline mass; at 301° C. it boils and distils with slight decomposition. It possesses a coumaric odour, but not to the same extent as the butyric coumarin. In boiling water it dissolves to a small extent, but is apparently insoluble in cold water. It is very soluble in alcohol, from which it crystallises in splendid transparent prisms nearly three-quarters of an

inch in length; they appear to be oblique six-sided prisms. This body is also very soluble in ether.

This coumarin appears to be insoluble in cold solutions of the alkalis. If added to a concentrated solution of hydrate of potassium, diluted with about a fourth of its volume of water, and gently heated, it melts and floats as an oil, but when heated further, perfectly dissolves. This solution, on being concentrated, becomes milky, and after standing a few moments, an oily layer forms on its surface, becoming a tenacious mass upon cooling; this is a compound of valeric coumarin and hydrate of potassium. This product is very deliquescent and easily soluble in water. Hydrochloric acid decomposes it, liberating the valeric coumarin. If heated strongly it decomposes, yielding an acid most probably valeric coumaric.

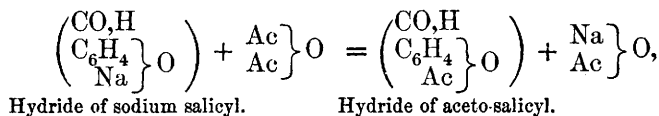
With fused hydrate of potassium this coumarin yields salicylic acid, hydrate of phenyl, and apparently a small quantity of valeric acid.

When distilled with pentachloride of phosphorous it yields a viscid oil, which, if gently heated, emits a turpentic odour, and when burnt, communicates a green colour to the edges of the flame, showing it to be a chlorinated body.

From the preceding results we see that coumarin is but a member of a whole series of homologous bodies producible from the hydride of sodium-salicyl by means of anhydrides. The question, therefore, which presents itself for consideration is, what is the nature of the reaction by which these bodies are formed, and their consequent constitution?

In this inquiry it will be well to consider the formation of ordinary coumarin, as the history of this substance is more complete than that of its homologues.

In the reaction by which this body is formed, there would appear to be two distinct stages, the first being the formation of the hydride of aceto-salicyl, thus :—



the second consisting in the formation of coumarin from this hydride of aceto-salicyl by the separation of an equivalent of water.



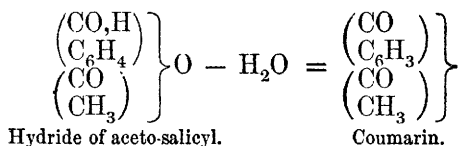
Respecting the first change I have found that by treating the hydride of sodium salicyl in a very careful manner the hydride of aceto-salicyl is actually formed.\*

The second part of this reaction is not so easy of explanation, viz., from what part of the hydride of aceto-salicyl is the equivalent of water removed.

Seeing that this change must be effected either by the dehydrating power of boiling acetic anhydride, or by a temperature not exceeding 300° C., it would not appear very probable that the acetylic radical was interfered with, especially as acetic acid is produced when coumarin or coumaric acid is decomposed with hydrate of potassium.

It is also evident that the hydride of aceto-salicyl loses its character as an acetate on changing into coumarin; otherwise, when dissolved in a strong solution of hydrate of potassium, coumarin should entirely split up, instead of forming coumaric acid.

Further, it is evident that it has lost its typical aldehydic hydrogen, otherwise coumarin would be an aldehyde. Assuming these considerations to be correct, the change which the hydride of aceto-salicyl undergoes on losing an equivalent of water, and thereby being converted into coumarin, may be represented thus:—

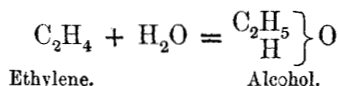
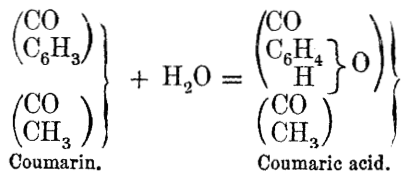


According to this formula, coumarin is a mixed acid radical, consisting of a molecule of acetyl, jointed to a molecule of a radical  $\text{C}_7\text{H}_3\text{O}$ . This would belong to the same series as cinnamyl, and I propose to name it *Diptyl*.

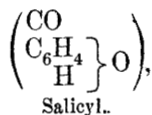
It will be well to see in what way the reactions of coumarin may be explained by this formula. I will first take the formation of coumaric acid.

\* This substance possesses all the properties pointed out by theory, namely, those of an aldehyde and an acetate. It freely combines with bisulphites and, with alcoholic hydrate of potassium, easily decomposes, yielding acetate of potassium, and the hydride of potassium-salicyl. I hope shortly to give a full account of this body.

This acid is formed by the assimilation of an equivalent of water by coumarin, through the intervention of hydrate of potassium, in the same way that alcohol is formed from ethylene by the intervention of sulphuric acid.

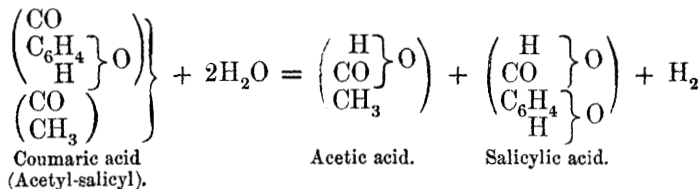


Thus expressed coumaric acid would be a phenol and not a true acid, and, if we regard the radical salicyl as a phenol as well as an acid radical,—



coumaric acid likewise becomes a mixed acid radical acetyl-salicyl.

The second reaction it will be well to consider is, the transformation of coumaric acid into acetic and salicylic acids. It will be seen that this change is easy of comprehension, the two radicals simply becoming hydrated.



To express the formation of the homologues of coumarin it is evidently only necessary to replace acetyl by other acid radicals.

Coumarin and its homologues probably have several isomers corresponding in number to the acids isomeric with salicylic, and

if coumarins are simply acid radicals, the possible number of such substances capable of existence is enormous.

The following is a table of the bodies described in this paper, written out according to the foregoing theoretical views. Also of coumaric acid, and its probable homologues not yet analyzed—

Acetic coumarin (Coumarin)	} C <sub>9</sub> H <sub>6</sub> O <sub>2</sub>	C <sub>7</sub> H <sub>3</sub> O C <sub>2</sub> H <sub>3</sub> O	} Acetyl-diptyl.
Propionic coumarin, wanting.			
Butyric coumarin ..	C <sub>11</sub> H <sub>10</sub> O <sub>2</sub>	C <sub>7</sub> H <sub>3</sub> O C <sub>4</sub> H <sub>7</sub> O	} Butyl-diptyl.
Valeric coumarin ..	C <sub>12</sub> H <sub>12</sub> O <sub>2</sub>	C <sub>7</sub> H <sub>3</sub> O C <sub>5</sub> H <sub>9</sub> O	} Valyl-diptyl.
Acetic coumaric acid } (Coumaric acid)	C <sub>9</sub> H <sub>8</sub> O <sub>3</sub>	C <sub>2</sub> H <sub>3</sub> O C <sub>7</sub> H <sub>4</sub> (HO)O	} Acetyl- salicyl.
Propionic coumaric acid, wanting.			
Butyric coumaric acid	C <sub>11</sub> H <sub>12</sub> O <sub>3</sub>	C <sub>4</sub> H <sub>7</sub> O C <sub>7</sub> H <sub>4</sub> (HO)O	} Butyl- salicyl.
Valeric coumaric acid	C <sub>12</sub> H <sub>14</sub> O <sub>3</sub>	C <sub>5</sub> H <sub>9</sub> O C <sub>7</sub> H <sub>4</sub> (HO)O	} Valyl- salicyl.

I am at present studying some new derivatives of coumarin and its homologues, with a view of obtaining a clearer insight into their nature.