XLVII.—*Brazilin, Haematoxylin, and their Derivatives.*
Part X. The Constitution of Trimethylbrazilone,
of α - and β -Anhydrotrimethylbrazilone, and of the
corresponding Haematoxylin Derivatives.

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IN Parts VIII and IX of this research (Trans., 1908, **93**, 489, 1115) we have brought forward evidence which, in our opinion,

clearly proves that the constitution of brazilin must be represented by the formula :

and it is there shown that this formula accounts in a comparatively simple manner for all the known reactions and decompositions of brazilin, trimethylbrazilin, and brazilein. In discussing trimethylbrazilone, one of the most important derivatives of brazilin, it was, however, found necessary to assume a rather complex series of molecular changes in order to derive a constitution which would account for the remarkable properties of this substance. It was suggested (*loc. cit.*, p. 498) that, during the oxidation of trimethylbrazilin to trimethylbrazilone, the central linking suffers disruption with the formation of an unstable diketone, which then undergoes internal condensation.

Before bringing our experiments on brazilin and hæmatoxylin to a conclusion, we thought it necessary still more thoroughly to investigate trimethylbrazilone in order to obtain further evidence which would leave no doubt as to its constitution and relationship to brazilin. Trimethylbrazilone is obtained from trimethylbrazilin

by oxidation with chromic acid, when the following change takes place :

When trimethylbrazilone is treated with dehydrating agents, it is converted, with loss of water, into α -anhydrotrimethylbrazilone, $\text{C}_{19}\text{H}_{16}\text{O}_5$, a substance which contains a hydroxyl group, since it is converted into acetyl- α -anhydrotrimethylbrazilone by treatment with acetic anhydride. We have suggested that the elimination of water from trimethylbrazilone takes place in a simple manner, and that the formula :

represents α -anhydrotrimethylbrazilone. According to this view, α -anhydrotrimethylbrazilone is a derivative of β -naphthol with one α -position free, and, in support of this, we showed that it possesses several of the properties characteristic of β -naphthol.

Thus, for example, it dissolves in dilute alkalis, and the solution combines with diazonium chlorides, yielding dyestuffs which are exactly similar to those produced in alkaline solutions of β -naphthol. We have continued our experiments in this direction (compare p. 391), and have prepared a number of interesting new derivatives of α -anhydrotrimethylbrazilone, the properties and decompositions of which afford further evidence that our view of the constitution of this substance is the correct one.

When α -anhydrotrimethylbrazilone is treated with ferric chloride, it is oxidised with formation of *di- α -anhydrotrimethylbrazilone*, and this substance is converted by phosphoryl chloride into the corresponding oxide. Using the central portion of the formulæ only :

it is seen that these changes are exactly similar to the conversion of β naphthol into β -dinaphthol and β -naphthylene oxide under the same conditions. Nitric acid reacts readily with acetyl α -anhydro-

trimethylbrazilone, with the formation of the acetyl derivative of *nitro- α -anhydrotetramethylbrazilone*,

and several derivatives of this substance have been prepared and are described in detail in the experimental part of this paper.

One of its most interesting reactions is its reduction by zinc dust and hydrochloric acid to the corresponding amino-derivative, which, when oxidised by ferric chloride, yields *trimethoxy- α -brazanquinone* (p. 394),

That this is an ortho-quinone is shown by its behaviour with *o*-tolylenediamine, with which it condenses with formation of a characteristic quinoxaline; on reduction, the quinone is converted into the corresponding dihydroxy-derivative, the diacetyl derivative of which is described on p. 396. Results exactly similar to those just described were obtained in the case of *α -anhydrotetramethyl-hæmatoxylone* (I).

(I.)

(II.)

Nitric acid converts the acetyl derivative of this substance into *nitroacetyl- α -anhydrotetramethylhæmatoxylone*, and this is readily reduced to the amino-derivative, which, on oxidation with ferric chloride, yields *tetramethoxy- α -brazanquinone* (II).

The investigation of the nature and constitution of the substances called *ψ* - and *β* -trimethylbrazilone and *ψ* - and *β* -tetramethyl-hæmatoxylone has proved to be a matter of very considerable difficulty. In 1904 (*Ber.*, 37, 631) Herzog showed that trimethyl-

brazilone undergoes isomeric change when it is dissolved in sulphuric acid, and is converted into a new substance, called by him ψ -trimethylbrazilone. In a previous communication (Trans., 1908, 93, 501) we described the results of a preliminary examination of this substance, during which we found that this carboxylic acid on oxidation with permanganate yielded large quantities of 2-carboxy-4:5-dimethoxyphenylacetic acid, $(\text{MeO})_2\text{C}_6\text{H}_2(\text{CO}_2\text{H})\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$. These and other considerations led us to suggest two possible expressions for ψ -trimethylbrazilone, namely :

The evidence available at that time was not sufficient to allow of a decision between these formulæ, but, as the result of further experiments (pp. 400—407), we are now in a position to show that formula (I) correctly represents the constitution of ψ -trimethylbrazilone. Before doing so it may be pointed out that this expression is readily derived from that of trimethylbrazilone by the following scheme of addition and subsequent elimination of water :

When ψ -trimethylbrazilone is treated with dehydrating agents, it loses the elements of water and is converted into β -anhydrotrimethylbrazilone. On the assumption that the above formula (I) is the correct expression for ψ -trimethylbrazilone, the most likely mechanism of this remarkable and interesting change is elimination of water

between the carboxyl group and the >CH group of the coumarone ring, leading to the expression

which, by intramolecular change, would then become

This formula represents β -anhydrotrimethylbrazilone as a derivative of α -naphthol with the second α -position free, and this view has been confirmed by further experimental investigation, since it has been found that, in its behaviour with diazo-solutions (p. 391) and in other respects, it exhibits properties exactly similar to those of α -naphthol. When acetyl- β -anhydrotrimethylbrazilone is treated with nitric acid, it yields *nitroacetyl- β -anhydrotrimethylbrazilone*,

and this, on reduction and subsequent treatment with nitrous acid, is converted into *trimethoxy- β -brazanquinone*,*

* The name "brazan" was given to the substance

by Kostanecki and Lloyd (*loc. cit.*; compare Bolina, Kostanecki, and Tambor, *Ber.*, 1902, **35**, 1675). When trimethylbrazilone is heated with hydriodic acid it yields, in the first place, tetrahydroxybrazan, which undergoes further reduction to trihydroxybrazan, and the latter, when distilled with zinc dust, yields brazan. The explanation of this process is obviously as follows: Trimethylbrazilone is first converted by the action of the hydriodic acid into ψ trimethylbrazilone, which loses

a para-quinone which had already been obtained by Kostanecki and Lloyd (*Ber.*, 1903, 36, 2194) from β -anhydrotrimethylbrazilone by oxidation with chromic acid.

During the course of our experiments on ψ -trimethylbrazilone, we investigated its behaviour with potassium hypobromite, and obtained a new series of derivatives, the examination of which has served to confirm our views as to the constitution of this substance.

When ψ -trimethylbrazilone is treated with potassium hypobromite in the cold, it yields a bromolactone, $C_{18}H_{15}O_6Br$, which, when digested with chloroform, readily loses hydrogen bromide with formation of a lactone, $C_{18}H_{14}O_6$. The bromolactone, $C_{18}H_{15}O_6Br$, is readily hydrolysed by alkalis, and the monobasic acid which is produced again readily yields a lactone, $C_{18}H_{16}O_7$. This latter substance contains a phenolic hydroxyl group, since it gives a violet coloration with ferric chloride, and is converted by methylation into a methyl ether, $C_{18}H_{15}O_7Me$, which is itself a lactone.

Important evidence bearing on the constitution of this methyl ether was obtained as the result of the observation that, when oxidised by permanganate, it suffers degradation with the formation of dimethylresorcylic acid and *m*-hemipinic acid.

This result seems to prove conclusively that the methyl ether, $C_{18}H_{15}O_7Me$, has the constitution :

and is the lactone of *tetramethoxybenzoincarboxylic acid*.

The acid, $C_{18}H_{18}O_8$, from which it was derived is therefore *hydroxy-trimethoxybenzoincarboxylic acid*,

water with formation of β -anhydrotrimethylbrazilone. At the same time the methoxy-groups are attacked with formation of the tetrahydroxybrazan of the formula

which, by the further action of the hydriodic acid and subsequently of zinc dust, is reduced to trihydroxybrazan and then to brazan :

But this acid is produced by the action of alkalis on the bromolactone, $C_{18}H_{15}O_6Br$, and as the latter substance has neither acid nor phenolic properties, it seems clear that its constitution must be represented by one of the formulæ:

It will be observed that the skeleton structure of this bromolactone is very similar to that of ψ -trimethylbrazilone, from which it is obtained by the action of hypobromite.

We have carefully considered the probable mechanism of the formation of the bromolactone from ψ -trimethylbrazilone and potassium hypobromite, and are of the opinion that the evidence is strongly in favour of the conclusion that formula (I) represents the constitution of the bromolactone, and we therefore propose the name *trimethoxy-coumaronoisocoumarin hydrobromide* for the substance.

The processes involved in the formation of this substance are probably of the following nature. ψ -Trimethylbrazilone (I) is, in the first

place, oxidised by the hypobromite with formation of the lactone (II). The lactone, on hydrolysis, yields the unsaturated acid, which reacts with the hypobromite with elimination of carbon dioxide and formation of the unsaturated bromo-derivative (III),

a process which is exactly similar to the formation of bromostyrene from cinnamic acid under the same conditions. The unsaturated bromo-derivative now unites with the elements of hypobromous acid, and the resulting dibromohydroxy-compound (IV) then loses water and hydrogen bromide and yields the bromolactone, $C_{18}H_{15}O_6Br$ (V).

It has already been mentioned that this bromolactone readily loses hydrogen bromide when it is boiled with chloroform, with formation of

a lactone, $C_{18}H_{14}O_6$, and there can be no doubt that this interesting substance has the constitution (VI) and is *trimethoxycoumaronoiso-*

coumarin. Experimental evidence in confirmation of this view is described and discussed on p. 402.

As far as we are able to judge, this series of investigations has produced evidence which has not only clearly demonstrated the constitutions of brazilin and hæmatoxylin, but has also afforded an explanation of each one of the remarkable series of decompositions which these substances undergo on treatment with reagents.

There are, however, two small exceptions to this which require discussion before this investigation is closed.

In Part VIII of this research (Trans., 1908, 93, 500) it was shown that the remarkable substance, nitrohydroxydihydrotrimethylbrazilone, $C_{16}H_{10}O_6N(MeO)_3$, which is produced when trimethylbrazilone is treated with nitric acid, has the constitution :

In an earlier paper (Part V, Trans., 1902, 81, 1053) the action of phenylhydrazine on this nitro-compound was described, and it was shown that during this process the molecule is decomposed with formation of *p*-methoxysalicylic acid and a substance of the formula $C_{24}H_{25}O_4N_5$. Similar experiments on the action of phenylhydrazine on the product of the action of nitric acid on tetramethylhæmatoxylone (nitrohydroxydihydrotetramethylhæmatoxylone) yielded the same substance, $C_{24}H_{25}O_4N_5$, and an acid which was not further examined, but which was doubtless dimethoxysalicylic acid.

Careful consideration of these curious decompositions has led us to the conclusion that the correct formula for this nitrogenous substance is $C_{28}H_{23}O_4N_5$, and not $C_{24}H_{25}O_4N_5$, and the new formula agrees well with the results of analysis. In attempting to explain the mechanism of the action of phenylhydrazine in these two cases, it will only be necessary to refer in detail to its action on nitrohydroxydihydro-

trimethylbrazilone. There can be little doubt that, in this decomposition, the molecule of the nitro-compound suffers scission in accordance with the scheme :

and that the latter compound then reacts with phenylhydrazine, yielding the condensation product :

a process which is very similar to the formation of glucosazone from fructose.

The other matter to which we wish to refer deals with the question of the methylation of α -anhydrotrimethylbrazilone.

Herzig (*Monatsh.*, 1902, 23, 178) heated trimethylbrazilone with potassium hydroxide and methyl iodide, and obtained two isomeric methyl derivatives of anhydrotrimethylbrazilone, namely, a sparingly soluble substance of melting point $163\text{--}165^\circ$ (α -tetramethyldehydrobrazilin), and a more readily soluble substance of melting point $130\text{--}135^\circ$ (γ -tetramethyldehydrobrazilin). We have twice repeated this experiment, and in both cases obtained considerable yields of the methyl ether of melting point $163\text{--}165^\circ$, and there can be no doubt that this is methyl α -anhydrotrimethylbrazilone,

On the other hand, although we used large quantities of material in both these experiments, we obtained no evidence of the existence of a methyl ether of melting point $130\text{--}135^\circ$. During the crystallisation of the product it was noticed that a small crop of crystals was sometimes obtained which melted roughly at 130° , but, on further crystallisation, the melting point rose to 165° . We are therefore of opinion that γ -tetramethyldehydrobrazilin does not exist.

EXPERIMENTAL.

Reactions which show the similarity in Properties between α - and β -Anhydrotrimethylbrazilones and Hæmatoxylohes and β - and α -Naphthol.

In the introduction (pp. 383, 386) it was stated that α -anhydro-trimethylbrazilone and α -anhydrotetramethylhæmatoxylohes have the properties of derivatives of β -naphthol with the α -position free, and that β -anhydrotrimethylbrazilone and β -anhydrotetramethylhæmatoxylohes have properties similar to derivatives of α -naphthol with the β -position free, and the constitutional formulæ given to these substances is in harmony with this view of their constitutions. The following qualitative comparison clearly brings out these points. The α -derivatives are soluble in dilute potassium hydroxide, and the β -derivatives are soluble even in cold sodium carbonate. They are all readily methylated by methyl sulphate and alkali under the same conditions as the corresponding naphthols. The azo-dyes obtained from the α -anhydro-derivatives have already been described (Trans., 1908, 93, 500) and shown to be similar to those obtained under the same conditions with β -naphthol, and we now find that the β -anhydro-derivatives also yield colour reactions with diazo-salts which correspond very closely with those exhibited by alkaline solutions of α -naphthol. The following table will illustrate this point :

Diazotised.	β -Anhydro-trimethylbrazilone.	β -Anhydrotetra-methylhæmatoxylohes.
Aniline	Deep crimson.....	Claret.
Sulphanilic acid	Crimson (blue shade)	Purplish-red.
α -Naphthylamine.....	Crimson (blue shade)	Purplish-red.
Benzidine	Purple.....	Purple.
<i>p</i> -Nitroaniline	Bluish-green	Bluish-green.
<i>m</i> -Nitroaniline	Crimson	Crimson.
Aminoazobenzene	Olive-green	Sage-green.

A very characteristic reaction shown by both α - and β -naphthol is that their solutions in potassium hydroxide acquire a Berlin-blue colour changing to green and finally to brown, when they are mixed with chloroform and heated at 40–50° (Lustgarten, *Monatsh.*, 1882, 3, 720). It is certainly remarkable that such complicated derivatives of the naphthols as the α - and β -anhydrotrimethylbrazilones and tetramethylhæmatoxylohes should not only show this reaction, but should reproduce almost exactly the same shades of colour. In carrying out the experiment, a few drops of chloroform were added to the solution of the anhydro-derivative in alcoholic potassium hydroxide,

and, on warming on the water-bath, the following behaviour was observed :

α -Anhydrotrimethylbrazilone	Berlin-blue changing to light green and then brown.
β -Anhydrotrimethylbrazilone	Bright green changing to brown.
α -Anhydrotetramethylhæmatoxylone.....	Prussian-blue changing to green and brownish-yellow.
β -Anhydrotetramethylhæmatoxylone.....	Intense Scheele-green changing to greenish-brown.

Di- α -Anhydrotrimethylbrazilone.

In order to prepare this substance, α -anhydrotrimethylbrazilone (5 grams) is dissolved in boiling methyl alcohol (200 c.c.) and digested with anhydrous ferric chloride (10 grams) on the water-bath for half an hour, when a green precipitate will have separated.

The whole is filtered hot, the precipitate washed with alcohol, and the pale green residue, which is very sparingly soluble in most organic solvents, crystallised from a large quantity of methyl ethyl ketone :

0.1219 gave 0.3138 CO_2 and 0.0495 H_2O . $\text{C} = 70.2$; $\text{H} = 4.5$.

$\text{C}_{38}\text{H}_{30}\text{O}_{10}$ requires $\text{C} = 70.6$; $\text{H} = 4.6$ per cent.

This interesting substance shrinks at 215° , and gradually melts with some decomposition to a green liquid, fusion being complete at 225° . When mixed with alcoholic sodium or potassium hydroxide, it yields sparingly soluble sodium or potassium salts ; it does not combine with diazonium salts, nor does it give any coloration with chloroform and potassium hydroxide, but sulphuric acid dissolves it with a yellowish-brown colour. In order to convert it into the derivative corresponding with β -naphthylene oxide, the substance was digested with phosphoryl chloride, the product decomposed by water, and the precipitate extracted repeatedly with dilute alcoholic potassium hydroxide. The greenish-grey residue resembles β -naphthylene oxide in a striking manner ; thus, for example, both substances dissolve in sulphuric acid, yielding a rose-red solution which, on warming, becomes successively red, violet, purple, and finally a beautiful indigo-blue.

Di- α -anhydrotrimethylbrazilone Diacetate.—This derivative is obtained when di- α -anhydrotrimethylbrazilone (2 grams) is boiled for ten minutes with acetic anhydride (20 c.c.) and anhydrous sodium acetate (3 grams). The product is poured into water, the crystalline precipitate collected, and crystallised first from methyl ethyl ketone and then from boiling acetic acid :

0.1236 gave 0.3117 CO_2 and 0.0532 H_2O . $\text{C} = 68.8$; $\text{H} = 4.8$.

$\text{C}_{42}\text{H}_{34}\text{O}_{12}$ requires $\text{C} = 69.0$; $\text{H} = 4.7$ per cent.

When this diacetate is slowly heated, a change is seen to occur, accompanied by slight shrinking, at about 170° — 175° , and there is no further change until the temperature reaches 278° , when the substance melts quite sharply. If the capillary tube containing the substance is plunged into sulphuric acid at 180° , the substance melts, but this is not the case with specimens which had previously been heated at 180° and allowed to cool. The diacetate exists evidently in two modifications, melting respectively at about 180° and at 278° .

The lower melting modification is always obtained when the substance is crystallised from acetic acid, and separates in four-sided plates, often united in the form of a cross. Its solution in methyl ethyl ketone exhibits a strong violet fluorescence.

Nitro- α -anhydrotrimethylbrazilone,

Considerable quantities of the acetyl derivative of this substance were prepared by dissolving acetyl- α -anhydrotrimethylbrazilone (Trans., 1902, 81, 1045), in quantities of 10 grams, in warm glacial acetic acid (150 c.c.), and, after cooling, adding nitric acid (10 c.c. of $D=1.42$) diluted with acetic acid (20 c.c.). The nitro-derivative crystallises almost immediately, and, after a few minutes, is collected and washed with alcohol, when a yield of 97 per cent. of that theoretically possible is obtained. For analysis, the substance was recrystallised from acetic acid :

0.1194 gave 0.2682 CO_2 and 0.0462 H_2O . $\text{C}=61.3$; $\text{H}=4.3$.

$\text{C}_{21}\text{H}_{17}\text{O}_8\text{N}$ requires $\text{C}=61.3$; $\text{H}=4.1$ per cent.

Nitroacetyl- α -anhydrotrimethylbrazilone is sparingly soluble in alcohol or cold glacial acetic acid, and separates from boiling acetic acid in small, brilliant yellow needles, which darken at 222° and melt at 235° with decomposition. It dissolves in sulphuric acid, yielding a purple solution, which becomes brown on dilution with water.

Nitro- α -anhydrotrimethylbrazilone may be obtained by the direct nitration of α -anhydrotrimethylbrazilone, but not so readily as by the hydrolysis of the acetyl derivative just described. The acetyl derivative is finely powdered and digested with a large excess of very dilute methyl-alcoholic potassium hydroxide for half an hour, the red solution is then filtered from any unchanged substance and undissolved potassium salt, and the filtrate acidified with acetic acid. The crys-

talline precipitate is collected, washed with alcohol, and dried at 100°; it is then pure :

0.1067 gave 0.2407 CO₂ and 0.0407 H₂O. C = 61.5 ; H = 4.2.

C₁₉H₁₅O₇N requires C = 61.8 ; H = 4.1 per cent.

Nitro-α-anhydrotrimethylbrazilone is very sparingly soluble even in hot glacial acetic acid, and is difficult to recrystallise.

It separates from a large quantity of boiling glacial acetic acid as a brick-red powder consisting of not very well defined microscopic prisms. It dissolves in alkalis with a yellowish-red, and in sulphuric acid with a reddish-purple, colour. When digested with acetic anhydride and sodium acetate, it is converted into the acetyl derivative described above.

Nitro-α-anhydrotrimethylbrazilone Methyl Ether.—This substance is readily obtained when nitric acid (3 c.c.) is added all at once to a cold solution of α-anhydrotrimethylbrazilone methyl ether (2.5 grams : see Herzig and Pollak, *Monatsh.*, 1902, 23, 177) in glacial acetic acid (25 c.c.). The yellow crystals, which soon separate, are collected, washed with alcohol, and crystallised from glacial acetic acid. The same substance is obtained when nitro-α-anhydrotrimethylbrazilone dissolved in boiling dilute methyl-alcoholic potassium hydroxide is treated with methyl sulphate until the red colour of the alkaline solution disappears :

0.1294 gave 4.4 c.c. N₂ at 10° and 751 mm. N = 4.0.

C₂₀H₁₇O₇N requires N = 3.7 per cent.

Nitro-α-anhydrotrimethylbrazilone methyl ether separates from acetic acid in bright yellow needles, melts at 226°, and dissolves in sulphuric acid, forming a reddish-violet solution.

Trimethoxy-α-brazaquinone,

This interesting new quinone has been obtained in a variety of different ways, of which the following may be particularly mentioned.

I. *By the Oxidation of Dihydroxytrimethoxy-α-braza*.—In carrying out this experiment, diacetoxytrimethoxybraza (p. 396 ; 3 grams) was dissolved in hot alcoholic potash (30 c.c. of 3 per cent.) and a current of air passed through the solution, when a flocculent precipitate

separated, which was green at first, but ultimately became brown. The precipitate was collected and crystallised from glacial acetic acid, from which the quinone separated as a brown, microcrystalline mass :

0.1105 gave 0.2726 CO_2 and 0.0437 H_2O . $\text{C} = 67.3$; $\text{H} = 4.4$.

$\text{C}_{19}\text{H}_{14}\text{O}_6$ requires $\text{C} = 67.5$; $\text{H} = 4.2$ per cent.

II. *By the Oxidation of Aminoacetyl- α -anhydrotrimethylbrazilone.*—Nitroacetyl- α -anhydrotrimethylbrazilone (p. 393 ; 5 grams) was suspended in boiling alcohol (500 c.c.) and reduced with zinc dust and hydrochloric acid on the water-bath until solution was complete. Water was then added, and the solution of the aminophenol oxidised by the addition of ferric chloride, chromic acid, or sodium nitrite, the latter appearing to give the best results. The well-cooled solution was mixed with sodium nitrite (2 grams), dissolved in water, and the brown precipitate, which rapidly separated, was collected, dried on porous porcelain, and crystallised from glacial acetic acid.

III. *By the Action of Potassium Hypobromite on α -Anhydrotrimethylbrazilone.*—In this experiment α -anhydrotrimethylbrazilone (2 grams) was dissolved in very dilute potassium hydroxide, mixed with powdered ice, and treated with an ice-cold solution of bromine (6 grams) in dilute potassium hydroxide. The brown precipitate of the quinone, which soon separated, was collected, and, after crystallisation from glacial acetic acid, was found to weigh 1.5 grams. The identity of the substances obtained in the above experiments was proved by careful comparison, and especially by the fact that they all yielded the same quinoxaline on treatment with 3:4-tolylenediamine, and were all converted into diacetoxytrimethoxy- α -brazan (p. 396) by treatment with zinc dust in the presence of acetic acid and acetic anhydride.

Trimethoxy- α -brazanquinone is very sparingly soluble in most solvents, and does not melt at 300° . It crystallises from much boiling acetic acid as a brown, microcrystalline powder, which consists of balls of needles. It dissolves in concentrated sulphuric acid with an intense crimson colour, and is precipitated unchanged on dilution with water.

Trimethoxy- α -brazotoluquinoxaline is obtained when the quinone (1 gram) is boiled with 3:4-tolylenediamine (1 gram), sodium acetate (1 gram), and glacial acetic acid (300 c.c.). As soon as the quinone has dissolved, the liquid is filtered and allowed to cool, when beautiful orange-brown, glistening needles separate. These are collected and recrystallised from glacial acetic acid :

0.1280 gave 0.3446 CO_2 and 0.0554 H_2O . $\text{C} = 73.4$; $\text{H} = 4.8$.

$\text{C}_{26}\text{H}_{20}\text{O}_4\text{N}_2$ requires $\text{C} = 73.6$; $\text{H} = 4.7$ per cent.

This quinoxaline melts at 257° without decomposition, and is moderately readily soluble in benzene, yielding a yellow solution which

exhibits an intense green fluorescence, but the solutions in alcohol or acetic acid do not fluoresce. It is coloured crimson by concentrated hydrochloric acid, and dissolves in sulphuric acid, yielding a magnificent royal-blue solution which, when diluted with water, gives a crimson solution and then a brown precipitate.

It is mentioned above that trimethoxy- α -brazanquinone is obtained in good yield from α -anhydrotrimethylbrazilone by oxidation with potassium hypobromite. When, however, chromic acid was employed as the oxidising agent, a different result was obtained.

α -Anhydrotrimethylbrazilone (7 grams) was dissolved in glacial acetic acid, and then chromic acid (4 grams), dissolved in a little water, gradually added, the solution being constantly stirred and carefully cooled.

After a quarter of an hour, the almost black precipitate was collected, dried on porous porcelain, and crystallised from a large quantity of boiling glacial acetic acid.

The deep green, microcrystalline mass yielded on analysis the following result:

0.1103 gave 0.2694 CO_2 and 0.0420 H_2O . $\text{C} = 66.6$; $\text{H} = 4.2$.

$\text{C}_{38}\text{H}_{50}\text{O}_{12}$ requires $\text{C} = 67.2$; $\text{H} = 4.4$ per cent.

Since this substance does not lose its green colour even after repeated crystallisation from acetic acid, it is probable that it is trimethoxy- α -brazanquinhydrone, a view which would be in agreement with the results of analysis.

Diacetoxytrimethoxy- α -brazan,

This interesting substance is obtained when trimethoxy- α -brazanquinone (5 grams) is boiled with acetic anhydride (20 c.c.), glacial acetic acid (50 c.c.), a trace of zinc chloride, and excess of zinc dust until the solution is colourless. The hot liquid is filtered into dilute sulphuric acid, the colourless, crystalline precipitate collected, and purified by repeated crystallisation from acetic acid:

0.1112 gave 0.2643 CO_2 and 0.0469 H_2O . $\text{C} = 64.8$; $\text{H} = 4.7$.

$\text{C}_{23}\text{H}_{20}\text{O}_8$ requires $\text{C} = 65.1$; $\text{H} = 4.7$ per cent.

Diacetoxytrimethoxy- α -brazan melts at 217° , and is sparingly soluble

Trimethoxy- β -brazanquinone,

This interesting substance was first prepared by Kostanecki and Lloyd (*Ber.*, 1903, **36**, 2194) by the oxidation of β -anhydrotrimethylbrazilone with chromic acid (compare p. 386). We have found that it may be obtained in a very good yield from nitroacetyl- β -anhydrotrimethylbrazilone by reduction, hydrolysis, and subsequent oxidation of the amino-derivative. Nitroacetyl- β -anhydrotrimethylbrazilone (1 gram) is dissolved in boiling alcohol and treated with zinc dust and hydrochloric acid until a colourless solution is obtained. After dilution with water, the liquid is filtered and mixed with a strong aqueous solution of sodium nitrite (1 gram), when an immediate voluminous, red precipitate separates; this is collected, washed with water, and crystallised from glacial acetic acid. The small, deep red threads obtained in this way melted at $261-262^\circ$, and were found by direct comparison to be identical with the trimethoxy- β -brazanquinone prepared by Kostanecki and Lloyd. This method of preparation is interesting, not only because it is exactly analogous to the formation of trimethoxy- α -brazanquinone from α -anhydrotrimethylbrazilone (p. 394), but also because it proves conclusively that the nitro-group in nitroacetyl- β -anhydrotrimethylbrazilone occupies the position assigned to it on p. 397.

That the quinone is a para- and not an ortho-quinone is confirmed by the fact that it does not yield a condensation product with *o*-tolyl-enediamine.

Nitroacetyl- α -anhydrotetramethylhaematoxylone,

In preparing this substance, acetyl- α -anhydrotetramethylhaematoxylone (10 grams: *Trans.*, 1902, **81**, 1062) was dissolved in glacial acetic acid (200 c.c.) and the well-cooled solution mixed with nitric acid (15 c.c. of $D=1.42$) diluted with glacial acetic acid (15 c.c.). In a short time, crystals commenced to separate, and, after two hours,

the precipitate was collected and a further quantity was obtained by diluting the filtrate with water. The mass was washed with alcohol and crystallised from acetic acid :

0.1270 gave 0.2784 CO₂ and 0.0489 H₂O. C = 59.8 ; H = 4.3.

C₂₂H₁₉O₉N requires C = 59.9 ; H = 4.3 per cent.

Nitroacetyl-α-anhydrotetramethylhaematoxylone separates from acetic acid in yellow needles, and melts, apparently without decomposition, at 215°. It is readily soluble in hot acetic acid or hot alcohol, but sparingly so in cold alcohol, and it dissolves in sulphuric acid, yielding an intense olive-green solution which, on dilution with water, changes to deep brown. It was mentioned on p. 393 that the solution of the corresponding brazilone derivative in sulphuric acid is purple, and it is remarkable that the introduction of a fourth methoxy-group should be sufficient to bring about so complete a change in colour.

Tetramethoxy-α-brazaquinone,

This interesting quinone was first obtained by methods similar to those described in the case of the corresponding trimethoxy-derivative (p. 394), but the most convenient method of preparation is probably the following. *Nitroacetyl-α-anhydrotetramethylhaematoxylone* (1 gram) is boiled in alcoholic solution with granulated zinc and hydrochloric acid until a colourless solution is obtained, and then for ten minutes longer. The hot solution is filtered, diluted with half its volume of water, and then sodium nitrite (1 gram), dissolved in water, is added, when a brownish-black precipitate separates. This is collected, washed with cold alcohol, and crystallised from much boiling alcohol :

0.1109 gave 0.2627 CO₂ and 0.0447 H₂O. C = 64.6 ; H = 4.4.

C₂₀H₁₆O₇ requires C = 65.2 ; H = 4.3 per cent.

Tetramethoxy-α-brazaquinone separates from alcohol in dark brown, microscopic prisms, and is very sparingly soluble in most solvents, but moderately readily so in hot acetic acid. It dissolves in sulphuric acid, yielding a deep violet solution. When it is boiled with acetic acid, acetic anhydride, and zinc dust (compare p. 396), it is reduced and converted into a colourless acetyl derivative, which was not further examined.

Tetramethoxy-α-brazotoluquinoxaline.—This derivative is obtained

when the quinone (1 gram) is digested for ten minutes with acetic acid (50 c.c.), 3:4-tolylenediamine hydrochloride (1 gram), and the same quantity of sodium acetate. The dark solution is mixed with water, the precipitate collected, washed with alcohol, and crystallised from a large quantity of toluene, from which it separates as a coffee-coloured powder consisting of microscopic needles :

0.1248 gave 0.3247 CO_2 and 0.0576 H_2O . $\text{C}=71.0$; $\text{H}=5.1$.

$\text{C}_{27}\text{H}_{22}\text{O}_5\text{N}_2$ requires $\text{C}=71.3$; $\text{H}=4.8$ per cent.

This quinoxaline shrinks at $205-210^\circ$, and is very similar in properties to trimethoxy- α -brazotoluquinoxaline described on p. 395. It dissolves in sulphuric acid with a deep indigo-blue colour, and the solution becomes pink on dilution with water. The solution of the substance in boiling toluene is brown, and, when diluted, exhibits an intense ivy-green fluorescence, and this property is so marked that, although the quinoxaline is almost insoluble in cold toluene, when it is shaken with the solvent and filtered, the almost colourless filtrate still shows a strong fluorescence.

Trimethoxycoumaronoisocoumarin Hydrobromide,

This substance is produced by the action of potassium hypobromite on ψ -trimethylbrazilone (Trans., 1908, 93, 501), the best conditions of preparation being apparently the following.

ψ -Trimethylbrazilone (20 grams) is dissolved in potassium hydroxide (4 grams) and water (150 c.c.), and the well cooled solution poured into potassium hypobromite, made by dissolving bromine (10 c.c.) in potassium hydroxide (24 grams), water (200 c.c.), and powdered ice (200 grams). In a few seconds the new substance commences to separate, the whole liquid soon becomes gelatinous, and, after standing for four to five hours, the gelatinous mass will have become crystalline.

The almost colourless, very finely-divided precipitate is collected by the aid of the pump, and is best washed by rubbing in a mortar with water and again transferring to the pump, and, after repeating the operation several times, the mass is left in contact with porous porcelain until dry. Finally, the substance is dissolved in cold chloroform and the filtered solution precipitated by light petroleum :

0.1230 gave 0.2404 CO_2 and 0.0446 H_2O . $\text{C} = 53.3$; $\text{H} = 4.0$.

0.1460 „ 0.0634 AgBr . $\text{Br} = 19.2$.

$\text{C}_{18}\text{H}_{15}\text{O}_6\text{Br}$ requires $\text{C} = 53.1$; $\text{H} = 3.7$; $\text{Br} = 19.6$ per cent.

Trimethoxycoumaronoisocoumarin hydrobromide separates from chloroform on addition of light petroleum as a precipitate which is very like flour, and under the microscope is seen to consist of prisms rather irregular in shape. It darkens somewhat at 95° , and melts at 121° to a green liquid which decomposes vigorously at about 130° ; it is rather sparingly soluble in the usual organic solvents in the cold, and is unstable, since it decomposes when it is boiled with acetic acid or chloroform (see below). It dissolves in sulphuric acid with elimination of hydrogen bromide, and the pale yellow solution gradually becomes red and develops a green fluorescence.

Trimethoxycoumaronoisocoumarin,

On one occasion when the action of potassium hypobromite on ψ -trimethylbrazilone was carried out apparently under the same conditions as usual (see the last section), the reaction took an abnormal course, and the product consisted entirely of yellow needles, which crystallised well from methyl alcohol and melted at 152° .

We have never been able to repeat this experiment, but we have prepared the same substance by the removal of hydrogen bromide from the hydrobromide described in the last section. This may be accomplished in many ways, but the most satisfactory is to boil the dry substance with chloroform. The hydrobromide, in quantities not larger than 0.5 gram, is digested in a test-tube with chloroform for a few minutes, and the bulk of the chloroform is then slowly distilled off, when, at a certain point in the concentration, the liquid becomes green and the solid passes into solution. As soon as the green colour is observed, the flame is removed, and the vigorous action which sets in with evolution of quantities of hydrogen bromide allowed to proceed without further heating until the green colour gives place to yellow. The product is mixed with 4 to 5 volumes of methyl alcohol, and the yellow, crystalline precipitate which separates is collected and recrystallised from methyl alcohol. Of the following analyses, the substance used in I was that

which had been obtained by the direct action of potassium hypobromite on ψ -trimethylbrazilone in the experiment mentioned above. Specimens II and III were prepared by the chloroform process:

- I. 0.1096 gave 0.2661 CO_2 and 0.0461 H_2O . C = 66.2; H = 4.6.
 II. 0.1378 „ 0.3360 CO_2 „ 0.0595 H_2O . C = 66.5; H = 4.3.
 III. 0.1226 „ 0.2965 CO_2 „ 0.0496 H_2O . C = 65.9; H = 4.5.
 $\text{C}_{18}\text{H}_{14}\text{O}_6$ requires C = 66.3; H = 4.3 per cent.

All the specimens of this substance were pale yellow, and it was not found possible to remove the colour by repeated recrystallisation from methyl alcohol or other solvents. When, however, the substance was digested with weak alcoholic potash for five minutes on the water-bath, a nearly colourless solution was obtained, which remained clear after diluting with water and removal of the methyl alcohol by evaporation, and, indeed, when the solution was saturated with carbon dioxide nothing separated. Addition of hydrochloric acid precipitated a white, caseous mass, and this crystallised from methyl alcohol in beautiful needles which were now quite colourless, but in other respects the substance proved to be identical with that described above, a fact which was controlled by analysis:

0.1162 gave 0.2824 CO_2 and 0.0449 H_2O . C = 66.3; H = 4.3.

Trimethoxycoumaronoisocoumarin melts at 152° , and dissolves rather readily in chloroform or acetic acid, but sparingly so in cold methyl or ethyl alcohols. It is not very soluble in boiling ethyl alcohol, and separates, on cooling, in small, colourless prisms. It dissolves in sulphuric acid, yielding a salmon-pink solution, which possesses a very intense, ivy-green fluorescence; addition of a trace of nitrite changes the colour to purple, and the fluorescence is destroyed.

That the substance is a lactone is shown by its behaviour with alcoholic potash, which has been already described. The formation of trimethoxycoumaronoisocoumarin by the elimination of hydrogen bromide from its hydrobromide may also be brought about by boiling with acetic acid or diethylaniline, but the product obtained in these cases is not so readily purified as when prepared by the chloroform method described above.

The Action of Bromine on Trimethoxycoumaronoisocoumarin.

In studying this action a dilute solution of bromine in chloroform was gradually added to the isocoumarin until an excess was present. The bromine was slowly absorbed with elimination of hydrogen bromide, and a quantitative experiment showed that 0.71 gram of the substance reacted with 0.39 gram of bromine, or in approximately molecular proportions. As soon as the reaction was finished, the

chloroform was evaporated in a vacuum desiccator, and the solid residue several times crystallised from alcohol. The air-dried substance yielded the following results on analysis :

0.1245 gave 0.2428 CO_2 and 0.0425 H_2O . $\text{C} = 53.2$; $\text{H} = 3.8$.

0.1300 „ 0.2547 CO_2 „ 0.0484 H_2O . $\text{C} = 53.4$; $\text{H} = 4.1$.

0.1207 „ 0.0552 AgBr . $\text{Br} = 19.4$.

$\text{C}_{18}\text{H}_{13}\text{O}_6\text{Br}$ requires $\text{C} = 53.3$; $\text{H} = 3.2$; $\text{Br} = 19.7$ per cent.

Monobromotrimethoxycoumaronoisocoumarin separates from alcohol as a satiny mass of yellow, prismatic plates ; it melts at 206° , and decomposes at 208° with formation of a red liquid. When it is digested with alcoholic potassium hydroxide, the lactone ring is hydrolysed, but the product obtained on acidifying still contains bromine, a proof that hydrogen in an aromatic nucleus had been substituted.

On the other hand, there is strong evidence that the reaction proceeds to some extent in another direction, bromine being added to the double linking. The bromine content of the crude product which remains after evaporating the chloroform is greater than that required for substitution, and yet too low for that required for the dibromide :

0.1114 gave 0.0643 AgBr . $\text{Br} = 24.5$.

$\text{C}_{18}\text{H}_{13}\text{O}_6\text{Br}$ requires $\text{Br} = 19.7$ per cent.

$\text{C}_{18}\text{H}_{14}\text{O}_6\text{Br}_2$ „ „ $\text{Br} = 32.8$ „ „

The presence of the dibromo-additive product seems to be borne out by the results of the following interesting experiment.

The crude product of bromination (2 grams) was dissolved in alcoholic potassium hydroxide, heated on the water-bath for half an hour, the solution diluted, evaporated until free from alcohol, cooled, and mixed with 10 c.c. of 30 per cent. hydrogen peroxide. After forty-eight hours, the solution was heated for one hour on the water-bath, acidified, filtered, saturated with ammonium sulphate, and repeatedly extracted with ether. The ethereal solution was dried, evaporated, and the solid residue, which crystallised from hot water in colourless needles, melted at 152° , and gave a violet coloration with ferric chloride, was easily recognised as *p*-methoxy-salicylic acid.

The mother liquors from these crystals yielded, on concentration, an acid which was shown, by conversion into the characteristic silver salt, to be *m*-hemipinic acid.

This interesting degradation is readily explained on the assumption that the product of the bromination of trimethoxycoumaronoisocoumarin contains the dibromo-additive compound (I), which is

hydrolysed by potassium hydroxide with formation of the hydroxy-trimethoxybenzilcarboxylic acid of the formula (II).

This acid is then oxidised by hydrogen peroxide with formation of *p*-methoxysalicylic and *m*-hemipinic acids (compare Proc., 1907, **23**, 166).

Hydroxytrimethoxybenzoic acid and its Lactone,

The hydroxy-acid is readily obtained by the action of alcoholic potash on trimethoxycoumaronoisocoumarin hydrobromide.

The hydrobromide (5 grams) is suspended in alcohol (100 c.c.) and warmed on the water-bath with a solution of potassium hydroxide (5 grams) in a small quantity of water, when decomposition rapidly takes place. As soon as solution is complete, the product is diluted with water, cooled, and acidified with dilute acetic acid; the gelatinous precipitate is then collected, dried on porous porcelain, and crystallised, first from methyl ethyl ketone and then from ethyl acetate :

0.1164 gave 0.2557 CO_2 and 0.0554 H_2O . $\text{C} = 59.9$; $\text{H} = 5.3$.

$\text{C}_{18}\text{H}_{18}\text{O}_8$ requires $\text{C} = 59.7$; $\text{H} = 5.0$ per cent.

Hydroxytrimethoxybenzoic acid melts at 195° , and is sparingly soluble even in boiling alcohol, but more readily so in ethyl acetate, from which it separates in clusters of pale yellow needles.

It is readily soluble in sodium carbonate, and dissolves in sulphuric acid, yielding a yellow solution which becomes redder on standing and develops an intense green fluorescence. Its alcoholic solution gives a brownish-violet coloration on the addition of ferric chloride.

The Lactone.—This substance was first obtained in small quantity from the product of the action of alkalis on trimethoxycoumaronoisocoumarin hydrobromide by extraction with ether, and, on concentrating the ethereal solution, it separated as a crystalline crust (analysis I). It is best prepared from the hydroxycarboxylic acid (1 gram) by digesting with glacial acetic acid (10 c.c.) and hydrochloric acid (1 c.c.). The precipitate, obtained on dilution with water, is collected and crystallised from ethyl alcohol (analysis II) :

I. 0.1227 gave 0.2795 CO₂ and 0.0525 H₂O. C = 62.2; H = 4.8.

II. 0.1131 ,, 0.2599 CO₂ ,, 0.0498 H₂O. C = 62.7; H = 4.9.

C₁₈H₁₆O₇ requires C = 62.8; H = 4.6 per cent.

The lactone of *hydroxytrimethoxybenzoincarboxylic acid* melts at 181°, and, although sparingly soluble in alcohol, is more readily so than the hydroxy-acid. It dissolves readily in potassium hydroxide, but is insoluble in sodium carbonate. Since the alcoholic solution gives a reddish-violet coloration with ferric chloride, it is clear that the phenolic hydroxyl has not taken part in the lactone formation, and it is therefore evident that the lactone contains the grouping :

Oxidation of Hydroxytrimethoxybenzoincarboxylic Acid.—When this acid is heated with excess of nitric acid (D = 1.17) on the water-bath for one hour, vigorous oxidation occurs, and, on dilution with water, a sticky, yellow oil is obtained, which gives the blood-red colour with ferric chloride characteristic of nitromethoxysalicylic acid, but from which nothing crystalline could be obtained. The clear liquid from this yellow oil was extracted with ether, and yielded, on evaporation, a crystalline residue, which was recognised, by conversion into the characteristic silver salt and ethylimide (m. p. 230°), as *m*-hemipinic acid.

The Lactone of Tetramethoxybenzoincarboxylic Acid,

In preparing this substance, the lactone of hydroxytrimethoxybenzoincarboxylic acid (1 gram) is dissolved in the least possible quantity of methyl alcohol, mixed with methyl sulphate (10 grams), and the solution kept distinctly alkaline by the addition, from time to time, of small quantities of 40 per cent. aqueous potassium hydroxide. The vigorous action is not checked, and when the solution remains alkaline, it is diluted with water and acidified with hydrochloric acid. The chalky precipitate is collected, and crystallised first from alcohol and then from methyl ethyl ketone containing a small quantity of light petroleum :

0.1012 gave 0.2369 CO₂ and 0.0481 H₂O. C = 63.8; H = 5.3.

C₁₉H₁₈O₇ requires C = 63.7; H = 5.0 per cent.

The lactone of *tetramethoxybenzoincarboxylic acid* melts at 200°, and is moderately soluble in methyl or ethyl alcohols, acetic acid, or acetone, but almost insoluble in light petroleum. The alcoholic solution gives no coloration with ferric chloride. It dissolves in

sulphuric acid, yielding a purple solution, which soon becomes carmine-red, and develops a deep green fluorescence. On long standing, the solution resembles in colour and fluorescence that of a solution of hydroxytrimethoxybenzoic acid in sulphuric acid. The lactone is insoluble in sodium carbonate and in dilute potassium hydroxide, but it dissolves in alcoholic potassium hydroxide, and the solution remains clear on dilution with water. If the alcohol is removed by evaporation and hydrochloric acid added to the well-cooled solution, a white, amorphous substance is precipitated, which is evidently the free hydroxy-acid, since it is soluble in sodium carbonate. In a short time, however, lactone formation takes place, and the precipitate becomes insoluble.

Oxidation of Tetramethoxybenzoic acid.—In carrying out this oxidation, the pure lactone (15 grams) was dissolved in alcoholic potash, the solution diluted, evaporated until free from alcohol, nearly neutralised with hydrochloric acid, mixed with powdered ice, and then cold saturated permanganate added until the colour remained permanent.

After removing the slight excess of permanganate by sulphurous acid, the product was heated on the water-bath, filtered, and the yellow solution evaporated to a small bulk, acidified, and extracted several times with ether. The ethereal solution was dried over anhydrous sodium sulphate, evaporated, and the semi-solid residue dissolved in hot water, when, on standing, a crystalline acid separated which melted at 107° . That this acid was dimethyl- β -resorcylic acid,

was proved by its properties, and especially by the fact that, when mixed with a specimen of this acid which had been obtained by the methylation of β -resorcylic acid, there was no alteration in melting point. The filtrate from the dimethyl- β -resorcylic acid was concentrated and allowed to stand, when large, prismatic crystals separated, which melted at 178° and were proved to consist of *m*-hemipinic acid by conversion into the characteristic silver salt and ethylimide (m. p. 230°).

The Action of Potassium Hypobromite on ψ -Tetramethylhaematoxylone.

In studying this decomposition, ψ -tetramethylhaematoxylone (5 grams) was dissolved in dilute potassium hydroxide and treated with a solution of bromine (3 c.c.) in dilute ice-cold potassium hydroxide, when a white precipitate soon separated, which, in appearance, closely resembled the substance obtained in the corresponding experiment with ψ -trimethylbrazilone (p. 401).

After five hours, the precipitate was collected, washed with water and alcohol, and left in contact with porous porcelain. The dry residue was extracted with boiling chloroform, and the extract mixed with alcohol, when a pink substance separated, which consisted of microscopic prisms or needles. After recrystallisation in the same manner, the substance was almost colourless :

0.1180 gave 0.2153 CO_2 and 0.0441 H_2O . $\text{C} = 52.1$; $\text{H} = 4.2$.

0.0985 „ 0.0412 AgBr . $\text{Br} = 17.8$.

$\text{C}_{19}\text{H}_{17}\text{O}_7\text{Br}$ requires $\text{C} = 52.2$; $\text{H} = 3.9$; $\text{Br} = 18.3$ per cent.

These analytical results indicate that the substance obtained in this matter is *tetramethoxycoumaronoisocoumarin hydrobromide*,

It melts at 158° with decomposition, and, in some of its properties, differs in a rather striking manner from the corresponding trimethoxy-derivative (p. 401). Thus, for example, whilst the latter is very readily decomposed by boiling with chloroform or acetic acid with elimination of hydrogen bromide, the tetramethoxy-derivative appears to be stable towards these reagents, and is even not immediately decomposed by diethylaniline. When it is digested with potassium hydroxide, it is readily hydrolysed, with formation of an acid, free from bromine, which in alcoholic solution gives a violet coloration with ferric chloride, and in appearance and other properties resembles hydroxytrimethoxybenzoic acid (p. 404).

The solution of the acid in potassium hydroxide was left in the cold with excess of 30 per cent. hydrogen peroxide for two days, and, after heating on the water-bath for an hour, acidified and repeatedly extracted with ether. The solid residue which remained after distilling off the ether consisted of two acids, one readily, and the other sparingly, soluble in water. The more soluble acid was recognised as *m*-hemipinic acid, and the less soluble acid, which gave an intense violet coloration with ferric chloride, was probably dimethoxysalicylic acid.

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