CLVII.—*The Constituents of Commercial Chrysarobin.*

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CHRYSAROBIN is a substance obtained from Araroba or Goa powder by extracting with certain solvents, for example, chloroform, evaporating to dryness, and powdering. It was first examined in 1875 by Attfield (*Pharm. J.* 1875, [iii], 5, 721), who found the chief constituent to be chrysophanic acid, $C_{15}H_{10}O_4$, identical with that previously obtained from rhubarb by Schössberger and Döpping (*Annalen*, 1844, 50, 213). In 1878, Liebermann and Seidler (*Ber.*, 11, 1603) showed that chrysarobin was not identical with chrysophanic acid, but contained a distinct substance, chrysarobin, $C_{30}H_{26}O_7$, together with a varying amount of chrysophanic acid into which it was converted by oxidation. The formula assigned to chrysarobin was deduced from analyses of the

recrystallised substance, which agreed fairly well with the formula proposed, but no determination of the molecular weight was made. A crystalline acetyl compound was obtained which, however, on analysis gave numbers differing from those required for the formula $C_{30}H_{22}O_7(C_2H_3O)_4$ (Found C=67.5; required C=68.5 per cent.). The subject was not again referred to for many years, and in the meantime the product has been sold indiscriminately as chrysarobin or chrysophanic acid.

In 1899, Hesse (*Annalen*, 309, 32) examined chrysarobin and obtained results differing from those recorded by previous investigators. He showed that crude chrysarobin contained no chrysophanic acid, but was a mixture of two parts of chrysarobin, $C_{15}H_{12}O_3$, with one of its methyl ether. He was, however, unable to obtain chrysarobin free from its methyl ether, and arrived at this conclusion from indirect evidence. Eight specimens, varying in melting point from 152° to 174° and purified by different means, were analysed, but all yielded methyl iodide by Zeisel's method, thus showing the presence of a methylated constituent. When the mixture was treated with hydrochloric or hydriodic acid, chrysophanohydroanthrone was obtained which was considered by Hesse to be isomeric with chrysarobin. On acetylation, however, the reverse change takes place, chrysophanohydroanthrone being converted into chrysarobin, since both yield the same triacetyl-chrysarobin. Chrysophanohydroanthrone and chrysarobin are both readily oxidised to chrysophanic acid, but if the impure chrysarobin is used a mixture of chrysophanic acid and its methyl ether results. Hesse thus regarded chrysarobin as the anthranole of chrysophanic acid.

Before stating the results of the present investigation, we desire to point out that some of Hesse's deductions are not in accordance with his observations, and further that simpler explanations than his can be given which are more in accordance with the facts.

In the first place, the analyses of the different specimens of chrysarobin do *not* agree with the assumption that they consist of a mixture of chrysarobin and its methyl ether. If this were so, the percentages of carbon and hydrogen found should lie *between* those required for the two substances, whereas in all cases they are *less* than that required for either substance :

$C_{15}H_{12}O_3$ requires C=75.0; H=5.0 per cent.

$C_{15}H_{11}O_3 \cdot CH_3$ requires C=75.6; H=5.5 per cent.

Found C=74.0 to 75.0; H=5.0 to 5.3 per cent.

It therefore follows that the methylated constituent must contain less than 75.0 per cent. of carbon.

Secondly, chrysarobin is assumed by Hesse to be isomeric and not

identical with chrysophanoanthrone (obtained by Liebermann by the reduction of chrysophanic acid). Yet both behave similarly to certain reagents and yield the same triacetylchrysarobin on complete acetylation. Their α -acetyl compounds showed similar properties although of slightly different melting points, 238° and 216° , but the latter contained some of the methylated constituent and was thus probably impure.

Furthermore, by the action of hydrochloric acid on the mixture, chrysophanoanthrone was obtained, and Hesse assumed that in this reaction the anthranole was converted into the isomeric hydroanthrone. In order, however, to explain the formation of triacetylchrysarobin from chrysophanoanthrone, it is necessary to assume that the reverse change, that is, conversion of the hydroanthrone to the anthranole takes place under the influence of acetic anhydride. These difficulties are removed by the simpler explanation that chrysophanoanthrone and chrysarobin are identical, and are the anthranole of chrysophanic acid. It is almost certain that the acetyl derivative of chrysophanoanthrone (m. p. $230-231^{\circ}$), described by Liebermann (*Ber.*, 1881, 21, 437), was triacetylchrysarobin, and had not the complex molecular composition assigned to it. Liebermann himself thought he had obtained this substance from natural chrysarobin (*Annalen*, 1882, 212, 41).

In view of the incomplete state of our knowledge of chrysarobin, and especially of the methylated constituent, we have made a thorough investigation of the subject in order to elucidate these points. After a very tedious and difficult process of separation, we have isolated from commercial chrysarobin the following substances:

Chrysarobin, $C_{15}H_{12}O_3$, m. p. 204° .

Dichrysarobin,* $C_{30}H_{24}O_7$, no sharp melting point.

Dichrysarobin methyl ether,* $C_{30}H_{23}O_7 \cdot CH_3$, m. p. 160° .

A substance, $C_{17}H_{14}O_4$, m. p. 181° .

Despite a very careful search, we have been unable to isolate any other definite substance, although a varying amount of amorphous product was always obtained.

Chrysarobin is shown to be identical with Liebermann and Seidler's chrysophanoanthrone, and since it yields chrysophanic acid on oxidation it must be regarded as the anthranole of this substance.

Dichrysarobin corresponds to Liebermann and Seidler's chrysarobin, but occurs only in very small amount in commercial chrysarobin,

* Although this substance does not correspond in composition with a polymeride of chrysarobin, we propose to retain for it the name "dichrysarobin" given by Hesse to a substance which he regarded as the polymeride, but which, as we show in this paper, had the composition now assigned to it.

which consists mainly of chrysarobin and dichrysarobin methyl ether.

Dichrysarobin is very different in its physical properties from chrysarobin, but as it yields the same oxidation and reduction products it must be closely allied to it. We therefore suggest for it the following constitutional formula, which differs but slightly from that first proposed by Liebermann and Seidler for chrysarobin.

This formula best explains the reactions of the substance and its relationship to chrysophanic acid and chrysarobin, but further experiments are needed to establish it definitely.

The action of acetic anhydride and of hydriodic acid on these substances has been studied, and the opportunity taken to prepare pure chrysophanic acid and its acetyl derivative. Several melting points have previously been given for this acid, and Hesse has shown that the acid as previously described is mixed with a varying quantity of a methylated constituent, which has not been isolated, but was supposed to be the methyl ether of chrysophanic acid.

The constants previously given have therefore been those for impure substances. Preliminary experiments on this point indicate that the methylated constituent is not the methyl ether of chrysophanic acid but that of dichrysarobin. In the cases both of crude chrysophanic acid and of chrysarobin, it was found easier to separate the acetyl compound than the original substance.

Both chrysarobin and dichrysarobin yield β -methylantracene on distillation with zinc dust.

EXPERIMENTAL.

This was prepared directly from the commercial chrysarobin by first extracting it with light petroleum, distilling the extract, and recrystallising the residue repeatedly from a large volume of hot ethyl acetate. By this means, after a very tedious fractional recrystallisation, it was obtained in beautiful, lemon-yellow scales melting at 202° (corr.), and further recrystallisation from different solvents did not alter the melting point. It was insoluble in aqueous sodium carbonate, but dissolved in caustic alkalis, forming a yellow solution which, however, rapidly absorbed oxygen from the air and became red. It gave a yellow colour with strong sulphuric acid, and its alcoholic solu-

tion became brown on the addition of ferric chloride. It was sparingly soluble in cold benzene, acetone, alcohol, glacial acetic acid, ethyl acetate, or light petroleum, but fairly soluble in these solvents when hot. When treated with hydriodic acid, no methyl iodide was formed. On analysis:

0.1156 gave 0.316 CO_2 and 0.0524 H_2O . $\text{C} = 74.6$; $\text{H} = 5.0$.

$\text{C}_{15}\text{H}_{12}\text{O}_3$ requires $\text{C} = 75.0$; $\text{H} = 5.0$ per cent.

When boiled with twice its weight of acetic anhydride for four hours, a product was obtained which melted at $191\text{--}192^\circ$, but by fractional crystallisation from glacial acetic acid was separated into two substances melting at 193° and $236\text{--}237^\circ$ respectively.

The substance melting at 193° furnished, on analysis, the following result:

0.0482 gave 0.124 CO_2 and 0.022 H_2O . $\text{C} = 70.1$; $\text{H} = 5.0$.

$\text{C}_{19}\text{H}_{16}\text{O}_5$ requires $\text{C} = 70.4$; $\text{H} = 4.9$ per cent.

It was therefore diacetylchrysarobin, $\text{C}_{15}\text{H}_{10}\text{O}_3(\text{C}_2\text{H}_3\text{O})_2$, and the other substance was the triacetyl compound.

When acetylated with acetic anhydride and sodium acetate, it yielded a triacetyl compound, $\text{C}_{15}\text{H}_9\text{O}_3(\text{C}_2\text{H}_3\text{O})_3$, crystallising from glacial acetic acid in hard, yellow cubes melting at 238° . This was insoluble in water and very sparingly soluble in cold or hot alcohol, but fairly soluble in hot glacial acetic acid. The alcoholic solution had a bluish fluorescence. On analysis:

0.1254 gave 0.317 CO_2 and 0.0566 H_2O . $\text{C} = 68.9$; $\text{H} = 5.0$.

$\text{C}_{21}\text{H}_{18}\text{O}_6$ requires $\text{C} = 68.9$; $\text{H} = 4.9$ per cent.

Chrysarobin (or the chrysophanohydroanthrone of Hesse) was also easily prepared directly from the crude petroleum extract of commercial chrysarobin in the following manner. The residue, after removal of the petroleum by distillation, was heated with four to five times its weight of hydriodic acid of sp. gr. 1.7 for two hours at $130\text{--}140^\circ$ and the mixture then poured into a large volume of water. The precipitate was dried and extracted with hot benzene in a Soxhlet apparatus, the benzene solution distilled, and the residue crystallised from hot ethyl acetate until of melting point 204° . On analysis:

0.1934 gave 0.5306 CO_2 and 0.0864 H_2O . $\text{C} = 74.8$; $\text{H} = 5.0$.

0.394 raised the b. p. of 19.1 benzene 0.21° . Mol. wt. = 262.

$\text{C}_{15}\text{H}_{12}\text{O}_3$ requires $\text{C} = 75.0$; $\text{H} = 5.0$ per cent. Mol. wt. = 240.

On acetylation with acetic anhydride or with sodium acetate and acetic anhydride, the same results were obtained as just described in connection with pure chrysarobin.

Chrysarobin, heated with an excess of hydriodic acid of sp. gr. 1.9 for one hour at 120° was recovered unchanged, as proved by the melting point 203—204°, and the analysis of the resulting product:

0.1268 gave 0.349 CO₂ and 0.06 H₂O C = 75.0; H = 5.2.

C₁₅H₁₂O₃ requires C = 75.0; H = 5.0 per cent.

These experiments prove that the chrysarobin originally present in commercial chrysarobin and the chrysophanohydroanthrone obtained from it by the action of hydriodic acid are not isomeric, as stated by Hesse, but identical.

When chrysarobin was oxidised in alkaline solution, chrysophanic acid was formed, as stated by Liebermann and Seidler and confirmed by Hesse. When distilled with zinc dust, a yellowish sublimate was obtained which, after recrystallisation from alcohol; formed yellowish plates melting at 199—200°. On analysis:

0.0592 gave 0.2038 CO₂ and 0.0332 H₂O. C = 93.9; H = 6.3.

C₁₅H₁₂ requires C = 93.7; H = 6.3 per cent.

This substance was therefore a methylantracene, probably the β-modification.

From these reactions and the fact that chrysarobin yields a triacetyl compound, it is clear that it must be regarded as the anthranole of chrysophanic acid. The anthranole formula for chrysarobin as proposed by Hesse is thus confirmed.

Dichrysarobin, C₃₀H₂₄O₇.

This substance is readily obtained from the crude petroleum extract of commercial chrysarobin as follows: the extract is heated with four or five times its weight of hydriodic acid of sp. gr. 1.7 for two hours at 130—140° in a reflux apparatus, and the mixture poured into water and filtered. The precipitate is washed with water, and then dried and extracted with hot benzene in a Soxhlet apparatus to remove the chrysarobin.

The residue insoluble in benzene is recrystallised from hot ethyl acetate or glacial acetic acid several times. It is thus obtained in beautiful, orange tabular crystals, which decompose at about 250° but have no sharp melting point. It is soluble in ethyl acetate or glacial acetic acid, but insoluble in benzene (distinction from chrysarobin), and appears to be more readily oxidised in alkaline solution than chrysarobin. It gives a yellow colour with sulphuric acid. As the purity of the crystals could not be determined by the melting point, three different specimens crystallised from various solvents were analysed:

- I. 0.1364 gave 0.363 CO_2 and 0.0594 H_2O . $\text{C} = 72.6$; $\text{H} = 4.8$.
 II. 0.1356 „ 0.3592 CO_2 „ 0.0600 H_2O . $\text{C} = 72.2$; $\text{H} = 4.8$.
 III. 0.1194 „ 0.316 CO_2 „ 0.0520 H_2O . $\text{C} = 72.2$; $\text{H} = 4.9$.
 $\text{C}_{30}\text{H}_{24}\text{O}_7$ requires $\text{C} = 72.6$; $\text{H} = 4.8$ per cent.

Owing to the sparing solubility of this substance in solvents, the molecular weight could not be determined. By using the acetyl compound of methyldichrysarobin, however, this constant was determined and the above formula thus confirmed.

The *acetyl* compound, $\text{C}_{30}\text{H}_{18}\text{O}_7(\text{C}_2\text{H}_3\text{O})_6$, was prepared by boiling dichrysarobin with considerable excess of acetic anhydride for three to four hours, cooling, and then adding alcohol. The acetyl compound separated in yellow cubes, which were recrystallised from acetic acid and alcohol, and thus obtained of constant melting point $179-181^\circ$. On analysis:

- 0.1044 gave 0.2568 CO_2 and 0.0456 H_2O . $\text{C} = 67.1$; $\text{H} = 4.8$.
 $\text{C}_{42}\text{H}_{36}\text{O}_{13}$ requires $\text{C} = 67.4$; $\text{H} = 4.8$ per cent.

Acetylation with acetic anhydride and sodium acetate yielded a product which could not be crystallised. Hexa-acetyldichrysarobin differs from the acetyl derivatives of chrysarobin in being much more soluble in organic solvents, such as alcohol, and in not giving fluorescent solutions.

Further treatment with hydriodic acid had no action on dichrysarobin, as after heating with the acid at 130° in a sealed tube the substance was recovered unchanged.

By oxidation with air in alkaline solution, chrysophanic acid was obtained, identified by its melting point, 190° , and its characteristic colour reaction with sulphuric acid. Although the oxidation proceeded more rapidly than in the case of chrysarobin, the yield of chrysophanic acid was less.

By distillation with zinc dust, a yellowish sublimate was obtained which, when recrystallised from hot alcohol, formed yellowish needles melting at $199-200^\circ$, and on analysis proved to be a methylanthracene, probably the β -modification:

- 0.0974 gave 0.3335 CO_2 and 0.0536 H_2O . $\text{C} = 93.3$; $\text{H} = 6.1$.
 $\text{C}_{15}\text{H}_{12}$ requires $\text{C} = 93.7$; $\text{H} = 6.3$ per cent.

*The insoluble residue, left after extraction of commercial chrysarobin with light petroleum, was crystallised from ethyl acetate and a substance separated which seemed to be identical with dichrysarobin, but was apparently less soluble in ethyl acetate or glacial acetic acid. After repeated recrystallisation from these solvents, it was obtained in crystals having no sharp melting point, but decomposing at about 250° . On analysis:

0.084 gave 0.2222 CO₂ and 0.0366 H₂O. C = 72.2 ; H = 4.8.

C₃₀H₂₄O₇ requires C = 72.6 ; H = 4.8 per cent.

The acetyl derivative was prepared in the usual way and analysed with the following result :

0.0402 gave 0.098 CO₂ and 0.0184 H₂O. C = 66.5 ; H = 5.0.

C₄₂H₃₆O₇ requires C = 67.4 ; H = 4.8 per cent.

Dichrysarobin Methyl Ether, C₃₁H₂₆O₇.

An examination of the petroleum extract of commercial chrysarobin indicated the presence of a methylated substance in addition to chrysarobin. The formation of chrysarobin and dichrysarobin by the action of hydriodic acid on the extract and their stability towards this reagent, rendered it highly probable that the methyl ether of dichrysarobin was present in commercial chrysarobin. The mother liquors, from which chrysarobin had been separated, were therefore worked up, and after a tedious process of fractional crystallisation a product was obtained melting constantly at 160°, which was slightly more soluble in ethyl acetate than chrysarobin but similar in other respects. On analysis :

0.2044 gave 0.5474 CO₂ and 0.0904 H₂O. C = 73.0 ; H = 4.9.

0.185, by Zeisel's method, gave 0.0604 AgI. CH₃ = 2.1.

C₃₁H₂₆O₇ requires C = 73.0 ; H = 5.1 ; CH₃ = 2.9 per cent.

The residue, after treatment with hydriodic acid, had the properties of dichrysarobin.

The *acetyl* compound, C₃₁H₂₁O₇(C₂H₃O)₅, was prepared by acetylating the mixture of chrysarobin and the methylated substance in the usual way and extracting it with hot alcohol. The portion insoluble in the solvent was triacetylchrysarobin, the soluble portion was precipitated from the alcoholic solution in three fractions with water. It was very soluble in alcohol, ethyl acetate, and glacial acetic acid, and could not be obtained crystalline. The middle fraction melted at 135°. On analysis :

0.123 gave 0.305 CO₂ and 0.0578 H₂O. C = 67.6 ; H = 5.2.

0.0684 „ 0.169 CO₂ „ 0.0326 H₂O. C = 67.4 ; H = 5.3.

0.206, by Zeisel's method, gave 0.0776 AgI. CH₃ = 2.4 per cent. *

0.721 raised the b. p. of 14.2 alcohol 0.085°, Mol. wt. = 687.

C₄₁H₃₆O₁₂ requires C = 68.3 ; H = 5.0 ; CH₃ = 2.1 per cent. Mol. wt. = 720.

It is extremely probable that this acetyl derivative is identical with, or is largely contained in, a substance examined by Hesse and regarded by him as hexacetyldichrysarobin, as it agreed with it in physical properties and chemical composition. Hesse found that his substance

THE CONSTITUENTS OF COMMERCIAL CHRYSAROBIN. 1583

melted at 125° and gave the following data: C = 68.0; H = 5.0 per cent. Mol. wt. = 692.

Hesse supposed that his substance was produced by the polymerisation of chrysarobin by the prolonged action of the acetylating agent. This, however, we find not to be the case, as the mixture of chrysarobin and dichrysarobin methyl ether, when treated with acetic anhydride and sodium acetate for half-an-hour, gave approximately equal quantities of triacetylchrysarobin and penta-acetyldichrysarobin methyl ether, whilst pure chrysarobin under exactly similar conditions gave a quantitative yield of triacetylchrysarobin. The polymeride, therefore, must pre-exist in the mixture. That it was a methyl ether was proved by treating the mixture with hydriodic acid and examining the alkyl iodide formed; it distilled completely below 50° and was therefore *methyl* iodide.

Substance, $C_{17}H_{14}O_4$. *M. p.* 181° .

In the process of working up the residual crude chrysarobin left after extraction with light petroleum, a small amount of a beautiful, crystalline substance melting constantly at 181° was obtained. It had the general properties of the substances associated with it in crude chrysarobin. On analysis:

0.108 gave 0.285 CO_2 and 0.052 H_2O . C = 72.0; H = 5.3.

0.19, by Zeisel's method, gave 0.141 AgI. CH_3 = 4.7.

$C_{17}H_{14}O_4$ requires C = 72.3; H = 5.0; CH_3 = 5.3 per cent.

The analytical data agree very well with this formula, and the large amount of methyl iodide formed on treatment with hydriodic acid precludes the possibility of it being a mixture of the other constituents previously mentioned.

The *acetyl* compound, prepared in the usual way,⁸ was crystallised from alcohol and formed orange-red crystals melting at $215-216^{\circ}$. The solution was not fluorescent. On analysis:

0.0938 gave 0.2276 CO_2 and 0.042 H_2O . C = 66.2; H = 5.0 per cent.

These figures unfortunately do not agree well with any likely formula, and we are unable at this stage of the inquiry to offer any suggestions as to the constitution of this substance.

Chrysophanic Acid, $C_{15}H_{10}O_4$.

For the sake of comparison, a preliminary examination was made of some chrysophanic acid prepared from rhubarb. This was obtained as a brown, indistinctly crystalline powder melting at 160° . On analysis:

1584 THE CONSTITUENTS OF COMMERCIAL CHRYSAROBIN.

0.1544 gave 0.398 CO_2 and 0.059 H_2O . $\text{C}=70.3$; $\text{H}=4.2$.

0.1906, by Zeisel's method, gave 0.0452 AgI . $\text{CH}_3=1.5$.

$\text{C}_{15}\text{H}_{10}\text{O}_4$ requires $\text{C}=70.9$; $\text{H}=3.9$ per cent.

The crude product obtained after treatment with hydriodic acid charred on heating, but had no sharp melting point. By recrystallisation it was separated into chrysarobin, melting at 203° , and a substance which charred and had no sharp melting point. On analysis, the latter gave figures agreeing with those required for dichrysarobin:

0.1668 gave 0.445 CO_2 and 0.0746 H_2O . $\text{C}=72.7$; $\text{H}=5.0$.

$\text{C}_{30}\text{H}_{24}\text{O}_7$ requires $\text{C}=72.6$; $\text{H}=4.9$ per cent.

The acetyl compound of chrysophanic acid, prepared in the usual way and recrystallised from glacial acetic acid, melted at 203° . On analysis:

0.1914 gave 0.4722 CO_2 and 0.0736 H_2O . $\text{C}=67.3$; $\text{H}=4.3$.

$\text{C}_{19}\text{H}_{14}\text{O}_6$ requires $\text{C}=67.4$; $\text{H}=4.1$ per cent.

Here, as in the case of crude chrysarobin, the acetyl derivative may be more readily separated from the methylated constituent than the parent substance. In order to determine the physical constants of pure chrysophanic acid, about which there has been hitherto much uncertainty, pure chrysarobin, after treatment with hydriodic acid, was converted by aerial oxidation in alkaline solution into chrysophanic acid and this recrystallised from several solvents until the melting point was constant. The pure substance melted at 190° . On analysis:

0.0984 gave 0.256 CO_2 and 0.0354 H_2O . $\text{C}=70.9$; $\text{H}=4.0$.

$\text{C}_{15}\text{H}_{10}\text{O}_4$ requires $\text{C}=70.9$; $\text{H}=3.9$ per cent.

The acetyl derivative, after several recrystallisations, melted constantly at 206° instead of 202 — 204° , as previously recorded. Attempts to prepare the methyl ether of chrysophanic acid were unsuccessful; even when heated in a sealed tube with methyl iodide and methyl alcohol at 100° , the original substance was recovered unchanged.

Finally, in order to prove beyond question that chrysarobin was identical with chrysophanohydroanthrone, chrysophanic acid was treated with hydriodic acid, and the product proved to be chrysarobin by its melting point, 204° , and that of its acetyl derivative, 234 — 235° . Liebermann and Seidler's chrysophanohydroanthrone is therefore not the hydroanthrone, but the anthranole of chrysophanic acid. Further, the methylated compound accompanying chrysophanic acid in rhubarb is not its methyl ether, as stated by Hesse, but is in all probability the methyl ether of dichrysarobin.

Chrysarobin and dichrysarobin are readily oxidised by alkaline

permanganate, but no product other than oxalic acid could be isolated from the result of the reaction. Fusion with caustic potash also yielded a negative result.

It was thought of interest to examine a commercial sample designated "absolutely chemically pure chrysarobin." This was found to have practically the same composition as that previously examined. After recrystallisation from ethyl acetate, it melted at 165—175°. On analysis :

0.103 gave 0.275 CO_2 and 0.0458 H_2O . $\text{C} = 72.8$; $\text{H} = 5.0$.

0.333, by Zeisel's method, gave 0.1166 AgI . $\text{CH}_3 = 2.2$.

$\text{C}_{15}\text{H}_{12}\text{O}_3$ requires $\text{C} = 75.0$; $\text{H} = 5.0$ per cent.

After treatment with hydriodic acid, it yielded a mixture of chrysarobin and dichrysarobin and was thus in all respects similar to that previously examined.

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