VIII.—*Occurrence of Orthohydroxyacetophenone in the Volatile Oil of Chione glabra.*

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SOME years ago, one of us (Dunstan, *Proc. Roy. Soc.*, **46**, 211) showed that the strong faecal odour of the wood of *Celtis reticulosa* is due to the presence of skatole, the substance to which the odour of human excrement is due. Through the interest of Mr. Thiselton Dyer, the Director of Kew Gardens, other plants having strong odours were then examined, but no definite information as to their constituents could be obtained, owing to the small quantity of material available for examination. Amongst these plants was a small specimen of the wood of *Chione glabra*, which had been sent to Kew by Mr. J. H. Hart, F.L.S., Superintendent of the Royal Botanic Gardens, Trinidad, with the suggestion that an examination of its constituents should be

undertaken, as the plant is reputed to possess valuable properties as a medicine and, in particular, is stated to be a powerful aphrodisiac. The bark and wood emitted a strong, unpleasant odour, chiefly aromatic, but partly fœcal. This was proved to be due to an oil which was volatile with steam, and although its chief physical and chemical properties were ascertained, the constitution of its principal constituent could not be determined owing to insufficiency of material. A further supply of the wood was afterwards obtained from the collections of the Imperial Institute. This was part of a large log which had been sent previously for exhibition at the World's Fair at Chicago. Now, however, it has completely lost its characteristic odour, owing to the escape of the volatile oil, and it proved to be quite useless for our purpose. Through the kind offices of Mr. Hart, the Trinidad Government undertook the collection of a fresh quantity of the wood, which has made it possible for us to complete the inquiry by identifying the odorous constituent of the tree, and in fact, proving its identity with the substance prepared synthetically in the laboratory.

The genus *Chione* of the Natural Order *Rubiaceæ* includes plants which are confined almost exclusively to the West Indies. The species *Chione glabra*, which is indigenous to Grenada, is a large flowering tree, known in the island as "Violette," a name which probably has reference to the aromatic smell of the flower. Through the kindness of Mr. E. J. Millard, F.C.S., we have received from Grenada a dried specimen of the stem, leaves, and flowers of this tree. The somewhat aromatic, somewhat fœcal, smell is associated with the bark and wood, especially with the former; on exposure to air, it gradually disappears. The results of the chemical investigation described in the subsequent part of this paper show that the volatile oil, which exhibits in a concentrated form the remarkable odour of the wood, is composed of two substances, the one a yellow oil boiling at 160° under 34 mm. pressure, and solidifying at low temperatures to a crystalline mass; the other, a colourless, crystalline substance melting at 82°. The former, which is the chief constituent, we have proved to be *orthohydroxyacetophenone*, $\text{OH} \cdot \text{C}_6\text{H}_4 \cdot \text{CO} \cdot \text{CH}_3$, and is identical with the compound prepared synthetically. The crystalline substance, which is present in very small quantity, has all the properties of an alkyl derivative of the oil; the amount of substance obtained, however, was insufficient to enable us to complete the examination. The fœcal odour of the fresh wood, which seems rather more pronounced than that of the constituents we have isolated from the oil, suggested the possibility that the plant might also contain a minute quantity of skatole or some other derivative of indole; but although the volatile oil contains traces of some nitrogenous substance, we have not been able to isolate any indole derivative from it. It is, however,

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interesting, and possibly significant from the biological standpoint, to observe that derivatives of orthohydroxyacetophenone may, by processes involving condensation and elimination of water, pass into compounds belonging to the indole group; the production of indoxyl from orthacetylamilidoacetophenone has, indeed, been accomplished by von Baeyer and Bloem (*Ber.*, 1884, 17, 963), and it is not difficult to conceive that the conversion may occur without difficulty and by shorter steps in the plant. The precursors of skatole and other indole derivatives in plants are at present unknown, but the occurrence of derivatives of acetophenone in the vegetable kingdom and particularly in *Chione glabra*, whose wood emits a faecal odour, indicates at least one possible direction in which search might be made.

Besides those whose names we have already mentioned, we are greatly indebted to Miss L. E. Boole, F.I.C., who conducted much of the preliminary examination of the constituents of this plant.

Extraction of the Volatile Oil.

The volatile oil was separated from the wood and bark by cutting these into fine shavings and distilling with steam; the distillate obtained was then shaken with ether, and the ethereal solution dried over calcium chloride and distilled. After removal of the ether, there remained a dark-coloured oil which distilled with some decomposition under the ordinary pressure; it was, therefore, distilled under reduced pressure, when a fraction boiling from 160° to 165°, under a pressure of 34 mm., was obtained. With the small quantity of material available, it was not possible to obtain a fraction of more definite boiling point.

Combustions of the liquid gave the following results.

0.0737 gave 0.1926 CO₂ and 0.0352 H₂O. C = 71.2; H = 5.29.

0.0607 „ 0.1586 CO₂ „ 0.0320 H₂O. C = 71.21; H = 5.76.

C₈H₈O₂ requires C = 70.57; H = 5.88 per cent.

The relative density of the oil is $d = 0.850$ 15°/4°.

It is slightly soluble in water, and has a peculiar and somewhat unpleasant odour, chiefly aromatic, but partly faecal. An aqueous solution of ferric chloride produces a deep purple coloration, and bromine water a faintly yellow, crystalline precipitate. The oil dissolves in alkaline solutions, and such solutions, on evaporation, leave a crystalline salt or metallic derivative; the potassium and sodium salts crystallise in yellow plates which quickly decompose on exposure to air; acids regenerate the oil from them.

Action of various Reagents on the Oil.

Action of Acetic Anhydride.—The liquid was mixed with acetic anhydride and warmed. The viscous oil precipitated on the addition of water to the product was removed by shaking with ether, the ethereal solution dried, and the ether removed by distillation. The crystalline residue of acetyl derivative obtained on standing was then recrystallised from methylic alcohol until the melting point was constant at 88°. A combustion gave the following result.

0.1331 gave 0.3254 CO₂ and 0.0776 H₂O. C = 66.66 ; H = 6.4.

C₈H₇O·C₂H₃O₂ requires C = 67.4 ; H = 5.61 per cent.

The substance is, therefore, a monacetyl derivative of the original liquid, and the existence of one hydroxyl group is thus proved.

Action of Hydroxylamine and Phenylhydrazine.—When an aqueous solution of hydroxylamine is added to the oil suspended in water and the mixture gently warmed, a red, resinous substance separates ; this dissolves in boiling water, and the solution deposits colourless needles as it cools. These, after recrystallisation, melt at 112°, and have all the properties of an oxime of the original substance.

0.1841 gave 0.4242 CO₂ and 0.1016 H₂O. C = 62.8 ; H = 6.12.

OH·C₈H₇·NOH requires C = 63.4 ; H = 5.96 per cent.

A phenylhydrazone was also obtained by the action of a 10 per cent. solution of phenylhydrazine on the liquid suspended in water ; after 24 hours, this mixture deposited a greenish-yellow oil which soon became crystalline. On recrystallisation, the hydrazone melted at 108°.

The production of an oxime and hydrazone indicate the presence of one ketonic group in the original substance.

Action of Bromine.—When bromine water is added to the oil suspended in water, a colourless precipitate forms immediately, and on standing becomes crystalline ; after recrystallisation from hot alcohol, it melts somewhat indefinitely at 108°, or, after prolonged heating at a lower temperature, at 95°. We are unable, at present, to represent its composition by any formula derivable from that of the parent substance. Combustions and two determinations of bromine by Carius' method gave the following results.

C. 32.6 per cent.	H. 2.52 per cent.	Br. 45.64 per cent.
32.3 "	2.04 "	46.2 "
32.96 "	2.09 "	
32.89 "	2.26 "	

It will be seen that these values for carbon, hydrogen, and bromine do not agree with those required for a mono- or dibromo-derivative.

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$C_8H_7O_2Br$ requires $C = 44.6$; $H = 3.2$; $Br = 37.2$.

$C_8H_6O_2Br_2$,, $C = 32.6$; $H = 2.04$; $Br = 54.4$.

When the bromine derivative is reduced with tin and hydrochloric acid, it yields a small quantity of a phenolic substance giving a bromine derivative melting at 86° . It is possible that the solid bromo-derivative is a mixture of one or more simple bromine derivatives, but this is not very probable, since its composition seems to be constant when prepared under various conditions, and its melting point is very definite.

Action of Fused Potash.—When the oil is boiled for some time (in a vessel fitted with an upright condenser) with 10 per cent. potash solution, it merely passes into a metallic derivative, and can be recovered by acidifying the solution; and even when heated with alkaline solutions in sealed tubes at 125° , it is not decomposed. When fused with excess of potash, the potassium salt of the oil floats for a time on the excess of potash, but is subsequently completely decomposed, forming a dark brown mass. When this is dissolved in water, acidified, and the mixture distilled, a solution containing *phenol* is obtained; this was identified by means of its tribromo-derivative. When the acid liquid left after distillation was extracted with ether, it furnished a crystalline substance which, after recrystallisation from hot water, melted at 151° , and gave all the reactions of *salicylic acid* m. p. 155°).

Action of Nitric Acid.—The residue from the Carius' estimations of bromine in the bromo-derivative was examined, and found to contain oxalic acid and a yellow, crystalline substance; the quantity of the latter, however, was too small to admit of satisfactory identification, but since it dyed silk yellow and did not dye cotton, and gave the chloropicrin reaction, there can be little doubt that it was *picric acid*.

These observations as to the chemical behaviour of the volatile oil of *Chione glabra* prove that its chief constituent is orthohydroxy-acetophenone [$OH : CO \cdot CH_3 = 1 : 2$].

The facts may be conveniently summarised here.

1. The parent substance has a composition represented by the formula $C_8H_8O_2$.

2. One of the hydrogen atoms can be replaced by the acetyl group, indicating the presence in the parent substance of one hydroxyl group.

3. The oil forms a monoxime, having a composition represented by the formula $C_8H_9O_2N$.

4. Fusion of the oil with potash furnished salicylic acid and phenol, the latter as the result of secondary action.

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The formation of all these substances is readily explained on the assumption that the chief constituent of the oil is orthohydroxyacetophenone, $\text{OH}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{CH}_3$. This compound has been described by Tahara (*Ber.*, 1892, 25, 1306) and by Feuerstein and Kostanecki (*Ber.*, 1898, 31, 710—719). The latter chemists described orthohydroxyacetophenone (obtained by the action of alcoholic soda on phenacylidenflavene) as a yellow oil of peculiar odour, distilling at 218° , giving a purple red colour with ferric chloride solution, and forming a yellow, crystalline, sodium salt. Tahara prepared the compound by the decomposition of orthomethoxybenzoylacetic acid. The acetyl derivative melted at 89° , and the phenylhydrazone at 107° .

We have prepared orthohydroxyacetophenone from nitrocinnamic acid, by the following series of reactions. Orthonitrocinnamic acid, $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{CH}\cdot\text{CH}\cdot\text{COOH}$, was converted successively into dibromonitrophenylpropionic acid, $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{CHBr}\cdot\text{CHBr}\cdot\text{COOH}$; orthonitropropionic acid, $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{C}\equiv\text{C}\cdot\text{COOH}$; orthonitrophenylacetylene, $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{C}\equiv\text{CH}$; orthamidophenylacetylene; $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{C}\equiv\text{CH}$; ortho-amidoacetophenone, $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{CH}_3$; and, finally, by diazotising into orthohydroxyacetophenone, $\text{OH}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{CH}_3$.

These compounds, with the exception of the last, have been prepared by Baeyer and Bloem (*Ber.*, 1880, 13, 2259), and we have made use of the methods of preparation and purification described by these chemists. The orthohydroxyacetophenone thus prepared had all the characteristics of the oil distilled from *Chione glabra*, and furnished derivatives having the same physical constants; thus the bromine derivative and the oxime melted at 108° and 112° respectively.

Orthomethoxyacetophenone.—The quantity of colourless, crystalline substance left as a residue in the distillation of the crude chione oil was too small to admit of an extended examination, but since it was decomposed by boiling with hydriodic acid, giving a volatile iodide, with the production of an oil having the properties of orthohydroxyacetophenone, it is probably an ether, possibly the methyl ether of this substance. The minute amount of this constituent present in the volatile oil has made it impossible for us more certainly to identify it.*

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* Since the work described in the present paper was completed, the following account of the volatile oil of *Chione glabra* has appeared (Paul and Cownley, *Pharm. Journ.*, [iv], 7, 51). The material examined was obtained from the Windward Islands. "From the aromatic odour of the bark, it was conjectured that it might contain a volatile oil, and on examination with that object we succeeded in isolating a volatile oil amounting to about 1.5 per cent. by weight.

"This volatile oil is of a pale yellow colour, and has a specific gravity higher than