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CC.—*The Constituents of the Essential Oil of Nutmeg.*

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ALTHOUGH the essential oil distilled from the nutmeg has been known for more than three centuries, and, being recognised by several national Pharmacopœias, has long been an established article of commerce, it is a remarkable fact that up to the present time very little of a definite character has been ascertained respecting the nature of its constituents. The previous investigations pertaining to this subject have been recorded by Gildemeister and Hoffmann in their work entitled "Die ætherischen Oele," Berlin, 1899, p. 474, and also by Semmler in his more recent work, "Die ætherischen Oele," Leipzig, 1906, Bd. I, p. 768; II, 314; III, 211; IV, 165. The correct interpretation of

* On the twofold position of mercury in the periodic system. See also Trans., 1905, **87**, 180. In this respect, mercury is comparable to thallium, which with variation of valency affords a remarkable instance of variation of chemical character.

† The researches of Sülc and recently of Watson have also conclusively proved the existence of silver peroxynitrates (Trans., 1906, **89**, 578).

the results of the earlier investigations is, however, rendered somewhat difficult by the fact that the essential oil of nutmeg has frequently been designated as oil of mace (compare *Pharmacopœia Germanica*, 4th Edition, p. 269), and that the source or genuineness of the oil employed has not always been clearly indicated. It is, indeed, generally assumed that the oils of nutmeg and mace are qualitatively identical, and that they differ only in the relative proportions of their constituents, but, inasmuch as neither of these oils has hitherto been completely examined, there is no direct evidence that this is the case.

Among the more important of the earlier investigations of oil of nutmeg, those of Gladstone may be considered. In his first communication on this subject (*Journ. Chem. Soc.*, 1864, 17, 11), he recorded the following observations. "The three specimens examined consisted of varying proportions of a hydrocarbon resembling carvene, and an oxidised oil with the boiling point 224° , and sp. gr. 0.9466. As it closely resembles carvol and menthol in its properties, it may by analogy be named myristicol." In a later communication (*Journ. Chem. Soc.*, 1872, 25, 3, 11), Gladstone suggested for the above-mentioned hydrocarbon the name "myristicene," and remarked further regarding "myristicol" as follows: "This oil has the characteristic smell of nutmeg, and . . . does not form a crystalline compound with hydro-sulphuric acid. It was found difficult to purify it by fractional distillation, indeed there was some reason to think that in the process of rectification it was subject to change. An ultimate analysis of portions boiling at somewhere about 220° yielded rather too much carbon and hydrogen for the formula $C_{10}H_{14}O$, suggesting the idea of its being still mixed with some amount of a hydrocarbon."

The constituents of nutmeg oil were next investigated by C. R. A. Wright (*Journ. Chem. Soc.*, 1873, 26, 549), who obtained "a considerable quantity of a mixture of hydrocarbons boiling below 180° and a small quantity of an oxidised constituent boiling above 210° , apparently the 'myristicol' of Gladstone." He noted that the purest myristicol boiled at $212-218^{\circ}$, and from an analysis of this fraction concluded that it contained as its principal constituent a body isomeric with camphor, $C_{10}H_{16}O$, but as he obtained from it, by repeated distillation, a portion boiling at $250-265^{\circ}$, which was assumed to be a polymerised product, the conclusion respecting the composition of the fraction was evidently not justified. With regard to the hydrocarbons, Wright stated that, "contrary to Gladstone's experiments, the hydrocarbon of oil of nutmeg is not a single body boiling at 167° and of formula $C_{10}H_{16}$, but a mixture of a terpene boiling at $163-164^{\circ}$ and a hydrocarbon, apparently cymene, boiling towards 177° ." As the cymene, however, was only isolated after treating the mixture with

sulphuric acid, no evidence was afforded of its pre-existence in the oil.

Brühl (*Ber.*, 1888, 21, 472), with consideration of the statements respecting the character of the so-called "myristicol," and from purely physical data, which apparently were obtained by the examination of a fraction of nutmeg oil boiling at 224° , was led to the conclusion that, as an alcohol of the formula $C_{10}H_{10}O$, myristicol was to be regarded as a cyclic compound containing two ethylenic linkings. He, moreover, suggested constitutional formulæ which were believed to be in accordance with the physical determinations.

Wallach (*Annalen*, 1889, 252, 105) examined the lower boiling portions of an oil which he designated as "mace oil," and positively established the presence of pinene and dipentene. In this connexion, he noted that "it was remarkable that the fractions containing pinene were nearly inactive (very slightly levorotatory). The crude oil, on the other hand, as also the fractions of higher boiling point, were strongly dextrorotatory. It is to be assumed that in the low boiling portion, + and - pinene neutralise each other. The nature of the higher boiling, dextrorotatory portions of mace oil still remains to be cleared up."

The investigation of the oils of nutmeg and mace was subsequently undertaken by Semmler (*Ber.*, 1890, 23, 1803; 1891, 24, 3818). The oil of nutmeg supplied to him had a density of 0.8611 at 15° , and was found to consist entirely of terpenes, but these were not further examined. He particularly noted the absence of cymene, "myristicol," and higher boiling oils of high specific gravity, and stated that the oil in question evidently represented the portions which are most volatile in steam. These results led Semmler to examine an oil of mace, which was found to have a specific gravity of 0.9309 at 14° , and to give a green coloration with ferric chloride, indicating the presence of a phenolic substance. A fraction collected between 70° and 144° at 10 mm. pressure was assumed to contain "myristicol," but was not further examined. From the higher boiling portions of the oil, after treatment with sodium, a crystalline substance was isolated, to which Semmler gave the name myristicin, and assigned to it the formula $C_{12}H_{14}O_3$. It was subsequently shown, however, that myristicin has the formula $C_{11}H_{12}O_3$, and is 3-methoxy-4:5-methylenedioxy-1-allylbenzene. This substance is a liquid, but, by treatment with metallic sodium or with alkalis, it is readily converted into the corresponding propenyl compound (m. p. 45°), which has been designated isomyristicin (compare Thoms, *Ber.*, 1903, 36, 3446; Richter, *Ber. Deut. pharm. Ges.*, 1907, 17, 152; Rimini, *Gazzetta*, 34, ii, 281; 35, i, 406; Rimini and Olivari, *Atti R. Accad. Lincei*, 1907, [v], 16, i, 663).

The purpose of the present investigation has been to ascertain the nature of the constituents of a genuine oil of nutmeg, and especially, among other points of interest, to determine the character of the so-called "myristicol." In addition to the statements (*loc. cit.*) regarding the occurrence of this compound in oil of nutmeg, Wright (*Journ. Chem. Soc.*, 1873, 26, 552) believed it to be also present in very small amount in the oil of sweet orange. He noted that "the portion passing over at 210—230° appeared to be identical with myristicol, as it gave numbers agreeing with the formula $C_{10}H_{16}O$." Quite recently, Thoms (*Ber. Deut. pharm. Ges.*, 1904, 14, 27) has indicated that the essential oil distilled from the seed of *Monodora Myristica*, Dumal, contains an oxygenated compound of the composition $C_{10}H_{16}O$, which he regarded as probably identical with "myristicol." In connexion with these later observations, it is, however, of interest to note that the constituent of oil of sweet orange which Wright had considered to be identical with "myristicol" has been shown by Stephan (*J. pr. Chem.*, 1900, [ii], 62, 531) to be nothing more than *d*-terpineol.

EXPERIMENTAL.

I. Examination of a Normal Oil of Nutmeg.

The oil employed in this investigation was specially distilled for us by Messrs. Stafford Allen & Sons, of London, from unlimed Ceylon nutmegs of good quality, and our thanks are due to them for the care with which the operation was conducted. The amount of oil obtained from 24.38 kilograms of nutmegs was 1693 grams, corresponding to a yield of 6.94 per cent. This oil was a nearly colourless, limpid liquid, having a density of 0.8690 at 15°/15°, an optical rotation of +38°4' in a 1-dcm. tube, and was soluble in three times its volume of 90 per cent. alcohol.

A determination of the amount of free acids and esters gave the following data: 20 grams of the oil required 2.9 c.c. of an *N*/10 alcoholic solution of potassium hydroxide to neutralise the free acids, corresponding to an acid value of 0.81. On subsequently adding an excess of the alkali and boiling for half an hour, it was found that 11.2 c.c. of the decinormal solution were required to hydrolyse the esters present, corresponding to an ester value of 3.15. The esters, if calculated as $C_{10}H_{17} \cdot C_2H_3O_2$, would therefore amount to 1.1 per cent.

As a preliminary test for the presence of aldehydes or ketones, 20 grams of the oil were shaken for some time with a saturated solution of sodium bisulphite. No solid compound was formed, but the aqueous liquid, after being freed from adhering oil by shaking with ether, gave on treatment with alkali a trace of an oil which possessed

a fragrant odour. The amount of this substance was, however, much too small to permit of its isolation.

Treatment with Sodium Hydroxide.—A quantity (1500 grams) of the oil was extracted several times with a 5 per cent. solution of sodium hydroxide, in order to remove the free acids and any phenolic substances present. The combined alkaline liquids and aqueous washings were shaken with ether to remove any adhering oil, and then acidified with sulphuric acid, when an oily liquid separated. This was extracted with ether, and the ethereal liquid shaken a few times with a 10 per cent. solution of sodium carbonate.

Identification of Myristic Acid.

The liquids resulting from the extraction with sodium carbonate were acidified with sulphuric acid and distilled with steam. The distillate contained no volatile acids, but there remained in the flask a quantity of a solid substance amounting to about 5 grams, which was collected on a filter and washed with water. On crystallisation from alcohol, it yielded a product melting sharply at 54°:

0.1482 gave 0.3990 CO_2 and 0.1690 H_2O . $C = 73.4$; $H = 12.7$.

$C_{14}H_{28}O_2$ requires $C = 73.7$; $H = 12.3$ per cent.

This substance was thus identified as myristic acid.

Identification of Eugenol and isoEugenol.

The ethereal liquid which had been extracted with a solution of sodium carbonate, as above described, was dried with anhydrous sodium sulphate, and the ether removed. About 3 grams of a dark brown oil were thus obtained, which possessed an intense odour of eugenol and gave with ferric chloride a deep green colour. By distillation under a pressure of 75 mm., it was resolved into the following three fractions: 164—174°; 174—180°; above 180°/75 mm., only a little non-volatile, resinous substance remaining in the flask. These products were then separately benzoylated, when from the first fraction (b. p. 164—174°/75 mm.) a benzoyl derivative was obtained, which, after fractional crystallisation from alcohol, separated in thick prisms, melting at 67—69°:

0.1705 gave 0.4760 CO_2 and 0.0955 H_2O . $C = 76.1$; $H = 6.2$.

$C_{17}H_{16}O_3$ requires $C = 76.1$; $H = 6.0$ per cent.

The substance yielding this compound was thus identified as eugenol.

The second fraction (b. p. 174—180°/75 mm.) yielded a mixture of benzoyl derivatives, for, when crystallised from alcohol, the first crop of crystals melted somewhat indefinitely between 68° and 84°. After

repeated fractional crystallisation, this product melted at 96—100°, and was then analysed:

0.1500 gave 0.4158 CO₂ and 0.0851 H₂O. C = 75.6; H = 6.3.

0.1385 „ 0.3862 CO₂ „ 0.0776 H₂O. C = 76.0; H = 6.2.

C₁₇H₁₆O₃ requires C = 76.1; H = 6.0 per cent.

From the melting point and analysis of this compound, it is evident that it was nearly pure benzoylisoeugenol, which is stated to melt at 103—104°. The identification of isoeugenol as a constituent of nutmeg oil is of considerable interest, inasmuch as hitherto but one instance appears to have been recorded of its occurrence in an essential oil (compare Semmler, "Die ätherischen Oele," Bd. IV, p. 130). The fraction of the phenols boiling above 180°/75 mm. yielded no solid benzoyl derivative.

Preliminary Examination of the Terpenes.

The oil from which the myristic acid and phenols had been removed, as above described, was washed with water, dried with anhydrous sodium sulphate, and distilled under a pressure of 60 mm. The portion boiling below 110°/60 mm., which would contain practically all the terpenes, was separately collected, and amounted to about 87 per cent. of the entire oil. This portion was subsequently subjected to several fractionations under a pressure of 20 mm., and a fraction boiling below 70°/20 mm. was collected. The density of the latter was found to be 0.8526 at 15°/15°, which proved the absence of any appreciable amount of an olefinic terpene. A portion of the oil which distilled at 170—172° under the ordinary pressure was specially tested for phellandrene, but with a negative result. The further examination of the terpenes was conducted after the hydrolysis of the higher boiling portions of the oil.

Hydrolysis of the Oil.

The portion of oil collected below 110°/60 mm., as also that boiling above this temperature, was distilled under the ordinary pressure, and the fraction passing over below 190° was collected.

The entire amount of oil boiling above 190° under the ordinary pressure was heated for an hour with an alcoholic solution of 10 grams of potassium hydroxide in a flask provided with a reflux condenser. After distilling off the greater part of the alcohol, water was added, and the mixture extracted with ether. The ethereal liquid was washed, dried, and the ether removed, after which the hydrolysed oil was distilled under 15 mm. pressure in order to remove any non-

volatile, resinous matter. The strongly alkaline, aqueous liquid, which remained in the flask after the extraction of the hydrolysed oil, was reserved for the examination of the acids.

Fractional Distillation of the Oil.

The hydrolysed oil, together with the portion boiling below 190°, which had previously been separated, was next submitted to a systematic fractional distillation at the ordinary pressure, a Young's rod and disc column having been used up to a temperature of 205°. The following fractions were ultimately obtained:

Boiling-point.	d_{20}^{20} .	α_D in a 1 dem. tube.	Amount in grams.
156—159°	0.8519	+ 31°36'	136.0
159—161	0.8513	+ 45 15	351.0
161—163	0.8515	+ 52 10	229.0
163—165	0.8516	+ 48 48	135.0
165—170	0.8514	+ 35 46	29.0
170—180	0.8521	+ 9 1	77.0
180—195	0.8754	+ 4 21	22.0
195—205	0.9149	+ 10 40	9.2
205—215	0.9351	+ 12 44	19.5
215—225	0.9504	+ 9 12	18.0
225—235	0.9656	+ 5 24	8.1
235—245	0.9812	+ 4 12	6.8
245—255	0.9931	+ 5 20	10.2
255—265	1.0166	+ 5 20	17.1
265—275	1.0436	+ 5 40	24.2
Above 275	1.0510	+ 2 25	5.0

Total ... 1097.1 grams.

Identification of Pinene.

Fraction 156—159°.—This was a colourless, limpid liquid, which possessed the odour of pinene:

0.1018 gave 0.3282 CO₂ and 0.1100 H₂O. C = 87.9; H = 12.0.

C₁₀H₁₆ requires C = 88.2; H = 11.8 per cent.

It is evident that this fraction consisted entirely of a hydrocarbon. The presence of pinene was determined by the formation of a crystalline nitrosochloride (m. p. 108°), and the conversion of the latter into the corresponding nitrolbenzylamine (m. p. 123°).

Fraction 159—161°.—This was the largest fraction obtained, and it resembled in its characters the preceding one:

0.0958 gave 0.3100 CO₂ and 0.1034 H₂O. C = 88.3; H = 12.0.

C₁₀H₁₆ requires C = 88.2; H = 11.8 per cent.

It was found to contain a considerable quantity of pinene, since it readily yielded the above-mentioned derivatives of this terpene.

Identification of Camphene.

Fraction 161—163°.—This was a large fraction, and resembled in odour the preceding one:

0.1441 gave 0.4650 CO₂ and 0.1555 H₂O. C = 88.0; H = 12.0.

C₁₀H₁₆ requires C = 88.2; H = 11.8 per cent.

The high optical rotation of this fraction suggested the presence of a considerable amount of camphene. Fifty grams of the liquid were therefore treated with a mixture of acetic and sulphuric acids according to the method of Bertram and Walbaum for the conversion of camphene into an *isoborneol* ester. After hydrolysing the product, a pale yellow oil was obtained, which was distilled under diminished pressure. A portion which passed over at 120—140°/25 mm. partially solidified in the receiver, and possessed a pronounced camphoraceous odour. On treating this fraction with phenylisocyanate in a sealed tube at 100° for several hours, a phenylurethane was obtained, which crystallised from alcohol in fine needles melting at 138°. The latter compound, on treatment with alcoholic potash, yielded a substance which, after crystallising from methyl alcohol, melted at 207—212°, and had all the characteristic properties of *isoborneol*. The presence of camphene in this fraction of the oil was thus established.

Fractions 163—165° and 165—170°.—These fractions were similar in their general characters to the preceding one, but had a somewhat lower rotatory power. The fraction 165—170° was analysed:

0.1062 gave 0.3430 CO₂ and 0.1150 H₂O. C = 88.1; H = 12.0.

C₁₀H₁₆ requires C = 88.2; H = 11.8 per cent.

It was evident that these two fractions consisted of mixtures of pinene and camphene with the constituents of the succeeding fraction.

Identification of Dipentene.

Fraction 170—180°.—This was a limpid, colourless liquid, possessing a distinctly lemon-like odour:

0.1171 gave 0.3778 CO₂ and 0.1244 H₂O. C = 88.0; H = 11.8.

C₁₀H₁₆ requires C = 88.2; H = 11.8 per cent.

The analysis of this fraction showed that it contained no oxygenated substances, such as cineol (b. p. 176°). The fraction readily yielded a bromo-derivative, which, after crystallisation from ethyl acetate, melted at 124—125°, thus establishing the presence of dipentene. No terpinene could be detected in it.

Fraction 180—195°.—This was a colourless liquid, possessing a somewhat lemon-like odour:

0.1567 gave 0.4867 CO₂ and 0.1650 H₂O. C = 84.7; H = 11.7.

The characters of this fraction indicated it to consist of a mixture of the constituents of the preceding and succeeding ones.

Identification of Linalool.

Fraction 195—205°.—This fraction possessed a pronounced odour of linalool:

0.1145 gave 0.3352 CO₂ and 0.1191 H₂O. C = 79.8; H = 11.6.

C₁₀H₁₈O requires C = 77.9; H = 11.7 per cent.

Although this fraction still contained some terpene, it evidently consisted largely of an oxygenated substance. A portion of it was gently oxidised with a chromic acid mixture and the product extracted with ether. The ethereal liquid was washed, dried, and the ether removed, when a small amount of a product was obtained, which, on distillation, yielded a fraction possessing an intense lemon-like odour. The latter fraction, on treatment with β -naphthylamine and pyruvic acid, yielded the crystalline α -citryl- β -naphthacinchoninic acid, melting at 200°. This result, together with the positive rotation of the original fraction, rendered it evident that *d*-linalool was present in the oil.

No semicarbazone, oxime, or solid bisulphite compound could be obtained from the above fraction, thus indicating the absence of aldehydes or ketones.

The subsequent fractions of the oil, as previously noted, were all relatively small in amount, but they were analysed with the following results:

Fraction 205—215°.

0.1193 gave 0.3441 CO₂ and 0.1210 H₂O. C = 78.7; H = 11.3.

Fraction 215—225°.

0.1684 gave 0.4855 CO₂ and 0.1634 H₂O. C = 78.6; H = 10.8.

Fraction 225—235°.

0.1691 gave 0.4893 CO₂ and 0.1526 H₂O. C = 78.9; H = 10.0.

Fraction 235—245°.

0.1359 gave 0.3930 CO₂ and 0.1191 H₂O. C = 78.9; H = 9.7.

Fraction 245—255°.

0.2367 gave 0.6796 CO₂ and 0.2026 H₂O. C = 78.3; H = 9.5.

Fraction 255—265°.

0.1435 gave 0.4049 CO₂ and 0.1139 H₂O. C = 77.0; H = 8.8.

Fraction 265—275°.

0.1855 gave 0.5090 CO₂ and 0.1386 H₂O. C = 74.8; H = 8.3.

Fraction above 275°.—The amount of this fraction was only 5 grams and, being obviously of an indefinite character, it was not analysed.

The fractions collected between 195° and 245° were all fragrant liquids, whereas the odour of those obtained between 245° and 275° was not so distinctive.

As all the fractions which distilled above 195° under ordinary pressure were too small in amount to admit of a satisfactory examination, the nature of the oxygenated constituents of the oil was more fully determined by means of a larger quantity of material, designated as heavy oil of nutmeg, which was kindly supplied to us by Messrs. Stafford Allen & Sons. The identification of these constituents will therefore be described in connexion with the examination of the so-called "heavy oil of nutmeg" in the second section of this paper. It may here be noted, however, that among the above fractions those boiling at 255—265° and 265—275° respectively contained a considerable amount of myristicin, for they both readily yielded the dibromo-myristicin dibromide, which crystallised in silky needles melting at 128—129° (*Ber.*, 1903, 36, 3446).

Acids Obtained by the Hydrolysis of the Oil.

The alkaline, aqueous liquid obtained by the hydrolysis of the oil, as previously described, was acidified with sulphuric acid and distilled with steam. The distillate contained some oily drops, and towards the end of the operation a small amount of solid passed over. It was therefore extracted with ether, the ethereal liquid washed with water, dried with anhydrous sodium sulphate, and the ether removed. About 1 gram of a dark brown, oily product was thus obtained, which was converted into a sodium salt, and from the latter five fractions of silver salts were prepared. These were washed, dried in a vacuum over sulphuric acid, and analysed:

Fraction	I.	0.1475 of silver salt gave	0.0459 Ag.	Ag = 31.1.
"	II.	0.1107 " " "	0.0366 Ag.	Ag = 33.1.
"	III.	0.1213 " " "	0.0534 Ag.	Ag = 44.0.
"	IV.	0.1601 " " "	0.0815 Ag.	Ag = 50.9.
"	V.	0.1583 " " "	0.0950 Ag.	Ag = 60.0.

It is evident from these results that the acids extracted by ether represented a rather complex mixture, apparently containing some myristic acid, since silver myristate requires Ag = 32.2 per cent. Their nature was, however, more fully ascertained by the subsequent examination of the corresponding product from "heavy oil of nutmeg."

The aqueous distillate, which had been extracted with ether as above-described, still contained some acid, which was converted into a barium salt. The hot solution of the latter, on cooling, deposited a quantity (about 2 grams) of a salt in glistening leaflets. This

was collected, washed with a little water, dried at 110°, and analysed:

0.8933 of the dried salt gave 0.8135 BaSO₄. Ba = 53.5.
(C₂H₃O₂)₂Ba requires Ba = 53.7 per cent.

By the evaporation of the mother liquors, a further quantity of a salt was obtained, the solution of which abundantly reduced mercuric chloride on heating. It was likewise dried at 110° and analysed:

1.4219 of the dried salt gave 1.4201 BaSO₄. Ba = 58.7.
(CHO₂)₂Ba requires Ba = 60.4 per cent.

These results established the presence of esters of both formic and acetic acid in the oil.

The contents of the distillation flask, after the removal of the volatile acids by steam, were extracted with ether, but only a little resinous matter was obtained.

II.—*Examination of a Heavy Oil of Nutmeg.*

This oil, which, as previously stated, had been kindly supplied to us by Messrs. Stafford Allen & Sons, represented a product obtained by the rectification of very large quantities of normal oil of nutmeg, and consisted chiefly of the oxygenated constituents of the latter, the terpenes having been to a large extent removed. It was a pale yellow liquid, possessing the following constants: $d_{20}^{20} = 1.102$; $n_D^{17} + 1^{\circ}17'$ in a 1-dcm. tube; saponification value 6.10.

Treatment with Sodium Hydroxide.—A quantity (6800 grams) of the oil was extracted several times with a 5 per cent. solution of sodium hydroxide. The combined alkaline liquids and washings were shaken with ether to remove any adhering oil, acidified with sulphuric acid, and the liberated acids and phenols extracted with ether. In order to remove the acids, the ethereal liquid was shaken with a 10 per cent. solution of sodium carbonate. The liquid obtained by extraction with the last-mentioned alkali, when acidified with sulphuric acid and distilled, yielded, however, only traces of acetic and butyric acids. No crystalline acid could subsequently be isolated from the contents of the distilling flask, and therefore the heavy oil, unlike the normal oil of nutmeg, did not contain any free myristic acid.

Identification of Eugenol and isoEugenol.

The above-mentioned ethereal liquid, from which the traces of acid had been extracted, was washed with water, dried with anhydrous sodium sulphate, and the ether removed. About 100 grams of crude

phenols were thus obtained, which were first distilled under diminished pressure to remove resinous matter, and then under the ordinary pressure, when the following fractions were collected: 245—250°; 250—260°; above 260°.

Fraction 245—250°.—This amounted to about 50 grams, and evidently consisted chiefly of eugenol. Its identity was confirmed by the formation of benzoyl-eugenol (m. p. 69°), and also of the diphenylurethane, melting at 107—108° (*Ber.*, 1907, 40, 1834).

Fraction 250—260°.—This amounted to 25 grams. In attempting to prepare from it a diphenylurethane, it was found that the product did not solidify so readily as in the case of the preceding fraction, and was obviously a mixture. With consideration of the probable presence of isoeugenol, and as the *diphenylurethane* of the latter had not hitherto been prepared, a little of this derivative was made from pure isoeugenol (Kahlbaum) and found to melt at 112—113°, which is but a few degrees higher than the melting point of the corresponding derivative of eugenol. It was thus evident that the diphenylurethanes are not well adapted for the differentiation of the above-mentioned isomeric phenols.

Fraction above 260°.—This amounted to about 10 grams. It readily yielded a crystalline benzoyl derivative melting at 105°, thus confirming the observation recorded in connexion with the normal oil of nutmeg, that the phenols consist of a mixture of eugenol and isoeugenol.

Hydrolysis of the Oil.

After the removal of the phenols by extraction with a solution of sodium hydroxide, as above described, the oil was heated with an alcoholic solution of potassium hydroxide (1 part KOH to 100 parts of oil). The greater part of the alcohol was then removed, water added, and the separated oil collected, washed, and dried; the aqueous, alkaline liquid being reserved for the subsequent examination of the acids.

Fractional Distillation of the Hydrolysed Oil.

The hydrolysed oil was subjected to a systematic fractional distillation, the portions boiling below 265° being finally collected under the ordinary pressure, whilst the remainder of the oil was fractionated under a pressure of 40 mm. The following results were obtained:

Boiling-point.	d_{20}^{20} .	α_D in a 1-dm. tube.	Amount in grams.
Below 195°	—	—	184
195—205	0·9136	+ 11°22'	35
205—215	0·9432	+ 11 31	440
215—225	0·9666	+ 5 5	238
225—235	1·0070	- 0 33	151
235—245	1·0469	- 0 5	82
245—255	1·0729	+ 1 4	74
255—265	1·1014	+ 1 48	182
165—169°/40 mm.	1·1316	+ 1 8	130
169—171	„ 1·1341	+ 0 51	560
171—173	„ 1·1437	+ 0 6	3420
Above 173	„ 1·1366	± 0 0	60
Total ...			5556 grams.

Fraction below 195°.—Since this fraction consisted chiefly of terpenes, which had been thoroughly investigated in connexion with the normal oil, it did not require further consideration.

Identification of Linalool.

Fraction 195—205°.—This was a colourless liquid, possessing the fragrant odour characteristic of linalool:

0·0988 gave 0·2881 CO₂ and 0·1046 H₂O. C = 79·5; H = 11·8.

C₁₀H₁₈O requires C = 77·9; H = 11·7 per cent.

The analysis of this fraction indicated that it still contained a small amount of terpene. A quantity of it was gently oxidised with a chromic acid mixture, and the product extracted with ether, when, after the removal of the solvent, a small amount of a yellow liquid was obtained, which was distilled under the ordinary pressure. The portion boiling between 215° and 235° possessed an intense odour of citral, and readily yielded α -citryl- β -naphthacinchoninic acid, melting at 197°, thus confirming the presence of linalool in the oil.

Identification of Borneol and Terpeneol, and Formation of a Diketone, C₈H₁₄O₂.

Fraction 205—215°.—This was a very large fraction. It was a colourless liquid, with an odour resembling that of terpeneol:

0·1409 gave 0·4015 CO₂ and 0·1445 H₂O. C = 77·7; H = 11·4.

C₁₀H₁₈O requires C = 77·9; H = 11·7 per cent.

Test for Terpeneol.—A portion of the liquid was shaken with a concentrated solution of hydriodic acid (sp. gr. 1·96), when a heavy, dark-coloured oil was formed. This was separated from the aqueous layer, dissolved in ether, and shaken with a dilute solution of sodium bisulphite to remove the free iodine. The ethereal solution was washed, dried with anhydrous sodium sulphate, and the ether removed,

when a thick oil was obtained which solidified in a freezing mixture. This solid was dried on a porous tile and crystallised from light petroleum, from which it separated in colourless prisms, melting at 80° . This melting point was identical with that of dipentene dihydriodide, $C_{10}H_{18}I_2$, prepared from terpineol (m. p. 35°), and, when the two preparations were intimately mixed, the melting point remained unchanged. It was thus evident that this fraction of the oil contained a considerable amount of terpineol, and its presence was confirmed by the isolation of the ketolactone, $C_{10}H_{16}O_3$, from the products of its oxidation.

Oxidation of the Fraction. Formation of the Ketolactone, $C_{10}H_{16}O_3$, a Diketone, $C_8H_{14}O_2$, and Camphor.—A quantity (150 grams) of the fraction (b. p. $205-215^{\circ}$) was oxidised with a chromic acid mixture in the proportions of potassium dichromate (8 parts), sulphuric acid (12 parts), and water (36 parts) to 1 part of oil. In the beginning of the oxidation the odour developed was that of citral, but finally it became distinctly camphoraceous. After the mixture had been gently heated on a water-bath for about an hour, it was allowed to cool, and then extracted several times with ether. The ethereal liquid was first washed with a solution of sodium carbonate to free it from acidic substances, then with water, and the ether removed. A yellow oil was thus obtained, which was distilled with steam, when the greater portion passed over. The non-volatile portion of the oxidation product was extracted by ether, the ethereal solution being washed, dried, and the ether removed. A small quantity of a viscid, brown oil was thus obtained, which deposited no solid, even on long standing. It was finally distilled under diminished pressure, when the fraction of highest boiling point was obtained as a viscid, yellow liquid, which solidified when stirred with light petroleum. This solid was dried on a porous tile and crystallised from ether, from which it separated in colourless prisms melting at $62-63^{\circ}$:

0.1165 gave 0.2782 CO_2 and 0.0907 H_2O . C = 65.1; H = 8.7.

$C_{10}H_{16}O_3$ requires C = 65.2; H = 8.7 per cent.

It is evident that this substance is identical with the ketolactone, $C_{10}H_{16}O_3$ (m. p. 64°), which was obtained by Wallach by the oxidation of terpineol with chromic acid. As it is the optically inactive modification of the ketolactone, it follows that the terpineol contained in the oil must be the racemic form (compare Wagner and Brickner, *Ber.*, 1899, 32, 2315).

The portion of the above-mentioned oxidation product which was volatile in steam possessed a strongly camphoraceous odour, although no solid substance separated. The distillate was then extracted with ether, the ethereal solution dried, and the solvent removed, when a

quantity of an oily liquid was obtained. One part of this oil, in alcoholic solution, was heated for some time on a water-bath with hydroxylamine hydrochloride (1 part) and sodium hydroxide (1.5 parts), after which water was added and the mixture carefully neutralised with sulphuric acid. As no solid oxime separated, the mixture was extracted with ether, the ethereal solution being washed, dried, and the solvent removed, when a brown oil was obtained which solidified on stirring with light petroleum. This solid substance was collected on a filter and crystallised from hot alcohol, from which, on cooling, it separated in small, rectangular prisms melting at 140° . The yield of this compound was about 3 grams:

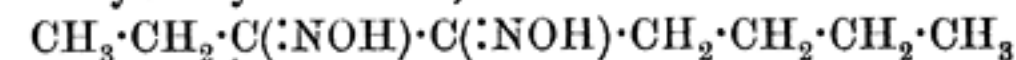
0.1368 gave 0.2804 CO_2 and 0.1187 H_2O . C = 55.9; H = 9.6.

0.1534 ,, 0.3137 CO_2 ,, 0.1272 H_2O . C = 55.8; H = 9.2.

0.1998 ,, 27.4 c.c. moist nitrogen at 16.5° and 762 mm. N = 16.1.

$C_8H_{16}O_2N_2$ requires C = 55.8; H = 9.3; N = 16.3 per cent.

From these results, it appears highly probable that this compound is the *dioxime* of a *diketone*, $C_8H_{14}O_2$. The only known compound of the formula $C_8H_{16}O_2N_2$ with which it might be identical is the *dioxime* of ethyl butyl diketone,



(m. p. $139-141^{\circ}$), which has been described by Fileti and Ponzio (*J. pr. Chem.*, 1898, [ii], 58, 364). These authors also prepared an osazone, which was found to melt at $96-97^{\circ}$. With the object of ascertaining whether our *dioxime* is identical with that prepared by Fileti and Ponzio, 50 grams of the fraction (b. p. $205-215^{\circ}$) were oxidised as previously described, and the portion of the oxidation product which was volatile in steam treated with an excess of phenylhydrazine in alcoholic solution. No solid osazone could, however, be obtained from the product of the reaction. An attempt was also made to obtain a semicarbazone of the diketone, $C_8H_{14}O_2$, from the volatile oxidation product of the fraction $205-215^{\circ}$, but without success. These results therefore do not permit of any conclusion respecting the identity of the compound $C_8H_{16}O_2N_2$, here described, with the *dioxime* of ethyl butyl diketone prepared by Fileti and Ponzio (*loc. cit.*).

The *dioxime*, $C_8H_{16}O_2N_2$, is a colourless, odourless substance, sparingly soluble in cold, but readily in hot, alcohol. It is also soluble in warm ethyl acetate, from which it crystallises in fine needles, but is only sparingly soluble in benzene, and insoluble in light petroleum and in water. When warmed with dilute sulphuric acid, it first dissolved, developing a fragrant odour, but, as resinification ensued, it was impossible by this means to regenerate the ketone from which it had been formed.

Since not more than a trace of substance of aldehydic or ketonic nature was present in the fraction of the oil employed, it is evident that the above-mentioned diketone must represent the oxidation product of an unidentified compound, which is doubtless an *alcohol*.

The light petroleum liquid which had been separated from the dioxime, as above described, possessed a strongly camphoraceous odour. After the removal of the solvent, a brown oil was obtained which did not solidify, and was therefore distilled under diminished pressure. From the first portions of the distillate a solid separated which had the characteristic odour of camphor, and, after drying on a porous tile, melted at 170—175°. This substance readily yielded a semicarbazone melting at 238°, and when the latter was mixed with camphorsemicarbazone the melting point remained unchanged. Not having obtained the camphor in the form of its oxime by the treatment of the original product of oxidation with hydroxylamine, it may be assumed that the amount of the latter was only sufficient to combine with the diketone which was present in the mixture.

The identification of camphor as a product of oxidation of the fraction boiling between 205° and 215° affords conclusive evidence of the presence of borneol in the original oil.

Identification of Geraniol.

Fraction 215—225°.—This was a comparatively large fraction. It was a colourless liquid, possessing a rose-like odour:

0.1109 gave 0.3136 CO₂ and 0.1055 H₂O. C = 77.1; H = 10.6.

This fraction was found to contain some terpineol, since it readily yielded the crystalline dipentene dihydriodide (m. p. 80°) on treatment with concentrated hydriodic acid, whilst the analytical results also indicated it to contain some of the constituents of the succeeding fraction.

A portion of the fraction was oxidised with a chromic acid mixture, when the odour of citral was at first strongly developed, and from the final product a further small amount of the diketone, C₈H₁₄O₂, was obtained in the form of its dioxime (m. p. 140°), which has been described in connexion with the preceding fraction.

As the odour of the fraction, together with the evident formation of citral by its limited oxidation, indicated the presence of geraniol, a portion of it was treated with diphenylcarbamic chloride in the presence of pyridine, according to the method suggested by Erdmann (*J. pr. Chem.*, 1897, [ii], 56, 8), when a product was obtained which crystallised from alcohol in thin, colourless needles melting at 81—82°. This was found to be identical with the diphenylurethane (m. p. 82°)

prepared from a specimen of pure geraniol, and the presence of the latter compound in the oil was therefore established.

Identification of Safrole.

Fraction 225—235°.—This was a pale yellow liquid, possessing a distinct odour of safrole, and also the rose-like odour of geraniol:

0.1129 gave 0.3154 CO₂ and 0.0933 H₂O. C = 76.2; H = 9.2.

The presence of a considerable proportion of geraniol in this fraction was evident from the fact that it yielded the diphenylurethane (m. p. 82°), and, when gently oxidised, some citral was obtained, which was identified by the formation of the α -citryl- β -naphthacinchoninic acid, melting at 195—197°. The odour of the fraction, together with its high density and the analytical figures, indicated, however, that it also contained safrole.

A portion was oxidised with a mixture consisting of potassium dichromate (8 parts), sulphuric acid (12 parts), and water (30 parts) to 1 part of oil. After heating gently for two hours, a distinct odour of piperonal was observed. The mixture, after being allowed to cool, was repeatedly extracted with ether, the ethereal liquids washed first with water, then with aqueous sodium carbonate, which removed only a trace of acidic substance, finally again with water, and the ether removed. A brown, oily residue was thus obtained, which was shaken with a saturated solution of sodium bisulphite, when a small amount of a solid compound separated. This was collected on a filter by the aid of the pump, and washed with ether. On warming with dilute alkali, a substance was liberated which had the odour of piperonal. This alkaline liquid was subsequently extracted with ether, the ethereal solution being washed, dried, and the ether removed. The residual oily liquid was placed in a freezing mixture and nucleated with a trace of piperonal, when crystallisation ensued, and the resulting product melted at 34—35°. This was identified as piperonal, thus proving the presence of safrole in the oil.

The fraction (b. p. 225—235°), as well as the two preceding ones, were treated with semicarbazide hydrochloride and sodium acetate in alcoholic solution, and the uncombined oil subsequently removed by distillation with steam, when a very small amount of a solid semicarbazone was obtained. On treatment with dilute sulphuric acid, this yielded a few drops of a yellow oil, which possessed an odour resembling that of citral, but gave a β -naphthacinchoninic acid derivative which, when crystallised from alcohol, separated in pearly leaflets melting at 248° with decomposition. The substance, evidently an *aldehyde*, which yielded this derivative was so small in amount that it was impossible further to characterise it.

As this fraction of the oil was slightly levorotatory, it must have contained a small amount of some undetermined substance, for both geraniol and safrole are optically inactive, and the preceding, as well as the principal succeeding, fractions were dextrorotatory.

Fraction 235—245°.—This was a colourless liquid, possessing a strong odour of safrole:

0.2001 gave 0.5502 CO₂ and 0.1417 H₂O. C = 75.0; H = 7.9.

The presence of safrole was proved, as described in connexion with the preceding fraction, by the isolation of a small quantity of piperonal, melting at 33—35°, from the products of its oxidation.

Fraction 245—255°.—This was a colourless liquid, which became slightly yellow on standing. It was comparatively small in amount:

0.1502 gave 0.4126 CO₂ and 0.1021 H₂O. C = 74.9; H = 7.6.

This fraction was specially tested for the methyl ether of eugenol, but with a negative result, since it yielded neither the corresponding bromo-derivative nor could any veratric acid be isolated from the products of its oxidation. On oxidation, however, it developed a strong odour of piperonal, indicating the presence of safrole, and yielded on treatment with bromine a compound which crystallised from alcohol in small needles melting sharply at 128—129°. This was identified as the bromo-derivative of myristicin, which will subsequently be described.

Fraction 255—265°.—This was considerable in amount:

0.1550 gave 0.4048 CO₂ and 0.0984 H₂O. C = 71.2; H = 7.1.

It was evident that this fraction consisted largely of myristicin, together with a small amount of some dextrorotatory substance, probably a sesquiterpene, which it was impossible to isolate.

The subsequent fractions, which had been distilled under diminished pressure, were analysed with the following results:

Fraction 165—169°/40 mm.

0.1500 gave 0.3854 CO₂ and 0.0956 H₂O. C = 70.1; H = 7.1.

Fraction 169—171°/40 mm.

0.1737 gave 0.4457 CO₂ and 0.1089 H₂O. C = 70.0; H = 7.0.

Each of these fractions evidently consisted chiefly of the constituent of the following fraction.

Identification of Myristicin, C₁₁H₁₂O₃.

Fraction 171—173°/40 mm.—This was by far the largest fraction of the heavy oil of nutmeg, amounting to 3420 grams, or more than one-half of the total quantity of oil employed. When freshly distilled, it was a colourless liquid, possessing only a faintly aromatic odour:

0.1469 gave 0.3728 CO₂ and 0.0844 H₂O. C = 69.2; H = 6.4.

0.1135 „ 0.2875 CO₂ „ 0.0677 H₂O. C = 69.1; H = 6.6.

0.2424 „ 0.6098 CO₂ „ 0.1400 H₂O. C = 68.6; H = 6.4.

C₁₁H₁₂O₃ requires C = 68.7; H = 6.2 per cent.

d 20°/20° = 1.1437; *a*_D + 0°6' in a 1-dcm. tube; *n*_D²⁰ 1.54032.

The results of analysis and the determination of the physical constants of this fraction rendered it evident that it consisted of nearly pure myristicin. This compound has previously been obtained from material designated as mace oil (Thoms, *Ber.*, 1903, 36, 3446), but proof of its occurrence in oil of nutmeg has hitherto been lacking.

Dibromomyristicin Dibromide, C₁₁H₁₀O₃Br₄.—This was prepared according to the method described by Thoms (*loc. cit.*). When crystallised from a mixture of alcohol and ethyl acetate, it separated in fine, colourless, silky needles, melting at 128—129°:

0.2085 gave 0.2000 CO₂ and 0.0402 H₂O. C = 25.2; H = 2.1.

C₁₁H₁₀O₃Br₄ requires C = 25.9; H = 2.0 per cent.

Thoms described this compound as a white, crystalline powder, melting at 130°.

isoMyristicin.—A quantity (20 grams) of the fraction (b. p. 171—173°/40 mm.) was heated on a water-bath for two days with an alcoholic solution of 50 grams of potassium hydroxide, and the product extracted with ether. After the removal of the solvent, it was distilled under diminished pressure, when practically all passed over at 166°/18 mm. as a colourless, viscid liquid, which, when placed in a freezing mixture, readily solidified. It was crystallised from alcohol, from which it separated in radiating clusters of needles, melting at 44°:

0.1345 gave 0.3380 CO₂ and 0.0757 H₂O. C = 68.5; H = 6.3.

C₁₁H₁₂O₃ requires C = 68.7; H = 6.2 per cent.

The refractive index of this substance, kindly determined for us by Mr. Frederic H. Lees, was *n*_D^{45°} 1.56551, whereas that of myristicin at the same temperature was 1.52927.

Dibromoisomyristicin Dibromide.—This was easily prepared by the same method as that employed for the corresponding bromo-derivative of myristicin. When crystallised from a mixture of alcohol and ethyl acetate, it separated in stout needles, melting at 156°:

0.2013 gave 0.1915 CO₂ and 0.0406 H₂O. C = 25.9; H = 2.2.

C₁₁H₁₀O₃Br₄ requires C = 25.9; H = 2.0 per cent.

Acids Obtained by the Hydrolysis of the Heavy Oil of Nutmeg.

The alkaline liquid and aqueous washings obtained by the hydrolysis of the oil, as previously described, were concentrated, acidified with sulphuric acid, and distilled with steam. The distillate

contained a quantity of acids in the form of a pale yellow oil, which was extracted by means of ether. From the aqueous liquid, which was still strongly acid, about 20 grams of a barium salt were obtained. This was fractionally crystallised, and each fraction analysed, when it was found to consist entirely of barium acetate.

Fraction	I.	0.8950	of the salt gave	0.8106	BaSO ₄ .	Ba = 53.3.
"	II.	0.7924	" "	0.7247	BaSO ₄ .	Ba = 53.8.
"	III.	0.4997	" "	0.4573	BaSO ₄ .	Ba = 53.8.
"	IV.	0.7443	" "	0.6802	BaSO ₄ .	Ba = 53.7.

(C₂H₃O₂)₂Ba requires Ba = 53.7 per cent.

The pale yellow, oily acids which had been extracted from the distillate by means of ether, as above described, amounted to about 6 grams. These were distilled under the ordinary pressure up to 270°, and the remainder at 20 mm. pressure, when the following fractions were obtained: (a) below 230°; (b) 230—250°; (c) 250—270°/760 mm.; (d) 190—230°/20 mm. Each of these fractions was converted into a sodium salt, from which, by fractional precipitation with a solution of silver nitrate, a number of silver salts were prepared. These were washed, dried in a vacuum over sulphuric acid, and analysed:

(a)	0.0882	gave	0.0386	Ag.	Ag = 43.8.
(b)	0.1150	gave	0.0492	Ag.	Ag = 42.8.
	0.1835	"	0.0789	Ag.	Ag = 43.0.
	0.1531	"	0.0664	Ag.	Ag = 43.4.
	0.1752	"	0.0790	Ag.	Ag = 45.1.
(c)	0.1044	gave	0.0434	Ag.	Ag = 41.6.
	0.1862	"	0.0806	Ag.	Ag = 43.3.
	0.1751	"	0.0765	Ag.	Ag = 43.7.
	0.1231	"	0.0544	Ag.	Ag = 44.2.
(d)	0.1272	gave	0.0503	Ag.	Ag = 39.5.
	0.2145	"	0.0856	Ag.	Ag = 39.9.
	0.2309	"	0.0968	Ag.	Ag = 41.9.

C₈H₁₅O₂Ag requires Ag = 43.0 per cent.
C₉H₁₇O₂Ag " " Ag = 40.8 " "

It would appear from these results that the volatile, oily acids obtained by the hydrolysis of nutmeg oil contain a considerable proportion of an octoic acid, with smaller amounts of acids of higher and lower molecular weight.

Isolation of a New Monocarboxylic Acid, C₁₂H₁₇O·CO₂H.

After the removal of the volatile acids by distillation with steam, as above described, there remained in the distillation flask a semi-

solid mass. This was spread on a porous plate, when a quantity of tarry matter became absorbed and a crystalline solid was obtained. The latter was purified by dissolving it in hot dilute acetic acid, from which it crystallised in hexagonal prisms, melting at 84—85°, which possessed a slightly yellow tint. When crystallised from dilute alcohol, it separated in needles. The substance is extremely soluble in the usual organic solvents, but is insoluble in water:

0.1150 gave 0.2972 CO₂ and 0.0861 H₂O. C = 70.4; H = 8.3.

0.1015 " 0.2620 CO₂ " 0.0758 H₂O. C = 70.4; H = 8.3.

C₁₃H₁₈O₃ requires C = 70.3; H = 8.1 per cent.

0.1640, in alcoholic solution, neutralised 7.4 c.c. N/10 NaOH.

C₁₂H₁₇O·CO₂H requires 7.4 c.c.

The only known monocarboxylic acid of the formula C₁₃H₁₈O₃ possessing properties similar to those of the above compound is carvacroxypropionic acid, which has been described by Bischoff (*Ber.*, 1900, **33**, 1270) as forming colourless prisms, melting at 81.5—82.5°. A specimen of the latter acid was therefore prepared for the purpose of comparison with the above described compound, but the two substances were found to be not identical. The substance isolated from nutmeg oil is therefore to be regarded as a new *monocarboxylic acid*, C₁₂H₁₇O·CO₂H.

Summary.

The results of this investigation have shown that the essential oil of nutmeg contains the following substances:

1. Eugenol, } about 0.2 per cent.
2. *iso*Eugenol, }
3. *d*-Pinene, } about 80 per cent.
4. *d*-Camphene, }
5. Dipentene, about 8 per cent.
6. *d*-Linalool, } about 6 per cent.
7. *d*-Borneol, }
8. *i*-Terpineol, }
9. Geraniol, }
10. A new *alcohol*, yielding on oxidation a *diketone*, C₈H₁₄O₂, in very small amount.
11. A trace of an *aldehyde* resembling citral, but yielding a *β-naphthacinchoninic acid* derivative melting at 248°.
12. Safrole, about 0.6 per cent.
13. Myristicin, C₁₁H₁₂O₃, about 4 per cent.
14. Myristic acid, in the free state, about 0.3 per cent., and apparently a small amount in the form of esters.
15. Formic, acetic, butyric, and octoic acids, and a new *mono-*

carboxylic acid, $C_{13}H_{18}O_3$, all in the form of esters, and in relatively small amount.

Although the proportions of the above-mentioned constituents are those indicated for what we have designated a normal oil of nutmeg, it is obvious that as the latter differed in its physical characters, particularly in its optical rotatory power, from the standards generally adopted for this oil, the composition is subject to considerable variation, according to the character of the material employed for distillation.

This investigation has, furthermore, shown that the portion of nutmeg oil which has hitherto been designated "myristicol" is a mixture of alcohols, of which terpineol appears to be the predominating constituent.

In view of the fact that narcotic properties are attributed to the nutmeg, the authors are at present engaged in an investigation of its constituents other than the essential oil.

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