THE CONSTITUENTS OF SOME INDIAN ESSENTIAL OILS. PART XXIII. THE ESSENTIAL OIL FROM THE FRUITS OF 'PIPER CUBEBA,' LINN.*

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Oil of cubeb is obtained from the dried, full-grown but unripe fruits of *Piper cubeba*, Linn. Although *P. cubeba* is not indigenous to India, and is not widely cultivated, the fruits are imported in considerable quantity. It appeared to us desirable, therefore, to examine carefully the oil obtained from fruits grown in Mysore. A quantity of oil from this source was prepared in 1923, but it was not studied in detail at the time (*J. Ind. Inst. Sci.*, 1925, 8A, 159).

Although oil of cubeb is official in the British Pharmacopœia, and has been repeatedly examined (cf. Finnemore, 'The Essential Oils,' 192 *seq.*), there would appear to be considerable doubt as to its main constituents, only the presence of *l*-cadinene having been established with certainty.

The fruits used in this investigation, which were of undoubted authenticity, gave on distillation in steam 7·5 per cent. of an oil as compared with a yield of 11·9 per cent. obtained in 1923 from fruits from the same source. It is possible that the fruits were slightly immature.

The terpene fraction of the oil (about 35 per cent.) consisted essentially of *d*-sabinene, which was identified by conversion into terpinene dihydrochloride, and by oxidation with potassium permanganate to *d*-sabinenic acid. From amongst the oxidation products a small quantity of *cis*-caronic acid was isolated indicating the presence of either Δ^3-carene or Δ^4-carene. By the oxidation of the appropriate fraction with potassium permanganate in acetone solution a small amount of a keto-acid was obtained, and this was identified as *d*-1 : 1-dimethyl-2-γ-ketobutyl*cyclo*propane-3-carboxylic acid by the preparation of the semicarbazone, m.p. 178–180°, thus confirming the presence of *d*-Δ^4-carene. No evidence was obtained of the presence of any other terpenes, although pinene, camphene, and dipentene were specially tested for.

The terpene fraction (b.p. 105–110°/100 mm.) had a camphoraceous odour resembling that of cineole and analysis indicated the

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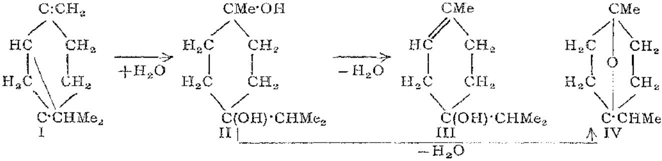
presence of an oxygenated compound. No derivatives of 1 : 8-cineole could be obtained, but on saturating a glacial acetic acid solution of this fraction of the oil with hydrogen chloride, an excellent yield of terpinene dihydrochloride separated, although the parent hydrocarbon itself was absent. The formation of this hydrochloride appeared to point to the presence of 1 : 4-cineole. This oxide has so far not been found to occur in nature, and was prepared synthetically by Wallach (*Annalen*, 1912, **392**, 62) by the dehydration of 1 : 4-terpin. Unfortunately, it is somewhat difficult to identify, since its only recorded properties are its conversion into terpinene dihydrochloride on treatment with hydrogen chloride, and its oxidation by potassium permanganate to an unidentified acid, m.p. 157°, which is sparingly soluble in water. Our specimen, which was contaminated with *d*-Δ^4-carene, yielded on oxidation under the conditions used by Wallach a sparingly soluble acid, m.p. 157°, which is at present under investigation, and there can therefore be little doubt that 1 : 4-cineole was present in the oil. In veiw of the probable occurrence of this oxide in other essential oils one of us (J.L.S.) proposes to make a further study of its properties.



The alcohols, which formed about 11 per cent. of the oil, were mainly tertiary. On hydration with dilute sulphuric acid *trans*-terpinene-terpin was formed together with what appeared to be *cis*-terpin. The latter was not obtained in sufficient quantity for complete characterisation, and it was not possible to confirm the presence of terpineol by other means. The *trans*-terpinene-terpin resulted from the hydration of *d*-1-methyl-4-*iso*propyl-Δ^1-*cyclo*hexen-4-ol (*d*-Δ^1-terpinen-4-ol), the presence of which was confirmed by oxidation to the glycerol, 1-methyl-4-*iso*propyl-1 : 2 : 4-trihydroxy*cyclo*hexane, m.p. 116–117° and m.p. anhyd. 128–129° (cf. Wallach, *Annalen*, 1906, **350**, 169).

The co-existence of *d*-sabinene (I), *d*-1-methyl-4-*iso*propyl-Δ^1-*cyclo*hexen-4-ol (III), and 1 : 4-cineole (IV) in the same oil is of considerable interest, since, as will be seen from a study of their formulæ, these substances are extremely closely related, their interconversion merely involving the addition or loss of water with the intermediate formation of 1 : 4-terpin (II).

In the sesquiterpene fraction *l*-cadinene was readily identified by the preparation of the dihydrochloride, but the low rotation pointed to the presence of a second hydrocarbon, the nature of which could not be determined.

In view of the marked difference in the rotation of the oil distilled in 1923 (Table I, sample B), it appeared desirable to determine if possible the cause of this, and the small remaining quantity of this oil was fractionated. The terpene fraction was found to be almost inactive and consisted of *dl*-sabinene, a hydrocarbon which has only once previously been described (Penfold and Simonsen, *J. Proc. Roy. Soc. N. S. W.*, 1925, **59**, 147). It was characterised by the preparation of *dl*-sabinenic acid, which was compared with the specimen obtained by the above-mentioned authors. The *l*-cadinene isolated from the sesquiterpene fraction had a much higher rotatory power than that which was obtained from sample *A*, and these two factors account for the marked difference in the rotatory powers of the two oils.

The composition of Mysore oil of cubeb is approximately the following:—*d*-sabinene (33 per cent.), *d*-Δ^4-carene and 1: 4-cineole (12 per cent.), *d*-Δ^1-terpinene-4-ol and other alcohols (11 per cent.), sesquiterpenes mainly *l*-cadinene (14 per cent.), sesquiterpene alcohols (17 per cent.), unidentified (13 per cent.).

EXPERIMENTAL.

The crushed fruits (21·8 kg.) were distilled in steam, yielding a light green oil (1·63 kg.). After drying over magnesium sulphate the oil had the constants given in Table I, column A, the constants for the sample of oil obtained in 1923 being given in column B.

TABLE I.

—	A	B
d^{30}_{30}	0·8937	0·9167
n^{30}_{D}	1·4811	1·4894
$[\alpha]^{30}_{D}$	+25·6°	−29·9°
Acid value	0·78	Nil
Sap. value	5·2	0·5
Do. after acetylation	54·6	24·1
Colour	Light green	Pale green, yellow on long keeping.

A quantity of the oil (*A*) was treated with an alcoholic solution of potassium hydroxide to hydrolyse the esters present, dried over magnesium sulphate, and distilled under diminished pressure, yielding the fractions given in Table II.

TABLE II.

No.	B.p./100 mm.	d_{30}^{30}	n_{D}^{30}	$[\alpha]_{D}^{30}$	Yield per cent.
1	1–100°	...	...	...	trace
2	100–104°	0·8435	1·4644	+59·78°	27·9
3	104–110°	0·8502	1·4667	+54·27°	9·2
4	110–115°	0·8570	1·4685	+44·83°	4·9
5	115–125°	0·8762	1·4706	+18·62°	2·7
6	125–135°	0·9186	1·4733	+16·22°	3·4
7	135–160°	0·9465	1·4795	+ 8·45°	6·6
8	160–180°	0·9562	1·4902	− 2·72°	10·9
9	180–200°	0·9779	1·5015	−10·45°	13·5
10	200–220°	1·0356	1·5142	...	11·4
	Residue and loss				9·5

The percentage weight is in all cases calculated on the original weight of the oil used.

Fractions 2 to 6, which were free from aldehydes and ketones, were repeatedly distilled under diminished pressure, the final fractionation being over sodium, and the results are summarised in Table III.

TABLE III.

No.	B.p. 100 mm.	d_{30}^{30}	n_{D}^{30}	$[\alpha]_{D}^{30}$	Yield per cent.	Terpinene, 2HCl from 5 c.c.	Sabinenic acid from 10 gms.
A	94–96°	0·8367	1·4603	+56·01°	1·3	*a*	5
B	96–97°	0·8382	1·4623	+65·45°	5·2	1·6	4·9
C	97–98°	0·8388	1·4630	+68·84°	9·9	1·6	4·9
D	98–100°	0·8390	1·4655	+64·86°	5·4	0·9	3·7
E	100–101°	0·8395	1·4656	+61·41°	2·2	0·5	*a*
F	102–103°	0·8398	1·4661	+56·81°	4·7	0·3	*a*
G	103–106°	0·8425	1·4686	+39·74°	1·1	*a*	1·4
H	106–108°	0·8459	1·4689	+35·42°	1·1	*a*	*a*
I	108–110°	0·8492	1·4702	+24·75°	0·8	0·9*	Nil
J	110–113°	0·8529	1·4706	+18·93°	1·3	*a*	*a*
K	113–116°	0·8605	1·4706	...	0·6	*a*	*a*
L	116–120°	0·8713	1·4706	...	0·3	*a*	*a*
M	120–125°	0·8920	1·4680	...	1·4	0·8*	*a*

(*a*) Not determined. * From 2·5 c.c.

d-*Sabinene*.—Fractions A to D consisted essentially of *d*-sabinene, the constants of fraction C agreeing well with those quoted for this hydrocarbon.

TABLE IV.

——	Fraction C.	*d*-Sabinene from savin oil.*
d_{30}^{30}	0·8382	d_{15}^{15} 0·8481
n_{D}^{30}	1·4630	...
$[\alpha]_{D}^{30}$	+68·8°	+68·9°

* Parry, "Essential oils," II, 56.

For a number of the fractions the yields of terpinene dihydrochloride and of *d*-sabinenic acid (Wallach, *Annalen*, 1908, **359**, 268) are given in the table. The *d*-sabinenic acid after recrystallisation from hot water had m.p. 55–57° and in alcoholic solution (*c.* 1·002) $[\alpha]_{D}^{30}$ +110·7° (Found: C, 64·9; H, 8·7: calc. C, 65·2; H, 8·7 per cent.). The identity was confirmed by careful comparison with an authentic specimen. The terpinene dihydrochloride after crystallisation from dilute alcohol had m. p. 52° which was not depressed on admixture with a specimen from another source (Found: Cl, 33·8; calc. 33·9 per cent.).

d-Δ^4-*Carene.*—From amongst the products of the oxidation with potassium permanganate of fractions H to L (Table III) a small quantity of an acid, m.p. 172–173°, was separated, which was identified as *cis*-caronic acid. Since this indicated the presence of either Δ^3-or Δ^4- carene a portion of these fractions was redistilled at the ordinary pressure and the fraction of b.p. 163–168°/685 mm. collected separately. This fraction was oxidised in acetone solution with potassium permanganate (*J.C.S.*, 1922, **121**, 2292), when a small quantity of a keto-acid was obtained which yielded a semicarbazone, m.p. 178–180°, not depressed when mixed with the original semicarbazone prepared from *d*-1 : 1-dimethyl-2-γ-ketobutyl*cyclo*propane-3-carboxylic acid.

1 : 4-*Cineole.*—The fractions H to M had a marked camphoraceous odour, which was more intense in the higher-boiling fractions. Analysis of fraction H showed the presence of an oxygenated substance mixed with the hydrocarbon (Found: C, 79·9; H, 11·7; $C_{10}H_{18}O$ requires C, 77·9; H, 11·7 per cent.), whilst fraction M on redistillation (b.p. 109–112°/100 mm.) gave on analysis C, 78·6; H, 11·7 per cent. This fraction, which did not give any of the characteristic reactions of

1 : 8-cineole, yielded on treatment with hydrogen chloride in acetic acid solution terpinene dihydrochloride, m.p. 52°, whilst on oxidation with potassium permanganate on the water bath it gave an acid, which was sparingly soluble in water and had m.p. 157° (cf. Wallach, *loc. cit.*). The aqueous solution from which this acid was separated yielded a small quantity of *cis*-caronic acid, and as has already been mentioned (p. 92) there can be little doubt that this fraction of the oil was a mixture of 1 : 4-cineole and *d*-Δ^4-carene.

Terpene alcohols: d-1-*methyl*-4-iso*propyl*-Δ^1-cyclo*hexen*-4-*ol*.—Fraction 7 (Table II) was refractionated under diminished pressure with the results given in Table V.

TABLE V.

No.	B.p./100 mm.	d^{30}_{30}	n^{30}_D	$[\alpha]^{30}_D$	Yield per cent.
i	130—135°	0·9380	1·4696	+18·66°	0·9
ii	135—138°	0·9481	1·4709	...	0·6
iii	138—140°	0·9503	1·4709	...	0·3
iv	140—142°	0·9536	1·4712	+18·72°	1·1
v	142—145°	0·9565	1·4716	+17·02°	0·6
vi	145—150°	0·9582	1·4776	+13·84°	1·5
vii	150—155°	0·9600	1·4812	...	0·6
viii	155—160°	0·9573	1·4844	+ 1·48°	1·2

Attempts to prepare crystalline phenylurethanes from the various fractions were not successful, whilst comparative experiments with phthalic anhyride showed that the percentage of primary alcohols present probably did not exceed 2 per cent. being greatest in fraction viii. The acid phthalate which was formed could not be induced to crystallise. On oxidation of this fraction with chromic acid, evidence was obtained of the formation of an aldehyde, but it could not be obtained pure.

Fractions iv to vi (5 c.c.) were shaken with dilute sulphuric acid (5 per cent.) for a week, and the reaction mixture was exhausted with ether. On removal of the solvent a solid (1·3 gms.) remained which, after crystallisation from methyl alcohol, had m.p. 136–137°, and was identified as *trans*-terpinene-terpin by analysis and by the method of mixed melting point (Found: C, 69·9; H, 12·0; calc. C, 69·8; H, 11·5 per cent.). The acid solution from which the terpinene-terpin had been removed was saturated with ammonium sulphate and thoroughly extracted with chloroform, when a solid was obtained which had m.p. 113–115°, and on resolidification m.p. 104–105°. No depression was observed on admixture with *cis*-terpin from another source, but, owing to the small quantity of material available, it was not possible to confirm the identity.

The presence of *d*-1-methyl-4-*iso*propyl-Δ^1-*cyclo*hexen-4-ol in fraction vi was supported by its conversion, on treatment with hydrogen chloride in acetic acid solution, into terpinene dihydrochloride. When this fraction of the oil was oxidised with alkaline potassium permanganate at 0° it yielded *d*-1-methyl-4-*iso*propyl-1 : 2 : 4-trihydroxy*cyclo*hexane, which after crystallisation from ether had m.p. 114–116°, anhydrous m.p. 126–128°. In alcoholic solution (*c* 10) $[\alpha]^{30}_D + 23·1°$ was observed (Wallach, *Annalen*, 1906, **350**, 169, gives m.p. 116–117° and 128–129° anhyd., $[\alpha]_D$ + 21·24°). The presence of the unsaturated alcohol was therefore fully established.

Sesquiterpenes.—Fractions 8 and 9 (Table II) were repeatedly redistilled and the residue boiling above 140°/12 mm. was added to fraction 10. The lower-boiling fractions were distilled twice over sodium yielding two main fractions : (*a*) 120–122°/13 mm., d^{30}_{30} 0·9095, n^{30}_D 1·4930, $[\alpha]^{30}_D - 10·1°$; (*b*) 126–130°/13 mm., d^{30}_{30} 0·9174, n^{30}_D 1·5013, $[\alpha]^{30}_D - 3·6°$.

From both fractions *l*-cadinene dihydrochloride, m.p. 117–118°, $[\alpha]^{30}_D - 38·1°$ (*c* 0·2546 in alcohol) was obtained (Found : Cl, 25·5 ; calc. 25·6 per cent.). The identity was confirmed by comparison with an authentic specimen. No other sesquiterpene could be characterised.

Sesquiterpene alcohols.—Fraction 10 (Table II) on redistillation yielded two main fractions (i) b.p. 150–155°/13 mm., d^{30}_{30} 1·0421, n^{30}_D 1·5150; C, 81·8, H, 10·8 ; (ii) 155–160°/13 mm., d^{30}_{30} 1·2050, n^{30}_D 1·5198, C, 81·6 ; H, 10·9 ($C_{15}H_{24}O$ requires C, 81·8 ; H, 10·9 per cent.). Neither of these fractions yielded a crystalline hydrochloride, and the presence of cadinol is therefore improbable. The alcohols did not react with phthalic anhydride at 130°.

EXAMINATION OF SAMPLE B (TABLE I).

A small specimen of the oil remaining from the 1923 distillation was hydrolysed with an alcoholic solution of potassium hydroxide and the terpene and sesquiterpene fractions were examined. The terpene fraction, after distillation over sodium, was separated into two main fractions : (*a*) b.p. 95–98°/100 mm., d^{30}_{30} 0·8302, n^{30}_D 1·4604, $[\alpha]^{30}_D + 3·1°$: (*b*) 98–100°/100 mm., d^{30}_{30} 0·8322, n^{30}_D 1·4625, $[\alpha]^{30}_D$ + 2·5°. On oxidation of fraction *b* with potassium permanganate *dl*-sabinenic acid, m.p. 83–84°, was obtained, thus establishing the presence of *dl*-sabinene in this fraction of the oil. The sesquiterpene fraction was found to have a higher rotation, $[\alpha]^{30}_{D} - 37{\cdot}5°$, than that of sample A. It yielded a specimen of *l*-cadinene dihydrochloride with a rotation identical with that previously obtained. The nature of the other hydrocarbon present was not determined.

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