III.—ESSENTIAL OIL FROM LEAVES OF *THYMUS SERPYLLUM*, LINN.

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Many varieties of thyme are found along the Himalayan range. One growing in parts of the Punjab and Kashmir yields about 0·5 per cent. of an essential oil and was identified by C. E. Parkinson, Forest Botanist, to be *Thymus serpyllum*, Linn. It is a slender, much-branched shrub commonly known as the wild thyme and ranges from Europe through Northern Africa to Western and Central Asia. French oil of thyme is the most esteemed variety of thyme oil and is distilled from the herb *Thymus vulgaris*, Linn., its value being chiefly dependent on the 20–40 per cent. of thymol contained. In the south of France the oil not infrequently suffers admixture with the oil of *Thymus serpyllum*. As a result of previous examinations by Febve (*Compt. rend.*, 1881, **92**, 1290) and Jahns (*Arch. Pharm.*, 1880, **216**, 277) the presence of *p*-cymene, carvacrol and thymol in the latter oil has been definitely established, and it is known to contain only a very small amount of phenols; thus Jahns found only 1 per cent. and Buri (*Arch. Pharm.*, 1878, **212**, 485) 3 per cent. in the oils examined by them.

The Indian oil examined in these laboratories has constants somewhat different from the usually accepted values for *Thymus serpyllum* and approximating to those of *Thymus vulgaris* (Table I). The two samples examined contained 52·7 and 42 per cent. of phenols mainly carvacrol; tests for thymol gave negative results, the derivatives obtained being inseparable mixtures. Besides carvacrol, there is another phenol which has not been characterised, and in this connection it is of interest to note that when French thyme plants were grown in Germany they yielded oils containing carvacrol but no thymol. The neutral portion of the oil is rich in *p*-cymene (17 per cent.), and γ–terpinene also appears to be present. Phenylurethanes of the terpene alcohols were obtained melting at 134–135°, 127–129° and 108–115° which, although not in good agreement, indicate the probable presence of borneol and α-terpineol. In the higher boiling fractions of the oil, the sesquiterpene zingiberene has been definitely recognised, hitherto known to occur only in oils of ginger and *Curcuma zedoaria* (*this Journal*, 1928, **XIA**, 196).

The percentage composition of the oil is approximately as follows:—Phenols (mainly carvacrol), 53; *p*-cymene, 17; terpenes (γ–terpinene and others), 8; terpene alcohols, 5; sesquiterpenes (zingiberene and others), 4.

Experimental.

The oil was dark reddish brown, and on drying over anhydrous magnesium sulphate had the physical and chemical characters shown in Table I, which also gives the constants for the commercial French thyme oil and limits for *Thymus serpyllum* oil.

TABLE I.

	Thymus serpyllum (Indian)	*Thymus vulgaris* (French Thyme)	*Thymus serpyllum** (French)
d^{30}_{30}	0·9269	0·905—0·935	0·890—0·920
n^{30}_{D}	1·4968	1·4800—1·4950	..
$[\alpha]^{30}_{D}$	—4·8°	—0·5° to —4°	—10° to —20°
Phenols	52·7 per cent. (mainly carvacrol)	20 to 40 per cent. (mostly thymol)	Below 5 per cent.
Absorption with potassium metabisulphite	Nil	..	..

* E. J. Parry. *The Chemistry of Essential Oils and Artificial Perfumes*, 4th edition, 1921, **1**, 246.

The oil is thus richer in phenols than that obtained from *Thymus serpyllum* grown in other parts of the world and the constants are comparable with those for French thyme oil.

Phenols.—The oil (500 g.) was washed with aqueous sodium carbonate and the phenols isolated by shaking with 4 per cent. sodium hydroxide on a water bath, acidifying the alkaline extract with dilute sulphuric acid and extracting the liberated phenols (52·7 per cent.) with ether. The ethereal solution was washed with water, dried and the ether distilled: the product (240 g.) on repeated fractionation with a 4–pear Young's column under 32 mm. pressure gave the following fractions:—

TABLE II.

Fractionation of Phenols.

Fraction	B.P.	d^{30}_{30}	n^{30}_{D}	Weight in gms.	Yield per cent. on	
					total phenols	original oil
1	127—130°	0·9613	1·5118	5·0	2·1	1·1
2	130—132	0·9701	1·5158	5·0	2·1	1·1
3	132—134	0·9710	1·5162	6·5	2·7	1·4
4	134	0·9719	1·5171	6·5	2·7	1·4
5	134	0·9719	1·5172	7·0	3·1	1·5
6	134—136	0·9719	1·5172	10·0	4·1	2·2
7	135—136	0·9719	1·5173	10·0	4·1	2·2
8	,,	0·9727	1·5175	10·8	4·4	2·4
9	,,	0·9727	1·5178	9·0	3·7	2·0
10	,,	0·9727	1·5178	77·0	33·3	16·9
11	,,	0·9728	1·5178	7·0	3·1	1·5
12	,,	0·9732	1·5178	54·0	22·4	11·9

The constants for pure thymol and carvacrol being as follows:—

	B.P.	d^{30}_{30}	n^{30}_{D}
Thymol	132°/32 mm.	0·965	1·5186 (superfused)
Carvacrol	136°/32 mm.	0·972	1·5200

It is evident that not more than a small proportion of thymol could be present; confirming this the fractions were cooled for two days at -5° without solidification. According to Sage and Dalton (*Perf. and Essent. Oil Rec.*, 1924, **15**, 345) mixtures of pure thymol and carvacrol containing 5, 10 and 20 per cent. thymol melt at about 1°, 3° and 9°, respectively, so that thymol, if present, did not exceed 5 per cent. in any fraction. The first two fractions alone were likely to contain this phenol and as they formed only 2·2 per cent. of the whole oil it follows that the amount of thymol was less than 0·1 per cent. The physical characters of the fractions showed that these were not pure carvacrol, but it was not found possible to identify other phenols. Attempts to detect thymol in the fractions by means of colour reactions applicable to thymol, carvacrol and their mixtures were unsuccessful due perhaps to the presence of a new phenol.

Phenylurethanes.—Fractions 1, 6 and 12 (5 g. each), phenyl *iso*cyanate (4·6 g.) and petroleum (b.p. 120–150°, 30 c.c.) were boiled in an acetylation flask during two hours. The cooled mixture deposited crystals which were recrystallised from petrol and ethyl alcohol in succession until the melting point was constant. The phenylurethane from fraction 12 showed no depression with carvacrol phenylurethane (m.p. 138°).

Nitrosophenols.—To 5 c.c. each of fractions 2, 6 and 12 dissolved in ethyl alcohol (25 c.c.) was added concentrated hydrochloric acid (25 c.c.), cooled to zero and gradually treated with a saturated solution of sodium nitrite (3·6 g.). On pouring into water a light yellow bulky solid was obtained which was recrystallised from benzene.

Benzoyl derivatives of nitrosophenols.—The nitrosophenol (3 g.) obtained from fractions 2, 6 and 12, was dissolved in 10 per cent. sodium hydroxide solution (10 c.c.) and benzoyl chloride (3·5 g.) added with shaking; the product separated as orange plates, and was recrystallised from alcohol. Table III shows the melting points of the derivatives obtained.

TABLE III.

Melting Points of Phenol Derivatives.

	Phenylurethanes	Nitroso derivative	Benzoyl derivatives of nitrosophenols
Fraction 1, 2	(1) 132—136° (2) 125—134 (3) 105—115	129°	(1) 93—98° (2) 77—85
Fraction 6	137	131	(1) 74—80 (2) 78—85
Fraction 12	138	152	(1) 73—76
	..	..	(2) 85
Thymol	106—107	160—164	109·5
Carvacrol	138	153	87, 85

Fraction 1 appears to be a mixture of carvacrol and thymol, although the latter could not be detected, and subsequent fractions become richer in carvacrol. Fraction 6 gives a pure phenylurethane of carvacrol but the nitroso- and benzoyl derivatives appear to be mixtures. Fraction 12 is pure carvacrol, all its derivatives having correct melting points.

To effect a separation of the phenols (1) ether extraction of alkaline solutions of varying strength, and (2) steam distillation were tried, but no separation could be effected. Shaking with a solution of normal potassium phosphate and examining the dissolved and undissolved phenols, gave a phenylurethane m.p. 103° from the dissolved portion, and this may be crude thymol phenylurethane.

Neutral oil.— After removing phenols by sodium hydroxide the residual oil was washed with water and dried over anhydrous magnesium sulphate when it had the following constants:—d_{30}^{30} 0·9017, n_{D}^{30} 1·4781, $[\alpha]_{D}^{30}$—7·65°, ester value 34·0, acetyl value 47·5. The oil (150 g.) was saponified with 10 per cent. alcoholic potash, diluted with water and extracted with ether. The ethereal solution was dried, the ether distilled and the residual oil fractionated under 50 mm. pressure with a 3-bulb Le-Bel column giving the results shown in Table IV.

TABLE IV.

Fraction	B.P.	d_{30}^{30}	n_{D}^{30}	$[\alpha]_{D}^{30}$	Weight in grams	Yield per cent. on original oil
1	below 80°	..	1·4708	..	..	..
2	80— 90	0·8449	1·4713	— 3·8°	19·0	6·0
3	90— 93	0·8473	1·4749	— 2·0	51·0	16·0
4	95—100	0·8540	1·4765	— 1·1	15·5	4·8
5	100—105	0·8684	1·4770	— 2·6	6·5	2·0
6	105—110	0·8744	1·4770	— 3·4	3·8	1·2
7	110—120	0·9019	1·4792	— 7·3	2·2	0·7
8	120—130	0·9217	1·4821	—10·5	5·5	1·7
9	130—140	0·9319	1·4888	—14·6	13·5	4·2
10	140—150	0·9227	1·4951	—22·8	9·5	3·0
11	150—160	0·8973	1·4925	—41·5	8·5	2·6
12	160—175	0·9325	1·5002	—23·1	3·5	1·1
	Residue and loss				11·5	3·6

Fractions 2, 3, 4 and 5 which consist of the greater part of the terpenes present in the oil were repeatedly fractionated with a Young's column under 50 mm. pressure, the results being shown in Table V.

TABLE V.

Fractionation of Terpenes.

Fraction	B.P.	d_{30}^{30}	n_D^{30}	$[\alpha]_D^{30}$	Weight in gms.	Yield per cent. on original oil
A	62—76°	..	1·4606	..	0·6	0·2
B	76—78	0·8436	1·4663	—7·3°	3·8	1·2
C	78—83	0·8436	1·4691	—5·5	7·0	2·2
D	84—88	0·8436	1·4720	—2·6	2·5	0·8
E	88—90	0·8441	1·4742	—2·4	19·8	6·2
F	90—91	0·8461	1·4751	—0·9	8·5	2·7
G	91—92	0·8496	1·4765	—0·7	30·5	9·6
H	92—93	0·8540	1·4770	—0·7	6·0	1·8

No ketones or aldehydes were detected in any of the fractions. A low boiling alcohol appeared to be present in A and B but no phenylurethane could be prepared. Attempts to prepare a solid hydrochloride from B, D and H, and a nitrosochloride, nitrosite or nitrosate from C, E and H were unsuccessful.

Fraction E (*γ–terpinene.*).— Fraction E (10 c.c.), potassium permanganate (60 g.), potassium hydroxide (16 g.), ice (500 g.) and water (500 g.) were mixed in a bottle and shaken mechanically. The unattacked terpene (3·5 c.c.) was distilled in steam. The filtrate after removal of manganese dioxide was evaporated to dryness and the residue extracted with alcohol. A small amount of a solid was obtained which melted at 231–234°, probably the erythritol $C_{10}H_{16}(OH)_4$ of γ–terpinene, which melts at 237–238°. The mother liquor from the erythritol on acidifying with dilute sulphuric acid yielded *p*–hydroxy*iso*propylbenzoic acid, m.p. 156–157° derived from *p*–cymene (see fraction G).

Fraction G (*p–cymene*).—Fraction G (5 c.c.) with potassium permanganate (20 g.) and water (400 c.c.) were boiled under reflux for two days and shaken occasionally. The potassium salts obtained by evaporation were boiled with alcohol and filtered. The soluble potassium salt on acidifying gave an acid m.p. 156–157° (equivalent 179·2) on recrystallisation from alcohol. A specimen of *p*–hydroxy*iso*propylbenzoic acid prepared from a sample of pure *p*–cymene had m.p. 156–157° and gave no depression when mixed with the acid obtained from fractions F, G and H confirming the presence of *p*–cymene.

Fractions 6 and 7 did not yield a phenylurethane or nitrosochloride.

Fractions 8, 9 *and* 10 yielded solid phenylurethanes on boiling with phenyl*iso*cyanate in petroleum solution, but all the derivatives were found to be complex mixtures melting over a wide range. On fractional crystallisation from petrol three crops were obtained with melting points 134–135°, 127–129° and 108–115°. An attempt to confirm the presence of α–terpineol by preparing the nitrosite was not successful. It is probable that borneol (phenylurethane, m.p. 138°) and α-terpineol (phenylurethane, m.p. 112-113°) are present in the fractions.

Fraction 11 (*zingiberene*).—On repeated distillation over sodium which reacted with a considerable proportion of the oil, 6 g. were obtained having the following constants:—B.p. 157-162°/45 mm., d^{30}_{30} 0.8886, n^{30}_{D} 1·4945, $[\alpha]^{30}_{D}$ —52°, $[R_L]_D$ 66.9. Zingiberene has b.p. 164-165°/45 mm., d^{30}_{30} 0·8639, n^{30}_{D} 1·4916, $[R_L]_D$ 68·4. The constants indicate the presence of a bicyclic sesquiterpene besides zingiberene. The fraction gave a nitrosochloride with amyl nitrite and hydrochloric acid melting at 95-96° after crystallisation from methyl alcohol and unchanged on mixing with zingiberene nitrosochloride. A nitrosate (m.p. 86-87°) was also obtained confirming the presence of zingiberene. In fraction 10, the fall in density and rise in refractive index and rotation, is due to admixture with zingiberene whose presence has been shown in fractions 11 and 12. The content of zingiberene in the oil is approximately 0·9, 2·0, 0·5 per cent. respectively in fractions 10, 11 and 12, or 3·4 per cent. in the whole oil.

Fraction 12 was apparently a mixture of sesquiterpenes and a small quantity of sesquiterpene alcohols. Zingiberene nitrosochloride was also obtained from this fraction. There was no reaction with phthalic anhydride at 130-140°, showing the absence of primary and secondary alcohols.