Essential Oils and Their Constituents XXXVII. Isolation and Structure of Khusenol, a New Sesquiterpenic Primary Alcohol from Oil of Vetiver

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A new sesquiterpenic tricyclic primary alcohol has been isolated from Angola vetiver oil. It was found to be identical with the product obtained by $LiAlH_4$ reduction of methyl khusenate, and on oxidation with CrO_3 and Ag_2O it gave khusenic acid. The alcohol has, therefore, been assigned structure I and named khusenol.

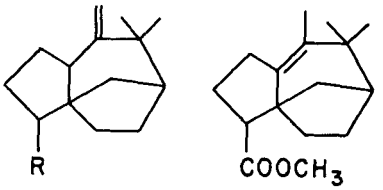
A NEW SESQUITERPENE alcohol has been determined to be the main constituent of the primary alcohol fraction of Angola vetiver oil. The present communication describes its isolation and properties, and records experimental evidence for its structure (I). The alcohol has been named "khusenol" in view of its structural relationship to another constituent of the oil, khusenic acid, which was shown to possess a novel carbon skeleton and assigned structure II (1).

A sample of angola vetiver oil, from which the free acids as well as the aldehydes and ketones had been removed previously, was treated with phthalic anhydride on a steam bath. The resulting hydrogen phthalate esters were saponified to give the primary alcohol fraction (35.5% of the oil sample), which was chiefly composed of khusenol (64% by GLC analysis). Fractional distillation of the primary alcohol fraction gave a 90% pure sample of khusenol. The alcohol may be characterized through its 3,5-dinitrobenzoate (m.p. 116°).

Dehydrogenation of khusenol with selenium at 300 ± 10° failed to yield any aromatic product. Catalytic hydrogenation showed the presence of one double bond, indicating the tricyclic nature of the compound. The infrared spectrum of the alcohol (Fig. 1) exhibited absorption bands at 1632 and 890 $cm.^{-1}$ characteristics of a $CH_2 = C <$ group. The NMR spectrum of the compound (Fig. 2) showed two triplets centered at 4.58 and 4.73δ, instead of the expected doublet for the olefinic protons, indicative of long range coupling. An additional NMR peak at 1.07δ with a shoulder ($\approx$1.06δ) was assigned to two methyl groups. A detailed study of the NMR spectra of khusenol, khusenic acid, and some related compounds will be reported shortly.

Treatment of khusenol with CrO_3–pyridine yielded a mixture of carbonyl compounds (mainly aldehydes, IR spectrum), which were oxidized with Ag_2O to the corresponding acids and converted into methyl esters by reaction with diazomethane. On gas chromatographic analysis, the mixture of esters was found to be chiefly composed of two products, one of which was methyl khusenate (III). Treatment of the ester mixture with HCl brought about isomerization of methyl khusenate to methyl isokhusenate (IV) (2).

The relationship between the alcohol and khusenic acid implied in these results was confirmed by comparing the properties of khusenol with those of the alcohol obtained by reduction of methyl khusenate with $LiAlH_4$. The IR and NMR spectra, and the m.p. of the 3,5-dinitrobenzoate of the two alcohols, as well as their gas and thin-layer chromatographic properties were identical. Khusenol is, therefore, assigned Structure I.



I, R = CH_2OH IV

II, R = COOH

III, R = $COOCH_3$

EXPERIMENTAL

Apparatus and other pertinent details for UV, IR, and NMR spectral measurements, microanalyses, and gas chromatographic determinations were described before (2).

Isolation of the Primary Alcohol Fraction of Angola Vetiver Oil—A sample of the oil (90.3 Gm.) from which the free acids as well as the aldehydes and ketones had been removed by reaction with Amberlite-IRA-400 ion-exchange resin (2, 3) and Girard T reagent (4), respectively, was treated with freshly sublimed phthalic anhydride (95 Gm.) on a steam bath for 2 hr. The resulting hydrogen phthalate esters of the primary alcohols were separated and saponified following the method of Elze as described by Sterrett (5). Yield of the primary alcohol fraction was 32.1 Gm. (35.5% of the oil). Gas-chromatographic examination of the isolate employing a 3% SE-30 column (2) showed the presence of one major constituent (64%; relative retention time 0.857, reference standard-phenanthrene).

Isolation of Khusenol—A portion (32.1 Gm.) of the fraction containing primary alcohols was submitted to fractional distillation (pressure: 3 mm.; reflux ratio: 10:1) using a Gallenkamp fractional distillation unit. When 11 fractions (total weight: 23.4 Gm.) had been collected, the distillation slowed down. At this stage the residue in the distillation pot was transferred to a small flask (25 ml.), and fractional distillation was resumed at 0.7 mm. pressure employing a Quickfit micro-distillation assembly. Three more fractions (total weight 5.3 Gm.) were collected. All 14 fractions were analyzed by gas chromatography on an SE-30 column (2) and found to be chiefly composed of khusenol. Fraction No. 13 (3.4 Gm.) was the purest (90%). An analytical specimen, prepared by gas chromatography on a 20% Reoplex 400 column (2), possessed the following properties. $b.p._{0.7}$ 140–142°; n_D^{27} 1.524;

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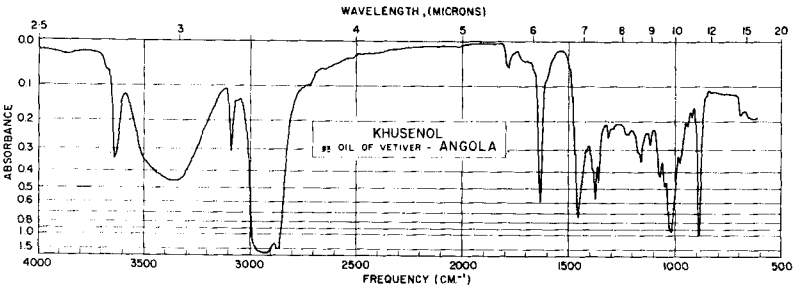

Fig. 1—Infrared spectrum of khusenol.

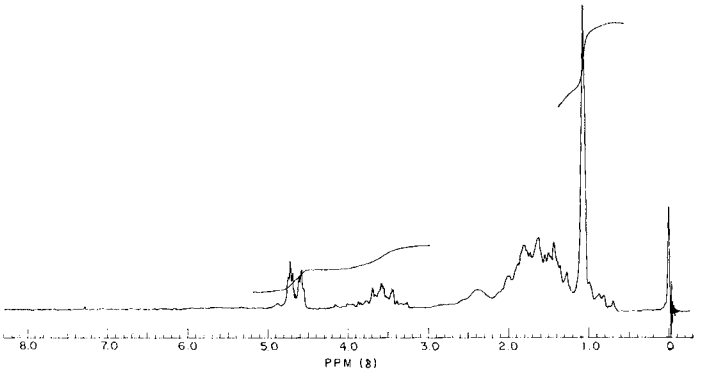

Fig. 2—NMR spectrum of khusenol. Solvent, $CDCl_3$; sweep width, 500. At sweep width of 100 a distinct shoulder near 1.06 δ was observed.

$[\alpha]_D^{29}$ + 14.5°; D_{26}^{26} 0.9740; 3,5-dinitrobenzoate, m.p. 116°.

Anal.—Calcd. for $C_{22}H_{26}O_6N_2$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.90; H 6.32; N, 6.75.

Dehydrogenation of Khusenol—A mixture of khusenol (381 mg.) and selenium (750 mg.) was heated at 300 ± 10° for 10 hr. under a stream of nitrogen. The reaction mixture was extracted with hexane (5 × 2 ml.), and the dark brown oil, which remained after evaporation of the solvent was chromatographed on alumina (grade I, 12 Gm.). Three fractions were collected: 1, (hexane, 30 ml.) 180 mg.; 2, (hexane, 30 ml.) 5 mg.; 3, (ether, 30 ml.) 58 mg. The fractions did not show any characteristic ultraviolet absorption and did not have any aromatic band in their infrared spectra.

Hydrogenation of Khusenol—Khusenol (135 mg. in glacial acetic acid (2 ml.) was hydrogenated in the presence of platinum oxide (5.2 mg.). The volume of absorbed hydrogen at 27°, 733 mm. was 16.6 ml. (1.2 moles).

Oxidation of Khusenol—Chromium trioxide (2.40 Gm.) in pyridine (36 ml.) was added to a solution of khusenol (2.98 Gm.) in pyridine (12 ml.) and the mixture was allowed to stand overnight at room temperature. The reaction mixture on conventional processing yielded a crude oxidation product (2.40 Gm.) which was purified by chromatography on grade II alumina (6) (Woelm; 100 Gm.). A mixture of hexane-benzene (3:1) eluted an oily product (468.2 mg., infrared absorption bands at 2712 and 1718 $cm.^{-1}$). Freshly prepared silver oxide, obtained from silver nitrate (169.2 mg.) (7) and a solution of sodium hydroxide (206.3 mg.) in water (2 ml.), was added to a portion of the product (107.1 mg.) dissolved in ethanol (0.2 ml.). The mixture was stirred at room temperature for 48 hr., filtered, acidified with 10% HCl, and extracted with ether. The yield of product was 100 mg.

Methylation of Acids—The above oxidation product (100 mg.) was dissolved in 3 ml. of a methanol–ether mixture (1:9) and methylated by introducing gaseous diazomethane (8). The product (99 mg.) on gas chromatographic analysis (SE 30 column) (2), showed 2 major peaks at 11.6 and 13.2 min. The former was identified as methyl khusenate.

Isomerization of Methyl Esters—The product of methylation (99 mg.) was refluxed with a mixture of ethanol (9 ml.) and concentrated HCl (1 ml.) for 1.5 hr. on a water bath. The usual processing of the reaction mixture yielded the isomerized esters (94 mg.). Gas chromatographic analysis of the product (SE-30 column) (2) showed the presence of two major constituents, appearing at 10.7 and 12.8 min. The earlier peak was identified as methyl isokhusenate. The peak corresponding to methyl khusenate was absent.

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Keyphrases

Khusenol—isolation, structure
Vetiver oil, Angola—khusenol isolation
UV spectrophotometry—structure
IR spectrophotometry—structure
NMR spectrometry—identity
GLC, TLC—identity