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A Constituent of Vetiver Oil: Bicyclic Primary Alcohol

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A bicyclic primary alcohol was isolated from vetiver oil. The structure was elucidated to be I, a member of the eremophilane series, by corelation with α-vetivone (isonootkatone).

The first investigation of the chemical composition of vetiver oil dates back to the beginning of the twentieth century, when Theulier[2] fractionated this substance and studied the physicochemical properties of the constituents of vetiver oil.

Isolation and characterization of alcoholic constituents from the essential oil of vetiver (*Vetiveria zizanoides* STAPF) has been reported by several investigators. Up to the present the following alcoholic constituents have been identified in vetiver oil: tricyclovetivenol[3] (khusimol),[4] bicyclovetivenol,[3] khusol[5], khusinol[6] (cussol),[7] juneol,[8] laevo-juneol,[8] and khusinoloxide.[9]

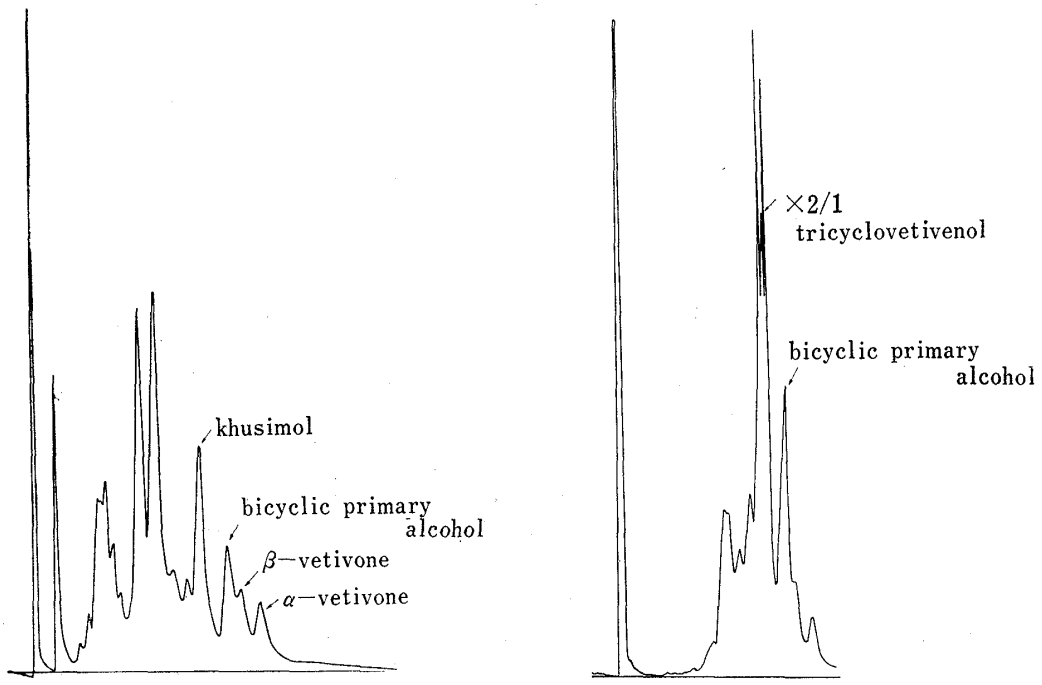

Fig. 1 alcoholic fraction

1) Location: *Shinagawa-ku, Tokyo.*
2) E. Theulier, *Bull. Soc. Chim. France*, **25**, 454 (1901).
3) L. Ruzicka, E. Capato, and H.W. Huyser, *Rec. Trav. Chim.*, **47**, 370 (1928); G. Chiurdoglu and J. Decot, *Tetrahedron*, **4**, 1 (1958).
4) D.C. Umarani, K.G. Gore, and K.K. Chakravarti, *Tetrahedron Letters*, 1966, 1255; F. Kido, H. Uda, and A. Yoshikoshi, *ibid.*, 1967, 2815.
5) S.N. Dhingra, D.R. Dhingra, and S.C. Bhattacharyya, *Perfum. Essent. Oil. Rec.*, 47, 350 (1960); P.S. Kalsi, K.K. Chakravarti, and S.C. Bhattacharyya, *Tetrahedron*, **19**, 1073 (1963).
6) A.A. Rao, K.L. Surve, K.K. Chadravarti, and S.C. Bhattacharyya, *Tetrahedron*, **19**, 233 (1963).
7) N.L. Zutschi and Sodgopal, *Perfum. Essent. Oil. Rec.*, **48**, 333 (1957).
8) S.C. Bhattacharyya, A.S. Rao, and A.M. Shaligram, *Chem. Ind.* (London), **1960**, 469.
9) R. Seshadri, P.S. Kalsi, K.K. Chakravarti, and S.C. Bhattacharyya, *Tetrahedron*, **23**, 1267 (1967).

In this paper the author reports the isolation and the structure determination of a new primary alcohol, which most probably is bicyclovetivenol (*vide* infra).

It is known[3,10] that vetiver oils, depending upon their origin and quality, contain from 45 to 65 per cent of free sesquiterpene alcohols, more than one half of which consists of a mixture of primary sesquiterpene alcohols. Most of the alcohols consist of tricyclic sesquiterpenes and approximately ten per cent of the alcohols consist of bicyclic sesquiterpenes.

By distillation on a small column the neutral fraction of the oil was divided into six fractions as shown in Table 1. Hydrocarbon and ketonic constituents were removed from the fifth fraction through alumina chromatography using benzene. The alcoholic fraction, obtained by further elution of the column by benzene–ethanol (10:1), was re-chromatographed on deactivated alumina in benzene solution. The eluent was shown to be a mixture of two components by gas chromatography. The major component (70 per cent) was proved to be tricyclovetivenol by its identification with the reduction product of zizanoic acid.[4] The minor component (10 per cent) was a bicyclic primary alcohol, a pure sample of which was obtained as a colorless oil after repeated column chromatography on silica gel.

Table I. Fractional Distillation of Vetiver Oil (3 kg)

Fraction No.	bp,	mmHg	Weight, g
1	—115°	3	400
2	115—128°	3	500
3	128—130°	3	500
4	130—135°	2	500
5	135—190°	2	400
6	residue		600

The alcohol (I), $C_{15}H_{24}O$, $[\alpha]_D^{25}$ +122.3°, boils at 150° (0.02 mmHg). The nuclear magnetic resonance spectrum (NMR) shows signals at 0.80 (3H, s), 0.93 (3H, d, J=6.0 cps), 1.82 (3H, s), 4.05 (2H, s), and 5.30 (1H, m) and the IR shows absorption bands at 3400, 1660, 890, 850, and 810 cm^{-1}. The alcohol (I) was oxidized to an α,β-unsaturated aldehyde (II) by manganese dioxide. The ultra violet spectrum (UV) of II shows an absorption maximum at 256 mμ and the infrared spectrum (IR) of II shows absorption bands at 1678 and 1637 cm^{-1}. The NMR data of II indicate that the trisubstituted double bond (5.40 (1H, m)) is not conjugated with the aldehyde group. Reduction of II with lithium aluminium hydride afforded the original alcohol. This result means that the alcoholic group of I should be situated allylicly to the tetrasubstituted double bond. The aldehyde (II) afforded the ethylene thioacetal derivative (III) upon treatment with ethylene thioglycol in the presence of boron trifluoride. Desulfurization of III with Raney nickel gave an unsaturated hydrocarbon (IV), $C_{15}H_{24}$, $[\alpha]_D^{23}$ +112° (c=6.5, $CHCl_3$).

Thioketalization of α-vetivone (isonootkatone)[11] followed by desulfurization with Raney nickel gave an unsaturated hydrocarbon, $C_{15}H_{24}$, $[\alpha]_D^{22}$ +116.4° (c=9.43, $CHCl_3$), which exhibited NMR and IR curves superimposable with those of the hydrocarbon (IV) obtained from the alcohol (I) and identical gas chromatographic retention times.

Consequently, the alcohol (I) has the same carbon skeleton, including the positions of alkyl substituents and double bonds, as α-vetivone. The structural formulas of the alcohol and its derivatives are depicted in figures I to IV.

10) E. Guenther, "The Essential Oils," D. Van Nostrand Company, Inc., N.Y., 1950, Vol. IV, pp. 170—171.
11) K. Endo and P. de Mayo, *Chem. Commun.*, **1967**, 89; J.M. Marshall, H. Faubl, and T.M. Warne, *ibid.*, **1967**, 753.

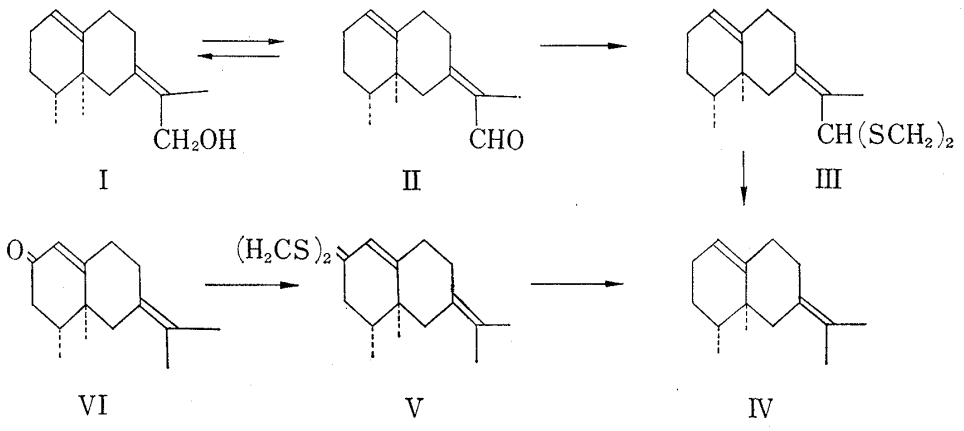

Chart 1

Recently, Marshall, *et al.*[12] refuted the previously proposed structure for β-vetivone and shawed that the list of sesquiterpenes containing a spiro[4,5]decane ring system, which previously contained only the acorones and agarospirol, must now be expanded to include β-vetivone, hinesol,[13] bicyclovetivenol,[3] α-isovetivenene,[14] and β-isovetivenene.[14] However, bicyclovetivenol was the only compound which has not been related to either β-vetivone or α-vetivone.

From a comparison of the physical constants of bicyclovetivenol with the alcohol (I) and a consideration of its content of vetiver oil and its chemical reactivity, bicyclovetivenol may be identical with the alcohol (I).

If bicyclovetivenol is identical with the alcohol (I), then a series of compounds having a perhydrovetivazulene carbon skeleton does not exist in nature.

Experimental[15]

Isolation of Alcohol (I)——The neutral fraction (400 g), bp 190° (2 mmHg), obtained by distillation of vetiver oil (3 kg), was chromatographed on Al_2O_3 (Woelm grade I, 4 kg) in benzene solution. After elution with benzene, the alcoholic fraction (100 g) was eluted with benzene–ethanol (10:1). The alcoholic fraction was chromatographed on Al_2O_3 (Woelm grade II) in benzene solution and benzene elution gave 70 g of alcohols, which showed two intense peaks, besides another small peaks, on gas chromatography (1.5% SE-30, 2.25 m, 180°, He 90 ml/min). One peak (*ca.* 70%) due to tricyclovetivenol and the other (*ca.* 10%) due to I. For separation, the mixture of the two compounds was chromatographed on silica gel–$AgNO_3$ (5%) in hexane solution. Elution with hexane–benzene (2:1) yielded I, bp 150° (0.02 mmHg), $[\alpha]_D^{25}$ +122.3° (c= 7.7, $CHCl_3$), as a colorless oil. *Anal.* Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.13; H, 10.83.

Subsequent elution with hexane–benzene (1:1) gave tricyclovetivenol, bp 150° (0.02 mmHg), as a colorless oil.

3,5-Dinitrobenzoate of I, mp 111—112°, was recrystallized from hexane. *Anal.* Calcd. for $C_{22}H_{26}O_6N_2$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.70; H, 6.30; N, 6.78.

Acetate of I, bp 150° (1 mmHg), was purified by distillation. *Anal.* Calcd. for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 76.51; H, 9.90.

Oxidation of I with Manganese Dioxide——A mixture of MnO_2 and I in $CHCl_3$ (30 ml) was stirred at room temperature for 24 hr. The filtered solution was evaporated to dryness *in vacuo*. The residue was chromatographed on silica gel in hexane solution and elution with hexane–benzene (5:1) gave 0.15 g of α,β-unsaturated aldehyde (II), mp 74—77°. *Anal.* Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.43; H, 10.20.

2,4-Dinitrophenylhydrazone of II, mp 209—211°, was recrystallized from ethanol–benzene. *Anal.* Calcd. for $C_{21}H_{26}O_4N_4$: C, 63.30; H, 6.58; N, 14.06. Found: C, 63.38; H, 6.69; N, 13.88.

12) J.A. Marshall and P.C. Johnson, *J. Am. Chem. Soc.*, **89**, 2750 (1967).
13) I. Yoshioka and T. Kimura, *Chem. Pharm. Bull.* (Tokyo), **13**, 1430 (1965).
14) M. Romanuk and V. Herout, *Collection Czech. Chem. Commun.*, **25**, 2540 (1960).
15) All melting points were uncorrected. NMR spectra were determined in CCl_4 solutions.

Semicarbazone of II, mp 229—231°, was recrystallized from EtOH. *Anal.* Calcd. for $C_{16}H_{25}ON_3$: C, 69.78; H, 9.15; N, 15.26. Found: C, 69.68; H, 9.08; N, 15.27.

Reduction of II with Lithium Aluminum Hydride——To a mixture of $LiAlH_4$ (0.2 g) in dry ether (10 ml) was added a solution of II (0.21 g) in dry ether (20 ml) and the mixture was refluxed for 4 hr. After usual work up, the product was distilled under reduced pressure to give an alcohol, which was identical to I, with respect to IR and NMR spectra and retention time of gas chromatography.

Ethylene Thioacetal of II——To a solution of II (0.5 g) in dry ether (10 ml) was added ethylene thioglycol (2 ml) and BF_3 etherate (2 ml). Stirring was continued at room temperature for 30 min. The reaction mixture was diluted with ether and the ether solution was washed with 10% K_2CO_3 and H_2O, dried (Na_2SO_4) and evaporated. The residue was recrystallized from acetone–ethanol to give 0.4 g of colorless plates (III), mp 114—116°. *Anal.* Calcd. for $C_{17}H_{26}S_2$: C, 69.36; H, 8.90; S, 21.36. Found: C, 69.29; H, 9.03; S, 21.71.

Desulfurization of III——The thioacetal (III) (0.3 g) in abs. EtOH (30 ml) was refluxed with Raney Ni (3 g) for 7 hr. After filtration, the filtrate was evaporated to give an oil (0.2 g) which was chromatographed on silica gel in hexane solution. Elution with hexane afforded an oil (0.15 g) which on distillation under reduced pressure gave a hydrocarbon (IV) as a colorless oil, $[\alpha]_D^{23}$ +112° (c=6.5, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.80; H, 11.86.

Ethylene Thioketal of α-Vetivone (VI)——To a solution of α-vetivone (VI) (1.4 g) in abs. ether (10 ml) was added to ethylene thioglycol (5 ml) and BF_3 etherate (5 ml). After the same work up as with III, the product (1.5 g) was chromatograhed on silica gel (10 g) in hexane solution. Fractions eluted with hexane afforded a solid (1 g), which was recrystallized from MeOH to give colorless plates (V), mp 77—79°. *Anal.* Calcd. for $C_{17}H_{26}S_2$: C, 69.36; H, 8.90; S, 21.36. Found: C, 69.07; H, 8.95; S, 21.63.

α-Vetivene——α-Vetivone thioketal (V) (0.5 g) in abs. EtOH (50 ml) was refluxed with Raney Ni (5 g) for 7 hr. Upon the usual work up, the product (0.3 g) was chromatographed on silica gel (5 g) in hexane solution. Elution with hexane afforded an oil which was distilled under reduced pressure to give α-vetivene, bp 130° (4 mmHg), $[\alpha]_D^{22}$ +116.4° (c=9.43, $CHCl_3$).