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THE STRUCTURE OF α-VETIVONE (ISONOOTKATONE)

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The naturally occurring sesquiterpenes β-vetivone and α-vetivone have long been regarded as isomeric hydroazulenones (1 and 2)[1,2] which differ only in the stereochemistry of their respective C-6 methyl substituents. Whereas detailed studies of β-vetivone have been reported,[2,3] α-vetivone has received little attention and, in fact, has never been chemically interrelated with its supposedly epimeric counterpart. In connection with synthetic studies aimed at settling the question of C-6 stereochemistry in the vetivones, we isolated a fairly pure sample of α-vetivone from natural sources. Our inability to reconcile its nmr spectrum with either structure 1 or 2 prompted us to further investigate this substance before attempting the projected synthetic work. In this report we present findings which establish α-vetivone as the hydronaphthalenone 3.

We secured samples of α-vetivone from Haiti oil of vetiver via separation of the ketonic components with Girard's reagent T and from vetivert acetate, Java origin, by partition between hexane and 1:1:5 pyridine-water-methanol. Final separation of the vetivones from each other and from various other contaminants was accomplished by means of preparative gas chromatography.[4] As shown in Table I, the physical constants of the material thus obtained agree with those reported for α-vetivone by previous workers. Further evidence for the identity of our sample came from a comparison of its infrared spectrum [λ_{max}^{film} 5.99 (CO), 6.17 (C=C), 7.23-7.27, 7.38, 7.76, 9.01, 10.02, 10.63, 11.07, 11.44, 11.74, 12.22, and 13.42 μ] with the published spectrum of α-vetivone[5]; the two were essentially identical. Finally, the mass spectrum[6] of this material confirmed the expected molecular formula, $C_{15}H_{22}O$.

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TABLE I
Some Properties of α-Vetivone

	This Study	Previously Reported
Melting Point	30-35°	51.0-51.5°,[1,7] liquid[2,5]
Refractive Index	n_D^{20} 1.5384	1.5370,[1] 1.5378,[2] 1.5360,[5] 1.5315[8]
Optical Rotation	$[\alpha]_D^{20}$ 248° ($CHCl_3$) 202° (dioxane) $[\alpha]_{405}$ 570° (dioxane)	238° (EtOH),[1] 225° (EtOH)[2] 234° (EtOH),[7] 218° (dioxane)[9] 620° (dioxane)[9]
Ultraviolet Absorption	λ_{max}^{EtOH} 238.5 mμ (ε 13,900)	240 mμ (ε 16,200)[7]

The nmr spectrum of α-vetivone is reproduced in Fig. 1. While most of its features appear compatible with structure **1** or **2**, one serious inconsistency stands out.

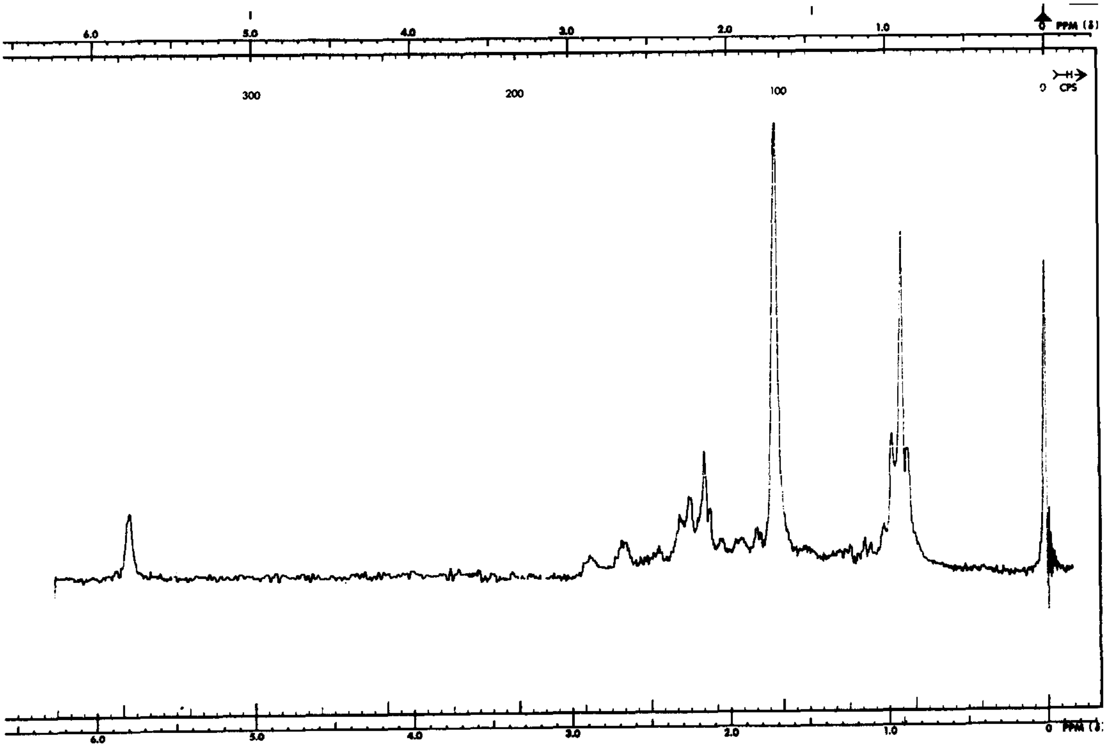


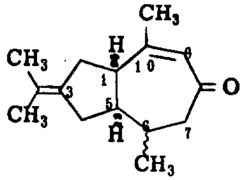
Fig. 1--The nmr spectrum of α-vetivone in 1:1 CCl_4-C_5H_5N

Specifically, this spectrum unexpectedly shows a prominent three-proton singlet at 0.91 ppm reminiscent of an angular methyl group in addition to the expected signals for a vinyl hydrogen (5.78 ppm, $W_{h/2}$ = 2.8 Hz), an isopropylidene grouping (1.70 ppm, $W_{h/2}$ ~ 3 Hz), and a CH_3-CH grouping (0.92 ppm, doublet, J = 6 Hz). Moreover, no peak suggestive of a methyl substituent on the β-position of an α, β-unsaturated ketone can be seen near 1.9 ppm. (The C-10 methyl group of β-vetivone gives rise to a peak at 1.89 ppm.)

α-Vetivone, upon treatment with lithium in ammonia-ethanol followed by oxidation of the resulting reduction product with chromic acid, afforded a dihydro derivative [5, λ_{max}^{film} 5.83 (CO), 7.24, 7.85, 8.02, and 8.78 μ; $\delta_{TMS}^{CCl_4}$ 2.74 (downfield portion of an A_2B_2 pattern, doublet, J_{AB} ~ 13 Hz - probably arising from the equatorial hydrogens at C-6 and C-8), 1.76 (isopropylidene), 0.95 (C-4 CH_3 doublet, J = 6.0 Hz), and 0.79 ppm (C-5 CH_3 doublet,[10] J = 0.7 Hz)]. Our analysis of the nmr spectra of α-vetivone and the dihydro α-vetivone suggested formulas 3 and 5 respectively (or the mirror images) as likely structural possibilities, a postulate which seemed particularly attractive in view of the related structure recently proposed for nootkatone (4).[11] The synthesis of trienone 6[11] [λ_{max}^{EtOH} 347 mμ (ε~21,000); λ_{max}^{film} 6.04, 6.14, 6.32 (conjugated trienone), 7.27, 7.36, 7.64, 7.78, 7.91, 8.30, 10.4, and 10.73 μ] by bromination and (spontaneous) dehydrobromination[12] of dihydro α-vetivone (5) substantiated this postulate. The material thus obtained was identified as isodehydronootkatone (6) by its infrared, nmr, and ultraviolet spectra.[11] Trienone 6 could also be prepared by treating α-vetivone with chloranil or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.[13] However, this route proved unsatisfactory owing to the formation of the cross conjugated dienone which could not be readily separated from its fully conjugated isomer.

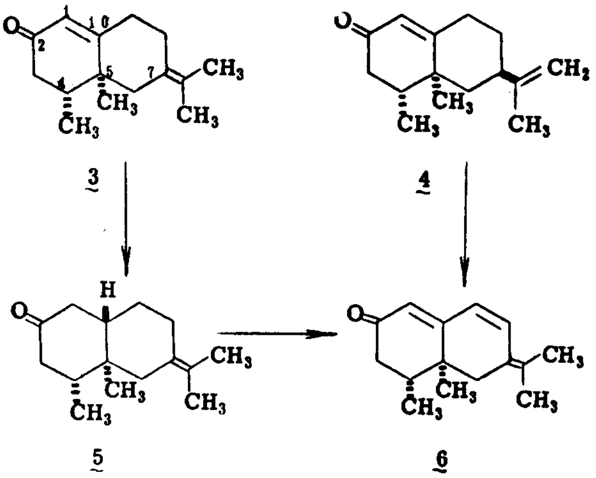
The remaining unknown structural feature of α-vetivone, its absolute configuration, can be assigned as indicated in formula 3 from the published ORD curve[9] which shows a positive Cotton effect. The similarity between this curve and those of related Δ^4-3-keto steroids supports the indicated assignment.

Since the naturally occurring sesquiterpene (3) described in this report can no longer be considered a member of the vetivane family[14] we recommend the name "α-vetivone" be dropped. In its place we suggest "isonootkatone", a name which emphasizes the close structural relationship of 3 to nootkatone (4).



1 β-vetivone*

2 α-vetivone**



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*The C-6 methyl group is probably β-oriented.[3]
**Alleged to be the C-6 epimer of β-vetivone.

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4. A 1/2 in. by 10 ft. column of 20% Carbowax 20-M on Chromosorb W was employed at 205°. Under these conditions, β-vetivone was eluted ahead of α-vetivone.
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10. The observed doublet must result from long-range coupling through a favorable "M" spatial arrangement. Cf. N S. Bhacca, J. E. Gurst, and D. H. Williams, ibid., 87, 302 (1965).

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12. The ketone was treated with 2 equivalents of pyridinium bromide perbromide in 1:1 EtOH-$CHCl_3$ containing a trace of pyridine at 55° for 50 min. Cf. C. Djerassi and C. R. Scholz, J. Am. Chem. Soc., 70, 417 (1948).

13. Cf. L. M. Jackman in "Advances in Organic Chemistry", Vol. 2, Interscience Publishers, Inc., New York, 1960, pp. 331 and 344.

14. Cf. T. Nozoe and S. Itô in "Fortschritte der Chemie Organisher Natustoffe", L. Zechmeister, Ed., Vol. XIX, Springer-Verlag, Vienna (1961), p. 52.

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