Tetrahedron Letters No.21, pp. 1759-1762, 1970. Pergamon Press. Printed in Great Britain.

STRUCTURES OF VETIVENENES AND VETISPIRENES[*,1]

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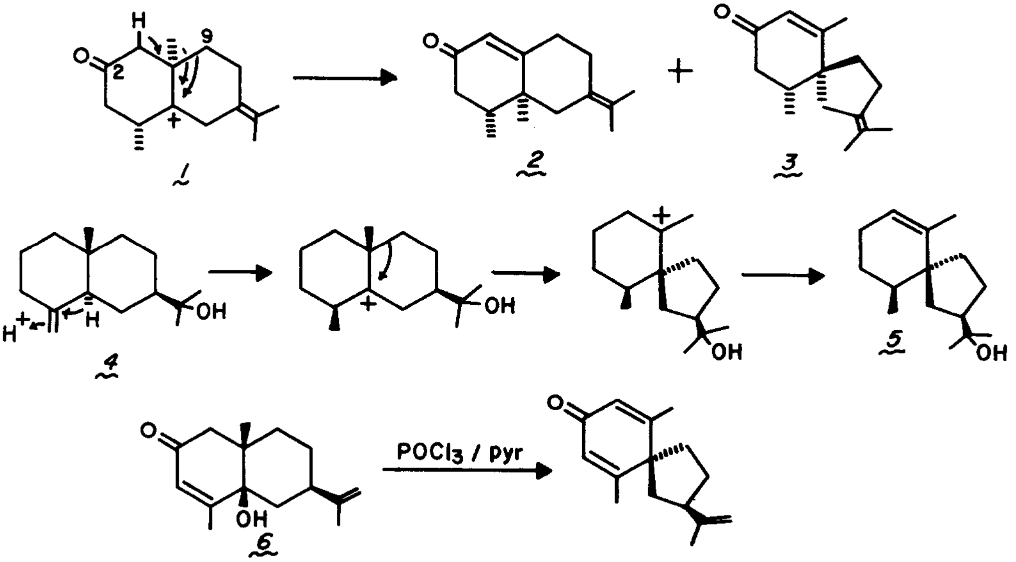
(Received in USA 16 March 1970; received in UK for publication 31 March 1970)

The presence of elemol, β-eudesmol, and vetiselinenol in vetiver oil (see preceding communication) bears on the questions concerning the genesis of the vetivones. It has been suggested[2] that an ion derived from a 2-keto-4,10-*epi*-eudesmane (1) could serve as a precursor of both α- and β-vetivone (2, 3). The same type of rearrangement (ring methylene migration) correctly predicts the now confirmed stereostructure of hinesol (5),[3] a congener of β-eudesmol (4). More recently the isolation of a 2-keto-5-hydroxyeudesmane, β-rotunol (6), has been reported.[4] The degradation of β-rotunol affords the first example of a chemically induced rearrangement of this type.



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[*] Paper III in the series "Vetiver Oil Constituents." Presented in part at the Symposium on the Chemistry of Essential Oils at the 158th Meeting, ACS, New York (Sept., 1969).

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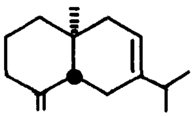

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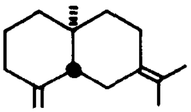

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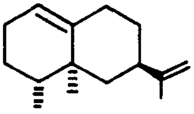

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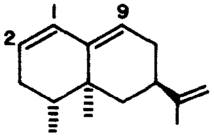

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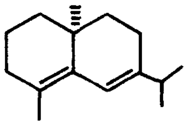

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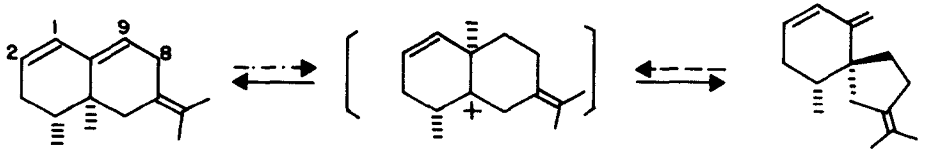
Our studies of the hydrocarbons of vetiver oil have centered on those of the eudesmane, nootkatane, and vetispirane[5] skeletons, in hopes of finding further examples consistent with this biosynthetic pathway. We found vetiselinene (7),(-)-selina-4(14),7(11)-diene (8), valencene (9), and nootkatene (10) among the minor constituents.[6] Vetiselinene was identical in all respects to the corresponding degradation product of vetiselinenol. Hydrocarbon 8 was identified by NMR and IR comparison with the same compound isolated from hops.[7,8] The absolute stereochemistry was defined by acid-catalyzed rearrangement to (-)-δ-selinene (11) which also occurs in vetiver oil. Valencene ($[\alpha]_D$ = +190°) was identical, in all respects, to an authentic sample. Nootkatene (10) showed the IR, RD, UV, and NMR spectra expected: RD $[\alpha]_D = -194°$, $\lambda_c \sim 230$ nm, a = -250! λ_{max}^{CH3OH} 235.5 nm (ε 18,000); $\delta_{TMS}^{CDCl_3}$ 0.89 (CH_3,d), 0.92 (CH_3, s), 1.75^{s} (vinyl-CH_3), 4.73^{s} ($C{=}CH_2$), 5.4 (H-9, mult.), 5.56 (H-2, mult.), and 5.97 ppm (H-1, d, 10 Hz). NMDR experiments confirmed the assignments. The hydrogenation of hydrocarbons 7-10 afforded the expected diastereomeric eudesmanes and nootkatanes.[9]

The major sesquiterpene hydrocarbon of vetiver oil is β-vetivenene (12):[10] n_D^{20}= 1.5361; RD $[\alpha]_D$ = -160°; UV, λ(ε) 228.5 (19,450), 236.5 (19,600), and 245 nm (inflec. 13,300). The NMR spectrum of β-vetivenene allowed an unambiguous assignment of double bond positions in the nootkatane skeleton (established by hydrogenation). Thus β-vetivenene showed the negative trending RD curve expected in analogy to nootkatene and also showed a nearly identical vinyl-H region of the NMR: H-1 @ 5.94, H-2 @ 5.6 and H-9 @ 5.4 ppm. The doubly allylic methylene (H-8) appeared at 2.87 ppm.



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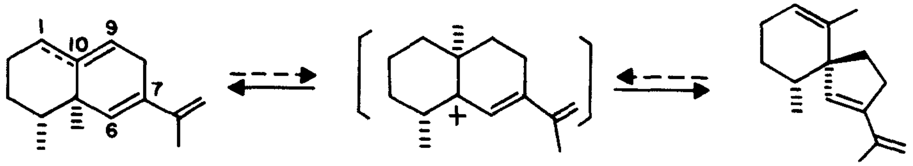

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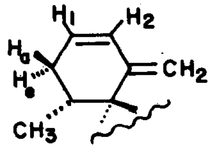
One of the remaining major hydrocarbons was also a nootkatane triene, γ-vetivenene (14): $C_{15}H_{22}$; RD positive trend, no measurable cotton effect (a < 30); $\lambda_{max}^{CH_3OH}$ 234.5 nm (ε 21,400), ν_{max} 3095, 3050 (=C-H), 1673, 1632, 1609 (C=C), 1219, 884, 872, and 810 $cm.^{-1}$ $\delta_{TMS}^{C_6D_6}$ 0.92 (CH_3, d, 6.8), 1.04 (CH_3, s); 1.915 (vinyl-CH_3), 2.32 (=C-$\underline{CH_2}$), 4.91 and 5.03 (C=CH_2), 5.38 (=CH-, ∿ triplet, ∿ 3.5 Hz), and 5.95 ppm (vinyl-H, singlet). The downfield position of the resonances for the isopropenyl group[11] and the singlet (W_h ∿ 3 Hz) vinyl-H (δ 5.95) indicate that the conjugated butadiene group must be as indicated. The remaining double bond must be in 1(10)- or 9(10)-position. We tentatively prefer the 9(10)-position on the basis of ORD[12] and hydrogenation results,[12] however it does not explain the NMR as well - in particular the doubly allylic methylene at C-8 would be expected to be downfield from the observed position (δ 2.32).

In addition we have isolated two trienes of the vetispirane skeleton, β- and α-vetispirene - identified by hydrogenation to vetispiranes (also obtained from β-vetivone, 3). The double bond placements were uniquely assigned from the NMR and NMDR experiments. The spectral characteristics are given below.

β-Vetispirene (13) $C_{15}H_{22}$: $[\alpha]_D$ = -90°; $\lambda_{max}^{CH_3OH}$ 232 nm (ε 13,500); ν_{max} 3085, 1780, 1637, 890 (C=CH_2); 3025, 1600, 779 (-CH=CH-, conj., cis); 1377 (=CMe_2); 1330, 1318, 1232, 1159, 1138, 1095, 990, 848, and 740 $cm.^{-1}$ $\delta_{TMS}^{CCl_4}$ 0.83 (CH_3, d, 6.6 Hz); 1.62 and 1.67 (C=CMe_2); 4.69 and 4.77 (C=CH_2); 5.50 (vinyl-H, complex multiplet); and 5.92 ppm (vinyl-H, d.d., J = 10.0, 2.6 Hz). Lit. for β-isovetivenene:[6b] $[\alpha]_D$ = -68°, λ_{max} 232 nm (ε 12,300).

α-Vetispirene (15): $C_{15}H_{22}$: $[\alpha]_D$ = +220°, $[\alpha]_{300}$ = +2300°; $\lambda_{Max}^{CH_3OH}$ 239.5 nm (ε 20,500); ν_{max} 3085, 1772, 1631, 883 (C=CH_2); 3045, 3020, 1660, 1599 (-CH=C<, conj.); 1378, 1201, 1076, 1060, 841, and 797 $cm.^{-1}$ $\delta_{TMS}^{CCl_4}$ 0.867 (CH_3, d, 5.6 Hz); 1.544 (vinyl-CH_3, ∿ d.)[13], 1.91 (vinyl-CH_3), ∿ 2.54 (a 10 line multiplet due to two hydrogens), 4.85 (C=CH_2, apparent quartet, S = 0.5 Hz), 5.33 (vinyl-H, trip of quartets, J_q = 1.4, J_t = 4 Hz)[13]; and 5.46 ppm (vinyl-H, s, W_h = 3.2 Hz).

The conjugated butadiene system of β-vetispirene was located as follows. The downfield vinyl-H (δ 5.92) is clearly an internal hydrogen on the conjugated system (H-2). The 10 Hz coupling indicates a cis double bond. The smaller coupling (2.6 Hz) must then be due to an axial allylic hydrogen which was located at δ 2.4 by NMDR experiments. Irradiation at δ 2.4 produced a doublet at δ 5.92 (J = 10 Hz) and in addition reduced the complex multiplet at δ 5.50 (due to H-1) to a doublet of doublets (J = 10, 5 Hz). Irradiation at δ 2.0 left H-2 unchanged but reduced the H-1 resonance to a doublet of doublets (J = 10, ∿ 2). Computer simulation of the pattern due to H-1 and H-2 led to the following coupling constants: J_{12} = 10.0, J_{2a} = 2.6, J_{1a} = 2.4, and J_{1e} = 5.2 Hz. For α-vetispirene, the isoprenyl group (CH_3, 1.91; C=CH_2, 4.85 ppm; downfield from the usual position) and the singlet vinyl-H (δ 5.46) must be in the conjugated system. The absence of significant coupling dictates its placement such that there are no allylic hydrogens at the H-terminus of the double bond.



The chart shows the relationship between the vetispirenes and vetivenenes isolated. Once again they fall into pairs that can be viewed as Wagner-Meerwein rearrangement products of the 4,10-*epi*-eudesmane intermediates shown. In our opinion this lends considerable support to the proposed vetivone biogenesis since it is difficult to accept the increasing occurrence of these structural relationships as coincidence.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Research Corporation, for support of this research.

REFERENCES

1. The molecular formula of new substances were confirmed by combustion analysis or exact mass determinations. Rotation data was obtained in methanol ($c < 0.04$). NMR data is reported in ppm downfield from internal TMS. Line separations (S) are indicated when exact analyses of couplings (J) were not obtained.

2. N. H. Andersen, *Photochem.*, **9**, 145 (1970). N. H. Andersen, M. S. Falcone, and D. D. Syrdal, *Abstracts of Papers*, AGFD-27, 158th Mtg. ACS, New York (Sept. 1969).

3. J. A. Marshall and F. Brady, *Tetrahedron Letters*, 1387 (1969).

4. H. Hikino, K. Aota, D. Kawano, and T. Takemoto, *ibid.*, 2741 (1969).

5. Vetispirane, a name suggested for spiranes related to β-vetivone.[2] This skeleton has also been designated spirovetivane.[3]

6a. Only one detailed study of the sesquiterpene hydrocarbons of vetiver oil has appeared.[6b] Romanuk and Herout reported zizaene, zizanene (an unknown bicyclic diene), three hydrocarbons of the α-vetivone skeleton (α - and β-vetivenene and dehydrovetivenene), and two hydrocarbons related to β-vetivone (α- and β-isovetivenene). We also found zizaene, zizanene, β-vetivenene, and β-isovetivenene (which we designate β-vetispirene).

6b. M. Romaňuk and V. Herout, *Coll. Czechoslov. Chem. Commun.*, **25**, 2540 (1960).

7. R. D. Hartley and C. H. Fawcett, *Phytochem.*, **8**, 637, 1793[8] (1969).

8. Selinadiene **8** of low rotation ($[\phi]_{270} = +20°$) is reported to occur with germacrene in hops. The authors imply that **8** is not an artifact from its rotation. Our sample of (-)-**8** ($[\alpha]_D = -110°$, $[\alpha]_{270} = -1000°$) afforded optically pure (-)-δ-selinene. We intend to synthesize optically pure (+)-**8** from (+)-β-selinene, and compare it to isolated examples.

9. Identified by glc with products from authentic β-selinene and valencene. Additional diastereomers are produced due to the sp^2-center at the isopropyl attachment.[12]

10. β-Vetivenene had been assigned a hydroazulenic skeleton on the basis of a correlation with α-vetivone. The reported physical constants: $[\alpha]_D = -191°$, $n_D^{20} = 1.5378$, λ(ε) 230 (21,400), 238 (21,400), and 246 nm (15,800).[6b]

11. The vinyl methyl appeared as a four line pattern ($^4J = 0.6$ and 1.3 Hz), the larger coupling being with the more shielded hydrogen of the *exo*-methylene. We take this to indicate a near planar transoid diene.

12. The 1(10)-isomre (see **14**) would be expected to show a large cotton effect due to the skewed homoconjugated system. Hydrogenation of γ-vetivenene afforded nootkatane, 7-*epi*-nootkatane, and 10 *epi*-nootkatane (eremophilane) - the proportion of the *cis*-fused product was much higher than observed for valencene, nootkatene, or the other vetivenenes. The conformation of the 9(10)-isomer suggested from models has a planar cyclohexadiene ring and as a result the 9(10)-bond is not hindered as much from the side of the angular methyl group.

13. NMDR experiments confirmed the coupling between the vinyl-H and -CH_3 (δ 1.544) suggested by the pattern of the vinyl-H resonance at δ 5.33.