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THE STRUCTURE OF β-SINENSAL

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β-Sinensal, a new oxygenated sesquiterpene, was isolated from California cold-pressed orange oil by a combination of vacuum distillation, silica gel chromatography, and preparative gas chromatography.* The purified compound** is quite unstable, polymerizing rapidly at room temperature on exposure to light and air.

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* Carbowax 20M on Anakrom AB, 12-ft. x 1-in. column at 185°. Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

** One peak at 72 min. when analyzed on a 75-ft. x 0.01-in. DC-550 capillary column in a Perkin-Elmer 226 gas chromatograph (programmed run).

A parent peak of m/e = 218 appears in the mass spectrum* of β-sinensal, with major peaks at m/e = 134, 119, 107, 93, 79, and 55. Infrared absorptions** at 2817, 2713, and 1688 cm^{-1} reveal the presence of an α,β-unsaturated aldehyde grouping, and a monosubstituted ethylene is indicated by bands at 3082, 1796, 1647, 992, and 893 cm^{-1}. A maximum appears at 231 mμ in the ultraviolet† with log ε = 4.57 (95% EtOH), suggesting that the α,β-unsaturated aldehyde is disubstituted.[1] However, the extinction coefficient is considerably higher than is usually observed with such a chromophore,[2] so that the presence of a second chromophore, also absorbing near 230 mμ with a log $\epsilon \simeq 4.3$, was suspected. NMR‡ reveals that the aldehyde has an α-substituent, for the aldehydic proton absorbing at 9.70 δ is unsplit. The vinyl region of the spectrum contains absorptions which integrate for six protons; 6.33 (triplet, J = 6.6 cps, 1H), 6.27 (dbl. doublet, J = 17.3 and 10.3, 1H), 5.36 (triplet, J = 7.1, 1H), 5.2 (triplet, J = 7.1, 1H),§ 5.02 (doublet, J = 17.5, 1H), and 4.88 δ (doublet, J = 10.4, 1H). The three bands at 6.27, 4.88, and 5.02 δ are assigned to the protons of the monosubstituted ethylene, the 4.88 and 5.02 δ protons being cis and trans respectively to the lone proton at 6.27 δ. The observed J values make these assignments rather straightforward; however, the lone proton's appearance at such a low-field position strongly suggests that the

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* Bendix Time-of-Flight Model 12.

** Beckman IR-5, 10% soln. in CCl_4, 0.1 mm. path length.

† Beckman DK-2, 95% EtOH soln.

‡ Varian A60, soln. in CCl_4 with 1% TMS.

§ Poorly resolved at 60 mc.; at 100 mc. the absorption appears as a triplet, with each peak further split, J = 7.1 and 1.3 cps.

monosubstituted ethylene is part of a conjugated system. The other proton absorptions appear at 2.82 (triplet, J = 7.2, 2H), 2.39 (multiplet, 2H), and 2.20 (multiplet, 2H) (allylic methylenes), and at 1.62-.75 δ (multiplet, 9H) (vinyl methyls). The 2.39 and 2.20 δ bands appear to be a triplet and a doublet respectively in the 60 mc. spectrum, but at 100 mc. the increased $\Delta_{\text{chem. shift}}$ reveals considerably more complex spin-spin interactions for both. Two of the NMR bands were found to shift positions when the 2,4-DNPH derivative (m.p. = 98.3-99.5°, uncorrected) was prepared. The 6.33 triplet (1H) was moved upfield to 5.94 δ, and the absorption band of one of the vinyl methyls was moved downfield from 1.7 to 1.93 δ.

Hydrogenation* of β-sinensal afforded two products, a saturated alcohol (m/e = 227, loss of H; m/e = 210, loss of H_2O) (major product) and a hydrocarbon (parent peak m/e = 212) presumably formed via hydrogenolysis of the saturated alcohol. The hydrocarbon was identified as farnesane (1) by comparison (MS, IR, and capillary gc. retention times) with authentic samples obtained by hydrogenation, dehydration, and hydrogenation of nerolidol, and by hydrogenation (50 psi, PtO_2 in 95% EtOH, tr. Fe^{+2}) and hydrogenolysis of farnesol. Hexahydrofarnesol (m/e = 227, loss of H; m/e = 210, loss of H_2O) was obtained as the major product in the corresponding hydrogenation of farnesol, with farnesane again the minor product. β-Sinensal therefore has a farnesane (1) skeleton in common with hexahydrofarnesol (2) and farnesol (3).

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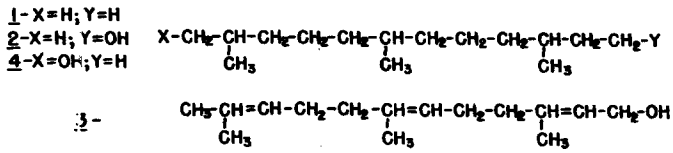
* 50 psi, PtO_2 in 95% EtOH, tr. Fe^{+2}.



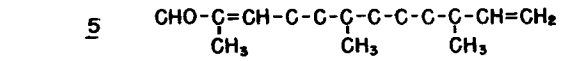
1-X=H; Y=H
2-X=H; Y=OH
4-X=OH; Y=H

X-CH2-CH(CH3)-CH2-CH2-CH2-CH(CH3)-CH2-CH2-CH2-CH(CH3)-CH2-CH2-Y

3- CH3-CH(CH3)-CH=CH-CH2-CH2-CH(CH3)-CH=CH-CH2-CH2-CH(CH3)-CH=CH-CH2-OH

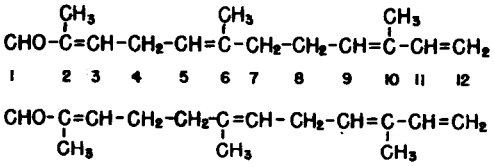
The infrared spectra of octahydrosinensol (228 - 218 - 10) and hexahydrofarnesol (2) differ in only two regions, 1370-90 and 1025-60 cm^{-1}. The spectrum of hexahydrofarnesol has a strong doublet centered at 1374 cm^{-1} (gem-dimethyl[3a]), as well as a somewhat stronger band at 1381 cm^{-1} (isolated methyl), in contrast to that of octohydrosinensol, which has only a 1380 cm^{-1} band. In the 1025-60 C-O stretch--OH deformation region, hexahydrofarnesol absorbs strongly at 1055 cm^{-1} (primary alcohol[3b]). This band is shifted to 1025 cm^{-1} in the spectrum of octahydrosinensol, indicating branching α to the functional group of the sinensal derivative[3b], in agreement with the aforementioned NMR evidence for α-branching in β-sinensal. These spectral differences require that the oxygen function in octahydrosinensol, and therefore in β-sinensal as well, be on one of the methyls of the farnesane (4) gem-dimethyl group.

A partial structure for β-sinensal may now be written:



5 CHO-C(CH3)=CH-C-C-C(CH3)-C-C-C(CH3)-CH=CH2

The hydrogenation data indicate that β-sinensal has four double bonds. Six vinyl protons appear in the compound's NMR spectrum, and four of these are accounted for in the partial structure 5. The two remaining double bonds must both be trisubstituted, and only two structures, 6 and 7, remain to be considered.



Three vinyl proton absorptions remain to be assigned; at 5.2 (triplet), 5.36 (triplet), and 6.33 δ (triplet). The corresponding protons are at positions 3, 5, and 9 in 6 or at 3, 7, and 9 in alternative structure 7. The high-field triplet may safely be assigned to the proton on the isolated central double bond, at C-5 (6) or C-7 (7).[4] The 6.33 δ triplet must arise from the proton at C-3, for it is shifted upfield in the spectrum of the 2,4-DNPH derivative. The 5.36 δ triplet therefore arises from the C-9 vinyl proton, and the two-proton triplet at 2.82 δ, which has been found by spin-decoupling experiments to be coupled to this 5.36 δ proton, must be at C-8. This methylene group's absorption at 2.82 δ is considerably farther downfield than are those of the other two allylic methylenes (2.20 and 2.39 δ), indicating that the C-8 position is di-allylic,* so 7 represents the structure of β-sinensal. The two remaining absorptions are then due to the two allylic methylenes at C-4 and C-5. The AB situation at positions 4 and 5 provides an explanation for the complex spin-spin splitting of the two allylic methylene bonds that is observed in the 100-mc. spectrum of β-sinensal.

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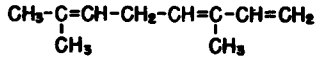
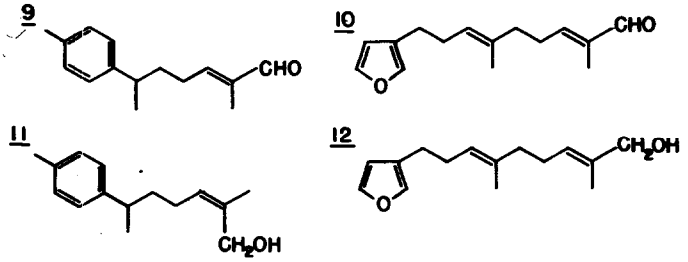
* The di-allylic C-11 protons of methyl linoleate were found to absorb at 2.74.

The NMR spectrum of ocimene (8),* a good model compound for the olefinic



portion of β-sinensal, is superimposable upon that of β-sinensal downfield from 2.6 δ with the exception of the 6.33 δ triplet and the 9.70 δ singlet, which are absent from the ocimene spectrum.

Very few terpenes or sesquiterpenes have been reported that have oxygen functions on a methyl of the isopropylidene (or isopropyl) group. However, Sakai, et al.,[6] have recently described four such sesquiterpenes, nuciferal (9), torreyal (10), nuciferol (11), and neotorreyol (12).**



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* From oil of opopanax (Fritszche extra). Ocimene constitutes 15-20% of the total oil, and is essentially the only monoterpene present.[5]

** There appears to be a discrepancy between the trans double bond configurations assigned to nuciferal and torreyal by Sakai and the NMR data which he and his co-workers quote.

The NMR spectra of nuciferal and torreyal both exhibit triplets at 6.27 δ, presumably due to the C-3 proton, for the absorption is moved upfield to 5.28 and 5.16 δ respectively on reduction of the two aldehydes 9 and 10 to the corresponding allylic alcohols.

Even more recently, Stevens, et al.,[7] have published the structure of sinensal (13), a double bond isomer of β-sinensal. We propose that Stevens' compound shall henceforth be referred to as α-sinensal. The NMR spectrum of α-sinensal contains a similar triplet at 6.31 δ, which is shifted upfield to 5.93 δ on formation of the 2,4-DNPH derivative.

Bates' method[8] was applied to the NMR spectra of β-sinensal and its 2,4-DNPH derivative in an attempt to assign cis or trans geometry to the C-6 double bond (too much uncertainty was introduced by conjugation of the other two trisubstituted double bonds at C-2 and C-9 to permit reliable geometric assignments). In both spectra, the highest field vinyl methyl group appears at 1.66 δ (8.34 τ). This suggests that the central double bond is cis, i.e., the C-6 methyl and C-7 proton are cis to one another, for Bates found that the vinyl methyl at the central double bond in the four isomeric farnesols (3) appears at 1.66 δ (8.34 τ) when the bond is cis, and at 1.59 δ (8.41 τ) when trans. However, in view of the small $\Delta_{chem.}$ shift being considered, and since no secondary internal standard such as t-butanol was employed, this cis assignment for the C-6 double bond can only be tentative.

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