

THE STRUCTURE OF PARADISIOL AND ITS IDENTITY TO INTERMEDEOL

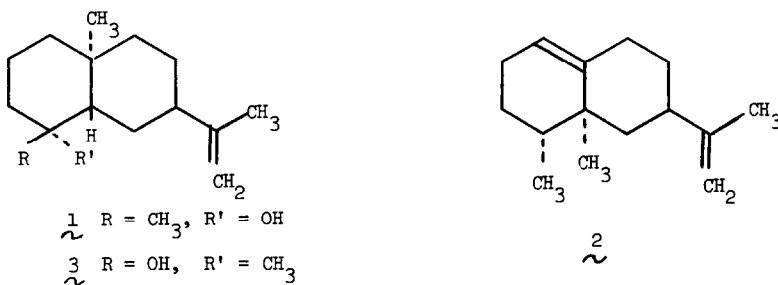
J. W. Huffman
 Department of Chemistry and Geology
 Clemson University
 Clemson, South Carolina 29631

and

L H Zalkow
 School of Chemistry
 Georgia Institute of Technology
 Atlanta, Georgia 30332

(Received in USA 30 November 1972; received in UK for publication 25 January 1973)

The currently accepted biosynthetic paths leading to the vetivane and nootkatane groups of sesquiterpenes require as intermediates various 10-epieudesmanes as precursors ¹ In recent years several of these compounds have been isolated and their structures determined ^{1b,2} Very recently, a new member of this group of sesquiterpenes, paradisiol, was isolated from grapefruit oil, and assigned structural formula 1.³ This compound appeared to be of particular biosynthetic importance due to the axial tertiary hydroxyl group which is sterically

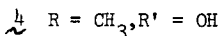
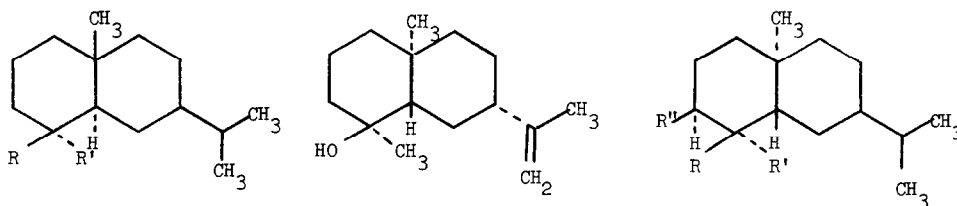


oriented such that it would favor the biosynthetic rearrangement to valencene (2)

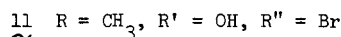
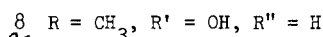
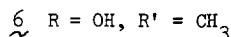
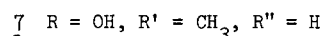
However, the reported spectral properties of paradisiol are remarkably similar to those of intermedeol, a compound reported by one of us several years ago, and which was assigned a structure (3), epimeric at C-4 to that of paradisiol ⁴ Direct comparison of the infrared

spectra of paradisiol and the dihydroparadisiol obtained by platinum catalyzed reduction with the spectra of intermedeol and dihydrointermedeol confirmed that these compounds are identical ⁵

Stevens *et al.*³ assigned the stereochemistry at C-4 in paradisiol on the basis of 1) The apparent lack of similarity of the spectral properties of dihydroparadisiol (palladium catalyzed) with those of selinan-4 α -ol(4),⁶ and 2) the rather pronounced change in the nmr



5



chemical shifts of both tertiary methyl signals in dihydroparadisiol (platinum catalyzed) when the spectra in carbon tetrachloride and pyridine-d₅ were compared.⁷ The stereochemistry of intermedeol at this center was assigned on the basis of dehydration experiments, and the identity of the mass spectrum of 5 with that of its enantiomer, prepared from β -eudesmol ⁴

In order to reconcile this apparent contradiction, β -eudesmol was converted to a mixture of the enantiomer of 5 and juniper camphor,^{4a} which was reduced to 4. The infrared spectrum of 4 was markedly different from that of the appropriate dihydroparadisiol and the stereochemistry of the hydroxyl group in 4 was confirmed on the basis of a comparison of the nmr spectra in carbon tetrachloride and pyridine-d₅ (Table 1). The C-4 epimer of 4,

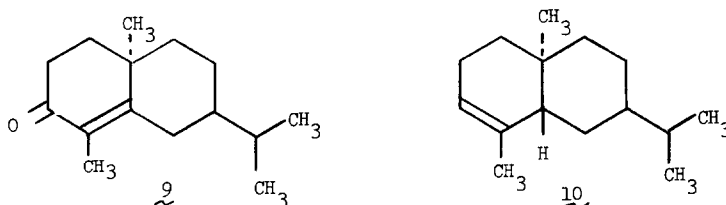
Table 1 Nmr Spectra of Compounds

Compound	δ (ppm in CCl ₄)		δ (ppm in pyridine-d ₅)	
	C-10 methyl	C-4 methyl	C-10 methyl	C-4 methyl
<u>3</u>	0.91	1.03	0.90	1.21
<u>4</u>	0.82	1.06	0.85	1.21
<u>6</u>	0.95	1.08	1.24 or 1.28	1.24 or 1.28
<u>7</u>	0.88	1.01	0.92	1.22
<u>8</u>	1.01	1.04	1.43 or 1.47	1.47 or 1.43
<u>10</u>	0.83	1.54(d, J=1)	----	----

dihydroeneointermedeol (6) was prepared from β -eudesmol by a modification of the published procedure⁸ Again, the infrared spectrum of this compound was not identical to that of dihydroparadisol, although the nmr spectrum in two solvents (Table 1) agreed with the assigned structure⁹

Reexamination of the nmr spectra of intermedeol (3) and dihydrointermedeol (7) showed that only one of the two tertiary methyl signals showed a significant downfield shift when the spectra in carbon tetrachloride were compared with those in pyridine-d₅ (Table 1) This confirms the equatorial nature of the hydroxyl group in intermedeol⁷ In view of the identity of the infrared spectra of intermedeol and paradisol and their dihydro derivatives this also indicates that the structure assigned to paradisol is incorrect, and that paradisol is in fact intermedeol

The conclusion was confirmed by the synthesis of a compound (8) having the structure assigned to dihydroparadisol³ 10-Epieudesm-4-en-3-one¹⁰ (9) was converted to 10 α -selin-3-ene (10)¹¹ by the method of Ireland and Pfister¹² Reaction with aqueous hypobromite gave



the unstable bromohydrin (11), which was reduced with lithium aluminum hydride to give 8¹¹ The nmr spectrum of 8 was in agreement with the assigned structure (Table 1), however, as expected, the infrared spectrum was markedly different from that of dihydroparadisol, which had previously been assigned this structure^{3,13}

Acknowledgements The mass spectrometer used in this work was obtained through a National Science Foundation Research Instrument Grant to Clemson University We would like to thank Professor A R Pinder for the gift of a quantity of β -eudesmol

REFERENCES

- 1a W Parker, J S Roberts and R Ramage, Quart Rev , Chem Soc , 21, 331 (1967)
- 1b N H Andersen, M.S Falcione and D D Syrdal, Tetrahedron Lett 1759 (1970).
- 1c N H Andersen, Phytochemistry, 9, 145 (1970)
- 2a H C Barrett and G Büchi, J Amer Chem. Soc., 89, 5665 (1967)

- 2b. N.H. Andersen, Tetrahedron Lett. 1755 (1970).
- 2c. R. Kaiser and P. Naegeli, Tetrahedron Lett. , 2009 (1972)
3. H Sulser, J.R Scherer and K.L Stevens, J. Org Chem , 36, 2422 (1971).
- 4a G L. Chetty, V.B. Zalkow and L.H Zalkow, Tetrahedron Lett., 3223 (1968)
- 4b L H. Zalkow, V.B Zalkow and D.R. Brannon, Chem. Ind (London), 38 (1963).
- 5 We would like to thank Dr. K L Stevens for supplying copies of the infrared spectra of paradisiol and the dihydroparadisiols.
6. R.E Corbett and R A.J. Smith, Tetrahedron Lett , 1009 (1967)
7. P.V. Demarco, E Farkas, D. Doddrell, B.L Mylari and E Wenkert, J Amer. Chem Soc , 90, 5480 (1968)
8. V.B. Zalkow, A M Shaligram and L H Zalkow, Chem. Ind. (London), 194 (1964)
- 9 Subsequent examination of the infrared spectra of compounds 4 and 7 indicates that palladium reduced paradisiol is probably a mixture of these C-7 epimers
10. H. Hikino, T. Kohana and T Takemoto, Tetrahedron, 25, 1037 (1968)
11. All new compounds were characterized by infrared, and nmr spectroscopy Their purity was monitored by glc, and the molecular formula confirmed by mass spectrometry.
12. R E Ireland and G Pfister, Tetrahedron Lett , 2145 (1969)
- 13 The only unresolved difference in the properties of paradisiol and intermedeol is the reported melting point for this compound ^{3,4b} This difference is probably due to either a difference in crystal structure or a considerable difference in purity of the two samples This problem could not be resolved due to the lack of a sample of paradisiol. The very small sample of intermedeol which was available could not be induced to crystallize following its use for spectroscopic measurements and the resolution of this question must await the isolation of an additional quantity of this compound.