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THE STEREOCHEMISTRY OF α- AND β-SANTALOL

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The major constituents of East Indian sandalwood, α- and β-santalol, have been known for some time. Extensive degradative studies[1] have established a gross structural relationship between α-santalol and α-santalene (III) as well as between β-santalol and β-santalene (IV, IVa) exclusive of stereochemistry. The interconversion of α- and β-santalol has also been reported.[2]

The stereochemistry of these alcohols has not been investigated, and we wish to present evidence herein which provides both a capstone for the structural investigations previously reported, as well as an assignment of stereochemistry to both alcohols.

The alcohols were obtained from East Indian sandalwood oil by an established procedure,[3] and carefully distilled through a spinning-band column. Although

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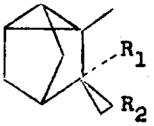
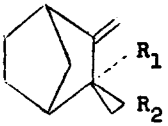
[1] For a summary of this subject, J. Simonsen, "The Terpenes," Vol. III, p. 179 ff., University Press, Cambridge (1952), should be consulted.

[2] Bhattacharyya, Science and Culture 13, 206 (1947).

[3] E. Gruenther "The Essential Oils," Vol. II, p. 266, D. Van Nostrand Co., New York (1949).

complete separation was not achieved by distillation, vapor phase chromatography permitted separation of the alcohols.





I $R_1 = Me$

$R_2 = -CH_2CH_2\underset{CH_3}{C} = \overset{H}{C}\,CH_2OH$

II $R_1 = Me$

$R_2 = -CH_2CH_2\underset{CH_3}{C} = \overset{H}{C}\,CH_2OH$

III $R_1 = CH_3$

$R_2 = -CH_2CH_2CH{=}C\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$

IIa $R_1 = -CH_2CH_2\underset{CH_3}{C} = \overset{H}{C}\,CH_2OH$

$R_2 = CH_3$

IV $R_1 = CH_3$

$R_2 = CH_2CH_2CH{=}CH\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$

IVa $R_1 = CH_2CH_2CH{=}C\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$

$R_2 = CH_3$

There are two major points of stereochemical interest, the configuration about the side-chain double bond, and the disposition of the side chain relative to the ring viz. exo or endo.

The configuration about the side-chain double bond was determined by an n.m.r. comparison of α- and β-santalol with the corresponding hydrocarbons. The successful application of this technique to the solution of stereochemical problems with the farnesols and related natural products has recently been reported.[4]

In systems of the type $ACH_2CCH_3 = CHCH_2B$ a <u>cis</u> relationship between the absorbing methyl group and the vinyl proton consistently gives the methyl protons the lower τ value (Δτ .07) as compared with the <u>trans</u> isomer. The santalol side chains are obviously of this general type with A = OH, B = CH_2–. The observed values are recorded in Table I.

TABLE I[a]

N.m.r. Absorption of Methyl Groups of Type ($ACH_2CH_3C = CHCH_2B$)

		<u>cis</u>	<u>trans</u>
α-Santalene	A = H B = CH_2	8.37	8.45
α-Santalol	A = OH B = CH_2		8.44
β-Santalene	A = H B = CH_2	8.43	8.50
β-Santalol	A = OH B = CH_2		8.49

a. Spectra taken in CS_2 with tetramethylsilane internal reference.

The consistency of these data with those previously recorded[4] makes it reasonably certain that the <u>trans</u> isomer predominates in both α- and β-santalol.

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[4] (a) R. B. Bates, D. M. Gale, and B. J. Gruner, <u>J. Org. Chem.</u> <u>28</u>, 1086 (1963). (b) R. B. Bates, D. M. Gale, <u>J. Am. Chem. Soc.</u> <u>82</u>, 5749 (1960).

The stereochemistry of the groups at the 3-position was investigated by reducing both α- and β-santalol in the corresponding hydrocarbons by use of sodium and methanol in liquid ammonia. It has been shown recently[5] that this method may be applied to the reduction of geraniol and nerol with little or no isomerization of the double bonds. This method, when applied to α- and β-santalol, gave only poor yields of olefin together with much unchanged alcohol. Nevertheless, the olefins obtained were conclusively identified as α-santalene from α-santalol, and β-santalene from β-santalol.

The hydrocarbons were identified <u>via</u> infra-red absorption, n.m.r. and vapor phase chromatographic retention time. These properties were identical with those of the natural materials.[6]

The hydrocarbons from β-santalene consisted of a mixture of 67% β-santalene (IV) and 33% epi-β-santalene (IVa). Both β-santalene and epi-β-santalene are available by synthesis.[7] We must therefore conclude that β-santalol is a mixture of epimeric alcohols II and IIa with β-santalol (II) predominating. α-Santalol is assigned the stereochemistry shown in (I).

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[5] Kenneth W. Greenlee and Vincent G. Wiley, J. Org. Chem. 27, 2304 (1962).

[6] Kindly supplied by Professor Sukh Dhev.

[7] (a) E. J. Corey, R. Hartman, and P. A. Vatakenchery, J. Am. Chem. Soc. 84, 2611 (1962). (b) Gottfried Brieger, to be published shortly.