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IDENTIFICATION OF *TRANS*-β-SANTALOL AND *EPI-CIS*-β-SANTALOL IN EAST INDIAN SANDALWOOD OIL*

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Key Word Index—*Santalum album*; Santalaceae; East Indian sandalwood oil; *trans*-β-santalol; *epi-cis*-β-santalol.

Abstract—An analysis of East Indian sandalwood oil (*Santalum album*) has resulted in the isolation and identification of *trans*-β-santalol and *epi-cis*-β-santalol.

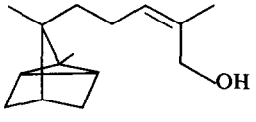
INTRODUCTION

Steam distillation of the heartwood of East Indian sandalwood trees (*Santalum album* L.) yields an oil which is highly prized by perfumers for its sweet woody, tenacious odor. Although the sesquiterpene alcohols α-santalol (**1**) and β-santalol (**2**) account for up to 90% of the oil, many of the minor components [1–3] also contribute to the overall odor character. This report describes the identification of two minor components of East Indian sandalwood oil, *trans*-β-santalol (**3**) and *epi-cis*-β-santalol (**4**).

RESULTS AND DISCUSSION

A comparison of GLC retention time data for synthetic (±)-*trans*-β-santalol (**3**) [4] and East Indian sandalwood oil indicates that **3** may be present in the natural oil at levels of about 2%. Preparative HPLC followed by preparative GLC gave the component in question in 89% purity. GLC retention time, mass spectral and 80 MHz ^{1}H NMR data for the isolate and for synthetic **3** are essentially identical, establishing the presence of **3** in the oil.

In 1963 Brieger [5] reported that Birch reduction of a mixture of santalols from East Indian sandalwood oil gave "a poor yield of olefins" which contained both β-santalene (**5**) and *epi*-β-santalene (**6**) in the ratio 2:1. This result is consistent with the proposed biosynthesis of the santalols [6], and the occurrence of *epi*-dihydro-β-santalol (**7**) [2], *epi*-β-santalene (**6**), and *epi-trans*-β-santalal (**8**) [1] in East Indian sandalwood oil. No additional evidence supporting the presence of *epi-cis*-β-santalol (**4**) in the natural oil has been reported. GLC retention time and mass spectral data for synthetic [7] *epi-cis*-β-santalol are identical with data for a minor component (*ca* 4%) of the natural oil (Fig. 1). The ratio of *cis*-β-santalol (**2**) to the peak in question is about 5:1. Separation of the minor component from **2** by preparative



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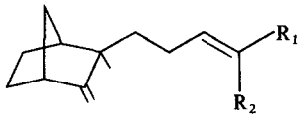
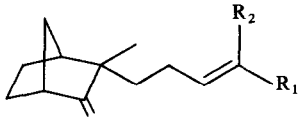
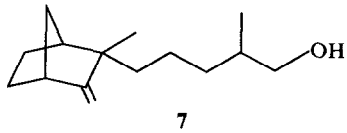


2 R_1 = Me, R_2 = CH_2OH
3 R_1 = CH_2OH, R_2 = Me
5 R_1, R_2 = Me



4 R_1 = Me, R_2 = CH_2OH
6 R_1, R_2 = Me
8 R_1 = CHO, R_2 = Me



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* Part 3 in the series "East Indian Sandalwood Oil". For Part 2 see ref. [7]. This work was presented at the 178th American Chemical Society meeting, Division of Agricultural and Food Chemistry, Washington D.C., 9 September 1979, paper No. 46.

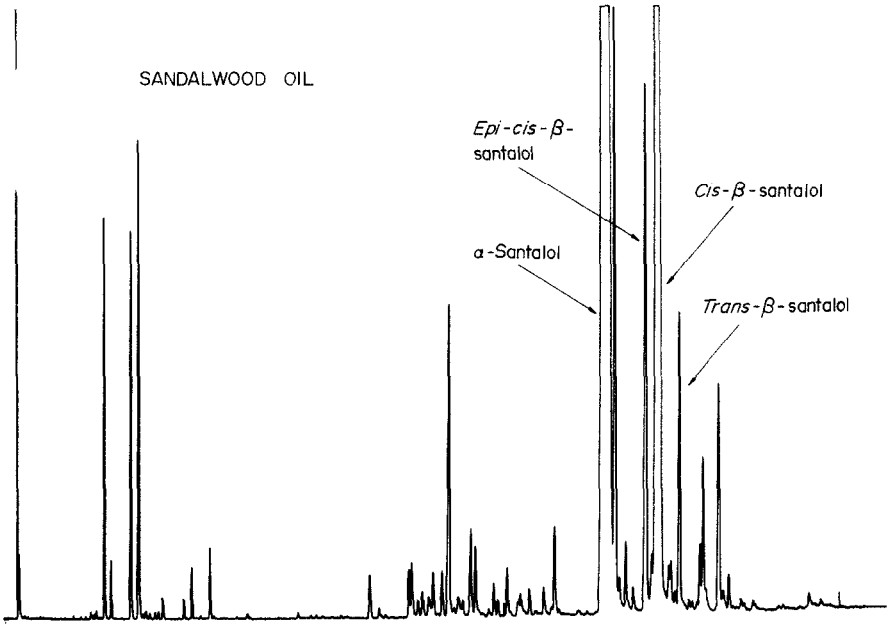

Fig. 1. Capillary column gas–liquid chromatogram of East Indian sandalwood oil. A sample of East Indian sandalwood oil was analysed by GLC (f.i.d. 260°) on a 12 m × 0.2 mm i.d. Carbowax 20M fused silica WCOT column, using temperature programming from 75° to 175° at 2°/min, and He (30 cm/sec) as carrier gas. Injector temperature was 220° and injection volume was 0.14 μl split 1201. The individual components were identified by their retention times and by co-injection with the synthetic compounds. The retention times of α-santalol (**1**), *epi-cis-β*-santalol (**4**), β-santalol (**2**) and *trans*-β-santalol (**3**) were respectively 37.8, 40.0, 40.9 and 42.1 min.

HPLC or GLC appeared to be impractical, consequently a mixture of the two was isolated. The 80 MHz ^{1}H NMR spectrum of the mixture shows a singlet at δ 1.04 corresponding to the *endo*-methyl group of **2** and a smaller signal at δ 1.01 for the *exo*-methyl group of **4**. Further evidence for the occurrence of *epi-cis-β*-santalol in East Indian sandalwood oil was provided by reduction of β-santalol to a mixture of β- and *epi-β*-santalenes. Treating synthetic β-santalol (ratio of β-:*epi-β*-, 19:1) with sulfur trioxide–pyridine, followed by lithium aluminum hydride [8] gave β-santalene (ratio of β-:*epi-β*-, 19:1) in 90% yield. Similarly, a mixture of β- and *epi-β*-santalols, isolated from the natural oil, gave a mixture of β- and *epi-β*-santalenes (ratio of β- to *epi-β*-, *ca* 5:1). The above evidence clearly establishes the presence of *epi-cis-β*-santalol in East Indian sandalwood oil.

EXPERIMENTAL

THF was distilled from Na and benzophenone. Moisture- or oxygen-sensitive reactions were carried out in flame-dried glassware under a N_2 atmosphere.

Prep. HPLC was carried out on a Waters Associates LC/System 500. Prep. GLC was carried out on a 3 m × 2.5 mm i.d. column packed with 10% Carbowax 20M on Chromosorb W 60/80 mesh, using He as a carrier gas (flow rate, 40 ml/min) and temp. programming from 120 to 220° at 4°/min. Unless otherwise indicated, GLC analyses were obtained using either a 3.5 m × 2 mm i.d. glass column packed with 2% Carbowax 20M on Chromosorb G 100/120 mesh, or a 4 m × 2 mm i.d. glass column packed with 3% OV-101 on Chromosorb W 100/120 mesh. Where indicated, percentages refer to computer-calculated peak areas without correction for response. Coupled GC/MS were carried out on a 10 m × 0.2 mm i.d. OV-101 glass WCOT column interfaced with a Hewlett–Packard 5985 mass spectrometer at 70 eV. ^{1}H NMR spectra were recorded at 80 MHz in $CDCl_3$ with TMS as internal standard.

Isolation of (E)-2-*methyl*-5-(2-endo-*methyl*-3-*methylenebicyclo* [2.2.1] *hept*-2-*yl*)-2-*penten*-1-*ol* (trans-*β-santalol*) (**3**). East Indian sandalwood oil (14.2 g) was chromatographed in two portions on a Waters Prep Pak-Silica cartridge (eluant: hexane–EtOAc: 41:9). The appropriate fractions were combined and rechromatographed to give, after kugelrohr distillation, 0.241 g of an oil containing 26% of *trans-β*-santalol (**3**). Further chromatography of the enriched oil (8 × 4 mg) on a 60 cm × 4 mm i.d. μ-Porasil column (eluant: hexane–EtOAc; 3:1) gave a sample containing 54% of **3**. Careful prep. GLC of the above sample gave material which by GLC analysis (25 m × 0.2 mm i.d. Carbowax 20M WCOT fused silica column) contained 89% of *trans-β*-santalol (**3**). The GLC retention time for this material was identical with that of the synthetic material [4] on OV-101 or Carbowax 20M. ^{1}H NMR: δ 1.06 (3 H, *s*, ≥CMe), 1.67 (3 H, *br s*, $-CH=C(CH_2OH)C\underline{H}_3$), 1.0–2.3 (12 H, *m*), 2.60–2.75 (1 H, *m* >CH—⟨), 3.99 (2 H, *s*, $-C\underline{H}_2OH$), 4.47 and 4.74 (2 H, 2*s*, >=CH_2), 5.2–5.6 (1 H, *m*, $-C\underline{H}=C(CH_2OH)Me$). MS *m/z*: 220, 202, 189, 187, 159, 122, 94, 79.

(Z)-2-*Methyl*-5-(2-exo-*methyl*-3-*methylenebicyclo* [2.2.1]*hept*-2-*yl*)-2-*penten*-1-*ol* (epi-cis-*β-santalol*) (**4**). A mixture of *cis-β*- and *epi-cis-β*-santalol (ratio 21:4) was isolated by prep. GLC. ^{1}H NMR: δ 1.01 (3 H, *s*, *exo*-Me for *epi-β*-santalol), 1.04 (3 H, *s*, *endo*-Me for *cis-β*-santalol), 1.79 (3 H, *br. s*, $=C(CH_2OH)C\underline{H}_3$), 1.0–2.3 (12 H, *m*), 2.60–2.75 (1 H, *m*, >CH—⟨), 4.14 (2 H, *s*, $-C\underline{H}_2OH$), 4.46 and 4.73 (2 H, 2*s*, >=CH_2), 5.15–5.35 (1 H, *m*, $-C\underline{H}=C(CH_2OH)Me$). MS (for *epi-cis-β*-santalol) *m/z*: 220, 202, 187, 161, 159, 122, 94, 79.

Reduction of cis-β-santalol (**2**). To a cold (0°) soln of *cis-β*-santalol (**2**) (0.055 g, p.25 mmol, synthetic material [4]

containing 93% *cis*-β-santalol and 5% *epi-cis*-β-santalol) in THF (2 ml) was added $SO_3 \cdot C_5H_5N$ (0.068 g, 0.437 mmol). After stirring for 26 hr at 0°, TLC analysis of the reaction mixture indicated that all of the *cis*-β-santalol had reacted. A soln of $LiAlH_4$ (0.066 g, 1.76 mmol) in THF (2 ml) was added and the mixture stirred at 0° for 30 min and then at 25° for 3 hr. After cooling to 0°, H_2O (0.1 ml), 15% NaOH (0.1 ml), H_2O (0.3 ml) and Et_2O (10 ml) were added consecutively. The solids were removed by filtration and washed with Et_2O, and the combined extracts dried (Na_2SO_4). The solvent was evapd and the residue kugelrohr distilled (130°, 0.5 mm) to give 0.046 g (90% yield) of an oil. GLC analysis indicated 93% of β-santalene (**5**) and 5% of *epi*-β-santalene (**6**). The ^1H NMR and combined GC/MS data for the products are consistent with previously reported data [4, 7].

Reduction of β-santalols from East Indian sandalwood oil. A sample of β-santalols (0.0190 g, 0.086 mmol) isolated from the natural oil was reduced as described above to give 0.011 g of an oil. GLC analysis indicated 76% of β-santalene (**5**) and 12.5% of *epi*-β-santalene (**6**).

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A LABDANE DERIVATIVE FROM *CHROMOLAENA COLLINA* AND A *p*-HYDROXYACETOPHENONE DERIVATIVE FROM *STOMATANTHES CORUMBENSIS**

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Key Word Index—*Chromolaena collina*; *Stomatanthes corumbensis*; Compositae; Eupatorieae; labdane derivative; *p*-hydroxyacetophenone derivative.

Abstract—A new labdane derivative, 7α-acetoxy-*trans*-communic acid was isolated from *Chromolaena collina*. Extraction of *Stomatanthes corumbensis* yielded a new *p*-hydroxyacetophenone derivative which was identified as 4-methoxy-3-[3′-methyl-4′-angeloyloxy-but-2-en-1′-yl]-acetophenone.

The results obtained so far on the chemistry of the genus *Chromolaena* (*Praxelis* group, tribe Eupatorieae) [1] are not very uniform [2–4]. We have now investigated a further species, *C. collina* (DC) K. et R. The roots only afforded germacrene D and *trans*-communic acid (**1**) [5], while the aerial parts yielded germacrene D, caryophyllene epoxide and **1**, and, in addition, the labdane derivative, **2a**, which on esterification gave **2b**. The structure of **2a** followed from the ^1H NMR data (Table 1). The stereochemistry at C-7 was deduced from the observed small coupling $J_{6,7}$, while the position of the acetoxy group could be established by spin decoupling. As the absolute configuration of **1** was established, **2a** most probably had the same configuration. These results again show the complexity of the chemistry of this genus.

The genus *Stomatanthes* is placed in the Eupatoriinae (tribe Eupatorieae, Compositae) [1]. So far, only the occurrence of coumarin in *S. africanus* has been reported [6]. We have now investigated *S. corumbensis* (B. L.

* Part 325 in the series "Naturally Occurring Terpene Derivatives". For Part 324 see Bohlmann, F., Dhar, A. K., Jakupovic, J., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1077.