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α-SANTALDIOL AND β-SANTALDIOL, TWO SANTALANE SESQUITERPENES FROM *SANTALUM INSULARE*

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Key Word Index—*Santalum insulare* var. *marchionense*; Santalaceae; sesquiterpenes santalane-type; α-santaldiol; β-santaldiol.

Abstract—Two new sesquiterpene alcohols, β-santaldiol and α-santaldiol, have been isolated from the heartwood of *Santalum insulare* var. *marchionense* and, by means of two-dimensional NMR experiments, shown to have the β- and α-santalane skeleton, respectively.

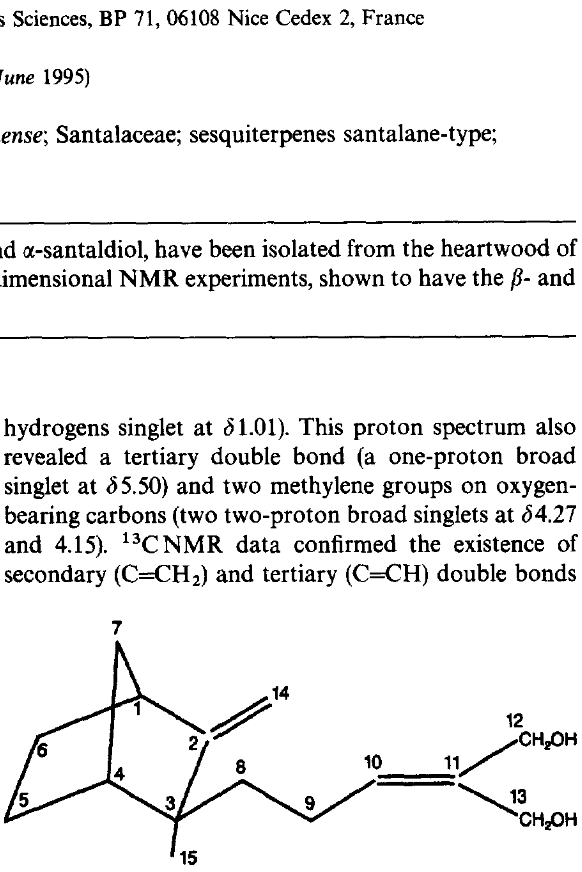
INTRODUCTION

Santalum insulare var. *marchionense* (Skottsberg) Fosberg and Sachet [1], commonly termed 'ahi' in French Polynesia [2], is a hemiparasite that grows in the wilderness in the Marquesas Islands (mainly in Hiva, Oa, Ua Pou and Fatu Hiva). The reddish heartwood part of this plant is widely used as raw material for various kinds of handicrafts, especially sculpture. Because of its strong sandalwood odour, the shavings from the sculpture work are used as fragrant ingredient of traditional monoï (locally prepared coconut oil); This 'ahi monoï' also had some traditional medicinal applications [2].

In the present paper we report the isolation of two new sesquiterpene alcohols, β-santaldiol (**1**) and α-santaldiol (**2**), and the establishment of their structures on the basis of their one- and two-dimensional NMR spectra.

RESULTS AND DISCUSSION

The ethanol extract *S. insulare* var. *marchionense* when subjected to the previously reported treatment [3, 4], give two new sesquiterpene alcohols, β-santaldiol (**1**) and α-santaldiol (**2**). The EIMS of compound **1** showed the molecular ion peak at *m/z* 236 corresponding to the molecular formula $C_{15}H_{24}O_2$. Its infrared spectrum had typical bands for a hydroxyl group and unsaturation absorptions at 3345 cm^{-1} and 1650 cm^{-1}, respectively. The ^1H NMR data established the presence of an exocyclic methylene group (two broad one-proton singlets at $\delta 4.71$ and 4.42) and a tertiary methyl resonance (three hydrogens singlet at $\delta 1.01$). This proton spectrum also revealed a tertiary double bond (a one-proton broad singlet at $\delta 5.50$) and two methylene groups on oxygen-bearing carbons (two two-proton broad singlets at $\delta 4.27$ and 4.15). ^{13}C NMR data confirmed the existence of secondary ($C{=}CH_2$) and tertiary ($C{=}CH$) double bonds



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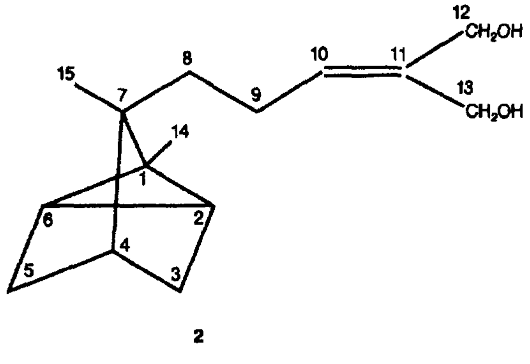

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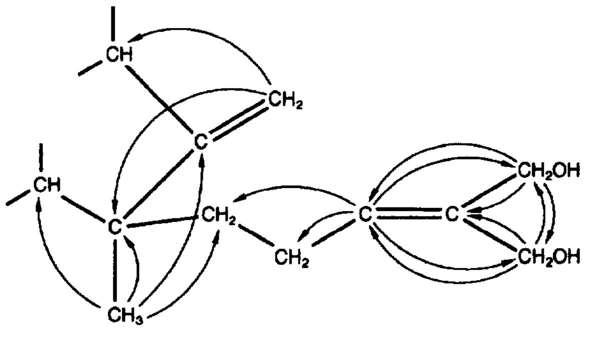

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Fig. 1. Selected long-range proton–carbon connectivities for structural unit A_1 derived from the HMBC plot of α-santaldiol (1).

Table 1. ¹H NMR and ¹³C NMR chemical shifts for compound **1**

$\delta^{13}C$*	Group†	Assignment‡	δ^1H*§
166.00	C	2	—
136.77	C	11	—
131.73	CH	10	5.50
99.93	CH_2	14	4.71 and 4.42
67.56	CH_2	12	4.15
59.93	CH_2	13	4.27
46.83	CH	1	2.64
44.77	C	3	—
44.74	CH	4	2.06
41.01	CH_2	8	1.38 and 1.22
37.12	CH_2	7	1.64 and 1.15
29.70	CH_2	6	1.63 and 1.20
23.72	CH_2	5	1.63 and 1.38
23.14	CH_2	9	2.04
22.65	CH_3	15	1.01

*In ppm with respect to TMS.
†Determined from DEPT spectra.
‡Information obtained from 2D experiments.
§Determined from 1D spectrum and from the cross-sections of the HMQC diagram.

Table 2. ¹H NMR and ¹³C NMR chemical shifts for compound **2**

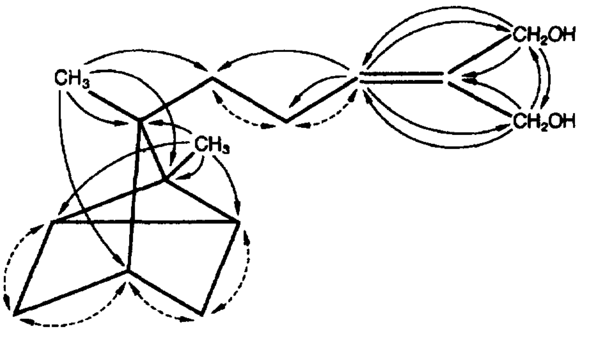
$\delta^{13}C$*	Group†	Assignment‡	δ^1H*§
136.53	C	11	—
132.08	CH	10	5.51
67.43	CH_2	12	4.14
59.73	CH_2	13	4.26
44.92	C	7	—
38.21	CH	4	1.54
34.56	CH_2	8	1.21 and 1.13
31.55	CH_2	3	1.57 and 1.03
31.06	CH_2	5	1.52 and 1.01
27.40	C	1	—
22.85	CH_2	9	1.99 and 1.95
19.58	CH	2	0.80
19.52	CH	6	0.80
17.54	CH_3	15	0.79
10.68	CH_3	14	0.95

*In ppm with respect to TMS.
†Determined from DEPT spectra.
‡Information obtained from 2D experiments.
§Determined from 1D spectrum and from the cross-sections of the HMQC diagram.

and two deshielded methylene carbons. The multiplicities of the other ¹³C NMR signals obtained from DEPT pulse sequence [5] indicated two methine, five methylene and one quaternary aliphatic carbons. As a consequence of the above considerations, compound **1** must contain two rings.

At this point compound **1** was identified from the concerted use of two-dimensional homonuclear and both direct and long-range heteronuclear chemical shift correlation techniques. By utilizing the contour plot of the long-range heteronuclear chemical multiple quantum bond connectivity (HMBC) experiment [6], the structural unit A_1 (Fig. 1) can be determined using the connectivities observed between the previously assigned protons and carbons α or β to these signals (^2J or ^3J couplings). On the basis of the combination of homonuclear ¹H–¹H (COSY) [7, 8] and ¹H-detected one-bond heteronuclear multiple quantum coherence (HMQC) [9] correlation diagrams, the remaining partial structures and fragment A_1 were assembled to afford a sesquiterpene with the β-santalane skeleton and two hydroxyl functions. This compound was named β-santaldiol. Moreover, its NMR data were in good agreement with those of β-santalol [10] and the stereochemistry at the C-3 position was deduced from the phase-sensitive NOESY [11] results. The ¹H NMR and ¹³C NMR chemical shifts of **1** are given in Table 1.

α-Santaldiol (**2**) displayed a large hydroxyl infrared band at 3335 cm^{-1}. In the EI mass spectrum no $[M]^+$ could be observed. However the significant fragment at m/z 218 $[M - H_2O]^+$ clearly showed that the molecular formula must be $C_{15}H_{24}O_2$. The ¹H NMR and ¹³C NMR chemical shifts are indicative of a tertiary double bond and two quaternary methyl groups; these spectroscopic data also exhibited signals for two oxygen-bearing methylene carbons. The DEPT experiment revealed the presence of two methyl groups, six methylene groups, three methine groups and two quaternary aliphatic carbons. From this information it was deduced that **2** was a tricyclic sesquiterpenoid. Moreover, the ¹H NMR spectrum of **2** resembled closely that of α-santalol [12] except for the different chemical shifts associated with the replacement of a vinyl methyl by an hydroxymethyl group. Finally, the molecular framework, and the complete ¹H NMR and ¹³C NMR chemical shift assignments of **2**, were deduced (Table 2), as for β-santaldiol (**1**), on the basis of various connectivities (Fig. 2) extracted from the two-dimensional experiments.



2

Fig. 2. Proton–carbon (——→) and proton–proton (→---→) coupling pathways of α-santaldiol (**2**) determined, respectively, from the HMBC and COSY experiments.

EXPERIMENTAL

Heartwood of *S. insulare* (27 g) was finely chopped and then extracted with EtOH for 8 hr by a Soxhlet apparatus yielding 5.3 g of an extract. The crude extract was distilled under red. pres. (vacuum: 0.03 mm Hg) to give the heavy fr. of the extract (1.25 g) This heavy fr. of *S. insulare* extract was chromatographed over a silica gel column using successively hexane and CH_2Cl_2 to separate the hydrocarbon fraction from the polar fraction. This last fr. (1.03 g), which contained mainly sesquiterpenoids, was then separated by CC on silica gel–$AgNO_3$ using a stepwise gradient system from toluene to EtOAc as described elsewhere [4]. Elution with toluene–EtOAc (50:50) gave **2** (153 mg). Compound **1** (54 mg) was obtained from toluene–EtOAc (80:20) eluted fr. Repeated elutions were necessary to purify every compound. All 1D and 2D NMR spectra were recorded in $CDCl_3$ solns (^1H at 400.13 MHz; ^{13}C at 100.61 MHz; TMS as standard in all measurements). Standard Bruker pulse sequences were used for homonuclear and heteronuclear correlation experiments. For other experimental details see [13, 14].

β-santaldiol (**1**): $C_{15}H_{24}O_2$. Oil, $[\alpha]_D^{25}$ − 66° ($CHCl_3$; *c* 0.1); IR ν_{max} cm^{-1}: 3345, 2968, 2917, 2869, 1650, 1456, 1004, 867. EIMS 70 eV, *m/z* (re. int.): 236 $[M]^+$ (1), 218 $[M - H_2O]^+$ (2), 200 (5), 187 (4), 171 (2), 159 (4), 134 (7), 122 (36), 107 (11), 94 (100), 93 (42), 91 (23), 79 (31), 67 (17), 55 (19), 43 (14), 41 (32).

α-santaldiol (**2**). $C_{15}H_{24}O_2$. Oil, $[\alpha]_D^{25}$ + 12,4° ($CHCl_3$; *c* 0.2); IR ν_{max} cm^{-1}: 3335, 2944, 2872, 1452, 1014, 852. EIMS 70 eV, *m/z* (rel. int.): 236 $[M]^+$ (0), 218 $[M - H_2O]$ (7), 200 (6), 187 (8), 175 (3), 161 (5), 143 (6), 129 (10), 121 (51), 107 (32), 94 (91), 93 (100), 91 (51), 79 (48), 77 (38), 67 (23), 55 (34), 43 (26), 41 (44).

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