

# A New Sesquiterpene Alcohol of the Copane Series from Angelica Root Oil

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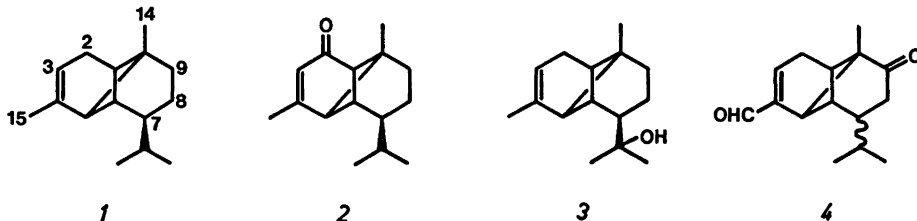
A new sesquiterpene alcohol was isolated from the volatile root oil of *Angelica archangelica* L. On the basis of spectral and chemical evidence structure **8**, *cis*- $\alpha$ -copaene-8-ol, was assigned to this compound.

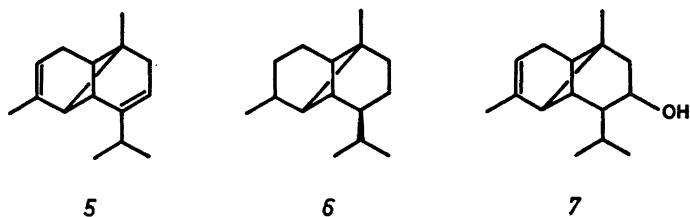
The tricyclic sesquiterpene hydrocarbons,  $\alpha$ -copaene (**1**) and  $\beta$ -copaene are reported to be present in a number of essential oils.<sup>1-6</sup> Two oxygenated copaene derivatives have been identified, mustakone (**2**) from *Cyperus rotundus*<sup>4</sup> and  $\alpha$ -copaene-11-ol (**3**) from *Parabenzoin preacox*.<sup>5</sup> Two sesquiterpenoid ketoaldehydes, called brachylaenalone A and B, have been isolated from the heartwood of *Brachylaena hutchinsii*.<sup>7</sup> The compounds (**4**) are thought to differ only in the configuration of the isopropyl group, so that one of them would have the configuration of copaene.

In a recent study the root oil of *Angelica archangelica* was found to contain  $\alpha$ -copaene-11-ol and an unknown alcohol (about 0.5 % of each) as the main sesquiterpene alcohol components.<sup>6</sup> The present paper describes the structure determination of this unknown, for which the structure and relative configuration **8**, *cis*- $\alpha$ -copaene-8-ol, is proposed.

The mass spectrum of **8** displayed  $M^+$  at  $m/e$  220, which obviously corresponds to the molecular formula  $C_{15}H_{24}O$ . A rearrangement ion corresponding to loss of water appeared at  $m/e$  202. The IR spectrum revealed the presence of a primary or secondary hydroxyl ( $\nu_{\max}$  3420 and 1020  $cm^{-1}$ ), a *gem*-dimethyl group ( $\nu_{\max}$  1383 and 1370  $cm^{-1}$ ) and a trisubstituted double bond ( $\nu_{\max}$  3020 and 783  $cm^{-1}$ ). The  $^1H$  NMR spectrum showed signals due to a methyl at a quaternary carbon ( $\delta$  0.83, 3 H, s), an isopropyl group (two 3 H doublets centered at  $\delta$  0.95 and 1.03,  $J$  6.5 Hz), a methyl attached to an olefinic carbon ( $\delta$  1.66, 3 H, m), one olefinic proton ( $\delta$  5.19, 1 H, m) and a methine proton adjacent to oxygen ( $\delta$  4.21, 1 H, m).

Hydrogenation of **8** with  $PtO_2$  in glacial acetic acid yielded a saturated alcohol with a molecular weight of 222 (MS, IR). This confirms that alcohol **8** has a tricyclic structure. The only tricyclic skeleton present in the sesquiterpenoids found in angelica root oil is that of copaene.<sup>6</sup> The structure derived from  $\alpha$ -copaene (**1**) with hydroxyl at the 2-, 8- or 9-position would be compatible with the spectral data including the unusual position of the C-H deformation band of the double bond. The lowered frequency





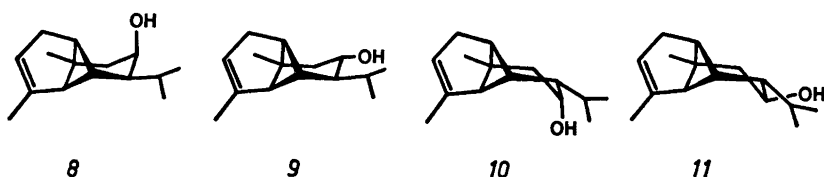
(about  $780\text{ cm}^{-1}$ ) is typical for the strained bicyclo[3,1,1]heptene system (e.g.  $\alpha$ -pinene,  $\alpha$ -copaene).<sup>9</sup>

Dehydration of **8** with thionyl chloride in pyridine afforded an unsaturated hydrocarbon, the mass spectrum of which displayed the molecular peak at  $m/e$  202. The IR spectrum of this hydrocarbon showed notable absorptions only at  $780\text{ cm}^{-1}$  in the region of C—H out-of-plane bending vibrations of double bonds. This could be expected if the new double bond is located at the 7,8-position as in **5**.

On catalytic hydrogenation of the diene **5**, two saturated hydrocarbons with molecular weights of 206 were obtained in a ratio of 2:3. The minor compound was identified as copane (**6**) by comparing its IR and mass spectra with those of the hydrogenation product of  $\alpha$ -copaene from angelica root oil. The other, with very similar spectra, was evidently the isopropyl epimer, ylangane. Formation of both is expected if the diene has the structure **5**.

This evidence suggests the structure **7** for the unknown alcohol, leaving the stereochemical details open. The four possible isomers differing in their configuration at C-7 and C-8 can be represented by the perspective figures **8–11**. Structures **8** and **9** are favoured by the fact that all the other cadalene-type sesquiterpenes found in angelica root oil belong to the muuro-lane group with related stereochemistry. Considering the smooth dehydration with thionyl chloride in pyridine, structure **8** is preferred as it has the C-7 hydrogen more favourably located for E2 elimination.

Further support for structure **8** was obtained from the relative lanthanide induced chemical shifts.  $^1\text{H}$  NMR spectra were recorded after successive additions of  $\text{Eu}(\text{dpm})_3$  to the alcohol sample in  $\text{CDCl}_3$ . The relative europium induced shifts (DEu values) of signals that could be correctly assigned were calculated as the slopes of the lines when the shifts were plotted against the  $\text{Eu}(\text{dpm})_3$  addition. The shift effect on the isopropyl methyl signals were found to be 2–3 times greater than on the other methyl signals. This is in agreement with the assignment of the hydroxyl at C-8. The average structure for the complex of **8–11** and the shift reagent was determined by iterative computer fitting of the relative shift effect values to the pseudo-contact equation of McConnell and Robertson.<sup>9,10</sup> The observed shift values of the C-3, C-8, C-14, C-15 and one of the C-9 proton signals were used. The Eu—O distances and  $\alpha$ -C—O—Eu angles obtained were 2.4 Å,  $165^\circ$  for the complex of **8**, 3.7 Å,  $128^\circ$  for the complex of **9**, 3.0 Å,  $129^\circ$  for the complex of **10**, and 3.9 Å,  $130^\circ$  for the complex of **11**. The corresponding data reported for *cis*-4-*t*-butylcyclohexanol, involving an axial hydroxyl group, are 2.2 Å,  $160^\circ$  and for *trans*-4-*t*-butylcyclohexanol, with an equatorial hydroxyl group, 2.5 Å,  $139^\circ$ .<sup>11</sup> Only the values for **8** are in reasonable agreement with the data for the 4-*t*-butylcyclohexanol with the corresponding configuration. Another conformation involving an axial isopropyl group is also possible for the compounds represented by structures **8–11**. In this conformation compound **11** would have given iden-



tical results to those calculated for **8**. This conformation, however, seems to be unfavorable. Moreover, the large shift effect observed in the signals due to the methyls of the isopropyl group seems to exclude this possibility. Accordingly, the relative configuration **8** was assigned to the sesquiterpene alcohol.

## EXPERIMENTAL

Gas chromatography was performed on a Hewlett-Packard 7620 A instrument with 6 mm  $\times$  3 m stainless steel columns packed with 10 % FFAP or 5 % SE-30 on Chromosorb W AW. IR spectra were recorded on a Perkin-Elmer 521 instrument. Mass spectra were run on JMS-D 100 mass spectrometer at the Technical Research Centre of Finland.  $^1\text{H}$  NMR spectra were determined in  $\text{CDCl}_3$  on a JEOL JMM PFT 100 spectrometer in the Department of Organic Chemistry, University of Helsinki. The average structures of the Eu-complexes were computed in the Department of Chemistry, University of Jyväskylä. The isolation of angelica root oil and separation of the fraction containing the oxygenated compounds have been described before.<sup>8</sup>

*cis- $\alpha$ -Copaene-8-ol* was separated from the fraction of oxygen containing compounds by preparative GLC first on the FFAP column. After rechromatography on SE-30 column about 10 mg of pure **8** was collected. MS:  $m/e$  (%) 220 ( $\text{M}^+$ , 1), 202 (10), 187 (6), 177 (5), 160 (45), 159 (85), 146 (12), 145 (59), 134 (14), 133 (31), 132 (36), 121 (15), 120 (25), 119 (100), 117 (18), 109 (15), 107 (19), 106 (14), 105 (50), 93 (23), 92 (13), 91 (33), 81 (10), 79 (15), 77 (16), 55 (14), 43 (12), 41 (22). IR:  $\nu_{\text{max}}$  3420, 3020, 1383, 1370, 1020, 783  $\text{cm}^{-1}$ . NMR:  $\delta$  ( $\text{CDCl}_3$ ) 0.83 (3 H, s), 0.95 (3 H, d,  $J$  6.5 Hz), 1.03 (3 H, d,  $J$  6.5 Hz), 1.66 (3 H, m), 4.21 (1 H, m), 5.19 (1 H, m). DEU values (% from the value of  $\alpha$ -proton): 100.0 (observed)/100.22 (calculated) (C-8 H); 65.5/65.0 (C-9  $\text{H}_{\text{eq}}$ ); 9.9/11.2 (C-14 3 H); 9.9/5.7 (C-3 H); 7.5/10.0 (C-15 3 H).

*Hydrogenation of 8*. 1 mg of **8** in glacial acetic acid (5 ml) containing  $\text{PtO}_2$  (5 mg) was shaken in a 20 ml ampule filled with hydrogen for 2 h at room temperature. The catalyst was filtered off and the filtrate neutralized with NaOH solution. The product was extracted into pentane and a saturated alcohol was isolated by GLC. MS:  $m/e$  (%) 222 (1), 204 (35), 189 (33), 161 (100), 149(28), 133 (24), 119 (30), 105 (70), 95 (48), 93 (42), 81 (54), 69 (40), 55 (45), 43 (40), 41 (65). IR:  $\nu_{\text{max}}$  3420, 1380, 1370, 1360, 1015  $\text{cm}^{-1}$ .

*Dehydration of 8*. 10  $\mu\text{l}$  of thionyl chloride in 200  $\mu\text{l}$  of pyridine was added to 2 mg of **8** in 200  $\mu\text{l}$  of pyridine at 0  $^\circ\text{C}$ . The solution was allowed to warm up to room temperature, neutralized and extracted with ether. Diene

**5** was isolated as the main product by GLC. MS:  $m/e$  (%) 202 (38), 187 (23), 159 (100), 145 (36), 131 (31), 119 (43), 106 (21), 105 (22), 91 (28), 77 (14), 41 (20). IR:  $\nu_{\text{max}}$  3020, 1377, 1369, 780  $\text{cm}^{-1}$ .

*Hydrogenation of diene 5*. 0.5 mg of **5** was hydrogenated in glacial acetic acid with  $\text{PtO}_2$  as above. The product consisted of two saturated hydrocarbons (3:2), which were separated by GLC. The mass spectra of both were almost identical with that published for copane.<sup>12</sup> The minor component was identified as the hydrogenation product of  $\alpha$ -copaene by comparing the IR spectra.

*Copane from  $\alpha$ -copaene*. 2 mg of  $\alpha$ -copaene was isolated from angelica root oil<sup>6</sup> and hydrogenated as above. The saturated hydrocarbon was identified as copane (**6**) by its mass spectrum.<sup>12</sup>

## REFERENCES

- Gildmeister, E. and Hoffmann, Fr. *Die Atherischen Öle*, Akademie Verlag, Berlin 1960, Vol. III a, p. 297.
- Westfelt, L. *Acta Chem. Scand.* 21 (1967) 152.
- Yates, R. L. and Wenninger, J. A. *J. Ass. Offic. Anal. Chem.* 53 (1970) 941.
- Kapadia, V. H., Nagasampagi, B. A., Naik, V. G. and Dev, S. *Tetrahedron* 21 (1965) 607.
- Ohara, K., Ohta, Y. and Hirose, Y. *Bull. Chem. Soc. Jap.* 46 (1973) 641.
- Taskinen, J. and Nykänen, L. *Acta Chem. Scand. B* 29 (1975) 757.
- Brooks, C. J. W. and Campbell, M. M. *Chem. Commun.* (1969) 630.
- Bellamy, L. J. *The Infra-red Spectra of Complex Molecules*, Methuen, London 1964, p. 388.
- Paasivirta, J., Häkli, H. and Widén, K.-G. *Org. Magn. Resonance* 6 (1974) 380.
- McConnell, H. M. and Robertson, R. E. *J. Chem. Phys.* 29 (1958) 1361.
- Demarco, P. V., Cerimele, B. J., Crane, R. W. and Thakkar, A. L. *Tetrahedron Lett.* (1972) 3539.
- Moshonas, M. G. and Lund, E. D. *Flavour Ind.* 1 (1970) 375.

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