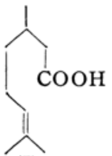
*The Structure of Chamenol**

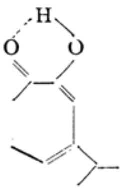
By Tetsuo NOZOE, Yoshio KITAHARA, and Tomio ARAI

(Received May 18, 1955)

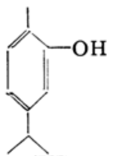
Some time ago, Nozoe and others[1] isolated two different phenolic substances from the acid portion of the essential oil of *Chamaecyparis taiwanensis Masamune et Suzuki*, together with *l*-rhodinic acid (I) and hinokitiol (II) (or β-thujaplicin), and designated the phenolic substances chamenol-A (oil) and chamenol-B (m.p. 41–42°, b.p. 122–124°/15 mmHg, $C_9H_{12}O_2$ or $C_{10}H_{14}O_2$). Later studies by Nozoe and others[2] revealed that chamenol-A is carvacrol (III).



(I)



(II)



(III)

By studies[2] on the acid portion of *Thujopsis dolabrata Sieb. et Zucc.*, *l*-rhodinic acid (I), hinokitiol (II) and carvacrol (III) were isolated; however the fraction (b.p. 122–125°/15 mmHg) that seemed to be chamenol-B, on seeding with crystals of chamenol-B, afforded crystals of α-thujaplicin, and chamenol-B could not be isolated from the essential oil of *Thujopsis*. Luckily, however, a minute amount of chamenol-B was brought back to Japan on repatriation from Formosa and its structural studies were again carried out.

Since chamenol-A has been found to be identical with carvacrol, chamenol-B will henceforth be referred to simply as *chamenol*.

The infrared spectra[3] (Figs. 1 and 2) of chamenol point to the presence of the following groups[4].

2.80 μ: hydroxyl group
3.24 μ (shoulder): probably C-H of benzene nucleus
3.37 and 3.45 μ: aliphatic C-H
6.24 and 6.60 μ: benzene nucleus
6.87, 7.32, 8.52 and 8.72 μ: isopropyl group[5]

---

* This work was presented at the XIIIth International Congress of Pure and Applied Chemistry at Stockholm, July 31st, 1953.

1) T. Nozoe, *Science of Drugs*, **3**, 174 (1949); *Science Repts. Tohoku Univ., First Ser.*, **34**, 199 (1950).

2) T. Nozoe, A. Yasue and K. Yamane, *Proc. Japan Acad.*, **27**, 15 (1951).

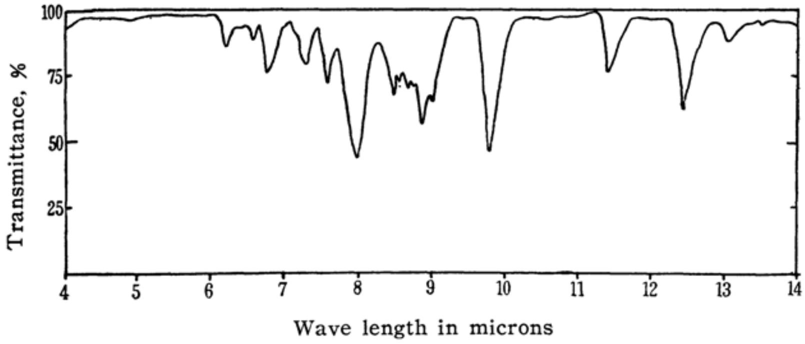
3) Infrared absorption spectrum was measured by Dr. M. Tsuboi of Faculty of Science, Tokyo University.

4) a) H.W. Thompson, *J. Chem. Soc.*, 328 (1948).
b) N.B. Colthup, *J. Optical Soc. Am.*, **40**, 397 (1950).
c) H.M. Randall, R.G. Fowler, N. Fuson and J.R. Dangl, *Infrared Determination of Organic Structures*. D. Van Nostrand Co., N.Y. (1949).

5) D.M. Simpson and G.B.B.M. Sutherland, *Proc. Roy. Soc.* (London), **A 199**, 169 (1949); *Chem. Abstr.*, **44**, 2372 (1950).

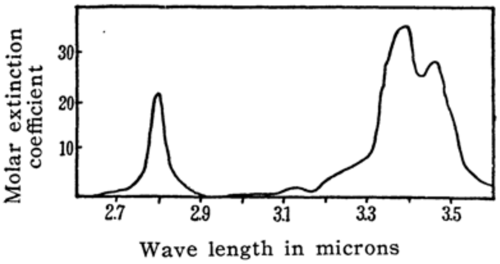
8.05 and 8.85 μ: aromatic ether (the absorption band due to C-O-C in trimethoxybenzaldehyde is at 8.87 μ[4c])

11.43 and 12.49 μ: 1, 2, 4-trisubstituted benzene.



Wave length in microns

Fig. 1. Infrared absorption spectrum of chamenol (solid).



Wave length in microns

Fig. 2. Near infrared absorption spectrum of chamenol in 0.01 mol./l. CCl_4 solution.

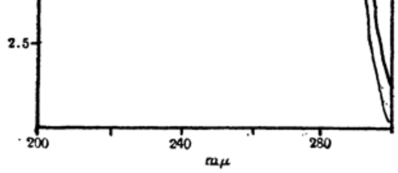


Fig. 3. Ultraviolet absorption spectra in methanol.

a) chamenol b) dihydroeugenol

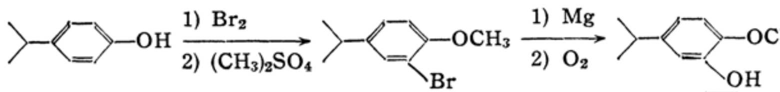
The fact that the 5.5–6.1 μ region lacks any absorption clearly shows that the molecule does not contain any carbonyl function.

Analytical values of chamenol correspond to the formula $C_{10}H_{14}O_2$, containing one methoxyl group. It is a phenolic substance and colors deep green with ferric chloride but did not give a red color in organic solvents (chloroform or benzene), characteristic of tropolones. It gives a monobenzoate, m.p. 64–65° and a *p*-nitrobenzoate, m.p. 87°. Chamenol shows a blue green coloration by the Liebermann reaction[6] and therefore the para-position of the phenol is apparently free of a substituent.

From the analytical results and infrared determination, chamenol may be assumed to be a phenol possessing a methoxyl and an isopropyl group. The ultraviolet spectrum of chamenol, as shown in Fig. 3, possesses an absorption maximum at 281 mμ while the maximum of dihydroeugenol is 281 mμ.

These results suggest that chamenol is an isopropyl derivative of guaiacol and could reasonably be represented by structure (IV).

Based on this surmise, the synthesis of (IV) was initiated from 2-bromo-4-isopropylanisole (V), obtained from *p*-isopropylphenol[7]. The bromide (V) was converted to the Grignard reagent in the presence of isopropyl bromide and followed by oxidation with oxygen to afforded 5-isopropylguaiacol, m.p. 41-42°. Both this substance and its *p*-nitrobenzoate showed no depression of the melting points on admixture with chamenol and its *p*-nitrobenzoate respectively; thus the structure of chamenol was confirmed as (IV).



(V) (IV)

---

[6] C. Liebermann, *Ber.*, **7**, 806, 1098 (1874); W.B. Deichmann, *Ind. Eng. Chem. Anal. Ed.*, **16**, 37 (1944).

[7] R.A. Smith, *J. Am. Chem. Soc.*, **56**, 718 (1934).

Experimental

Chamenol[1]—Colorless scales from petroleum ether, b.p. 122–124°/15 mmHg, m.p. 41–42°. Anal. Found: C, 72.44; H, 8.31; Mol. wt. (Rast method), 169; OCH_3 (by Zeisel method), 18.01. Calcd. for $C_{10}H_{14}O_2$: C, 72.44; H, 8.48; Mol. wt., 166; OCH_3, 18.67. *p-Nitrobenzoate*: Pale yellow prisms from ethanol, m.p. 86–87°. Anal. Found: C, 64.42; H, 5.46; N, 4.65. Calcd. for $C_{17}H_{17}O_5N$: C, 64.76; H, 5.40; N, 4.44. *Benzoate*: Colorless scales from ethanol, m.p. 64–65°. Anal. Found: C, 75.24; H, 6.95. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71.

2-Bromo-4-isopropylphenol—To a solution of 12 g. of 4-isopropylphenol[7] in 40 cc. of chloroform, 17 cc. of chloroform containing 14 g. of bromine was added under ice-cooling. Removal of the solvent followed by distillation furnished monobromo compound (15.7 g., 83%), b.p. 119–120°/15 mmHg. *p-Nitrobenzoate*: Colorless prisms from ethanol, m.p. 83–84°. Anal. Found: N, 4.08. Calcd. for $C_{16}H_{14}O_4NBr$: N, 3.87.

2-Bromo-4-isopropylanisole (V)—To a stirred mixture of 16.5 g. of 2-bromo-4-isopropylphenol, and 6 g. of sodium hydroxide in 30 cc. of water, 10.5 g. of dimethyl sulfate was added dropwise, the reaction mixture was heated at 60–70° for five hours after the last addition, and extracted by ether. Removal of the solvent from the extract followed by distillation furnished the anisole (V, 11.9 g., 68%), b.p. 113–116°/4 mmHg. Anal. Found: C, 52.38; H, 5.53. Calcd. for $C_{10}H_{13}OBr$: C, 52-42; H, 5.72.

5-Isopropylguaiacol (IV)—Grignard reagent prepared from 4 g. of (V), 3.2 g. of isopropyl bromide, and 1 g. of activated magnesium was oxidized by the introduction of dry oxygen for four hours. After standing for fifteen hours, the reaction mixture was refluxed with dilute sulfuric acid for one hour. The ethereal layer was extracted with 20 cc. of 5 % sodium hydroxide solution and the alkali layer was acidified and extracted with ether. Removal of the solvent from dried ether solution followed by distillation furnished colorless solid (1.1 g. 38%, b.p. 115–124°/10 mmHg, m.p. 38–40°), which after recrystallization from petroleum ether, afforded colorless scales, m.p. 41–42°, 5-isopropylguaiacol (IV). (IV) and its derivatives (*benzoate*, m.p. 64–65°, *p-nitrobenzoate*, m.p. 86–87°) were respectively found by admixture to be identical with chamenol and its derivatives.

Summary

The structure of chamenol, a phenolic substance isolated from the acid fraction of the essential oil of *Chamaecyparis taiwanensis*, was proved to be 2-methoxy-5-isopropylphenol.

Chemical Institute, Faculty of Science,
Tohoku University, Sendai