*Polyterpenes I. Permanganate Oxidation of Thujopsene, Part 1**

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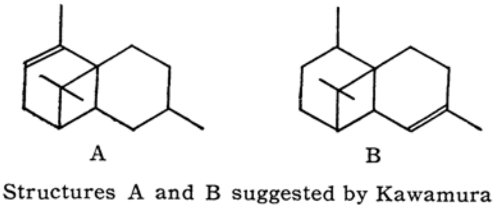
Hiba, *Thujopsis dolabrata Sieb. et Zucc.* is an arbor native to Japan, abounding especially in the northern parts of Honshū island, namely Ōu, Hokuriku, and Tōhoku district. In view of the strong resisting power of Hiba wood against saprophytes, the wood oil has long been a target of much attention, and both Yano¹⁾ and Uchida²⁾ proved in their early investigation that its main constituent is a tricyclic sesquiterpene, which was subsequently named thujopsene by Kawamura³⁾. It may be noted that the anti-saprophytic property is due to the minor acidic parts of the oil, the components of which were elucidated by Nozoe, Yasue and Yamane⁴⁾.

By the permanganate oxidation of thujopsene, Kawamura³⁾ obtained a glycol $C_{15}H_{26}O_2$, m.p. 92—3°, a keto-aldehyde $C_{15}H_{24}O_2$, b. p. 170—7°/11 mm, disemicarbazone m. p. 221° (decomp.), and a keto-carboxylic acid $C_{15}H_{24}O_3$, b. p. 180—5°/4 mm, semicarbazone m. p. 219° (decomp.). The ketonic acid was further degradated with hypobromite to a dicarboxylic acid $C_{14}H_{22}O_4$, m. p. 208—9°. On the basis of these degradations and several other observations, he suggested the structure A or B for thujopsene. Unfortunately little has been known about this paper in foreign countries, as it was written only in Japanese and was not introduced in abstracting journals.


A B

Structures A and B suggested by Kawamura.

Later Obata and Fukushi⁵⁾ stated that they could not find thujopsene in Hiba wood oil and that its main constituent has the constants between the dicyclic and the tricyclic. To make clear of this discrepancy, Fujita⁶⁾ collected ten samples of Hiba wood from various districts where it grows, and confirmed the fact that the main constituent of the oil obtained from them was a tricyclic sesquiterpene. Recently Tanaka and Aikawa⁷⁾ reported that thujopsene is a mixture of endo- and semicyclic double bond isomer.

As it is regrettable that the study on the structure of this interesting substance has been interrupted for long years, the authors have decided to take it up at this time. The present paper deals with some of the degradation products by the oxidation of thujopsene with potassium permanganate in acetone solution. Unlike the procedure followed by Kawamura, the authors did not add water to the reaction mixture.

The main product was a crystalline keto-carboxylic acid $C_{15}H_{24}O_3$ (I), m. p. 164—5°, which was oxidized with hypobromite to a dicarboxylic acid $C_{14}H_{22}O_4$, m. p. 210°. This dicarboxylic acid was easily converted into an anhydride m. p. 109—110° by the treatment with acetic anhydride, which shows infrared absorption at 1799 and $1752\,cm^{-1}$ (in carbon tetrachloride), agreeing with glutaric anhydride derivatives⁸⁾. The ring containing double bond, therefore, becomes five membered and Kawamura's formulae are rejected. Since the dicarboxylic acid can be esterified into monomethyl ester m. p. 60°, for the most part, with methanol and sulfuric acid, one of the carboxyl groups may be considered to be attached to the tertiary carbon atom. The ketonic acid I was

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* Presented before the 10th Annual Meeting of the Chemical Society of Japan held in Tokyo, April, 1957. Simultaneously two other reports on the same subject were presented independently by Tanaka et al. and Nozoe et al. at this meeting.

1) M. Yano, *J. Soc. Chem. Ind. Japan*, **16**, 443 (1913).

2) S. Uchida, ibid., **31**, 501 (1928).

3) J. Kawamura, *Bull. Govt. Forest Expt. Station*, **30**, 59 (1930).

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

5) Y. Obata and S. Fukushi, *J. Agr. Chem. Soc. Japan*, **26**, 113 (1952).

6) N. Fujita, *Bull. Govt. Forest Expt. Station*, **76**, 175 (1954).

7) J. Tanaka and T. Aikawa, 9th Annual Meeting of the Chemical Society of Japan, Kyoto, April 1956.

8) H. H. Wasserman and H. E. Zimmerman, *J. Am. Chem. Soc.*, **72**, 5787 (1950); G. Stork and R. Breslow, ibid., **75**, 3291 (1953); G. Büchi and R. E. Erickson, ibid., **78**, 1262 (1956).

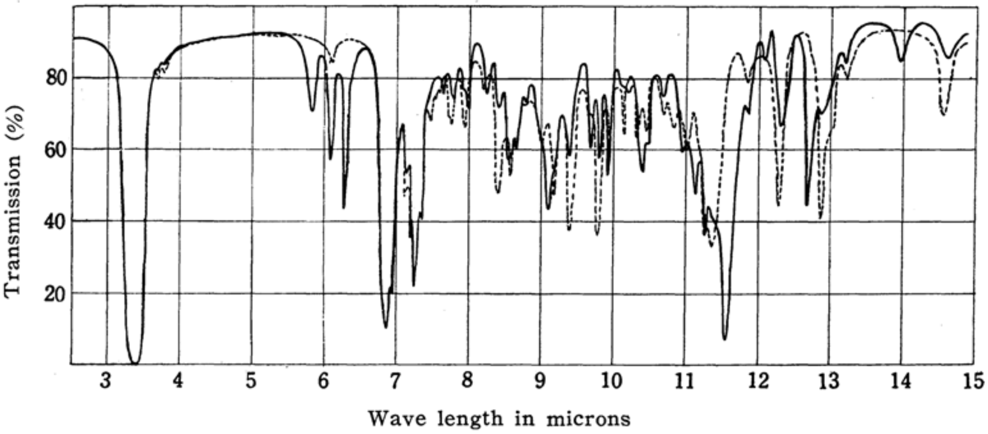

Fig. 1. Infrared spectra of thujopsene and isomerized hydrocarbon.
…… Thujopsene —— Isomerized hydrocarbon

soluble gradually into concentrated hydrobromic acid or sulfuric acid and a ketonic γ-lactone m. p. 56° was obtained from the solution. Curiously, attempted esterification of the acid I with methanol and sulfuric acid gave the same lactone.

Besides this ketonic acid, the authors separated, from the acidic portion of the oxidation product, three crystalline substances, namely an oxylactone $C_{15}H_{22}O_4$ (II), m. p. 123.5°; a hydroxyketonic acid $C_{15}H_{22}O_4$ (III), m. p. 193° (decomp.); and a hydroxylic acid $C_{12}H_{14}O_3$ (IV), m. p. 153°. The acid III was converted into a dehydrated ketonic acid, m. p. 206—7°, by heating it to the decomposing point.

The neutral portion of the oxidation product was fractionated into unchanged thujopsene, isomerized hydrocarbon, and an oxygen-containing high boiling fraction, from which an unsaturated ketone $C_{14}H_{20}O$ (V), m. p. 70° was separated by alumina chromatography.

Experimental*

Thujopsene.—Hiba wood oil was purchased from the Soda Aromatic Co. and the Takasago Perfumery Co. The former was transparent, free from acidic portion, d_4^{25} 0.9341, n_D^{21} 1.5035 and the latter raw oil of dark red color, d_4^{15} 0.9518. The thujopsene fraction with following constants was obtained from both oils with an yield of 50—60%. B. p. 121—2°/12 mm, d_4^{25} 0.9311, n_D^{25} 1.5015, $[\alpha]_D^{20}$ −79.7° MR 64.71 infrared and ultraviolet spectra are shown in Figs. 1 and 2.

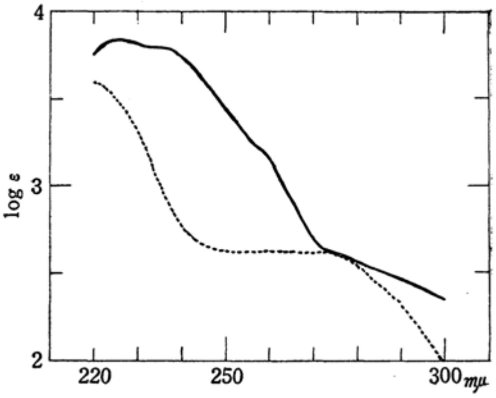

Fig. 2. Ultraviolet spectra of thujopsene (……) and isomerized hydrocarbon (——) in hexane.

Permanganate Oxidation.—To a mixture of 100 g. thujopsene and 400 cc. acetone, 120 g. of powdered potassium permanganate was added in portions in the course of 7 hours. The temperature was kept under 30° during the reaction. With the consumption of permanganate, manganese dioxide was filtered off, washed with acetone and the filtrate was concentrated. Manganese dioxide was further extracted several times with hot water, the extract was combined with acetone solution, acidified and extracted with benzene. Then the benzene solution was extracted with 7% sodium bicarbonate solution and 10% sodium hydroxide solution successively, washed with water and dried with sodium sulfate. The semi-solid substance, which was separated from the sodium bicarbonate extract by acidification with hydrochloric acid, was crystallized from benzene. The keto-acid I was obtained at first; removal of the keto-acid I by condensing the mother liquor several times, gave oxylactone (II). Acidifying the sodium hydroxide extract in the presence of benzen precipitate of III was separated between benzene and water layer. From the benzene extract, acid I and acid IV were separated by fractional crystallization. Analytical data of these substances were shown in Table I. Semicarbazone of I, prisms. m. p. 219° (decomp.), 2, 4-Dinitrophenylhydrazone of I, yellow, m. p. 187—9°; III, red, m. p. 250—252° (decomp.).

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* All melting points are corrected.

TABLE I

OXIDATION PRODUCTS OF THUJOPSENE

	m. p.	Formula	Analysis				Yield* (g.)
			Found		Calcd.		
			C	H	C	H	
I	164—5°	$C_{15}H_{24}O_3$	71.15	9.36	71.39	9.59	4.4
II	122.5—3.5°	$C_{15}H_{22}O_4$	67.47	8.44	67.64	8.33	0.2
III	193° (decomp.)	$C_{15}H_{22}O_4$	67.24 67.89	8.35 8.49	67.64	8.33	0.7
IV	152.5—3.5°	$C_{12}H_{14}O_3$	69.95	7.16	69.88	6.84	0.3
V	68—70°	$C_{14}H_{20}O$	82.09 82.13	9.92 9.89	82.30	9.87	0.2

* In another run, using 200 g. of permanganate, there was obtained 7.0 g of I and 1.4 g. of III.

The neutral portion was about 60 g. and was fractionated into the following three fractions with a concentric column 20 cm high: (1) recollected thujopsene about 30 g.; (2) isomerized hydrocarbon about 10 g. n_D^{25} 1.5111, d_4^{25} 0.9297, MR 65.74: infrared and ultraviolet spectrum Figs. 1 and 2; (3) oxygen-containing high boiling fraction 9 g.

Fraction 3 was chromatographed with alumina column, 5 cm. in diameter and 8 cm. high, developed successively with petroleum ether, benzene, ethyl acetate and methanol. From the benzene eluate a ketone $C_{14}H_{20}O$ (V) was crystallized. It has infrared absorption at 1653 and 1618 cm^{-1} (in Nujol) and is probably an α,β-unsaturated ketone. Semicarbazone m. p. 239° (decomp.).

Dicarboxylic Acid.—The keto-carboxylic acid (I) (2.0 g.) in 10 cc. of 10% sodium hydroxide solution, was added to the hypobromite solution prepared from 8.0 g. sodium hydroxide, 125 cc. water and 3.5 cc. bromine, under ice cooling. After being set aside for 1 hour, the solution was acidified with hydrochloric acid and the needles of dicarboxylic acid were separated. m. p. 205—6° (from dil. ethanol), yield 1.47 g. (73%). The melting point rose to 209.5—210.5° by further recrystallization.

Anal. Found: C, 66.12; H, 8.62; N. E. 127. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72%, N.E. 127.

Dicarboxylic Acid Anhydride.—The dicarboxylic acid (75 mg.) was dissolved in 3 cc. of acetic anhydride and refluxed for 3 hrs. Acetic anhydride was removed under reduced pressure and the residue was crystallized by rubbing. M. p. 109—110° (from acetic anhydride). The anhydride (20 mg.) was added to 0.4 cc. of 10% sodium hydroxide solution, allowed to stand overnight, warmed for few min., and then acidified. The crystals obtained were recrystallized from dil. ethanol, m. p. 210.5—211°. This was mixed with dicarboxylic acid (m. p. 208°) and melted at 208—210°. The infrared spectra of the two coincided.

Esters of Dicarboxylic Acid.—A mixture of the dicarboxylic acid (494 mg.), methanol (20 cc.), and conc. sulfuric acid (8 drops) was refluxed for 5 hr., poured into ice-water and extracted with ether. The ether solution was extracted twice with 7% sodium bicarbonate solution, washed with water and dried. Evaporation of the ether gave 70 mg. of dimethyl ester m. p. 71—3°. By acidifying the sodium bicarbonate extract with hydrochloric acid, monomethyl ester was obtained in needles, (300 mg.) m. p. 59—60° (from methanol-water). Infrared absorption max. 3490, 1705 cm^{-1} (in Nujol) N. E. 308, calcd. for $C_{15}H_{24}O_4 \cdot 2H_2O$ N. E. 304. The sample was kept in a desiccator for 2 weeks and analysed (infrared max. of 3490 cm^{-1} disappeared, and an ester band appeared at 1736 cm^{-1}).

Anal. Found: C, 67.16; H, 9.27. Calcd. for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02%.

Saponification of the monomethyl ester gave the dicarboxylic acid m. p. 209—210°.

Isomerization of the Keto-acid (I) to the Keto-lactone.— (a) To 10 cc. of conc. hydrobromic acid was added 810 mg. of I, which gradually dissolved to yield pink color. After being set aside overnight, the solution was poured onto crushed ice, the needle crystals were collected (470 mg.) and recrystallized twice from ether-petroleum ether mixture and finally with petroleum ether, m. p. 55—56°, yield 200 mg. The ether extract of the aqueous solution produced 100 mg. of the same crystals m. p. 56°. When 50% sulfuric acid was used instead of hydrobromic acid, the same substance was obtained. (b) A mixture of I (100 mg.), methanol (3 cc.) and conc. sulfuric acid (3 drops) was refluxed for 1 hr., poured into water and extracted with ether. The ether was evaporated, and the residue was crystallized by rubbing, yield 75 mg., recrystallized from petroleum ether m. p. 54.5—55.5°. Infrared max. 1774 and 1723 cm^{-1} (in carbon tetrachloride). Semicarbazone, leaflets m. p. 205° (decomp.), 2, 4-dinitrophenylhydrazone, yellow orange leaflets m. p. 162°.

Anal. Found: C, 71.42; H, 9.83. Calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%.

Thermal Dehydration of Hydroxyketonic Acid (III) — The acid (210 mg.) was heated to 210° in an oil bath. The crystals melted with bubbles, and dehydration was completed within 2 min. When the reaction tube was pulled up from the bath, the product crystallized immediately, m. p. 206—7° (from benzene), yield

130 mg. 2,4-Dinitrophenylhydrazone, red prisms m. p. 251—3°.

Anal. Found: C, 72.36; H, 8.01. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.

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