

The Identity of Thujopsene and Widdrene and of Hinokiic and Widdrenic Acids

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Widdrene is identical with the main constituent of thujopsene. Widdrenic acid is identical with hinokiic acid. The structure of this acid requires modification. Tentative structures are suggested for thujopsene and hinokiic acid.

The wood oil of the Hiba tree, *Thujopsis dolabrata* (L.f.) Sieb. et Zucc. has been studied by Japanese chemists over a long period. Both Yano¹ and Uchida² concluded from their early investigations that the main neutral constituent of the oil was a tricyclic sesquiterpene $C_{15}H_{24}$. This was given the name thujopsene by Kawamura³ who investigated it in some detail and suggested two alternative structures. Obata and Fukushi⁴ reported that they had been unable to isolate thujopsene from Hiba oil but Fujita⁵ definitely confirmed its presence. These investigations and especially the important contribution of Kawamura, published in Japanese, have remained largely unknown in the West.

The chemistry of thujopsene has recently attracted considerable interest in Japan and several groups are now studying its structure. A careful description of this compound was published (in English) a short time ago by Akiyoshi and Nagahama⁶ in a paper which is a repetition and extension of Kawamura's work and from which most of the above details have been taken. Their paper records the UV and IR absorption of thujopsene and some results of permanganate oxidation including the isolation, together with other degradation products, of a C_{15} -ketocarboxylic acid. This on oxidation with hypobromite furnished a C_{14} -dicarboxylic acid from which an anhydride and a dimethyl ester were prepared.

During studies in this laboratory on the constituents of heartwood extracts from trees of the South African genus *Widdringtonia*⁷ a tricyclic sesquiterpene $C_{15}H_{24}$ was obtained, which was called widdrene and according to its IR absorption and gas chromatographic behaviour was undoubtedly a pure compound. Further studies have demonstrated the presence of the same compound in several other conifers of the family *Cupressaceae* (*Chamaecyparis*

*thyoides*⁸, *Biota orientalis*⁹ and some species of *Juniperus*¹⁰) and it appears that it is a common constituent of woods that have the characteristic sweet fragrance of "pencil wood".

On ozonisation widdrene gave a C₁₅-ketocarboxylic acid that was oxidised by hypobromite to a C₁₄-dicarboxylic acid.

Table 1 shows the constants for thujopsene and widdrene and some of their degradation products.

Table 1.

<i>Thujopsene</i> C ₁₅ H ₂₄	<i>Widdrene</i> C ₁₅ H ₂₄
B. p. 121–122°/12 mm	B. p. 118–120°/10 mm
$n_D^{25} = 1.5015$, $[\alpha]_D^{20} = -79.7^\circ$	$n_D^{25} = 1.5033$, $[\alpha]_D^{20} = -109^\circ$
<i>Ketocarboxylic acid</i> C ₁₅ H ₂₄ O ₃	<i>Ketocarboxylic acid</i> C ₁₅ H ₂₄ O ₃
M. p. 164–165°	M. p. 166–168°, $[\alpha]_D^{20} = -129^\circ$
Semicarbazone, m. p. 219° (decomp.)	Semicarbazone, m. p. 220° (decomp.)
2,4-Dinitrophenylhydrazone, m. p. 187–189°	2,4-Dinitrophenylhydrazone, m. p. 153–154°
<i>Dicarboxylic acid</i> C ₁₄ H ₂₂ O ₄	<i>Dicarboxylic acid</i> C ₁₄ H ₂₂ O ₄
M. p. 209.5–210.5°	M. p. 215°, $[\alpha]_D^{20} = -57^\circ$
Anhydride, m. p. 109–110°	Anhydride, m. p. 113°, $[\alpha]_D^{20} = -39^\circ$
Dimethyl ester, m. p. 71–73°	Dimethyl ester, m. p. 71–73°, $[\alpha]_D^{20} = -59^\circ$

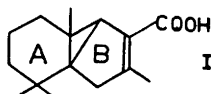
From the close similarity of these constants (apart from those of the ketocarboxylic acid 2,4-dinitrophenylhydrazones) and since widdrene is of widespread occurrence it seemed very probable that thujopsene and widdrene were identical but that the former was not a pure compound. This was confirmed by comparison of the IR spectrum of thujopsene with that of pure widdrene.

Through the courtesy of Dr. S. Katsura, Takasago Perfumery Co, Tokyo, it has been possible to investigate a large sample of Japanese hiba oil. The neutral fraction gave pure widdrene, only the small fractions at the beginning and end showing boiling point and rotation changes. The IR absorption curves of both *Thujopsis* and *Widdringtonia* widdrenes were superimposable and the crystalline oxidation products were identical. Pure widdrene shows a single sharp carbon-carbon double bond stretching vibration band at 1682 cm⁻¹. Impure samples of widdrene from *Widdringtonia* and thujopsene from *Thujopsis* gave an additional band at 1647 cm⁻¹ together with other minor differences.

Hirose and Nakatsuka¹⁹ arrived at the same conclusion as regards the identity of thujopsene and widdrene. Oxidation of their "thujopsene" ($[\alpha]_D -92^\circ$) with selenium dioxide gave an aldehyde identical with that obtained by similar oxidation of "widdrene" from *Biota orientalis*.

Since the name thujopsene has considerable priority we suggest that it should be retained but reserved for the fraction of thujopsene that corresponds to widdrene.

In the investigation of thujopsene from *Widdringtonia* it was oxidised with selenium dioxide to give a characteristic aldehyde "widdrenal" (thujopsenal) which was oxidised further with silver oxide to a monocarboxylic acid, "widdrenic acid", $C_{15}H_{22}O_2$. This acid was also isolated directly from the *Widdringtonia* heartwood extracts and has recently been found in several other woods containing thujopsene including *Chamaecyparis thyoides*⁸ and several *Juniperus* species¹⁰. Uchida¹¹ long ago isolated an acid, which he called hinokiic acid, from the steam volatile oil obtained from the leaves of the Japanese hinoki tree, *Chamaecyparis obtusa* Endl. Hinokiic acid has also been shown to occur in small amounts in the leaves of *Chamaecyparis taiwanensis* Masamune et Suzuki¹² and has recently been obtained by Masamura¹³ from a garden variety of hinoki, "chyabohiba". Uchida thought that the composition was $C_{15}H_{24}O_2$ but Moroe and Hara¹⁴ have shown that the correct composition of hinokiic acid is $C_{15}H_{22}O_2$. Okuda^{15a-f} has made an extensive investigation of hinokiic acid and has proposed the structure (I).



It was noticed that there were considerable similarities between the physical constants of hinokiic acid and widdrenic acid but there were also certain discrepancies. According to Okuda, permanganate oxidation of hinokiic acid gave a dicarboxylic acid containing only thirteen carbon atoms. However the melting point of this acid agreed with that of our C_{14} -widdrenedicarboxylic acid which has also been obtained by permanganate oxidation of widdrenic acid. The optical rotation of Okuda's dicarboxylic acid^{15f} was reported to be almost exactly 100° lower than that of the widdrene dicarboxylic acid (misprint?). The analytical data recorded for the " C_{13} -dicarboxylic acid" were not very satisfactory and it seemed probable that it was not a pure compound. Okuda also obtained the dicarboxylic acid by ozonisation of hinokiic acid followed by further oxidative degradation. From the neutral fractions of the ozonisation products he isolated an oily ketone, $C_{13}H_{20}O$.

Okuda's papers are all in Japanese and we are grateful to Dr. Y. L. Chow for translating them.

Ozonisation of widdrenic acid followed by oxidation with hypobromite also gave acid and neutral products. From the former there was isolated widdrene dicarboxylic acid and from the latter a dibromoketone, m.p. $99-100^\circ$. (Found: C 44.6; H 5.2; Br 46.0. $C_{13}H_{18}OBr_2$, requires C 44.6; H 5.2; Br 45.7) which on treatment with zinc and acetic acid gave a crystalline ketone, m.p. $49.5-50.5^\circ$. (Found: C 81.3; H 10.4. $C_{13}H_{20}O$ requires C 81.3; H 10.4.)

Some constants for hinokiic acid and widdrenic acid and some of their degradation and transformation products are shown in Table 2.

From the close similarity of these constants (apart from those of the dicarboxylic acid) it seemed very probable that hinokiic acid and widdrenic acid were identical. Dr. Okuda very kindly supplied a generous sample of crude hinokiic acid from which the pure acid was obtained and direct comparison

Table 2.

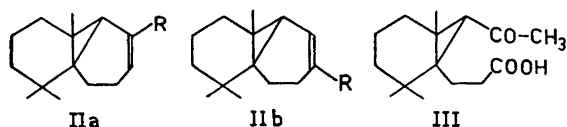
<i>Hinokiic acid</i> C ₁₅ H ₂₂ O ₃	<i>Widdrenic acid</i> C ₁₅ H ₂₂ O ₃
M. p. 166°, [α] _D ²⁰ = -90.4°	M. p. 169–171°, [α] _D ²⁰ = -86°
Methyl ester, m. p. 107°	Methyl ester, m. p. 109–110°, [α] _D ²⁰ = -99°
Dihydroderivative ("iso-dihydrohinokiic acid") (Pd in EtOH), m. p. 159°, [α] _D ²⁰ = 77°	Dihydroderivative (PtO ₂ in EtOH), m. p. 160–161°, [α] _D ²⁰ = 75°
Tetrahydroderivative (PtO ₂ in HAc), m. p. 143–144°, [α] _D ²⁰ = 61.3°	Tetrahydroderivative (PtO ₂ in HAc), m. p. 145–146°, [α] _D ²⁰ = 60°
<i>Dicarboxylic acid</i> C ₁₃ H ₂₀ O ₄	<i>Dicarboxylic acid</i> C ₁₄ H ₂₂ O ₄
M. p. 210–211°, [α] _D ²⁰ = -156.2°	M. p. 215°, [α] _D ²⁰ = -57°
Dimethyl ester, m. p. 69°	Dimethyl ester m. p. 71–73°, [α] _D ²⁰ = -59°
<i>Oily ketone</i> C ₁₃ H ₂₀ O	<i>Ketone</i> C ₁₃ H ₂₀ O, m. p. 49.5–50.5°
Semicarbazone, m. p. 224–225°	Semicarbazone, m. p. 225–226°

of this acid and widdrenic acid (mixed m.p., IR) showed that they were identical. The name widdrenic acid is thus redundant and should be abandoned*.

The structure (I) proposed for hinokiic acid cannot, however, be entirely correct. In ring B there can be no C=C—CH₃ grouping since the dicarboxylic acid, m.p. 215° (thujopsene dicarboxylic acid) and hinokiic acid on oxidation according to Kuhn-Roth gave almost the same yield of acetic acid (0.62 and 0.57 moles; thujopsene 1.49 mole). The oxidation of thujopsene to hinokiic acid and further to the C₁₄-dicarboxylic acid shows that there is only one substituent, the carboxyl group on the double bond.

Further investigation here has now shown that the ketone, m.p. 49.5–50.5°, from the ozonolysis products obtained from hinokiic acid is identical with a ketone formed by a Dieckmann condensation from the dimethyl ester of thujopsene dicarboxylic acid. According to the IR and UV absorption this ketone contains a bicyclo[3.1.0]hexane system with a carbonyl group in conjugation with the cyclopropane ring ($\nu_{\max}^{\text{CCl}_4}$ 1 723 cm⁻¹; $\lambda_{\max}^{\text{EtOH}}$ 210.5 mμ, ε 4 900). Dihydroumbellulone¹⁶ which has a similar structure shows the same absorption ($\nu_{\max}^{\text{CCl}_4}$ 1 722 cm⁻¹; $\lambda_{\max}^{\text{EtOH}}$ 210 mμ, ε 2 470). Dihydrolumiprednisone acetate¹⁷ and dihydrolumisantonin¹⁸ are also similar. The presence of both the cyclopropane ring and the double bond is also indicated by the results of the hydrogenation experiments of thujopsene and hinokiic acid (cf. Table 2). There is at present no reason to doubt Okuda's conclusions on the nature of ring A. The structure of thujopsene and hinokiic acid are therefore presumably either IIa or IIb (with R = CH₃ and COOH, respectively):

* It may in the future be found advantageous to rationalise the nomenclature of these compounds by abandoning the name hinokiic acid altogether in favour of names based on thujopsane.



The UV spectra of the ketocarboxylic acid obtained by ozonolysis of thujopsene ($\lambda_{\max}^{\text{EtOH}}$ 210.5 $m\mu$, ϵ 4 700), of the C_{14} -dicarboxylic acid (no maximum above 205 $m\mu$ in EtOH, $\epsilon_{205 \text{ m}\mu}$ ca. 800), and of a lactone, m.p. 126—128°, obtained by potassium borohydride reduction of the ketoacid (no maximum above 205 $m\mu$ in EtOH, $\epsilon_{205 \text{ m}\mu}$ ca. 150) indicate that the ketogroup of the ketocarboxylic acid is conjugated with the cyclopropane ring (structure III). Structure IIa ($R = \text{CH}_3$) is therefore preferred for thujopsene and IIa ($R = \text{COOH}$) for hinokiic acid.

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