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The Chemistry of the Natural Order Cupressales

40 *. The Structure of Thujopsene and Hinokiic Acid

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The structures of thujopsene and hinokiic acid are proved to be (*1a*) and (*1b*), respectively. On catalytic hydrogenation of these compounds a conjugate addition of hydrogen takes place with formation of the corresponding dihydro-compounds (*2a*) and (*2b*), respectively.

Yano [1] and Uchida [2] found that the wood oil of the Japanese Hiba tree, *Thujopsis dolabrata* (L.f.) Sieb. et Zucc., contained a tricyclic sesquiterpene. Kawamura [3] gave this product the name thujopsene and investigated it in some detail. He also suggested two possible structures (*3* and *4*) for this compound.

Erdtman and Thomas [4] isolated a hydrocarbon, $C_{15}H_{24}$ called widdrene, from the heartwood of various species of the South African genus *Widdringtonia* and Erdtman and Pelchowicz [5] later found the same hydrocarbon in the heartwood of *Platycladus (Biota) orientalis*. On oxidation with selenium dioxide widdrene gave a crystalline α,β-unsaturated aldehyde [4]. This aldehyde can be obtained even from fairly impure widdrene fractions. Widdrene was also found in many genera belonging to the natural order Cupressales [6–9].

Hirose and Nakatsuka [10] later oxidised thujopsene from *Thujopsis* and obtained an aldehyde which was identical with that obtained from *Platycladus*. This was confirmed by Erdtman and Norin [6]. Most of the hydrocarbon fractions isolated by the Japanese authors were impure, exhibiting lower rotations than that of pure widdrene, but in view of the fact that the name thujopsene has priority over the name widdrene it was suggested that the name thujopsene should be retained for the pure hydrocarbon [6].

The α,β-unsaturated aldehyde, "widdrenal" (now thujopsenal, *1c*), could be oxidised with silver oxide to an α,β-unsaturated acid, "widdrenic acid" (now thujopsenic acid, *1b*). The identity of this acid with hinokiic acid was long suspected. Hinokiic acid was first isolated by Uchida [11] from the leaf oil of the hinoki tree, *Chamaecyparis obtusa*, and was extensively investigated by

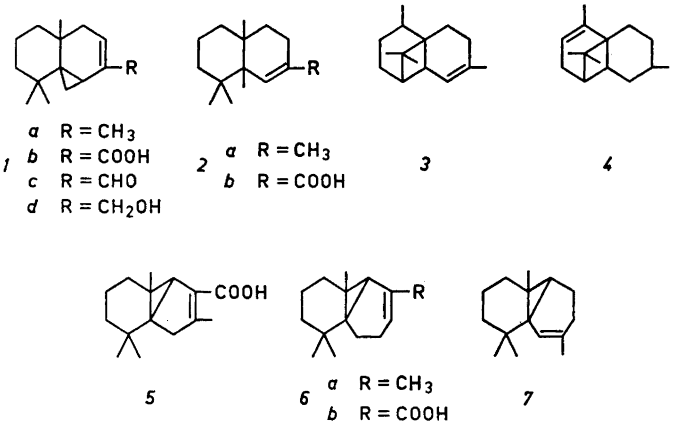
* Part 39: *Acta Chem. Scand.* **15** (1961) 1313.

Okuda [12a–f] who suggested structure (*5*) for this acid. Hinokiic acid was later found to be a common congener of thujopsene [6].

However, due to some ambiguities in Okuda's paper, the identity of thujopsenic and hinokiic acids could not be settled. It was not until a direct comparison of both acids was made possible that Erdtman and Norin [6] were able to establish the identity of these compounds.

As the results of degradation studies and consideration of Okuda's structure (*5*) for hinokiic acid, Erdtman and Norin [6] tentatively suggested the structures (*6a*) and (*6b*) for thujopsene and hinokiic acid respectively. Independently, and almost simultaneously, Kobayashi, Nagahama and Akiyoshi [13] arrived at the same structure as regards the hydrocarbon. Without adducing any further experimental evidence Sisido and Nozaki [14] proposed structure (*7*) for thujopsene. However, continued degradative studies and spectral investigations soon indicated that the structures (*6a*) and (*6b*) for thujopsene and hinokiic acid required modification. Based on the new evidence Erdtman and Norin [15] suggested that thujopsene and hinokiic acid were correctly represented by structures (*1a*) and (*1b*), respectively.*

In this paper conclusive evidence for the revised structures (*1a*) and (*1b*) for thujopsene and hinokiic acid is presented.



1 *a* R = CH_3; *b* R = COOH; *c* R = CHO; *d* R = CH_2OH

2 *a* R = CH_3; *b* R = COOH

3

4

5

6 *a* R = CH_3; *b* R = COOH

7

The thujopsene used for this investigation was obtained by a careful distillation of Japanese "hiba oil" and was a pure compound according to its infrared spectrum (Fig. 1) and gas-chromatogram [16].

Titration with perphthalic acid indicated the presence of only one double bond in thujopsene and, according to the oxidation of thujopsene with selenium dioxide, the hydrocarbon must contain the grouping $>C=C(CH_3)-$ [4].

On ozonisation thujopsene gave a ketocarboxylic acid (*8a*) together with small amounts of a hydroxyketocarboxylic acid (*8b*). Hypobromite oxidation

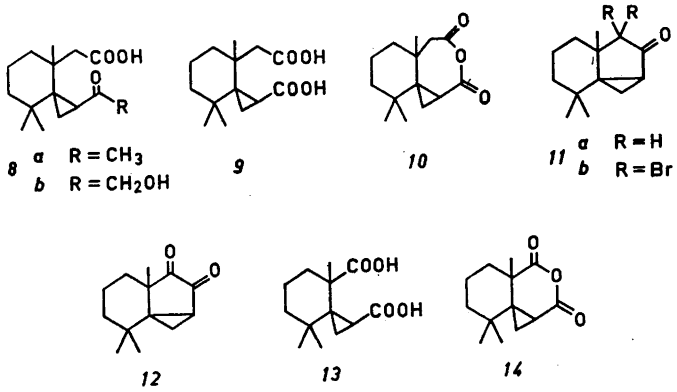
* *Added in proof.* Structure (1a) for thujopsene has now been accepted by several investigators (Kobayashi, H., Nagahama, S. and Akiyoshi, S. *Bull. Chem. Soc. Japan* **34** (1961) 1123, Sisido, K., Nozaki, H. and Imagawa, T. *J. Org. Chem.* **26** (1961) 1964 and Nozoe, T., Takeshita, H., Ito, S., Ozeki, T. and Seto, S. *Chem. and Pharm. Bull. Japan* **8** (1960) 936).

of the ketocarboxylic acid (*8a*) furnished a C_{14}-dicarboxylic acid (*9*) and bromoform. This dicarboxylic acid (*9*) could readily be converted to an anhydride (*10*) with acetic anhydride. A Dieckmann condensation of the dimethyl ester of (*9*) followed by hydrolysis and decarboxylation afforded a ketone (*11a*). Oxidation of this ketone (*11a*) with selenium dioxide gave the diketone (*12*) which on further oxidation with hydrogen peroxide gave the C_{13}-dicarboxylic acid (*13*). The latter seems to be identical with the C_{13}-dicarboxylic acid that Okuda [12e,f] obtained by an oxidation of hinokiic acid with permanganate. On heating it gave a remarkably stable anhydride (*14*).

Hinokiic acid on ozonisation followed by hypobromite oxidation gave an oil which was separated into a neutral and an acidic fraction. The neutral fraction consisted mainly of a dibromoketone (*11b*). By chromatography of the oily, acidic fraction the C_{14}-dicarboxylic acid (*9*) was obtained. The dibromoketone (*11b*) was transformed into the ketone (*11a*) by a reductive debromination with zinc and acetic acid. It was also possible to obtain the dibromoketone (*11b*) by bromination of the ketone (*11a*) although in poor yield.

Hypobromite oxidation of the ozonised hinokiic acid may appear to be a somewhat surprising procedure, but when this experiment was carried out Okuda's structure (*5*) for hinokiic acid [12f] was believed to be correct.

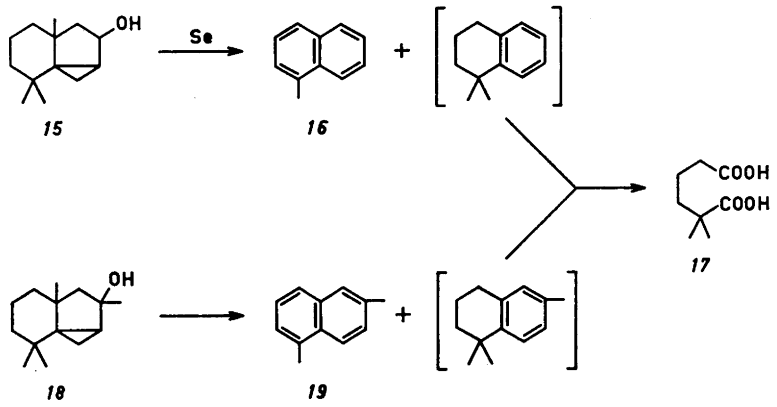
Hinokiic acid methyl ester gave the primary alcohol (*1d*) on reduction with lithium aluminium hydride. This alcohol on ozonisation furnished the hydroxyketocarboxylic acid (*8b*). Hypoiodite oxidation of compound (*8b*) gave the C_{14}-dicarboxylic acid (*9*). No iodoform was formed.



Selenium dehydrogenation of the alcohol (*15*) obtained by potassium borohydride reduction of the ketone (*11a*) furnished a crude mixture. This mixture was separated by chromatography into α-methylnaphthalene (*16*) and an oily product which according to its ultra-violet spectrum appeared to contain a tetralin derivative. Ozonisation of the latter followed by hydrogen peroxide oxidation gave α,α-dimethyladipic acid (*17*).

The ketone (*11a*) was converted to the alcohol (*18*) by treatment with methylmagnesium iodide. This alcohol gave on selenium dehydrogenation 1,6-

dimethylnaphthalene (*19*) and an oil possessing the ultra-violet characteristics of a tetralin derivative. The latter furnished *α,α*-dimethyladipic acid (*17*) on oxidation as above.



15 *16* *17* *18* *19*

On catalytic hydrogenation thujopsene (*1a*) and hinokiic acid (*1b*) readily formed di- and tetrahydroderivatives. The results of the ozonisation and titration experiments with perphthalic acid, however, indicated the presence of only one double bond in compounds (*1a*) and (*1b*). It therefore seemed probable that thujopsene and hinokiic acid contained a *cyclo*propane ring. This was also indicated by the molecular refraction ($[R_L]_D$ 64.9) which showed an exaltation compared with that of a tricyclic sesquiterpene with only one double bond ($[R_L]_D$ 64.4). Such exaltations are known from alkenyl*cyclo*propane systems (compare sabinene, *α*- and *β*-thujene, Δ^3-, Δ^4-carene and related compounds) [17]. The alcohols (*15*) and (*18*) gave pale yellow colour reactions with tetranitromethane which also indicated the presence of a *cyclo*propane ring [18,19].

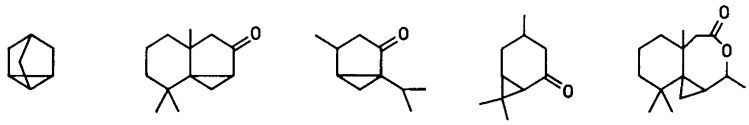
Infra-red bands at 1 000—1 020 cm^{-1} and 850—860 cm^{-1} have been reported to be characteristic for *cyclo*propane rings [20–22]. The infra-red spectra of thujopsene, hinokiic acid and their degradation products exhibit absorption at these frequencies, but the bands are not characteristic enough to be assigned to a *cyclo*propane ring [20,21].

Compounds having a *cyclo*propane ring with a CH_2-group are reported to show a characteristic infra-red band at 3 050—3 090 cm^{-1} [21–23]. The reliability of this assignment has been questioned by Allen *et al.*[24] Moreover, several compounds of tricyclene type exhibit this band, *e.g.* nortricyclene (*20*) 3 085 cm^{-1} [21]. Thus, the appearance of a band at about 3 050 cm^{-1} in compounds having no interfering groups, such as olefinic hydrogens, seems to provide clear evidence for the presence of hydrogens attached to a *cyclo*propane ring, but the band does not prove the presence of a CH_2-groups in such a ring.

In thujopsene, hinokiic acid and especially in some of their degradation products such as ketone (*11a*), dibromoketone (*11b*), diketone (*12*) and alcohols (*15*) and (*18*), there is a band at about 3 050 cm^{-1} which must be due to hydrogens attached to a *cyclo*propane ring.

Thujopsene shows an ultra-violet maximum at 212 mμ (ε 4 680), which is in good agreement with a *cyclo*propane-ene chromophore. When such a chromophore is part of a seven-membered ring the observed maximum is at about 222—224 mμ (ε 4 000—6 000) and when part of a six-membered ring no maximum is observed down to 205 mμ (λ_{205} about 5 000) [25].

The spectral data of the ketone (*11a*), λ_{max}^{EtOH} 210 mμ (ε 4 900) and the infra-red band at 1 723 cm^{-1}, show the presence of a *cyclo*propane ring conjugated with the keto group. The data are in good agreement with those for dihydroumbellulone (*21*), λ_{max}^{EtOH} 210 mμ (ε 2 470); carbonyl band at 1 721 cm^{-1} [26–28] but not with those for carone (*22*), λ_{max}^{EtOH} 210 mμ (ε 3 970); carbonyl band at 1 685 cm^{-1} [22]. The *cyclo*propane ring is shown to be conjugated with the keto group of the ketocarboxylic acid (*8a*) by the spectral data of this acid, λ_{max}^{EtOH} 210 mμ (ε 4 700), and infra-red band at 1 700 cm^{-1} [29]. This is confirmed by the fact that the dicarboxylic acid (*9*), its dimethylester and a lactone (*23*), obtained by potassium borohydride reduction of the ketocarboxylic acid (*8a*), do not show any ultra-violet maxima above 205 mμ.



20 *11a* *21* *22* *23*

From the above results thujopsene may be formulated as (*1a*) or (*6a*). Conclusive evidence for structure (*1a*) is presented below.

In the infra-red spectra of thujopsene (Fig. 1) and hinokiic acid (Fig. 2) a band of medium intensity is observed at 1 487 cm^{-1}. This band is not present in the di- and tetrahydrocompounds. Ring strain can lead to alterations in the CH_2-deformation frequency as in ethylene oxide with one band at 1 500 cm^{-1} [30] and in *cyclo*propane with a Raman band at 1 505 cm^{-1} [31]. It has been reported that when *cyclo*propane rings are situated within larger systems,

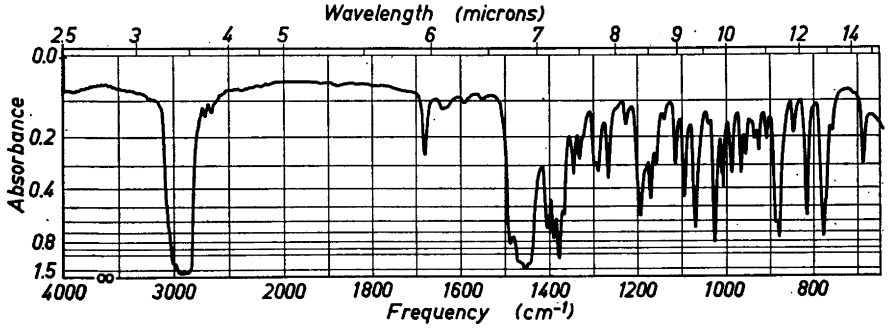


Fig. 1. Infra red spectrum of thujopsene (*1a*) as a pure oil in a 0.025 mm NaCl-cell.

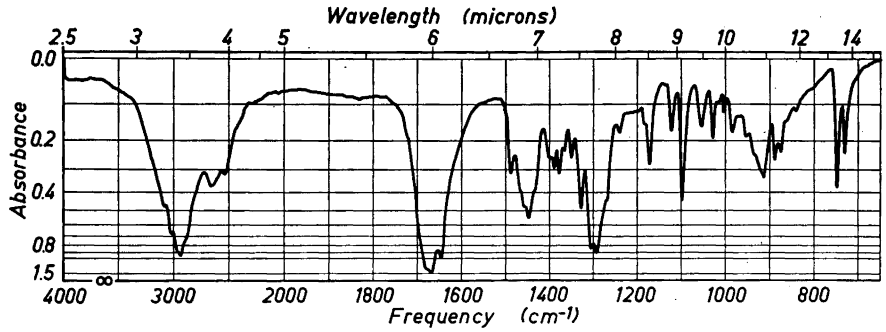
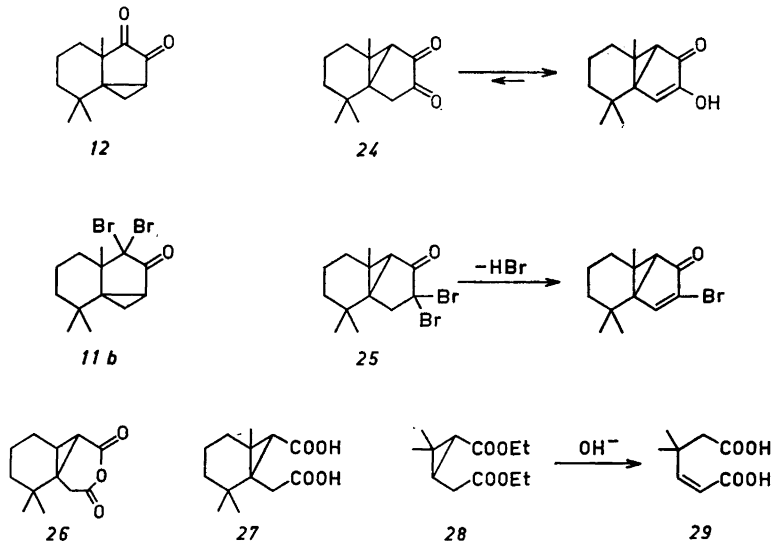


Fig. 2. Infra red spectrum of hinokiic acid (*1b*) in a KBr-disc.

such as triterpenes, the CH-deformation frequencies are not distinct enough for identification [32]. In the case of thujopsene and hinokiic acid, however, the band at 1 487 cm^{-1} may be assigned to a CH_2-group in the *cyclo*propane ring.

The diketone (*12*) did not show any tendency to enolise under neutral conditions (see experimental). If the structure (*6a*) for thujopsene was correct this compound should have furnished a diketone (*24*) which would have been expected to be more or less completely enolised [33,34].

The dibromoketone (*11b*) failed to undergo dehydrobromination with both collidine and lithium bromide in dimethylformamide. The corresponding dibromoketone (*25*) derived from structure (*6a*) for thujopsene should, on the other hand, undergo such a dehydrobromination.



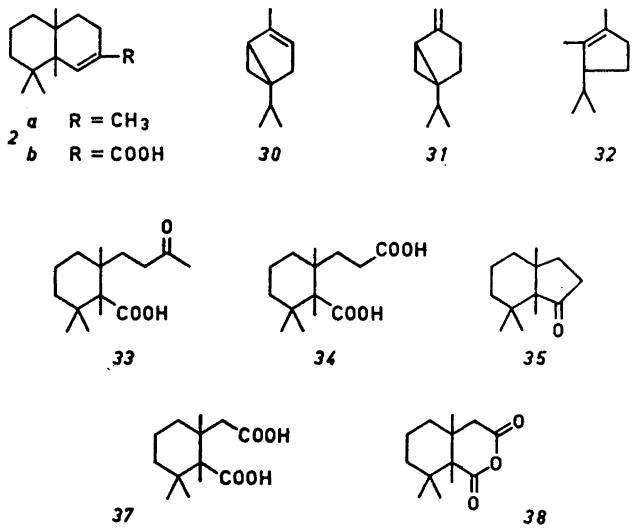
In the infra-red spectrum of the C_{14}-dicarboxylic acid anhydride (*10*) there is a band at 1 418 cm^{-1} indicating the presence of a CH_2-group adjacent to a carbonyl. The C_{13}-dicarboxylic acid anhydride (*14*) did not show such a band. If the structure (*6a*) originally proposed for thujopsene were correct this compound should have furnished a C_{13}-anhydride (*26*) exhibiting this absorption.

The C_{13}-dicarboxylic acid (*13*) is stable towards strong alkali. If structure (*27*) were correct it would be expected to rearrange as in the hydrolysis of homocaronic acid diethyl ester (*28*) to the acid (29) [35].

A proton magnetic resonance investigation on the structure of thujopsene and hinokiic acid confirmed that their structures must be (*1a*) and (*1b*), respectively [36].

On catalytic hydrogenation of thujopsene (*1a*) and hinokiic acid (*1b*) with palladised charcoal in methanol solution, a conjugate addition of hydrogen evidently takes place with formation of the corresponding dihydro-compounds (*2a* and *2b*). Further hydrogenation gave saturated tetrahydro-compounds. This type of conjugate addition of hydrogen has been observed in vinyl-*cyclo*propane systems [37,38].

The formation of a new methyl group due to fission of the *cyclo*propane ring on the catalytic hydrogenation of thujopsene and hinokiic acid has been studied in detail as it proves the presence and position of this ring. The proof of the structures (*2a* and *2b*) for the dihydro-compounds is also of importance since the hydrogenation of the alkenyl-*cyclo*propane systems in *a*-thujene (*30*), sabine (*31*) and related compounds is reported to give di- and tetrahydro-derivatives where the cleavage of the *cyclo*propane ring has occurred in another way [17]. *a*-Thujene (*30*) and sabinene (*31*) both gave the same dihydro-compound (*32*). These catalytic hydrogenations are now being reinvestigated in this Laboratory.



Ozonisation of dihydrothujopsene (*2a*) gave the dihydroketocarboxylic acid (*33*) which on further oxidation with hypobromite gave the dihydro-C_{14}-dicarboxylic acid (*34*) and bromoform. Dieckmann condensation of the dimethyl ester of this acid (*34*) followed by hydrolysis and decarboxylation yielded a five-membered ring ketone (*35*). Selenium dioxide oxidation of this ketone (*35*) furnished the diketone (*36*) which was further oxidised with hydrogen peroxide to the dihydro-C_{13}-dicarboxylic acid (*37*). This acid (*37*) on heating gave the dihydro-C_{13}-anhydride (*38*).

Similarly, dihydrohinokiic acid (*2b*) was ozonised to an aldehyde-acid (*39*) which on further oxidation with silver oxide gave the same dicarboxylic acid (*34*) as was obtained from dihydrothujopsene (*2a*).

The appearance of a new methyl group on hydrogenation of thujopsene and hinokiic acid is indicated by the results of Kuhn-Roth determinations. The increase in the carbon-methyl content of the dihydrocompounds compared with the non-hydrogenated products corresponds to a value expected for a new angular methyl group.

Thujopsene (*1a*) exhibits infra-red absorption at 1 380 cm^{-1} (ε 68). This band is much stronger in the dihydro-derivative (*2a*) (ε 101) as shown from Fig. 3, which also indicates the formation of a new methyl group on hydrogenation. This could be further proved by comparing the intensities of the infra-red maxima at 1 380 cm^{-1} of a dihydro-compound and its corresponding dideutero-derivative. It is known from a similar case that the number of CH_3-groups contributing to this band is proportional to its intensity [39]. Catalytic deuteration has been used for the preparation of some steroids deuterated in certain positions [40–42]. Thujopsene on catalytic deuteration formed a dideutero-derivative which, as shown from Fig. 3, had a band at 1 380 cm^{-1} of lower intensity compared with that of dihydrothujopsene.

However, it has also been shown by a mass spectrometric investigation that an extensive replacement of hydrogen by deuterium takes place on catalytic deuteration of unsaturated fatty acid esters. Deuterium was found to have entered the chain not only where the double bond was situated [43]. Such a deuterium exchange can occur during the catalytic dideuteration of thujop-

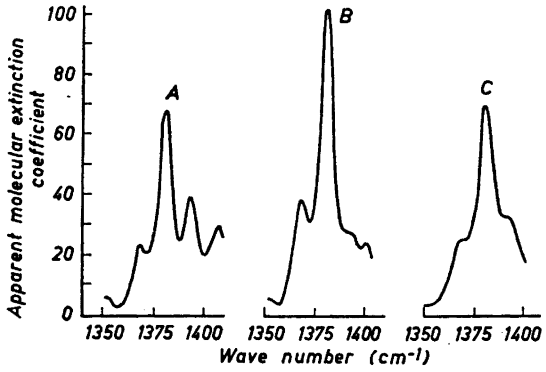


Fig. 3. Infra-red spectra in the region of the symmetrical methyl C—H bending vibration in CCl_4-solutions. A. Thujopsene (*1a*). B. Dihydrothujopsene (*2a*). C. Dideuterothujopsene.

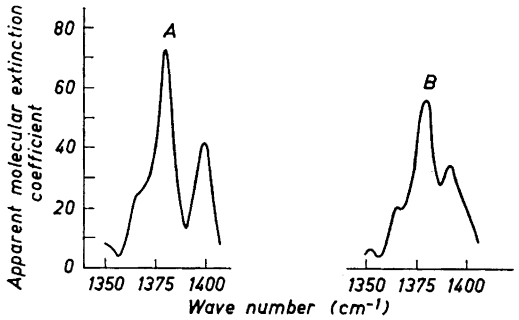
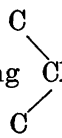


Fig. 4. Infra-red spectra in the region of the symmetrical methyl C—H bending vibration in CCl_4-solutions. A. Dimethylester of the dihydro-C_{14}-dicarboxylic acid (*34*). B. Dimethylester of the corresponding dideutero-C_{14}-dicarboxylic acid.

sene and the exchange can take place with the hydrogens of a methyl group. The results from a direct comparison of the infra-red bands at 1 380 cm^{-1} for dihydro- and dideuterothujopsene can in such a case be misleading. The methyl group attached to the double bond is, however, the only one to which the double bond can shift. Such shifts are known to occur during catalytic hydrogenation of olefins and are also believed to be the cause of the deuterium exchange[43]. This methyl group was therefore removed by degradation of the dideuterothujopsene to the dideutero-compound corresponding to the dihydro-C_{14}-dicarboxylic acid (*34*) . The dimethylester of this deutero-dicarboxylic acid showed a decrease in intensity of the infra-red band at 1 380 cm^{-1} compared with that of the dimethylester of the dihydro-C_{14}-dicarboxylic acid (*34*) as shown from Fig. 4. This proves that a new methyl group had been formed during the hydrogenation.

In the proton magnetic resonance spectrum of dideutero-thujopsene there is a signal at 224 cps (from benzene as internal standard on a 40 Mc instrument[36]) that can be assigned to a methyl group on the double bond[36]. This shows that the deuterium exchange in this methyl group is negligible. Therefore it is possible by a direct comparison of the infra-red maxima at 1 380 cm^{-1} of the dihydro- and dideuterothujopsene to determine the number of methyl groups contributing to this band. The ratio (101—69) of the intensities of this band corresponds almost to the calculated (3—2), as shown from Fig. 3.

The PMR-spectrum of dihydrothujopsene shows signals at 252, 253.5 and 254.5 cps which are assigned to four methyl groups (the average area of these signals corresponds to 12 protons)[36]. In the spectrum of dideuterothujopsene there is a decrease in the intensity of this signal group. The decrease in intensity corresponds to one methyl group (the average area corresponds almost to 9 protons). This is also in agreement with the formation of a new methyl group during hydrogenation.

The dihydroketone (*35*) contains the grouping  (A).

Evidence in favour of this grouping was obtained in the same way as described by Barnes *et al.*[44]

(i) The ketone did not afford a 2,4-dinitrophenylhydrazone even when refluxed for 1 h in ethanolic solution (*cf.* 2β-8β-11α-triacetoxylanan-17-one[43]) but on the other hand the ketone (*11a*) rapidly gave a 2,4-dinitrophenylhydrazone.

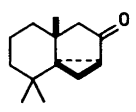
(ii) Quantitative bromination experiments clearly show that the dihydroketone contains only two α-hydrogen atoms replaceable by bromine. The dibromoketone was isolated.

(iii) The ketone (*11a*), which evidently has one α-CH_2-group, exhibits infrared absorption at 1 415 cm^{-1} with almost the same apparent integrated intensity ($I = 23.0$) as the dihydroketone ($I = 21.9$).

The number of hydrogen atoms in the α-position to the keto group in the dihydroketone (*35*) was also determined by deuterium exchange. A mass spectrum of the deutero-compound showed that two hydrogen atoms had been exchanged which confirms the presence of grouping (A) in the dihydroketone (*35*).

The structures of dihydrothujopsene and dihydrohinokiic acid must therefore be (*2a*) and (*2b*) respectively as shown also by Forsén and Norin[36] from a proton magnetic resonance investigation. Thus the hydrogenation experiments conclusively prove the presence and position of the *cyclo*propane ring in thujopsene and hinokiic acid and their structures must be represented by (*1a*) and (*1b*) respectively.

Application of the "octant rule"[45] to the ketone (*11a*), which exhibits a strong positive Cotton effect, suggests that the *cyclo*propane ring stands out of the plane of the paper as indicated in (*40*).* The ring junction of the dihydrothujopsene (*2a*) is proposed to be *cis* for the following reasons: (i) The dihydro-C_{13}-dicarboxylic acid (*37*) formed the anhydride (*38*) readily by heating to its melting point. (ii) The dihydro-ketone (*35*) has an extremely low carbonyl frequency (1 728 cm^{-1}, in CCl_4) for a five-membered ring ketone, which is in good agreement with a *cis* fusion of the five- and six-membered rings in this ketone[46]. From the above reasons it is believed that the angular methyl group of the ketone (*11a*) stands out of the plane of the paper as indicated in (*40*). Further work on the stereochemistry and absolute configuration of thujopsene is in progress.*



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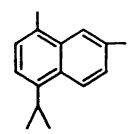

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* See footnote p.1886.

Finally, it is of interest to note that on selenium dehydrogenation thujopsene (*1a*) affords 1,7-dimethyl-4-*iso*propylnaphthalene (*41*) in an unexpectedly high yield (15 %) together with other compounds which have not yet been completely characterised. The results of the dehydrogenation of thujopsene (*1a*) will be discussed in a following paper. Widdrol, a frequent congener of thujopsene[4,7], the structure of which is presently being investigated, also gives this naphthalene derivative on dehydrogenation [4]. Nagahama [47] recently reported that on hydration with oxalic acid thujopsene gives widdrol.*

EXPERIMENTAL

Melting points are uncorrected and were taken on a Kofler micro hot stage unless otherwise stated. The infra-red spectra were recorded on a Perkin-Elmer No. 21 instrument (NaCl-prism; liquids as pure oils in 0.025 mm NaCl-cell and solids in KBr-discs, unless otherwise stated). The ultra-violet spectra were measured in alcohol (95 %) on a Beckman DK 2 spectrophotometer. Rotations were measured in chloroform ($c \approx 2.0$ unless otherwise stated). Light petroleum refers to a fraction b.p. 40–60°. Alumina used for chromatography was supplied by Merck A.G., Darmstadt, Germany, and the degree of activity was according to Brockmann.

Thujopsene. Gas chromatographically pure thujopsene was obtained by a careful distillation of the neutral fraction of Japanese "hiba oil" (wood oil of *Thujopsis dolabrata* (L.f.) Sieb. et Zucc.) [16]. B.p. 120/10 mm, $[\alpha]_D$ −110° (*c* 2.0), n_D^{25} 1.5031, d^{24} 0.932, $[R_L]_D$ 64.9, λ_{max} 212 mμ (ε 4 680), infra-red spectrum see Fig. 1. (Found: C 88.1; H 11.8; C–CH_3 (Kuhn-Roth) 1.49 moles HOAc/mole. $C_{15}H_{24}$ requires C 88.2; H 11.8).

Hinokiic acid. A combined acidic fraction (10 g) from several *Widdringtonia* species remaining from the work of Erdtman and Thomas [4] was fractionally crystallised as described by the authors. The material which was slightly less soluble in ether gave on recrystallisation from this solvent "Widdringtonia acid II" [4] (3 g), m.p. 190–192°, $[\alpha]_D$ −79° (*c* 1.9). The more soluble material gave on recrystallisation from ether/light petroleum and then from methanol small amounts of *hinokiic acid*, "Widdringtonia acid I", (*1b*) (0.5 g), m.p. 169–170°, $[\alpha]_D$ −86° (*c* 1.8), identical with a sample of hinokiic acid kindly supplied by Dr. Okuda [13]. The infrared spectrum of hinokiic acid is shown in Fig. 2 and the ultraviolet data are λ_{max} 245 mμ (ε 5 000). (Found: C 76.8; H 9.3; C–CH_3 0.57

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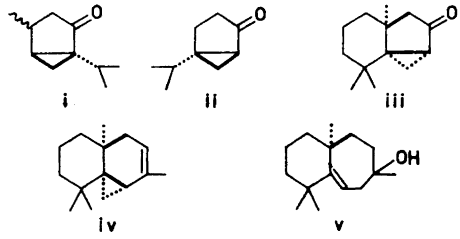
* *Added in proof:* The absolute configuration of the monoterpenes of the thujane group has recently been determined (Norin, T. *Acta Chem. Scand. In the press* and Walborsky, H. M., Sugita, T., Ohno, M. and Inouye, Y. *J. Am. Chem. Soc.* **82** (1960) 5255). The optical rotatory dispersion curves of dihydroumbellulone (i) (Djerassi, C., Riniker, R. and Riniker, B. *J. Am. Chem. Soc.* **78** (1956) 6377) and sabinaketone (ii) show negative Cotton effects. By analogy and contrary to earlier findings, the CH-group of the *cyclo*propane ring in the ketone (*11a*) lies below the plane of the paper as shown in formula (iii). The stereochemistry and absolute configuration of thujopsene will thus be represented by formula (iv) and formula (v) will represent the related alcohol widdrol [4,47], the structure of which now has been assigned (Enzell, C. *Acta Chem. Scand.* **15** (1961) 1303 and Ito, S., Endo, K., Takeshita, H., Nozoe, T. and Stother, J. B. *Chem. & Ind. London* **1961** 1618). Full details and further evidence will be presented in a separate paper.



moles HOAc/mole. $C_{15}H_{22}O_2$ requires C 76.9; H 9.5). The mother liquors afforded a solid fraction which after several recrystallisations from different solvents gave a constant melting material (4 g), m.p. 137—139°. According to paper chromatography (dimethyl sulphoxide-light petroleum system)[48] this fraction consisted of a mixture of cuparenic acid [49] and hinokiic acid. The mixture was separated by chromatography on silica gel (250 g); elution with chloroform/methanol (200:1) gave hinokiic acid (3 g) m.p. 169—170°; further elution with chloroform/methanol (20:1) gave *cuparenic acid* (1 g), m.p. and mixed m.p. 158—160°, $[\alpha]_D$ + 63° (*c* 2.0), infra-red and ultra-violet spectra identical with those of an authentic sample.

The selenium dioxide oxidation of thujopsene (*1a*) was carried out according to Erdtman and Thomas [4] and the *aldehyde* (*1c*) was obtained, m.p. 75—76°, $[\alpha]_D$ —27° (*c* 1.9), λ_{max} 255 mμ (ε 6 800). Silver oxide oxidation [4] of this aldehyde (*1c*) gave hinokiic acid (*1b*), m.p. and mixed m.p. 169—170°, $[\alpha]_D$ —86° (*c* 1.9), and infra-red spectrum identical with that of an authentic sample.

Ozonisation of thujopsene (*1a*). Thujopsene (*1a*) (15 g) in ethyl acetate/methanol (6:1, 200 ml) was ozonised at —70° until a blue colour appeared. Excess ozone was removed by bubbling nitrogen through the solution until the colour disappeared. When the reaction mixture had reached room temperature zinc dust (30 g), activated with acetic acid, was added in portions. A vigorous reaction began and the mixture started to boil. After about 1 h the reaction was complete and ether (200 ml) was added followed by dilute sulphuric acid (1 %, 200 ml). The reaction mixture was filtered, the zinc residue washed with ether and the organic phase separated. The water phase was shaken with ether and the combined ether extracts washed with water, dried and taken to dryness. The residue was recrystallised from ethyl acetate and gave large crystals of the *ketocarboxylic acid* (*8a*) (11.5 g), m.p. 166—168°, $[\alpha]_D$ —129° (*c* 2.0), λ_{max} 210.5 mμ (ε 4 700), strong infra-red absorption at 1 700 cm^{-1} (double peak, carbonyl and carboxyl). (Found: C 71.2; H 9.7; C—CH_3 1.36 moles HOAc/mole, $C_{15}H_{24}O_3$ requires C 71.4; H 9.6.) *Semicarbazone* m.p. 220° (decomp.). *2,4-Dinitrophenylhydrazone* (yellow-orange) m.p. 153—154°. More of the ketocarboxylic acid (*8a*) (1 g) was obtained by working up the mother liquors and also a compound that was less soluble in ether (0.6 g, needles). The latter compound was the *hydroxyketocarboxylic acid* (*8b*) m.p. 193 (decomp.), λ_{max} 212 mμ (ε 6 050), strong infra-red absorption at 3 420 and 3 200 cm^{-1} (hydroxyl), 1 718 and 1 688 cm^{-1} (carbonyl and carboxyl). (Found: C 67.4; H 9.3. $C_{15}H_{24}O_4$ requires C 67.1; H 9.0.)

Potassium borohydride reduction of the ketocarboxylic acid (8a). The ketocarboxylic acid (*8a*) (250 mg) was dissolved in methanol (2 ml) and aqueous sodium hydroxide (10 %, 0.5 ml). This solution was added to a solution of potassium borohydride (300 mg) in methanol (2 ml) and water (4 ml). The reaction mixture was acidified and diluted with water until it became cloudy and then warmed until a clear solution was obtained. After cooling the product that crystallised was sublimed to give the *lactone* (*23*), m.p. 125—127°, characteristic infra-red bands at 3 060 cm^{-1} (hydrogens attached to the *cyclo*propane ring) and 1 720 cm^{-1} (seven-membered ring lactone), no maximum above 205 mμ in the ultra-violet spectrum (ε_{205} 150). (Found: C 77.0; H 9.4. $C_{15}H_{22}O_2$ requires C 76.9; H 9.5).

Hypobromite oxidation of the ketocarboxylic acid (*8a*). The ketocarboxylic acid (*8a*) (5 g) was dissolved in aqueous sodium hydroxide (10 %, 50 ml) and excess sodium hypobromite solution (freshly prepared from 25 g sodium hydroxide, 400 ml water and 9 ml bromine) at ice-bath temperature. The mixture was kept at room temperature for 3 h and then extracted with ether to remove bromoform. The solution was decolourised with sodium bisulphite. The solution was acidified and extracted with ether and the ether extract washed with water and evaporated. Recrystallisation of the crude product from ethyl acetate gave the *C_{14}-dicarboxylic acid* (*9*) (4.5 g), m.p. 215°, $[\alpha]_D$ —57°, (*c* 1.7), no maximum above 205 mμ in UV (ε_{205} 800). (Found: C 66.1; H 8.7; C—CH_3 0.62 moles HOAc/mole. $C_{14}H_{22}O_4$ requires C 66.1; H 8.7).

Hypoiodite oxidation of the hydroxyketocarboxylic acid (*8b*). The hydroxyketocarboxylic acid (*8b*), (100 mg) was dissolved in aqueous sodium hydroxide and aqueous iodine-potassium iodide solution (10 % iodine, 20 % potassium iodide) added until there was a slight excess of iodine present. The solution was warmed to 60° and more iodine added until the colour persisted for 2 min and then aqueous sodium hydroxide (10 %) until the colour just disappeared. The solution was allowed to cool to room temperature and water (10 ml) was added. No iodoform was obtained. Sulphuric dioxide was bubbled through the solu-

tion which was then acidified and extracted with ether. The ether extract was washed with water and evaporated to give crystals which on recrystallisation from ethyl acetate gave the *C_{14}-dicarboxylic acid* (*9*), m.p. and mixed m.p. 215° and infra-red spectrum identical with the substance obtained by hypobromite oxidation of the ketocarboxylic acid (*8a*).

Preparation of the anhydride (*10*). The C_{14}-dicarboxylic acid (*9*) (200 mg) was refluxed in acetic anhydride (10 ml) for 1 h and the reaction mixture then evaporated to dryness to give oily crystals which were sublimed *in vacuo* and crystallised from light petroleum-chloroform to give the *anhydride* (*10*), m.p. 113°, $[\alpha]_D$ + 39° (*c* 2.4), characteristic infra-red bands at 1 803 and 1 726 cm^{-1} (in CCl_4, in KBr these bands were displaced to 1 778 and 1 740 cm^{-1}) and at 1 418 cm^{-1} (CH_2-group adjacent to carbonyl). (Found: C 71.0; H 8.5. $C_{14}H_{20}O_3$ requires C 71.2; H 8.5.)

The dimethyl ester of the C_{14}-dicarboxylic acid (*9*) was prepared with diazomethane and purified by recrystallisation from methanol-water and sublimation, m.p. 71—73°, $[\alpha]_D$ —59° (*c* 1.7). (Found: C 68.3; H 9.2. $C_{16}H_{26}O_4$ requires C 68.1; H 9.3.) Saponification of the ester gave unchanged starting material; m.p. 214—215° (from ethyl acetate).

Preparation of the ketone (*11a*). The dimethyl ester of the dicarboxylic acid (*9*) (2.82 g) was dissolved in dry benzene (30 ml). Sodium methoxide (0.54 g) was added and the mixture refluxed for 3 h under an atmosphere of dry nitrogen. The solution (nearly all the sodium methoxide had dissolved) was cooled and poured into an ice-cooled mixture of ether (30 ml) and water (60 ml). The organic phase was separated and the water phase extracted with two portions (20 ml) of ether. The combined ether extracts were washed with water and dried.

The aqueous phase was acidified and extracted with ether and the extract dried and evaporated to give an oil (0.180 g) which after crystallisation from methanol-water and sublimation *in vacuo* gave needles of *a monomethyl ester of the C_{14}-dicarboxylic acid* (*9*), m.p. 115—116°. (Found: C 67.0; H 8.9. $C_{15}H_{24}O_4$ requires C 67.1; H 9.0). Saponification gave the C_{14}-dicarboxylic acid (*9*), m.p. and mixed m.p. 213—215° and infra-red spectrum identical with that of an authentic sample.

The combined organic extract was evaporated to give an oil which was dissolved in a solution of methanol (20 ml) and aqueous sodium hydroxide (10 %, 10 ml) and refluxed for 2 h. The mixture was cooled and diluted with water, acidified and extracted with ether. The dried ether extract was evaporated to give an oil which was distilled *in vacuo* to give the crystalline ketone (*11a*) (1.720 g). Crystallisation from methanol-water and sublimation *in vacuo* gave pure (*11a*). The crystals became isotropic at 49—50° (at this temperature under crossed Nicols the crystals lost their polarisability) and melted at 119—121° (sealed tube). $[\alpha]_D$ + 65°, λ_{max} 210 mμ (ε 3 490). Characteristic infra-red bands at 3 060 cm^{-1} (hydrogens attached to the *cyclo*propane ring), 1 723 cm^{-1} (carbonyl) and 1 415 cm^{-1} ($C-CO-CH_2-C$, in CCl_4 with apparent integrated intensity, *I* 23.0). (Found: C 81.3; H 10.4; $C-CH_3$ 0.65 moles HOAc/mole. $C_{13}H_{20}O$ requires C 81.2; H 10.5). *2,4-Dinitrophenylhydrazone* (orange) m.p. 215—217°. *Semicarbazone*, m.p. 225—226° (decomp.). The rotatory dispersion curve of the ketone (*11a*) (in methanol) showed a maximum at 300 mμ, [M] + 12 600°, and the lowest value recorded was 265 mμ [M] —17 800°.

Preparation of the alcohol (*1d*). Hinokiic acid (*1b*) was esterified with diazomethane and the methyl ester[4] treated with lithium aluminium hydride in the usual way. The primary *alcohol* (*1d*) so obtained was recrystallised from petroleum ether, m.p. 103—104°, $[\alpha]_D$ —102°. (Found: C 81.7; H 11.0. $C_{15}H_{24}O$ requires C 81.8; H 11.0).

Ozonisation of the alcohol (*1d*). The alcohol (*1d*) (0.30 g) was ozonised according to the method used for thujopsene (*1a*). The crystalline product obtained gave, after recrystallisation from ether-ethyl acetate, the *hydroxyketocarboxylic acid* (*8b*) (0.21 g), m.p. 190—193° (decomp.) and infra-red spectrum identical with the compound obtained as a byproduct on ozonisation of thujopsene (*1a*).

Ozonisation of hinokiic acid (*1b*). Hinokiic acid (*1b*) (1.5 g) was dissolved in ethyl acetate-methanol (5:1, 20 ml) and treated with ozone at a temperature of —70° until the solution turned blue. Excess ozone was removed with nitrogen and water added. The organic solvents were removed by distillation and aqueous sodium hydroxide (40 %, 1 ml) was added to the residue of water and oily organic material. After cooling in ice-water an excess of freshly prepared sodium hypobromite solution (from 5 g sodium hydroxide, 100 ml water and 1.5 ml bromine) was added and the mixture was allowed to stand for

3 h at room temperature. No bromoform could be isolated but a crystalline neutral product was obtained (0.21 g). This was recrystallised from methanol-water to give the *dibromoketone* (*11b*), m.p. 99—100°, $[\alpha]_D$ + 87°, λ_{max} 211 mμ (ε 4 100), characteristic infra-red bands at 3 060 cm^{-1} (hydrogens attached to the *cyclo*propanering) and 1 733 cm^{-1} (carbonyl). (Found: C 44.5; H 5.2; Br 45.9. $C_{13}H_{18}OBr_2$ requires C 44.6; H 5.2; Br 45.7). The filtrate was acidified and extracted with ether. The extract was dried and evaporated to give an oil (0.95 g) which after standing for one week gave a small amount of crystalline material (0.08 g). After recrystallisation from ethyl acetate the m.p. was 213—215° and undepressed when mixed with the *C_{14}-dicarboxylic acid* (*9*) (identical infra-red absorption). After evaporating the solvent from the mother liquors the oily residue was dissolved in chloroform (2 ml) and chromatographed on silica gel (50 g). Methanol-chloroform (4 %) eluted the *monomethyl ester* (0.150 g) of the *C_{14}-dicarboxylic acid* (*9*), m.p. 115—116°, which was also obtained as a by-product of the Dieckmann-condensation of the dimethyl ester of the C_{14}-dicarboxylic acid (*9*). (Mixed m.p. and identical infra-red spectra). Methanol-chloroform (10 %) eluted the *C_{14}-dicarboxylic acid (9)* m.p. and mixed m.p. 213—215° (identical infra-red spectra).

Reductive debromination of the dibromoketone (*11b*). A mixture of the dibromoketone (*11b*) (0.160 g) in acetic acid (3 ml), zinc dust (1.0 g) and sodium acetate (0.5 g) was refluxed for 1 h. After filtration the inorganic residue was washed with ether. The ether phase was washed with water and sodium bicarbonate, dried and evaporated to give the *ketone* (*11a*) (0.080 g). Sublimation *in vacuo* gave the pure (*11a*), m.p. and mixed m.p. 119—121° (sealed tube). Infra-red spectrum identical with that of an authentic sample.

Bromination of the ketone (*11d*). The ketone (*11a*) (0.100 g) was dissolved in carbon tetrachloride (3 ml) and bromine (0.160 g) added. The reaction mixture was stirred overnight by which time the bromine colour had disappeared. Ether (20 ml) was added and the solution dried over sodium sulphate. After evaporation of the solvents an oil remained, which, after the addition of some methanol, furnished crystals of the *dibromoketone* (*11b*) (0.020 g), m.p., mixed m.p., 99—100°. The infra-red spectrum was identical with that of an authentic sample. From the mother liquor crystals were obtained which, after recrystallisation from methanol, furnished a tribromo compound (0.040 g), m.p. 174—177° (decomp.). (Found: C 36.0; H 4.4; Br 55.9. $C_{13}H_9OBr_3$ requires C 36.1; H 4.4; Br 55.6).

The dehydrobromination experiments [50]. The dibromoketone (*11b*) (35 mg) in dimethyl formamide (2.5 ml) was heated with lithium carbonate (80 mg) and lithium bromide (95 mg) and the mixture stirred in an atmosphere of dry nitrogen. After 24 h at 100° the product was extracted with ether. After crystallisation from methanol, the product obtained was found to be unchanged starting material (28 mg), m.p. and mixed m.p. 99—100°, infrared and ultra-violet spectra identical. Even the crude product did not exhibit any ultra-violet absorption indicating the presence of an α,β-unsaturated ketone. The dibromoketone (*11b*) (20 mg) was heated under reflux with γ-collidine (1 ml). No precipitate of the collidine salt was formed even after 2 h heating. The crude residue did not exhibit any ultra-violet absorption corresponding to that of an α,β-unsaturated ketone. The crystalline material obtained from this residue was unchanged starting material.

Selenium dioxide oxidation of the ketone (*11a*). The ketone (*11a*) (0.380 g) was dissolved in acetic acid (5 ml), selenium dioxide (0.400 g) added and the mixture refluxed for 1 h. The selenium formed was removed by filtration and washed with ether. The ether solution was washed with water and sodium bicarbonate. The ether layer was dried and evaporated to give an orange oil (0.400 g). This oil was chromatographed on alumina (neutral, activity I, 40 g). Ether-light petroleum (50 %) eluted starting material (0.150 g), m.p. and mixed m.p. 119—120°, and infra-red spectrum identical with that of the ketone (*11a*). Ether eluted the *diketone* (*12*) (0.170 g) which after sublimation *in vacuo* gave pure (*12*). At 68° the crystals became isotropic (*cf.* ketone(*11a*)) and melted at 177° (sealed tube). Characteristic infra-red bands at 3 080 cm^{-1} (hydrogens attached to the *cyclo*propane ring), 1 752 and 1 727 cm^{-1} (non-enolised diketone), λ_{max} 233 mμ (ε 2 200). (Found: C 75.7; H 8.8. $C_{13}H_{16}O_2$ requires C 75.7; H 8.8).

Hydrogen peroxide oxidation of the diketone (*12*). The diketone (*12*) (0.150 g) was dissolved in methanol (5 ml) and methanolic potassium hydroxide (10 %, 5 ml) at ice-bath temperature. Hydrogen peroxide (30 %, 2 ml) was added and a white solid began to separate from the solution. After standing overnight in a refrigerator, the mixture was refluxed on a water bath for 10 min. After cooling the mixture was diluted with water

(20 ml) when the white solid obtained went into solution. The aqueous phase was acidified and extracted with ether. The ether extract was dried and evaporated to give a solid which, after sublimation *in vacuo*, gave crystals of the *C_{13}-anhydride* (*14*) (0.140 g). At 92—93° the crystals became isotropic (*cf.* ketone (*11a*)) and melted at 211—213° (sealed tube). Characteristic infra-red bands at 3070 cm^{-1} (hydrogens attached to the *cyclo*propane ring), 1795 and 1750 cm^{-1} (in CCl_4, anhydride). (Found: C 70.1; H 8.2. $C_{13}H_{18}O_3$ requires C 70.2; H 8.2).

The anhydride (*14*) could be recrystallised from methanol-water without being hydrolysed and also a rapid recrystallisation from acetic acid-water yielded unchanged anhydride. A slow crystallisation from this mixture gave large crystals of the *C_{13}-dicarboxylic acid* (*13*) which could be recrystallised from methanol-water. The acid did not analyse well probably due to partial anhydride formation on drying in a vacuum. (Found: C 66.5; H 8.3. $C_{13}H_{20}O_4$ requires C 65.0; H 8.4). On rapid heating the crystals began to melt at about 180° giving an oil which solidified and remelted at 211—213° when it also sublimed. The sublimed product showed an identical infra-red spectrum and undepressed mixed m.p. (sealed tube) with the C_{13}-anhydride (*14*).

Potassium borohydride reduction of the ketone (*11a*). A solution of potassium borohydride (0.900 g) in water (15 ml) and methanol (6 ml) was added to the ketone (*11a*) (0.500 g) in methanol (6 ml). The mixture was allowed to stand overnight at room temperature and water (25 ml) was added. Extraction with ether gave a product which was crystallised from methanol-water to give the *alcohol* (*15*) (0.425 g). At 87° the crystals became isotropic and melted at 133—135°. No absorption in the ultra-violet above 205 mμ, characteristic infra-red bands at 3360 cm^{-1} (hydroxyl) and 3060 cm^{-1} (hydrogens attached to the *cyclo*propane ring). (Found: C 80.6; H 11.5. $C_{13}H_{22}O$ requires C 80.4; H 11.4).

Selenium dehydrogenation of the alcohol (*15*). The alcohol (*15*) (0.500 g) and selenium (0.600 g) were heated under reflux in a salt bath kept at 280—290° for 24 h in an atmosphere of carbon dioxide. The product was distilled giving an oil (0.33 g) which was chromatographed on alumina (standard, activity I, 30 g). Elution was carried out with light petroleum (20 ml fractions). Fractions 3 and 4 gave an oil (0.195 g) which, according to its ultra-violet spectrum contained a tetralinic compound, λ 260 mμ (inflexion, ε 400), 263 mμ, (inflexion, ε 520), 267 mμ (maximum, ε 530), 272 mμ (minimum, ε 310), 274 mμ (maximum, ε 450) (the extinction coefficients are calculated for an assumed molecular weight of 160). The fractions 6—8 gave an oil (0.100 g) which according to its ultra-violet and infra-red spectra was identical with *α-methyl-naphthalene* (*16*); *picrate*, m.p. and mixed m.p. 139—140°.

Preparation of the alcohol (*18*). The ketone (*11a*) (0.730 g) in ether (5 ml) was added dropwise to a stirred solution of methyl magnesium iodide (from 0.250 g magnesium and 0.64 ml methyl iodide in 10 ml ether) at ice-bath temperature. The stirring and cooling were continued for 4 h. The reaction mixture was then stirred for half an hour at room temperature followed by 1 h heating under reflux. The mixture was poured into a mixture of ice (30 g) and ammonium chloride (4 g). The organic phase was separated, washed with aqueous sulphuric acid (1 %, 2 × 20 ml), and water and then dried. After evaporation of the ether, oily crystals (0.750 g) were obtained. Recrystallisation from methanol-water gave the *alcohol* (*18*), m.p. 62—63°, having characteristic infra-red bands (in CCl_4) at 3580 and 3450 cm^{-1} (hydroxyl) and 3070 cm^{-1} (hydrogens attached to the *cyclo*propane ring) (Found: C 80.7; H 11.6. $C_{14}H_{24}O$ requires C 80.7; H 11.6).

Selenium dehydrogenation of the alcohol (*18*). This reaction was carried out in the same way as with alcohol (*15*). The alcohol (*18*) (0.500 g) also gave an oily product (0.300 g) which was chromatographed on alumina as described above. Fractions 3 and 4 gave an oil (0.175 g) with tetralinic properties. λ 265 mμ (inflexion ε 590), 270 mμ (maximum, ε 700), 272 mμ (inflexion, ε 640), 276 mμ (minimum, ε 490), 278 mμ (maximum, ε 670) (the extinction coefficients were calculated for an assumed molecular weight of 174). Fractions 6—8 gave an oil which according to its ultra-violet and infra-red spectra was identical with (1,6-dimethylnaphthalene *19*). The m.p. and mixed m.p. of the styphnates, 119—120°, and of the picrates, 112—114°, were identical with those of authentic samples.

Ozonisation of the tetralinic compounds. The tetralinic compounds obtained from the selenium dehydrogenation of the alcohols (*15*) and (*18*) were treated as follows:

Ozone was passed through a solution of the compound (0.200 g) in methanol (7 ml) for 12 h at room temperature. Most of the methanol was removed by evaporation and the residue refluxed with a mixture of aqueous sodium hydroxide (5 %, 2 ml) and hyd-

rogen peroxide (30 %, 0.3 ml) on a water bath for 1 h. After cooling the mixture was extracted with ether. The alkaline solution was acidified and extracted with ether (4 × 20 ml). The ether solution was dried and the solvent removed, yielding an oil (0.120 g), which was suspended in a solution of copper acetate (0.5 g) in water (10 ml). A few drops of ether were added and the mixture stirred for 3 h. The copper salts were collected and washed with water (20 ml) and ether (25 ml), suspended in aqueous sodium hydroxide (10 %, 10 ml) and the mixture saturated with hydrogen sulphide. More sodium hydroxide was added and the mixture stirred for 2 h. The copper sulphide was removed by filtration and washed with water and the filtrate acidified and extracted with ether (5 × 15 ml). The combined ether extracts were dried and evaporated to give an oil (0.055 g) which did not crystallise. According to paper chromatography (dimethyl sulphoxide-ether system) [48] the main spot had the same R_F-value (0.15) as *a,a*-dimethyladipic acid. A sheet of paper (15 × 30 cm, Whatman 3 MM) was impregnated by passing it through a solution of dimethyl sulphoxide in toluene (25 % v/v), uniformly blotted between layers of filter paper and dried in an oven at 60° for 3 min. This process was repeated and the paper immediately placed between glass plates leaving only the starting line and the paper above it uncovered. After application of the crude oil (0.050 g) the paper was transferred to the chromatogram tank in such a manner as to prevent absorbtion of moisture. Sodium dried ether containing small amounts of dimethyl sulphoxide (4 % v/v) was used as eluent. The chromatogram was run until the diffuse ether front had moved about 20 cm. Three thin slips were cut out along the paper and developed by spraying with indicator in the usual way [18]. The part of the paper that contained the main product was cut out, extracted with ether and the combined ether extracts washed with water and dried. After evaporating the solvents an oil (0.020 g) was obtained which on standing partly crystallised giving *a,a-dimethyladipic acid* (*17*), m.p. and mixed m.p. 86—88°. The infra-red spectrum was identical with that of an authentic sample.

Catalytic hydrogenation of thujopsene (*1a*). Thujopsene (*1a*) (4.040 g, 20 mmoles) in methanol (30 ml) and ether (3 ml) was hydrogenated over a 10 % palladium on charcoal catalyst. When the theoretical amount of hydrogen (20 mmoles) had been consumed the mixture was filtered, diluted with water and extracted with ether. The ether extract was dried and the solvent evaporated to give *dihydrothujopsene* (2a), $[a]_D$ + 24°, n_D^{25} 1.5100, characteristic infra-red bands at 1 675 cm^{-1} (double bond) and in the 1 375 cm^{-1} region as shown from Fig. 3. (Found: C 87.3; H 12.7; C—CH_3 1.55 moles HOAc/mole. $C_{15}H_{26}$ requires C 87.3; H 12.7).

On further hydrogenation in the same solvent and catalyst system the rate of hydrogen uptake decreased to about one sixth of that of the first molar equivalent of hydrogen. After the uptake of a further 0.90 molar equivalent of hydrogen the reaction stopped. The *tetrahydrothujopsene* was isolated, $[a]_D$ + 27, n_D^{25} 1.4922, no infra-red bands in the range 1 600—1 700 cm^{-1}. (Found: C 86.7; H 13.4. $C_{15}H_{28}$ requires C 86.5; H 13.5).

The hydrogenation products were not completely homogeneous and there seemed to be 10 % of the normal 1:2 addition of hydrogen besides the main 1:4-addition, since only 1.9 molar equivalents of hydrogen were consumed.

Catalytic hydrogenation of hinokiic acid (*1b*). Hinokiic acid (*1b*) (0.469 g) in methanol (30 ml) was hydrogenated over a 10 % palladium on charcoal catalyst. The reaction was stopped when one molar equivalent of hydrogen had been consumed. The catalyst was filtered off. On evaporation to half the volume and addition of a little water needles of dihydrohinokiic acid separated. Recrystallisation from methanol and sublimation under reduced pressure gave pure *dihydrohinokiic acid* (*2b*), m.p. 158—160°, $[a]_D$ + 75°, λ_{max} 219 mμ (ε 9 000) characteristic infra-red bands at 1 685 and 1 640 cm^{-1} (carboxyl with conjugated double bond). (Found: C 76.1; H 10.2; C—CH_3 0.79 moles HOAc/mole. $C_{15}H_{24}O_2$ requires C 76.2; H 10.2).

With platinum in acetic acid hinokiic acid rapidly consumed 1.85 molar equivalents of hydrogen. No further hydrogen uptake took place. Evaporation under reduced pressure gave a product which after several recrystallisations from methanol gave pure tetrahydrohinokiic acid, m.p. 144—146°, $[a]_D$ + 60°. (Found: C 75.7; H 10.9. $C_{15}H_{26}O_2$ requires C 75.6; H 11.0).

Ozonisation of dihydrothujopsene (*2a*). Dihydrothujopsene (*2a*) (4.0 g) in ethyl acetate-methanol (6:1, 50 ml) was treated with ozone at —70° as described for thujopsene (*1a*).

The crystalline acidic fraction obtained (3.1 g) gave on recrystallisation from ethyl acetate pure *dihydroketocarboxylic acid* (*33*), m.p. 160–161°, $[\alpha]_D$ + 7.1°, no ultra-violet maximum above 205 mμ, characteristic infra-red bands at 1 722 cm^{-1} (carbonyl) and 1 692 cm^{-1} (carboxyl). (Found: C 70.9; H 10.2; C–CH_3 1.55 moles HOAc/mole. $C_{15}H_{26}O_3$ requires C 70.8; H 10.3). *2,4-Dinitrophenylhydrazone*, m.p. 227–228°.

Hypobromite oxidation of the dihydroketocarboxylic acid (*33*). The dihydroketocarboxylic acid (*33*) (3.0 g) was treated with sodium hypobromite as described for the ketocarboxylic acid (*8a*). The *dihydro-C_{14}-dicarboxylic acid* (*34*) (2.2 g) was obtained which on recrystallisation from acetonitrile gave pure (*34*), m.p. 185–187°, $[\alpha]_D$ –10°. (Found: C 65.8; H 9.3; C–CH_3 0.8 moles HOAc/mole. $C_{14}H_{24}O_4$ requires C 65.6; H 9.4).

Ozonisation of dihydrohinokiic acid (*2b*). The dihydrohinokiic acid (*2b*) (0.500 g) was dissolved in ethyl acetate-methanol (5:1, 10 ml) and treated with ozone at –70° until the blue colour appeared. Excess ozone was removed by bubbling nitrogen through the solution. Activated zinc (about 1 g) was added at room temperature and the mixture allowed to stand for 3 h. Ether (30 ml) and aqueous sulphuric acid (1 %, 30 ml) were added and the organic phase separated. The water phase was extracted with further amounts of ether (2 × 20 ml) and the combined organic extracts washed with water and dried. On evaporation an oil was obtained which crystallised overnight. Recrystallisation from methanol-water gave the *acid-aldehyde* (*39*) (0.310 g), m.p. 111–113.5°, characteristic infra-red bands at 1 735 cm^{-1} (aldehyde) and 1 688 cm^{-1} (carboxyl). This compound did not give a good analyses probably because of slow autoxidation.

Silver oxide oxidation of the acid-aldehyde (*39*). A saturated solution of silver nitrate (0.350 g) in water was added with stirring to a solution of aqueous sodium hydroxide (4 %, 2 ml) and dioxane (2 ml). The acid-aldehyde (*35*) (0.100 g) in dioxane (5 ml) was added to the mixture which was then heated with mechanical stirring for 24 h on a water bath. A silver mirror was formed. After filtration the filtrate was diluted with water, acidified and extracted with ether. The extract was dried and evaporated and the crystalline residue recrystallised from acetonitrile to give pure *dihydro-C_{14}-dicarboxylic acid* (*34*) (0.068 g), m.p. and mixed m.p. 185–187°. The infra-red spectrum was identical with that of an authentic sample.

Preparation of the dihydroketone (*35*). The oily dimethyl ester (1.42 g, 0.050 mole) of the dihydro-C_{14}-dicarboxylicacid obtained with diazomethane was dissolved in dry benzene (20 ml). Sodium hydride (0.050 mole) was added and the mixture refluxed for 3 h under an atmosphere of dry nitrogen. The sodium hydride passed into solution. The reaction mixture was cooled and poured into a mixture of ether (30 ml) and water (50 ml) at ice-bath temperature. The organic phase was separated and the aqueous phase extracted with ether (2 × 20 ml). The combined ether extract was washed with water, dried and evaporated to given an oil which was dissolved in methanol (20 ml) and aqueous sodium hydroxide (10 %, 10 ml) and refluxed for 2 h. The mixture was cooled, diluted with water (30 ml) and extracted with ether. The alkaline phase was acidified and extracted with ether. The dried ether extract was evaporated to give a crystalline residue which, after decarboxylation by heating on a water bath under reduced pressure, gave the *dihydroketone* (*35*) which sublimed (0.805 g), m.p. 202° (sealed tube, the crystals were isotropic at room temperature *cf.* ketone *(11a)*) $[\alpha]_D$ + 82°, characteristic infra-red bands at 1 728 cm^{-1} (in CCl_4, 5-membered ring ketone) and at 1 415 cm^{-1} (C–CO–CH_2–C, in CCl_4 with apparent integrated intensity: *I* 21.9). (Found: C 80.4; H 11.4; $C_{13}H_{22}O$ requires C 80.4; H 11.4).

Attempts to prepare the 2,4-dinitrophenylhydrazone of the dihydroketone (*35*) failed even on refluxing an ethanolic solution of the compound for 1 h in the presence of hydrochloric acid (with 70 % recovery of starting material).

Quantitative bromination experiment of the dihydroketone (*35*). A quantitative bromination experiment was carried out according to Barnes *et al.*[44] but the excess bromine was decreased to about 10 moles bromine/mole ketone. The uptake of bromine (in moles/mole ketone) was after 1 day, 2.1; 2 days, 2.0; 3 days, 2.1; 4 days, 2.1. The dibromodihydroketone was isolated and, after sublimation *in vacuo*, the pure compound was obtained, m.p. 119–120°, characteristic infra-red band at 1 755 cm^{-1} (*a,a*-dibromosubstituted 5-membered ring ketone). (Found: C 42.1; H 5.7; Br 47.9. $C_{13}H_{20}OBr_2$ requires C 41.9; H 5.4; Br 48.2).

Deuteration of the dihydroketone (*35a*)[22,51]. A mixture of the dihydroketone (*35a*) (100 mg), potassium deuteroxide (60 mg), deuterium oxide (2.5 ml) and dioxane (6 ml) was heated under reflux in an atmosphere of nitrogen for 30 min. Half the volume of the

reaction mixture was evaporated (care was taken as the dihydroketone is volatile). The mixture was cooled to room temperature and light petroleum added. The organic phase was collected, washed with two portions of deuterium oxide, dried over anhydrous magnesium sulphate and the light petroleum evaporated. Sublimation of the crystalline residue (80 mg) afforded pure *deuteroketone*, m.p. 202° (sealed tube), no infra-red band at about 1 415 cm^{-1}. The mass spectrum of the compound (kindly recorded by Dr. R. Ryhage, Laboratory for Mass Spectrometry, Karolinska Institutet, Stockholm) showed a mass peak at 196 *m/e*, corresponding to the dideuterated ketone.

Selenium dioxide oxidation of the dihydroketone (*35*). The dihydroketone (*35*) (0.300 g) was dissolved in acetic acid (3 ml) and oxidised with selenium dioxide (0.180 g) as described for ketone (*11a*). The yellowish oily product obtained was chromatographed on alumina (neutral, activity I, 15 g). Ether-light petroleum (10 %) eluted unchanged starting material (0.065 g). Ether-light petroleum (25 %) eluted the *diketone* (*36*) (0.130 g). Recrystallisation from methanol gave pure (*36*), m.p. 125—126°, λ_{max} 278 mμ (ε 1 800), characteristic infra-red bands (in CCl_4) at 1 700 and 1 600 cm^{-1} (enolised diketone). (Found: C 74.9; H 9.6. $C_{13}H_{20}O_2$ requires C 75.0; H 9.7).

Hydrogen peroxide oxidation of the diketone (*36*). The diketone (*36*) (0.100 g) was dissolved in methanolic potassium hydroxide (5 %, 10 ml) and cooled in ice water. Hydrogen peroxide (30 %, 2 ml) was added. After standing overnight in the refrigerator the mixture was refluxed on a water bath for 10 min. After cooling the mixture was diluted with water (20 ml) acidified and extracted with ether. On evaporation the dried ether extract gave oily crystals of the *dihydro-C_{13}-dicarboxylic acid* (*37*) which, after recrystallisation from methanol-water, gave the pure compound (0.070 g), m.p. 225—227° (decomp.). (Found: C 64.7; H 9.1. $C_{13}H_{22}O_4$ requires C 64.4; H 9.2).

On heating to the melting point the dihydro-dicarboxylic acid lost water and the *dihydro-C_{13}-dicarboxylic acid anhydride* (*38*) sublimed. At 64°, the crystals became isotropic (*cf.* ketone (*11a*))and melted at 216—218° (sealed tube). Characteristic infra-red bands at 1 800 and 1 760 cm^{-1} (in CCl_4, 6-membered ring anhydride). (Found: C 69.6; H 8.9. $C_{13}H_{20}O_3$ requires C 69.6; H 9.0).

Catalytic deuteration of thujopsene (*1a*). Thujopsene (*1a*) (0.741 g) in deuteromethanol (MeOD, 8 ml) and ether (2 ml) was deuterated over a 10 % palladium on charcoal catalyst (previously saturated with deuterium) until one molar equivalent of deuterium had been taken up. The dideuterothujopsene was isolated as described for dihydrothujopsene (*2a*): $[a]_D$ + 22°, n_D^{25} 1.5013. Characteristic infra-red bands at 2 185 and 2 125 cm^{-1} (carbon-deuterium stretching) 1 675 cm^{-1} (double bond). The bands in the 1 375 cm^{-1} region are shown in Fig. 3.

The nuclear magnetic resonance spectrum of dideuterothujopsene was recorded under the same conditions as for dihydrothujopsene [36]. The shifts given in the discussion are from benzene as internal standard (on a 40 Mc/s instrument).

The ozonisation of the dideuterothujopsene was carried out in the same way as described for dihydrothujopsene (*2a*) and gave the *deuteroketocarboxylic* acid, m.p. 159—160°.

The hypobromite oxidation of the deuteroketocarboxylic acid was carried out in the same way as described for the dihydroketocarboxylic acid (*33*) and gave the *deutero-C_{14}-dicarboxylic acid*, m.p. 185—187°. This acid on esterification with diazomethane gave the dimethylester with infra-red absorption in the 1 375 cm^{-1} region as shown from Fig. 4.

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