

Proton Magnetic Resonance Investigations on the Structure of Thujopsene and Hinokiic Acid

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The position of the *cyclopropane* ring in the sesquiterpene thujopsene and the corresponding acid, hinokiic acid, has been investigated by proton magnetic resonance (PMR) studies. The structure Ia for thujopsene and hinokiic acid has been confirmed.

On catalytic hydrogenation of the alkenyl-*cyclopropane* system in thujopsene and hinokiic acid, a conjugate addition of hydrogen takes place giving dihydroderivates which, as shown by the PMR spectra, have structure II.

The sesquiterpene thujopsene¹ occurs in the woods of many conifers². It can be oxidised to an α,β -unsaturated carboxylic acid^{3,4} identical with the naturally occurring hinokiic acid². From the results of oxidative degradation and of earlier work on hinokiic acid⁵ the structure Ib was tentatively suggested for thujopsene and hinokiic acid². Kobayashi, Nagahama and Akiyoshi independently arrived at the same structure for the hydrocarbon⁶. However, further studies have shown that this structure requires modification.

The chemical investigations on the structure of thujopsene and hinokiic acid leading to structure Ia, R = CH₃ and R = COOH, respectively, have been published^{7,8}. A simplified reaction scheme showing the relationships between thujopsene, hinokiic acid and some of their degradation products is given in Fig. 1.

On ozonisation thujopsene I gave the ketocarboxylic acid III which could be further oxidised to the C₁₄-dicarboxylic acid IV and easily transformed into the 5-membered ring ketone V. On treatment with potassium borohydride and then with acid the ketocarboxylic acid III furnished the corresponding lactone VII. The ketone V was oxidised to a C₁₃-dicarboxylic acid, which on heating gave a remarkably stable 6-membered ring anhydride VI. The C₁₄-dicarboxylic acid IV, however, gave a 7-membered ring anhydride VIII. The ketone V on reduction with potassium borohydride furnished the corresponding alcohol IX, which on dehydrogenation with selenium gave α -methylnaphthalene X. With methylmagnesium iodide the ketone V gave the alcohol XI, which on dehydrogenation with selenium gave 1,6-dimethylnaphthalene XII.

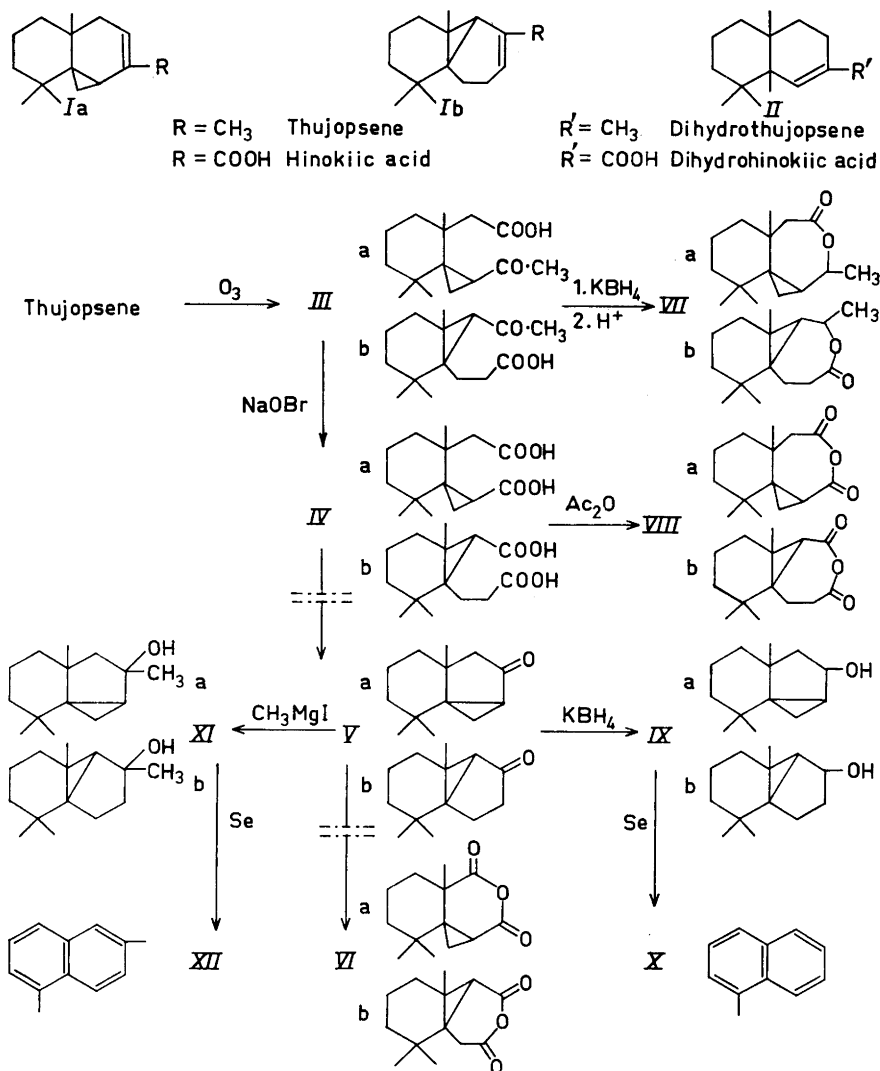


Fig. 1. Simplified reaction scheme showing relationships between thujopsene, hinokiic acid and their degradation products.

The dehydrogenation experiments established the carbon skeleton for the ketone V and located the position of the carbonyl function. UV- and IR-data for this ketone showed that the *cyclopropane* ring is "conjugated" with the carbonyl group. Structures Va and Vb are therefore both possible for the ketone. The keto group in the ketocarboxylic acid III was also shown to be "conjugated" with the *cyclopropane* ring. The problem was therefore to decide between structures Ia and Ib for thujopsene and hinokiic acid.

It was clear that if the number of hydrogens on the *cyclopropane* ring could be determined it would be possible to make a choice between the two structures Ia and Ib for thujopsene and hinokiic acid. The high PMR frequency of the protons on a *cyclopropane* ring (282 cps from benzene at a field of 9 400 gauss)⁹ made a PMR approach to this problem seem feasible. It was found, however, that the signal from the hydrogens on the *cyclopropane* ring in thujopsene, hinokiic acid and many of their degradation products appeared at frequencies lower than 282 cps. As a consequence they interfered with signals from angular and geminal methyl groups thus making the interpretation of the PMR spectra difficult. The signals from the *cyclopropane* ring protons could be definitely distinguished in only a few compounds.

The PMR spectrum of thujopsene I is shown in Fig. 2. The signal at 90 cps is clearly due to the proton on the double bond; it may indicate coupling with two non-equivalent hydrogens in a methylene group. The peak at 266 cps is due to the angular methyl group. The shift is somewhat higher than is usually observed for methyl groups at junctions between 5- and 6-membered rings^{10,11}. Methyl groups at double bonds in 6-membered rings are usually found at about 216 cps from benzene⁹ and this suggests that the peak at 218 cps is due to the methyl group on the double bond in thujopsene I. The area is about that expected and the splitting found may be due to long range coupling with the hydrogen atom on the double bond. In the PMR spectrum of hinokiic acid I, in which this methyl group is oxidised, there is no signal near 218 cps.

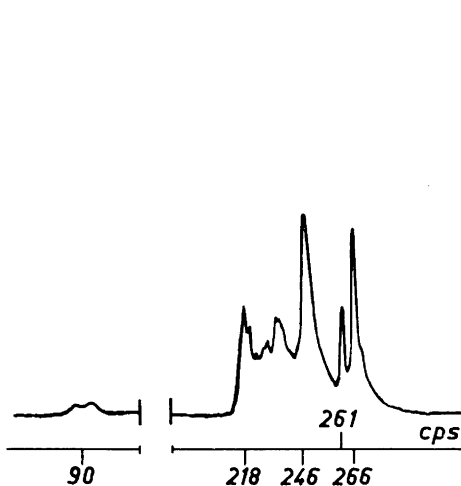


Fig. 2. The PMR spectrum of thujopsene, I, ($R = CH_3$). Solution in carbon tetrachloride, mole fraction 0.06. Benzene as internal reference.

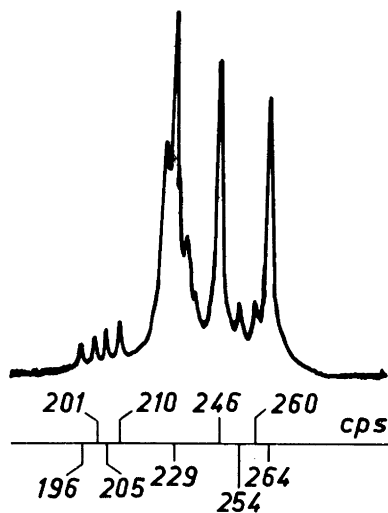


Fig. 3. The PMR spectrum of the C-13 anhydride, VI. Solution in carbon tetrachloride, mole fraction 0.05. Benzene as internal reference.

The signal at 261 cps and the unresolved signal at the base of the 266 cps signal are presumably due to protons on the *cyclopropane* ring. This interpretation favours structure Ia, since structure Ib cannot account for more than one PMR signal from the hydrogen on the *cyclopropane* ring.

The PMR spectrum of the C₁₃-dicarboxylic acid anhydride VI is shown in Fig. 3. Each of the three strong signals at 229 cps (on top of the methylene signals), 246 cps, and 264 cps corresponds to a methyl group. The geminal methyl groups are thus clearly non-equivalent. Models of the anhydride show that in structure VIa the CH₂ group of the *cyclopropane* ring comes very close to one of the geminal methyl groups and the non-equivalence of these two methyl groups may well be due to steric interactions. Inspection of the models indicates that structure VIb is not as crowded as structure VIa. The signals at 246 and 264 cps can be assigned to the geminal methyl groups and the signal at 229 cps to the angular methyl group (see below).

The four peaks at 196, 201, 205, and 210 cps could be due to the methylene group in the α -position to one of the anhydride carbonyl group in structure VIb. Two non-equivalent protons on this α -carbon should, however, give rise to an AB-spectrum (for nomenclature see Ref.¹⁰) with its characteristic small-large-large-small pattern and the spin coupling constant would be about 12–15 cps. This would not explain the two signals at 254 and 260 cps and is clearly not in agreement with the observed spectrum which is more consistent with structure VIa. As the two methylene protons on the *cyclopropane* ring can be expected to be non-equivalent the spectrum of the three *cyclopropane* ring hydrogens should be of the ABC- or, more likely, the ABX-type. Theoretically the X-part of the ABX-spectrum should consist of six lines. Two lines are however very weak and are not always observed (see Ref.¹⁰ pp. 132–8) and the X-part of the ABX-spectrum can appear as a quartet with peaks of almost equal intensity (see Ref.¹⁰ pp. 245 and 335). The signals at 254 and 260 cps can then be considered as a part of the AB-pattern. Unfortunately, the ABX-spectrum in Fig. 3 is not sufficiently distinct to permit a detailed analysis, but the X-part at about 200 cps can be described by $J_{AX} = 9.0$ cps and $J_{BX} = 5.0$ cps.

The proton on the *cyclopropane* ring and in α -position to one of the carbonyl groups in the C₁₃-anhydride VI has its resonance position at a comparatively low field which may be due to the fact that this proton lies in the C—C—O-plane of the carbonyl group. Jackman has given many examples of a carbonyl group causing shifts towards lower fields of neighbouring protons when these lie in this plane, and has discussed this in terms of the diamagnetic anisotropy of the carbonyl group¹².

Similarly the anisotropy of the other carbonyl group may account for the low resonance field (229 cps) assigned to the protons of the angular methyl group. In the C₁₄-anhydride VIIIa, where the angular methyl is in a β -position to the carbonyl group and thus where the shifts towards lower field should be considerably weaker, the angular methyl signal is at about 260 cps.

In the PMR spectra of the other degradation products containing carbonyl groups (V, VII, and VIII) the region around 200 cps is obscured by signals from the methylene groups in α -positions to the carbonyl group. The two protons on these methylene groups are clearly non-equivalent and give rise to

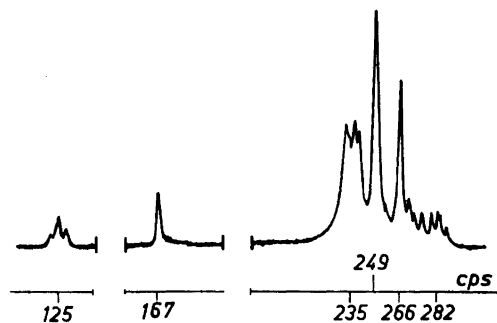


Fig. 4. The PMR spectrum of the alcohol, XI. Solution in carbon tetrachloride, mole fraction 0.06. Benzene as internal reference.

typical AB-patterns with a spin coupling constant $J_{AB} = 15\text{--}15.5$ cps. (For other examples of non-equivalent methylene protons see Refs.^{11,13}.)

The PMR spectrum of the alcohol IX is shown in Fig. 4. The position of the signal at 167 cps is sensitive to temperature and concentration and it is therefore assigned to the OH-group. The small triplet at 125 cps corresponds to the proton on the same carbon atom as the OH group. The pattern and the coupling constant $J = 2.6$ cps suggests spin coupling with equivalent or nearly equivalent methylene protons. According to this interpretation the coupling with the neighbouring *cyclopropane* proton is quite small. The disappearance of the spin coupling is not unexpected in the light of the dependence of the coupling on the dihedral angle between protons on adjacent carbon atoms^{14,15}. Inspection of molecular models show the dihedral angle in this case to be close to 90° when the spin coupling should be very small. The strong signal at 249 cps corresponds to the geminal methyl groups and the signal at 266 cps to the angular methyl group. The pattern at about 280 cps

Table 1. Methyl group shifts in thujopsene, hinokiic acid and related compounds. (Solutions in carbon tetrachloride, mole fractions 0.04–0.06. Shifts in cps at 40 Mc/s relative to benzene as internal reference.)

Gem-dimethyls	Angular methyls	Compound
246	266	thujopsene (Ia, R = CH ₃)
243 and 246	263.5	hinokiic acid (Ia, R = COOH)
253	253	dihydrothujopsene (II, R = CH ₃)
250	250	dihydrohinokiic acid (II, R = COOH)
245 and 251	267.5	ketone (Va)
246 and 264 (tentative)	229	C-13 anhydride (VIa)
244 and 252	265	lactone (VIIa)
243 and 259 (tentative)	262	C-14 anhydride (VIIIa)
249	266	alcohol (IXa)

is due to the protons on the *cyclopropane* ring. The observed pattern can hardly be interpreted in terms of structure IXb but can well be part of an ABC-spectrum as would be expected from structure IXa.

The collected evidence from the PMR spectra in Figs. 2—4 leaves little doubt that thujopsene and hinokiic acid must have structure Ia.

As judged from models there seems to be a rough correlation between the non-equivalence of the *gem*-dimethyl groups expressed as difference in the PMR shifts and the degrees of steric interaction between the *cyclopropane* ring and the axial geminal methyl group. It is hoped to discuss this effect in a forthcoming paper. The observed positions of the PMR signals of the geminal methyl and angular methyl groups in the compounds studied in this work are listed in Table 1.

On hydrogenation of thujopsene and hinokiic acid (Ia) over palladised charcoal in methanol, a conjugate addition of hydrogen to the alkenyl*cyclopropane* system evidently takes place. From chemical and infrared evidence, structure II seemed to be correct for dihydrothujopsene and dihydrohinokiic acid⁸. This type of conjugate addition of hydrogen in catalytic hydrogenation has been observed in vinyl*cyclopropane* systems¹⁶.

The PMR spectrum of dihydrothujopsene (Fig. 5) shows three signals, at 252, 253.5, and 254.5 cps, with areas corresponding to four methyl groups. The signal at 224 cps can be assigned to a methyl group on a double bond by comparison with the spectra of hinokiic acid and dihydrohinokiic acid. The signal at 235 cps corresponds to methylene groups.

The PMR spectrum of dihydrohinokiic acid shows a strong signal at 250 cps with an area corresponding to four fortuitously overlapping methyl groups.

The proton on the double bond in dihydrothujopsene II gives rise to a comparatively sharp line at 83 cps (Fig. 5) and the absence of spin splitting would suggest the grouping :C—CH=C: . The relative sharpness of the signal from the proton on the double bond in dihydrohinokiic acid II also suggests the presence of the same grouping.

The observed PMR spectra for dihydrothujopsene and dihydrohinokiic acid are thus in good agreement with structure II for these compounds.

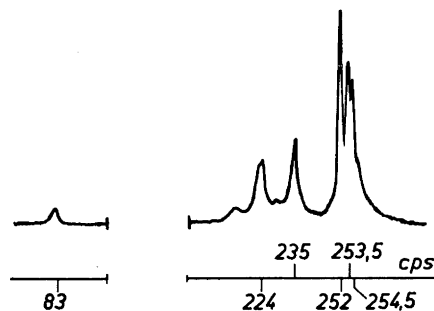


Fig. 5. The PMR spectrum of dihydrothujopsene, II. Solution in carbon tetrachloride, mole fraction 0.05. Benzene as internal reference.

EXPERIMENTAL

The PMR measurements were made with a Varian V-4300 Spectrometer operating at 40 Mc/s and equipped with a Varian V-K 3506 Stabilizer. The sample cells were thin-walled glass tubes with a good filling factor permitting studies at low concentrations. The spectra were recorded with comparatively dilute solutions in carbon tetrachloride (mole fractions 0.04–0.06). The proton chemical shifts in this work were obtained relative to benzene as internal standard. As, however, association between the small amounts of benzene used as internal standard and the substances under study could introduce large errors in the measured shifts, most shifts were also determined against an external benzene standard. The difference in the shifts determined with external and internal benzene standards were approximately constant and equal to 30 cps when no correction was made for macroscopic susceptibility effects. This seemed to justify the use of benzene as internal standard in the dilute carbon tetrachloride solutions.

The shifts were determined in cps by the audio frequency sideband method using a Hewlett-Packard 200 CD Audio Oscillator. The shift measurements were generally reproducible to within ± 1 cps.

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