# Terpenoids. IX.[1] Permanganate Oxidation of Thujopsene. 2.[2] Neutral Products

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**Synopsis.** Permanganate oxidation of thujopsene **1** in dry and aqueous acetone was reexamined with a careful separation of the neutral part of the products. In dry acetone, the major products were $\Delta^9$-thujopsen-8*β*- and 8*α*-ols (**2** and **3**) which easily decomposed to thujopsadiene **6**. In aqueous acetone, **1** gave 8*β*-hydroxythujopsan-9-one **8** and thujopsane-8*α*,9*α*-diol **11** as main products, besides 8*β*,9*β*-diol **10**, 8*α*-hydroxythujopsan-9-one **9**, and epimeric allyl alcohols **2** and **3**. The hydroxy ketone **8** was isomerized to a ring contracted compound, 4*α*-acetyl-4*β*-hydroxy-6*α*,10,10-trimethyltricyclo[4.4.0.0$^{1,3}$]decane **4** during alumina chromatography. 8*β*,9-Epoxy-10-thujopsanone **5** was isolated as a minor product. Kawamura's glycol was an eutectic mixture of **10** and **11**.

For the structural elucidation of thujopsene **1**, permanganate oxidation of this compound in dry acetone has been studied.[2,3] From the neutral part of the products, a considerable amount of "isomerized hydrocarbon" was isolated by distillation[2] and identified later as thujopsadiene **6** by the author.[4] The formation of such a diene **6** by permanganate oxidation is interesting and a reexamination was undertaken.

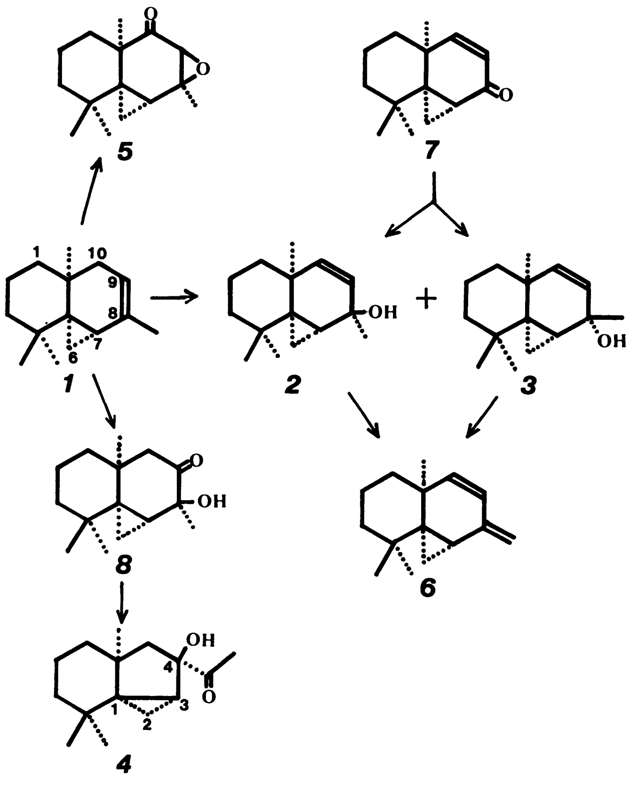
Kawamura[5] obtained a glycol, mp 92—3 °C, from thujopsene by permanganate oxidation in aqueous acetone. Later Traas et al.[6] obtained thujopsane-8*β*,9*β*-diol **10** (mp was not announced) and 8*α*,9*α*-diol **11**, mp 79—80 °C, from thujopsene by osmium tetraoxide oxidation. To clarify the relation of these products, permanganate oxidation in aqueous acetone (Kawamura's conditions) has also been carried out.

## Results and Discussion

**Oxidation in Dry Acetone:** The neutral products showed two main peaks on GLC analysis (PEG-HT), in a ratio of about 2 : 1, accompanying at least 8 minor peaks, besides unchanged hydrocarbon **1**. The mixture was chromatographed on an alumina column and the main product isolated as an oil. The IR spectrum of the oil showed the presence of an OH group. The NMR spectrum showed four tertiary methyl groups, two vinyl protons and some protons on a cyclopropane ring. The structure was considered to be $\Delta^9$-thujopsen-8*β*-ol **2**.

The second main product **3** (produced in about half the amount of **2**) crystallized and was identified as $\Delta^9$-thujopsen-8*α*-ol, mp 110—2 °C (lit, mp 110—2 °C).[7] It was unstable and decomposed, on standing, to a liquid from which thujopsadiene **6** and mayurone **7** could be separated. The amount of **6** in the neutral product was estimated as about 1% from the analysis of the hydrocarbon fraction separated by column chromatography. Therefore most of **6** previously obtained[2] was considered to be a secondary product from these allyl alcohols by dehydration during distillation.

Two major by-products were separated as crystals. One was previously described as "oxyketone," $C_{15}H_{24}O_2$, mp 68—70.5 °C.[3] The NMR data showed one acetyl group at 2.31 ppm as well as three tertiary methyl groups and some protons on the cyclopropane ring. Thus a ring contracted structure, 4*α*-acetyl-4*β*-hydroxy-6*α*,10,10-trimethyltricyclo[4.4.0.0$^{1,3}$]-decane **4** was proposed for this compound. The *β*-hydroxy configuration was based on a high field shift of H*α*-C(2) upon $NaBH_4$ reduction of **4** to the corresponding glycols. The NMR analysis of the initial mixture showed the absence of **4** and the presence of 8*β*-hydroxy-9-thujopsanone **8** (see below). Thus **4** was formed from **8** by *α*-ketol rearrangement during separation on the alumina column. Another by-product mp 75—7 °C possessed an IR band at 1690 cm$^{-1}$ which is characteristic of a C=O group adjacent to a three membered ring. NMR data showed one singlet proton on an epoxy ring at $\delta$ 3.14, four tertiary methyl groups and cyclopropane protons. Thus, the 8*β*,9-epoxy-10-thujopsanone **5** structure was assigned to this compound. The *β*-configuration of the epoxy ring was proposed, based on the high magnetic field shift of H*α*-C(6).



Since the formation of allyl alcohols on permanganate oxidation of alkenes is unfamiliar to our knowledge, further study of the structure of **2** and **3** was required. Grignard methylation of mayurone **7** gave **2** and **3** in a ratio of 1:9. Relative values of the lanthanoide-induced shift (LIS) using Eu(fod)$_3$ and Pr(fod)$_3$ are summarized in Table 1. The data show that the OH group of **3** is closer to the cyclopropane ring than that of **2**. Thus, the OH group in **3** must be in an $\alpha$-configuration, and that in **2** in a $\beta$-configuration. Interestingly, all of the three tertiary methyl groups remote from the OH group in the epimers **2** and **3** showed the same chemical shifts. The difference in the LIS values of the bridge head proton, H-C(7), in **2** and **3** is small. These results show that the epimers have the same ring conformation in which the cyclohexene ring has a boat form with a flag pole of a C(1) atom. The LIS data observed for two vinyl protons and two methylene protons on the cyclopropane ring are consistent with this conformation.

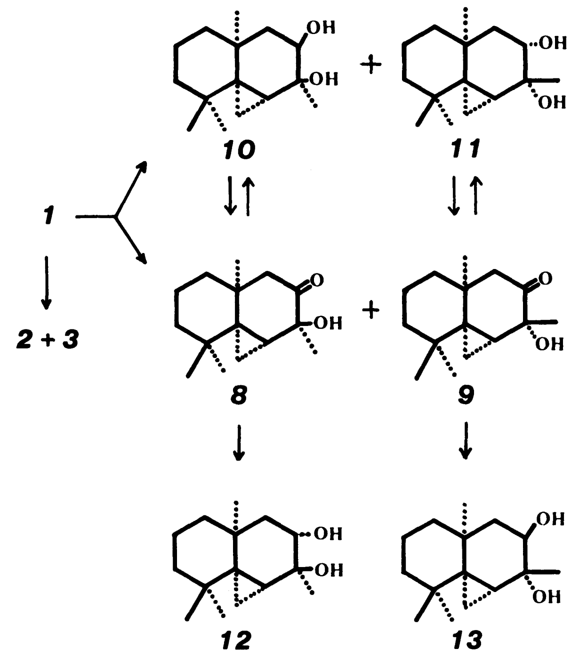


Table 1. Lanthanoide-Induced Shift (LIS) of **2** and **3**

| Proton | Chemical shift δ/ppm | | Relative LIS | |
|---|---|---|---|---|
| | **2** | **3** | **2** | **3** |
| (Cyclopropane) | | | | |
| Hα on C(6) | 0.02 | 0.22 | 0.449 | 0.754 |
| Hβ on C(6) | 0.44 | 0.39 | 0.321 | 0.465 |
| H on C(7) | 1.55 | 1.48 | 0.990 | 0.916 |
| (Vinylic) | | | | |
| H on C(9) | 5.24 | 5.10 | 0.786 | 0.983 |
| H on C(10) | 5.15 | 4.92 | 0.368 | 0.340 |
| (Methyl) | | | | |
| Me on C(8) | 1.28 | 1.40 | 1.00 | 1.00 |
| Me | 0.66 | 0.65 | 0.152 | 0.207 |
| Me | 1.07 | 1.06 | 0.143 | 0.156 |
| Me | 1.17 | 1.15 | 0.216 | 0.216 |

**Oxidation in Aqueous Acetone:** Gas chromatographic analysis of the neutral product obtained under Kawamura's conditions showed two main peaks besides more than 12 minor peaks. Chromatographic separation with silica gel gave a mixture of *cis*-8,9-diols **10** and **11** as one of the main products. The mixture of **10** and **11** showed a single peak on gas chromatography. The ratio of **10** to **11** was about 1:4 by NMR analysis. Further chromatography of the mixture on neutral alumina gave 8$\beta$,9$\beta$-diol **10**, mp 68—71 °C and 8$\alpha$,9$\alpha$-diol **11**, mp 71—3 °C. Repeated recrystallization of a mixture of **10** and **11** from hexane gave binary eutectic crystals of mp 92 °C corresponding to Kawamura's glycol.

Another main product **8** was separated as an oil. IR showed the presence of OH and C=O groups. NMR showed an isolated CH$_2$-(C=O) group, four tertiary methyl groups and a cyclopropane ring. NaBH$_4$ reduction of **8** gave **10** and a *trans*-diol **12**, mp 62—3 °C in a ratio of 2:1. CrO$_3$ oxidation of **10** in pyridine gave **8**. Thus **8** was 8$\beta$-hydroxythujopsan-9-one. Semicarbazone, mp 230 °C.

The epimeric 8$\alpha$-hydroxythujopsan-9-one **9** was obtained as a crystalline minor product, mp 97—8 °C. NaBH$_4$ reduction of **9** gave **11** and a *trans*-diol **13**, mp 76—8 °C in a ratio of about 2:3. CrO$_3$ oxidation of **11** gave **9**. $\alpha$-Ketol rearrangement of **8** was easy as described above. However, the rearrangement of **9** was found to be slow.

$\Delta^9$-Thujopsen-8$\beta$-ol (**2**) and -8$\alpha$-ol (**3**), the main products under nonaqueous conditions, became minor products.

## Experimental

The $^1$H NMR spectra were measured with JEOL JNM-PMX 60si in CDCl$_3$ solution. GLC analyses were performed on a Shimadzu GC-5A gas chromatograph with PEG-HT glass column 1.0 or 1.5 m. The column temperature was elevated from 100 to 220 °C at a rate of 5 °C min$^{-1}$.

Thujopsene **1** was separated from Hiba wood neutral oil perchased from Soda Aromatic Co., by a spinning band distillation with Tokyo Kagaku Seiki Co., Model SB 818 (1.8 m height) and the fraction of bp 124—6 °C/10 mmHg† (purity 95% up) was used immediately after passing through a silica-gel column to eliminate some autoxidation products.

**Oxidation in Dry Acetone:** Thujopsene **1** 30.4 g (0.149 mol) was dissolved in 250 ml of dry acetone and 47 g (0.30 mol) of KMnO$_4$ was added portionwise below 6 °C under nitrogen atmosphere. The mixture was stirred for 12 h and MnO$_2$ was filtered off. Evaporation of the acetone left 11.8 g of residue. The MnO$_2$ was washed twice with acetone and additional 7.7 g of extract was obtained. The combined residue was dissolved in hexane and shaken with aqueous Na$_2$CO$_3$ solution and NaOH solution successively, giving 14 g of neutral products. Gas chromatography showed unreacted hydrocarbon **1** 33.5%, thujopsadiene **6** 2%, **2** 28.5%, **3** 14.5%, **8** 6.5% and **5** 5%. Extraction of MnO$_2$ with hot water gave neutral product 1.1 g. Gas chromatography showed 67% of thujopsane-8,9-diol.

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† 1 mmHg=133.322 Pa.

**Separation by Column Chromatography:** The separation was accomplished by passage through an alumina column (320 g). Hexane eluted hydrocarbons and **5** successively. Hexane–$CH_2Cl_2$ (4:1) eluted **2**, hexane–$CH_2Cl_2$ (1:1) eluted **3** and $CH_2Cl_2$ eluted **4**. $\Delta^9$-Thujopsen-8$\beta$-ol (**2**): Oil. IR (neat) 3400 (OH), 3060, 1665, 1100, 910, and 760 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.02 (1H, dd, $J$=5 and 4 Hz), 0.44 (1H, dd, $J$=9 and 4 Hz), 0.66 (3H, s), 1.07 (3H, s), 1.17 (3H, s), 1.28 (3H, s), 1.0—1.7 (6H, m), 1.55 (1H, ddd, $J$=9, 5 and 2 Hz), 5.15 (1H, d, $J$=10 Hz), and 5.24 (1H, dd, $J$=10 and 2 Hz). $\Delta^9$-Thujopsen-8$\alpha$-ol (**3**): mp 110—2 °C. IR (KBr) 3300 (OH), 3060, 1660, 1125, 1090, 940, 750, and 738 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.29 (1H, dd, $J$=5 and 4 Hz), 0.39 (1H, dd, $J$=9 and 4 Hz), 0.65 (3H, s), 1.0—1.7 (6H, m), 1.06 (3H, s), 1.15 (3H, s), 1.40 (3H, s), 1.48 (1H, ddd, $J$=9, 5 and 2 Hz), 4.92 (1H, d, $J$=10 Hz), and 5.10 (1H, dd, $J$=10 and 2 Hz). Ring contracted hydroxy ketone **4**: mp 69—70 °C. IR (KBr) 3450, 3370, 3200, 1698, 1350, 1235, and 1048 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.35—0.82 (2H, m), 0.60 (3H, s), 1.03 (3H, s), 1.13 (3H, s), 1.3—2.3 (7H, m, broad), 1.33 (1H, d, $J$=14 Hz), 1.72 (1H, d, $J$=14 Hz), 2.31 (3H, s), and 3.75 (1H, broad). 8$\beta$,9-Epoxy-10-thujopsanone (**5**): mp 75—7 °C. IR (KBr) 3050, 3025, 1690 (C=O), 1372, 1250, 1090, 850, and 818 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.00 (1H, dd, $J$=6 and 5.5 Hz), 0.78 (1H, dd, $J$=8.5 and 6 Hz), 0.67 (3H, s), 1.05 (3H, s), 1.33 (3H, s), 1.52 (3H, s), 1.3—2.3 (6H, m), 1.77 (1H, dd, $J$=8.5 and 5.5 Hz) and 3.14 (1H, s).

**Isomerization of 8-Hydroxy-9-thujopsanone 8 to 4 by Alumina:** Eighty three mg of **8** was dissolved in hexane and loaded on a column containing 10.5 g alumina deactivated with 1.05 ml of water. After one day, 82 mg of **4** was eluted with ether as the sole product.

**Synthesis of 2 and 3 from Mayurone (7):** To a Grignard reagent from 0.080 ml of methyl iodide in 3 ml ether was added dropwise 21 mg of mayurone in 1 ml ether. After 15 min at 0 °C, the mixture was cooled on a Dry Ice methanol bath, hydrolyzed with aqueous ammonium acetate, and extracted with hexane–ether (1:1). The extract was washed twice with saturated sodium chloride, dried over sodium sulfate and evaporated to give 21 mg of residue. GLC of the residue showed 7% of **2**, and 63% of **3** besides 11% of **6** and 12% of an unidentifiable product.

**Lanthanoide-Induced Shift (LIS) of 2 and 3:** $^1$H NMR spectra were measured for ca. 20 mg of **2** and **3** in 0.35 ml $CDCl_3$ by adding stepwise Eu(fod)$_3$ and Pr(fod)$_3$ (3—5 mg for each measurement). The LIS values of $CH_3$-C(8) were from +2.4 to −8.0 ppm for **2** and from +3.4 to −5.5 ppm for **3**. A good straight line was obtained when the chemical shift values of each proton at various concentrations of the shift reagents were plotted against the corresponding values of $CH_3$-C(8). The relative value of LIS (1.00 for $CH_3$-C(8)) was obtained from the slope. The chemical shift values of cyclopropane ring protons were also obtained by extrapolating the concentration of the shift reagents to zero. The results are summarized in Table 1.

**Oxidation in Aqueous Acetone:** Potassium permanganate 14.0 g (88.6 mmol) was added portionwise to a mixture of thujopsene 14.0 g (68.5 mmol) in 140 ml of acetone and 14 ml of water under ice water cooling. The mixture was stirred overnight and filtered. The filtrate was evaporated under reduced pressure, and the residue was dissolved in hexane. The $MnO_2$ was extracted with hot water several times. The oil which separated from the water layer was extracted with hexane. The hexane solutions were combined and extracted with aqueous sodium carbonate solution. They afforded 13.4 g of neutral product and 1.7 g of acidic product. Gas chromatography of the neutral product yielded unreacted hydrocarbon **1** 26%, thujopsadiene **6** 0.4%, **2** 8.0%, **3** 4.0%, **8** 22.1%, **9** 4.5% and cis-diols (**10** and **11**) 25.1%.

**Separation:** The neutral product 27 g was chromatographed on a column (45 mm i.d. ×49 cm) packed with 350 g of Fuji gel CQ-3 silica gel. The eluent was fed with a Chemco Low Prep Pump Model 81-M-2. Hexane eluted hydrocarbons. Most of **2** and **3** were dehydrated to **6** on a $SiO_2$ column. Hydroxy ketone **8**, 5.86 g was eluted with hexane –$CH_2Cl_2$ (4:1). Hydroxy ketone **9**, 0.95 g was eluted with hexane–$CH_2Cl_2$ (1:1). Then, a mixture of *cis*-diols, **10** and **11**, 6.95 g was eluted with $CH_2Cl_2$. A similar oxidation product was chromatographed on alumina containing 10% $H_2O$ gave **4** instead of **8**. **8**: oil. IR(neat) 3480, 3050, 1715, 1140, 1090, and 958 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.43—0.86 (2H, m), 0.62 (3H, s), 1.06 (3H, s), 1.1—1.66 (7H, m), 1.20 (3H, s), 1.28 (3H, s), 1.66 (1H, d, $J$=14 Hz), 2.35 (1H, d, $J$=14 Hz), and 3.37 (1H, broad). **9**: mp 97—8 °C. IR(KBr) 3480, 3070, 3050, 1704, 1168, and 1106 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.44—0.80 (2H, m), 0.70 (3H, s), 1.06 (3H, s), 1.18 (3H, s), 1.4—1.75 (7H, m), 1.52 (3H, s), 2.10 (1H, d, $J$=16.5 Hz), 2.31 (1H, d, $J$=16.5 Hz) and 2.92 (1H, broad).

**Reduction of 8 and 9:** **8** (385 mg) was dissolved in methanol (20 ml) and reduced with excess $NaBH_4$. The product (319 mg) was chromatographed on a silica-gel column (10 g). Methylene chloride eluted 175 mg of **10**, mp 68—71 °C. Ether eluted 85 mg of 8$\beta$,9$\alpha$-diol **12**. **12**: mp 61—3 °C (recrystallized from hexane). IR (Nujol) 3440, 3150, 1170, 1140, 1103, 1080, and 1035 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=−0.01—0.57 (2H, m), 0.55 (3H, s), 0.9—1.9 (9H, m), 0.96 (3H, s), 1.07 (3H, s), 1.18 (3H, s), 2.47 (2H, broad), and 3.75 (1H, X part of ABX, $J_{AX}+J_{BX}$=16.5 Hz).

Hydroxy ketone **9**, 387 mg was reduced similarly, to give 53 mg of **11**, mp 72—3 °C and 82 mg of 8$\alpha$,9$\beta$-diol **13**. **13**: mp 76—8 °C (from hexane). IR (Nujol) 3300, 1145, 1106, and 1082 cm$^{-1}$. $^1$H NMR ($CDCl_3$) $\delta$=0.29—0.66 (2H, m), 0.79 (6H, s), 1.09 (3H, s), 1.1—1.7 (9H, m), 1.33 (3H, s), 2.25—2.57 (3H, m, broad), and 3.51 (1H, X part of ABX, $J_{AX}+J_{BX}$=16.5 Hz).

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