BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 51 (8), 2439—2440 (1978)

Oxidation of Thujopsene with Thallium Triacetate in Acetic Acid

Haruo SEKIZAKI,* Masaaki ITO, and Shoji INOUE**

Chemistry Laboratory, Department of General Education, Higashi Nippon Gakuen University, Onbetsu-cho, Hokkaido 088-01

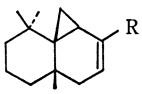
***Faculty of Pharmacy, Meijo University, Tenpaku-ku, Nagoya 468*

(Received January 17, 1978)

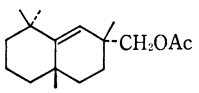
Synopsis. Oxidation of thujopsene with thallium triacetate in acetic acid at room temperature gave a stereospecifically ring-contracted ketone (**3**) in 76% yield, whereas oxidation at 50 °C afforded an allylic oxidation product in 72% yield. The configuration of **3** was estimated by the NMR spectrum of a compound derived from it.

Oxidation of thujopsene (**1a**) with metal acetate was first described in 1959 by Nagahama *et al.*,[1] who used lead tetraacetate to try to determine the partial structure of **1a**. Recently, one of us[2] reported that oxidation of **1a** with mercury diacetate gave a mixture of allylic oxidation products, (**1b**) and (**1c**), and an acid-catalyzed isomerization-acetoxylation product (**2**).

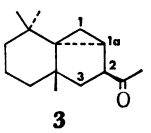
This report describes some interesting results about the oxidation of thujopsene (**1a**) with thallium triacetate.[3] We have found that oxidation of **1a** with thallium triacetate in acetic acid at room temperature gave a stereospecifically ring-contracted product (**3**) and **1b** in 76 and 10% yield respectively, whereas, oxidation of **1a** at 50 °C gave mainly the product (**1b**) (72%), resulting from allylic oxidation of **1a**, together with the ketone **3** (8%). The product (**3**) was already reported by Nagahama *et al.*,[1] but the configuration of the acetyl group in **3** has not been reported.



1a: R=CH_3
1b: R=CH_2OAc
1c: R=CHO



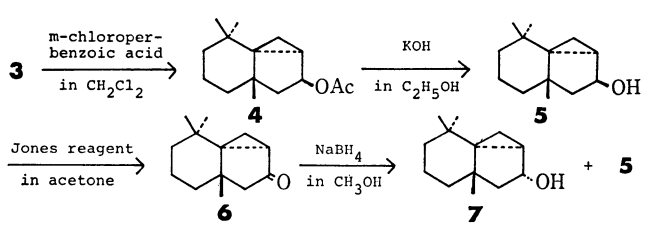
2



3

We estimated the relative configuration of the ketone **3** as follows. Alcohols, **5** (β-OH) and **7** (α-OH), were derived from **3** according to the method shown in Scheme 1. The structures of **1b**, **3**, **4**, **5**, and **6** were identical with authentic specimens (mp, IR).[1,2]

The NMR spectrum of C_2–H in the ketone **3** shows a doublet of doublets of doublets ($J_{C_2H-C_{1\alpha}H}$=10.0, $J_{C_2H-C_{3\beta}H}$=10.0, and $J_{C_2H-C_{3\alpha}H}$=4.0 Hz) at 3.07 ppm. On the other hand, the spectrum of C_2–H in the β-hydroxy alcohol **5** shows a doublet of doublets of doublets ($J_{C_2H-C_{1\alpha}H}$=8.0, $J_{C_2H-C_{3\beta}H}$=8.0, and $J_{C_2H-C_{3\beta}H}$=1.8 Hz) at 4.46 ppm, but that of C_2–H in the α-hydroxy alcohol **7** shows a doublet of doublets ($J_{C_2H-C_{3\beta}H}$=6.0, and $J_{C_2H-C_{3\beta}H}$=6.0 Hz) at 4.11 ppm. In these results, the spectrum of the C_2–H proton in **3** showed a pattern for the C_2–H which was in close agreement with the corresponding proton observed in β-hydroxy alcohol **5**, and therefore the acetyl group of **3** was assigned to be β.



Scheme 1.

Oxidation of thujopsene (**1a**) with mercury diacetate[2] gave two allylic oxidation products, **1b** and **1c**, in 14.4 and 11.1% yield respectively, together with the other product **2** (5.4%). With lead tetraacetate,[1] **1a** was oxidized to the ring-contracted ketone **3** in 35% yield. However, with thallium triacetate, the ring-contracted ketone **3** was obtained in higher yield at room temperature and the acetate **1b** was obtained in higher yield at 50 °C on allylic oxidation. It is interesting that oxidation of thujopsene (**1a**) with thallium triacetate gives different products up to reaction temperature. The extention of oxythallation reaction to other compounds including allyl methyl moiety in their molecules would be valuable.

Experimental

The melting points were determined on a Yanagimoto micro melting point apparatus and uncorrected. The NMR spectra were recorded on a JEOL PMX-60 spectrometer at 60 MHz and on a JEOL PS-100 spectrometer at 100 MHz, using Me_4Si as an internal standard.

The IR spectra were determined on a Shimadzu IR-400 spectrometer.

Oxidation of Thujopsene (1a) at Room Temperature. To a stirred solution of thallium triacetate (1.19 g, 5 mmol) in acetic acid (10 ml) was added dropwise a solution of **1a** (1.02 g, 5 mmol) in acetic acid (20 ml) under nitrogen atmosphere at room temperature in 30 min. The mixture was stirred for 10 h, then poured into ice–water and extracted with ether. The extract was washed with aqueous $NaHCO_3$ solution, water, dried (Na_2SO_4), and evaporated to give an oily residue (1.32 g). The products were separated by column chromatography using silica gel. Elution with benzene gave **3** (791 mg) and **1b** (130 mg) as colorless liquids. The pure samples of **3** and **1b** were obtained by distillation under reduced pressure. **3**: bp 127—129 °C/7 mmHg. NMR ($CDCl_3$) 0.75 (s, 3, CH_3), 1.15 (s, 3, CH_3), 1.13 (s, 3, CH_3), 2.20 (s, 3, Ac), and 3.07 (ddd, 1, J=10.0, 10.0, and 4.0 Hz, C_2–H); 2,4-dinitrophenylhydrazone: mp 168—169 °C (lit,[1] mp 170—170.5 °C). Found: C, 62.11; H, 7.05; N, 13.99%. Calcd for $C_{19}H_{24}O_4N_4$: C, 62.98; H, 7.05; N, 13.99%. **1b**: bp 148—150 °C/6 mmHg.

Oxidation of Thujopsene (1a) at 50 °C. To a stirred solution of **1a** (1.02 g, 5 mmol) in acetic acid (30 ml), kept at 50 °C, was added thallium triacetate (1.91 g, 5 mmol) in portions under nitrogen atmosphere over 30 min. The mix-

ture was stirred for 7 h at the same temperature, then the same work up as that mentioned above gave **1b** (997 mg) and **3** (83 mg).

Oxidation of ***3***. To a stirred solution of **3** (2.20 g, 10 mmol) in dichloromethane (20 ml), kept at 7 °C, was added dropwise a solution of *m*-chloroperbenzoic acid (2.60 g, 11 mmol) in dichloromethane (20 ml) in 1 h. The mixture was stirred at room temperature overnight, then the usual work up gave crude **4** (2.61 g), which was chromatographed on a silica gel column. Elution with benzene gave **4** (2.28 g): colorless liquid; NMR ($CDCl_3$) 0.56 (s, 3, CH_3), 1.01 (s, 3, CH_3), 1.06 (s, 3, CH_3), 2.01 (s, 3, OAc), and 5.21 (m, 1, olefinic proton).

Hydrolysis of ***4***. The compound **4** (2.28 g) was hydrolyzed in alcohol (20 ml) with potassium hydroxide (860 mg) for 3 h. After the usual workup a crude product (2.23 g) was obtained. Sublimation under a reduced pressure gave **5** (1.91 g): mp 82—83 °C (lit,[1] mp 78 °C; NMR ($CDCl_3$) 0.51 (s, 3, CH_3), 1.01 (s, 3, CH_3), 1.05 (s, 3, CH_3), and 4.46 (ddd, 1, J=8.0, 8.0, and 1.8 Hz, C_2–H).

Oxidation of ***5***. The compound **5** (776.8 mg) was oxidized in acetone (10 ml) with the Jones reagent (8N, 1.1 ml) at room temperature for 2 h. The mixture was evaporated and ice-cooled water was poured into the resulting residue, which was then extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to give crude crystals (778.2 mg). Recrystallization from hexane gave pure **6** (761.8 mg): mp 126—127 °C (lit,[1] mp 118—121 °C); NMR ($CDCl_3$) 0.66 (s, 3, CH_3), 1.13 (s, 3, CH_3), and 1.21 (s, 3, CH_3).

Reduction of ***6***. The compound **6** (407.8 mg) was reduced in methanol (10 ml) with sodium borohydride (200 mg) at 15 °C for 2 h. The usual workup gave a crude product (414.7 mg), which was chromatographed on a silica gel column. Elution with benzene gave α-hydroxy alcohol **7** (267.8 mg) and β-hydroxy alcohol **5** (100.7 mg). **7**: mp 107—108 °C (hexane); IR (KBr) 3350 (OH) and 3050 (cyclopropyl) cm^{-1}; NMR ($CDCl_3$) 0.60 (s, 3, CH_3), 1.05 (s, 6, CH_3), and 4.11 (dd, 1, J=6.0 and 6.0 Hz, C_2–H); Found: C, 79.17; H, 11.66%. Calcd for $C_{13}O_{20}O$: C, 80.35; H, 11.96%.

The authors are grateful to Takasago Perfumery Co. Ltd. for giving us the sample of crude thujopsene.

References

1) S. Nagahama, H. Kobayashi, and S. Akiyoshi, *Bull. Chem. Soc. Jpn.*, **32**, 366 (1959).

2) M. Ito. K. Abe, and H. Takeshita, *Bull. Chem. Soc., Jpn.*, **45**, 1913 (1972).

3) A. Mekillopand E. C. Taylor, *Chem. Brit.*, **9**, 4 (1973).