Oxidation of Thujopsene with Lead Tetraacetate

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Synopsis. We inveatigated the oxidation of thujopsene with lead tetraacetate. In the hydrolysis product, two new sesquiterpenoids were found to be afforded: 6α,10,10-trimethyl-4β-acetyltricyclo[4.4.0.0^{1,3}]decane and its $C_{(4)}$-stereoisomer.

It has been reported by Nagahama *et al.*[1] that the lead tetraacetate oxidation of **1** was accompanied by ring contraction; this was a new reaction. However, the structures of the oxidation product were not well-defined. In the course of our investigation of the oxidation, therefore, we have now isolated the components of the oxidation product and defined their structures well on the basis of the MS, IR, and NMR spectra.

Results and Discussion

The reaction was carried out by adding minium trilead tetraoxide to a mixture of thujopsene, **1**, acetic acid, and acetic anhydride. The reaction product was hydrolyzed to give three components (**2**: **3**: **4**=6: 87: 7 in GLC). The hydrolysis product was fractionated by distillation under reduced pressure, and each component was isolated by GLC. Their products are shown in Fig. 1. Compound **4** was identified with authentic widdrol on the basis of the MS, IR, and NMR spectra.

Compound **2** was determined to have a molecular formula of $C_{15}H_{24}O$ on the basis of the MS spectra and the results of the elemental analysis, and it was characterized as a saturated ketone on the basis of the IR (C=O, 1700 cm^{-1}) absorption band. The ^{1}H-NMR spectra revealed the presence of the following functional groups: a *gem*-dimethyl (6H, two s), a tertiary methyl (3H, s), an acetyl (3H, s), a methine (1H, dd), and a methylene of a cyclopropane ring (2H, m). The ketone

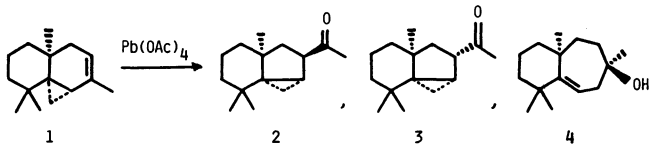

Fig. 1. Oxidation products of thujopsene **1**.

was deduced to be 6α,10,10-trimethyl-4-acethyltricyclo-[4.4.0.0^{1,3}]decane.

Compound **3** was determined to have a molecular formula of $C_{15}H_{24}O$ on the basis of the MS spectra and the results of the elemental analysis; it was characterized on the basis of the close resemblance to most of the fragment ions of the MS spectrum of **2**. Also the ^{1}H-NMR spectra revealed the presence of the same functional groups as **2**. These findness supported the idea that **3** was the $C_{(4)}$stereoisomer of **2**.

In order to define each configuration of the acetyl group and the $C_{(2)}$-methylene of **2** and **3**, the coupling constant of $C_{(4)}$-methine, the variation in the chemical shift of each proton with an increase in the concentration of the shift reagent (Eu(dpm)$_3$: Tris(dipivaloylmethanato)europium(III)), and the NOE were measured in the ^{1}H-NMR spectra (Table 1). As a result, the $C_{(4)}$-methine of **2** revealed double doublet (J=2.5 Hz, 10 Hz), while the $C_{(4)}$-methine of **3** revealed a double quartet (ddd, J=5 Hz, 8.5 Hz, 10 Hz). The chemical shift of the $C_{(10\alpha)}$-methyl of **3** was enlarged further in comparison with those of **2** with an increase in the concentration of Eu(dpm)$_3$. Besides the NOE was observed on **3**, because, when the $C_{(2)syn}$-proton of **3** at 0.33 was irradiated, the integration of the acetyl proton of **3** at δ 2.19 was increased (44% of NOE), while the $C_{(6\alpha)}$-methyl of **3** at δ 1.09 was enlarged (42% of NOE). This behavior showed their structures

Table 1. Variation in the chemical shift for different protons of (**2**) and (**3**) (1×10^{-4} mol in 0.5 ml of $CDCl_3$) with an increase in Eu(dpm)$_3$

Eu(dpm)$_3$ 10^{-4} mol	δ ppm(ΔEu(dpm)$_3$[a])							
	2				**3**			
	$COCH_3$	$C_{(6\alpha)}$-CH_3	$C_{(10\beta)}$-CH_3	$C_{(10\alpha)}$-CH_3	$COCH_3$	$C_{(6\alpha)}$-CH_3	$C_{(10\beta)}$-CH_3	$C_{(10\alpha)}$-CH_3
0	2.18	1.07	0.63	1.00	2.19	1.09	0.60	1.01
0.1	2.49 (0.31)	1.12 (0.05)	0.66 (0.03)	1.03 (0.03)	2.58 (0.39)	1.15 (0.06)	0.65 (0.05)	1.06 (0.05)
0.2	3.10 (0.92)	1.19 (0.12)	0.76 (0.13)	1.06 (0.06)	3.32 (1.13)	1.27 (0.18)	0.78 (0.18)	1.14 (0.13)
0.3	4.02 (1.84)	1.35 (0.28)	0.90 (0.27)	1.10 (0.10)	4.27 (2.08)	1.38 (0.29)	0.88 (0.28)	1.22 (0.21)
0.4	4.90 (2.72)	1.44 (0.37)	1.02 (0.39)	1.18 (0.18)	5.14 (2.95)	1.52 (0.43)	1.00 (0.40)	1.31 (0.30)
0.5	5.80 (3.62)	1.61 (0.54)	1.14 (0.51)	1.29 (0.29)	6.12 (3.93)	1.68 (0.59)	1.16 (0.56)	1.43 (0.42)

a) Δ Eu(dpm)$_3$=δ Eu(dpm)$_3$−δ $CDCl_3$.

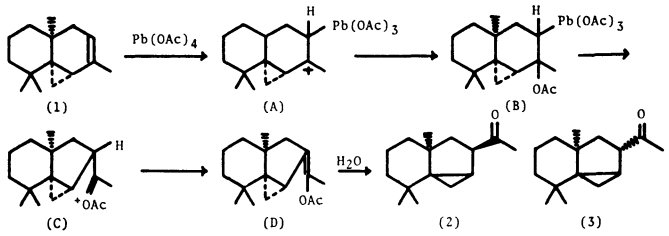

Fig. 2. Mechanism for the formation of **2** and **3**.

to be 6α,10,10-trimethyl-4-acetyltricyclo[4.4.0.$0^{1,3}$]-decane **2** and its $C_{(4)}$-stereoisomer, **3**.

In the reaction, the formation of the products, **2** and **3**, could be explained by the reaction sequence shown in Fig. 2: firstly, the addition of lead tetraacetate to the olefin of **1** may give an intermediate (**B**); the degration of **B** will give an enol acetate (**D**) (it was difficult to isolate **D**), accompanied by ring-contraction. The resulting stereoisomers (**2** and **3**) may be formed by the hydrolysis of **D**.

Experimental

Materials. Thujopsene, **1**, was obtained by distillation from chinese cedar wood oil (provided by the Takasago Perfumary Co., Ltd.); bp 118—120 °C/10 Torr, $d_4^{25}=0.9316$, $n_D^{25}=1.5019$, $[\alpha]_D^{29}=-77.4°$ (neat), purity in GLC 99%.

Measurements. The MS spectra were measured on a Shimadzu LKB 9000 gas chromatography mass spectrometer (acceleration voltage, 3500V; ionization potential 70 eV). The IR spectra were recorded on a Nihonbunko IRA-2 apparatus (Diffraction Grating Infrared Spectrophotometer). The ^{1}H-NMR spectra were recorded on a Hitachi Parkin-Elmer R-24 (60 MHz) spectrometer, using TMS as the internal standard, unless otherwise mentioned, in $CDCl_3$. The column chromatography depended on silica gel (Wako-gel C-300). The GLC was carried out with a separation column (3 mm×4 m) packed with 5% PEG-20M or 5% OV-17 on Chromosorb AW-DMCS (60—80 mesh).

Reaction of Thujopsene (1) with Lead Tetraacetate. To a mixture of 5 g (0.025 mol) of **1**, 48 g of acetic acid, and 17 g of acetic anhydride, we added 17.2 g of minium trilead tetra oxide in portions over a period of 1.5 h, the temperature being kept below 60 °C. Stirring was then continued for one additional hour. Water was added, and the solution was neutralized with sodium carbonate, filtered, and extracted with benzene. This benzene solution was washed with water again and dried over sodium sulfate. When the solvent was then removed, 6.4 g of a residue were obtained. $n_D^{25}=1.4941$, $d_4^{25}=0.9838$, $EV=10.6$, $[\alpha]_D^{25}=-0.07°$ (neat), The residue (3.5 g) was hydrolyzed with a 2 mol dm^{-3} sodium hydroxide-ethanol solution. After the ethanol had been removed, water and benzene were added with shaking and the organic layer was separated. This organic layer was washed and dried over sodium sulfate. The benzene was then removed; subsequent distillation gave 3.1 g of products which had three components (**2**: **3**: **4**=6: 87: 7). Bp 134—139 °C/2 Torr, $n_D^{25}=1.4975$, $d_4^{25}=0.9836$, $[\alpha]_D^{25}=-0.05°$(neat). Semicarbazone: mp 236—237 °C (dec, from 90% ethanol). A ketone regenerated from the semicarbazone had two components (**2**: **3**=2: 98) in GLC.

6α,10,10-Trimethyl-4β-acetyltricyclo[4.4.0.$0^{1,3}$]decane (2). Found: C, 81.59; H, 11.05%. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98%. MS(*m/e*) 220 (M^+, 62%), 205 ($M-CH_3$, 42), 177 ($M-COCH_3$, 100), 161 (39), 137 (83), 123 (84), 121 (87), 107 (72), 105 (56), 95 (72), 91 (56), 81 (50). IR ν-(cm^{-1}) 3400, 1700 (C=O), 3050, 1020 (cyclopropane ring), 1380, 1368 (*gem*-CH_3). NMR ($CDCl_3$) δ (ppm) 0.17—0.80 (2H, m), 0.63, 1.00, 1.07 (9H, each s, *t*-CH_3), 2.18 (3H, s, $-COCH_3$), 2.63 (1H, dd, $J=2.5$ Hz, 10 Hz, -COCH).

6α,10,10-Trimethyl-4α-acetyltricyclo[4.4.0.$0^{1,3}$]decane (3). Found: C, 81.63; H, 11.01%, Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98%. $d_4^{25}=0.9773$, $n_D^{25}=1.4918$. MS (*m/e*) 220 (M^+, 27%), 205 ($M-CH_3$, 27), 177 ($M-COCH_3$, 100), 161 (19), 137 (26), 123 (46), 121 (50), 107 (58), 105 (29), 95 (62), 93 (34), 91 (30), 81 (50), 69 (31). IR ν(cm^{-1}) 3400, 1700 (C=O), 3050, 1020 (cyclopropane ring), 1378, 1366 (*gem*-CH_3). NMR ($CDCl_3$) δ (ppm) 0.33 (1H, s, $C_{(2)syn}$-H), 0.44 (1H, br. s, $C_{(2)anti}$-H), 0.58, 1.00, 1.08 (9H, each s, *t*-CH_3), 2.17 (3H, s, $-COCH_3$), 3.05 (1H, ddd, 5 Hz, 8.5 Hz, 10 Hz, -COCH).

Widdrol (4). Mp 97.5—98 °C (colorless needle, from hexane). MS (*m/e*) 222 (M^+, 14%), 204 ($M-H_2O-CH_3$, 22), 151 (100), 121 (38), 119 (51), 93 (44). IR ν(cm^{-1}) 3350, 1100 (OH), 1382, 1368 (*gem*-CH_3). NMR ($CDCl_3$) δ (ppm) 1.08 (6H, s, $C(CH_3)_2$), 1.18 (3H, s, *t*-CH_3), 1.20 (3H, s, $C(OH)CH_3$), 1.42 (1H, s, OH), 5.48 (1H, m, =CH–).

Reference

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