Furanoeremophilan-14β,6α-olide. A New Furanosesquiterpene Lactone of an Eremophilane-type from *Ligularia Hodgsoni* Hook, f.[1)]

Yoshiaki Ishizaki, Yoshiaki Tanahashi, Takahiko Tsuyuki,
Takeyoshi Takahashi,* and Kazuo Tori**

Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113
***Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553*

(Received October 21, 1978)

A new sesquiterpene lactone of an eremophilane-type was isolated from *Ligularia Hodgsoni* Hook, f., and the structure including the absolute stereochemistry was shown to be furanoeremophilan-14β,6α-olide.

In connection with chemical investigations[2)] on plants of the genus *Ligularia* (Compositae), we examined sesquiterpene constituents of *Ligularia Hodgsoni* Hook, f. (Japanese name: Tōgebuki), and isolated a new sesquiterpene lactone together with furanoeremophilane,[3,4)] bakkenolide-A[5)] (fukinanolide[6)]) and eremophilenolide.[4,7)] This paper describes the structure determination leading to furanoeremophilan-14β,6α-olide (**1**) for this new sesquiterpene lactone.

A benzene extract of dried roots of the plant was further treated with petroleum ether and the petroleum ether-soluble fraction was subjected to purification by sublimation and recrystallization to afford a furanolactone (**1**) (pink color to the Ehrlich test) as crystals, mp 136—138 °C. Elemental analysis and the mass spectrum indicate the formula $C_{15}H_{18}O_3$. The IR, UV, and ^1H NMR spectra showed the presence of a tertiary methyl, an olefinic methyl, a γ-lactone, and a β-methyl-substituted furan moiety with an α-proton.[8)] Signals due to a secondary methyl was absent (*cf.* Table 1 and Experimental).

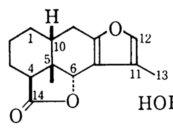
The lactone (**1**), on reduction with lithium aluminium hydride, gave a diol (**2**), which was readily converted into an ether (**3**) by treatment with *p*-toluenesulfonyl chloride in pyridine. The ^1H NMR spectrum of **3** showed signals due to the AB part of an ABX spin system; this implies the presence of methylene protons in the α-position and of a methine proton in the β-position to the ether oxygen atom. The presence of a tertiary methyl and a proton on a carbon atom bearing the ether oxygen atom was also shown in the NMR spectrum (Table 1).

The carbon skeleton and the absolute configuration of the lactone (**1**) were shown by the following transformation. The lactone (**1**) was subjected to hydrogenolysis in the presence of 10% palladium–charcoal in ethanol to afford a carboxylic acid (**4**). The presence of the carboxyl group and the absence of the hydroxyl group in **4** were suggested by the IR spectrum and the formation of an ester. Reduction of the carboxylic acid

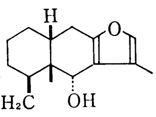
Table 1. Chemical shifts (δ) and coupling constants (Hz) of **1**, **3**, **8**, and **10**

	1		**3**	**8**		**10**	
	$CDCl_3$	$(CD_3)_2CO$	$CDCl_3$	$CDCl_3$	$(CD_3)_2CO$	$CDCl_3$	$(CD_3)_2CO$
5-Me	1.26	1.24	1.16	1.25	1.27	1.12	1.11
11-Me	2.03	2.01	2.03	2.05	2.02	2.02	1.97
9α-H	2.7	2.76	2.64	2.45	2.43	2.28	2.28
9β-H		2.62	2.48	2.87	2.90	2.82	2.82
4-H	a)	a)	a)	a)	2.67	a)	a)
6β-H	5.08	5.08	4.63	4.90	4.97	4.17	4.10
14α-H	—	—	3.91	—	—	4.00	3.91
14β-H	—	—	3.53	—	—	3.78	3.75
12-H	7.06	7.19	7.01	7.09	7.21	7.04	7.10
J-values							
9α,9β		−17.3	−16.6		−17.1		−16.9
9α,10		11.3	11.5		1.7		1.9
9β,10		5.9	6.1		6.3		5.6
6,9α		1.8	1.8		0.3		b)
6,9β		1.2	1.3		1.5		1.5
9α,12		b)	b)		0.5		0.5
9β,12		b)	b)		0.9		0.9
11,12		1.0	1.0		1.2		1.1
12,13		1.1	1.1		1.1		1.1
14α,14β		—	−7.4		—		−9.0
4,14α		—	7.3		—		8.6
4,14β		—	11.3		—		3.6

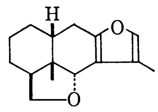
a) Undeterminable. b) Not measured.



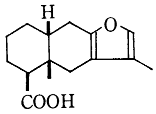
1



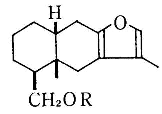
2



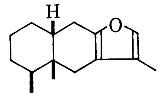
3



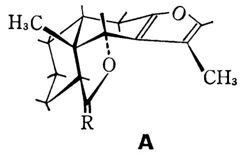
4



5 R = H
6 R = Ts



7



A

1 R = O
3 R = H₂

(**4**) with lithium aluminium hydride gave an alcohol (**5**), which was subsequently converted into a tosylate (**6**). The tosylate (**6**) was treated with lithium aluminium hydride to furnish the known furanoeremophilane (**7**).[3,9)]

Since the basic skeleton of the lactone (**1**) was shown to consist of furanoeremophilane, the structure, furanoeremophilan-14β,6ξ-olide, is suggested for this lactone on the basis of the spectral data, showing the absence of the secondary methyl and the presence of the γ-lactone. The structure **3** for the ether is compatible with the spectral data. However, the configuration of the carbon atom in the 6-position bearing the ether-type oxygen atom in the lactone moiety was still obscure. The configuration at C-6 and the stereostructure could be established by the NMR measurement using spin-decoupling experiments and intramolecular nuclear Overhauser effect (NOE) measurements.[10)] The result on **1** is shown in Tables 1 and 2. The fact that 6-H is only coupled weakly ($^5J<2$ Hz) to the allylic 9α- and 9β-protons, suggests that the 6-H is adjacent to the furan ring and that the other neighbor, C-5, bears no proton. On saturation of the signals due to the tertiary methyl at C-5β and the β-methyl on the furan ring, the signal due to the 6-H showed increases by 28 and 6% in area, respectively. These observations imply that the 6-H is situated *cis* to the tertiary methyl, indicating 6β-H orientation, and is attached to the other β-position on the furan ring. On triple irradiation at the resonance frequencies of 6-H and 12-H in acetone-d_6, the signals due to 9α-H and 9β-H exhibited the AB part of an ABX spin system, which gave $^2J_{9\alpha,9\beta}=-17.3$, $^3J_{9\alpha,10}=11.3$, and $^3J_{9\beta,10}=5.9$ Hz. Therefore, one of the methylene protons on C-9 was shown to be in *trans* or eclipsed conformation with respect to 10β-H. Triple irradiation on 12-H and 11-methyl signals determined two homoallylic coupling constants, $^5J_{6,9\alpha}=1.8$ and $^5J_{6,9\beta}=1.2$ Hz.[11)] These two large ^5J values indicate that the 6-H has a quasi-axial conformation.

Interpretation of the NMR spectrum of **3**, as shown in Table 1, is in full accord with that of the data on the lactone (**1**). This means that no stereochemical change occurred during the transformation of **1** to **3**. The β-configuration of C-14 methylene was supported by the following NOE measurement. On saturation of the signal due to the 5β-methyl by double irradiation, the signal due to one of the methylene protons, 14β-H, at δ 3.53 ($^3J_{4,14\beta}=11.3$ and $^2J_{14\alpha,14\beta}=-7.4$ Hz) showed a substantial increase in area, while 14α-H signal at δ 3.91 ($^3J_{4,14\alpha}=7.3$ and $^2J_{14\alpha,14\beta}=-7.4$ Hz) caused no increase in area (Table 2).

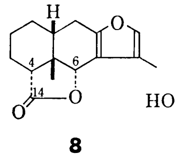
Table 2. Nuclear overhauser effects ($\pm$2%, in $CDCl_3$)

Observed proton	Saturated proton	1	3	8	10
12-H	11-Methyl	22	17	22	16
6β-H	11-Methyl	6	7	4	6
6β-H	5-Methyl	28	23	20	16
14β-H	5-Methyl	—	8	—	8
14α-H	5-Methyl	—	−2	—	0
9β-H	5-Methyl	a)	a)	a)	0
4-H	5-Methyl	b)	b)	≈15	b)

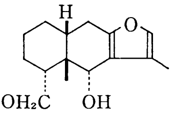
a) Not measured. b) Unobservable.

It is concluded that the structure including the absolute configuration of the new lactone (**1**) should be formulated as furanoeremophilan-14β,6α-olide and the stereostructure could be depicted as shown in **A**.

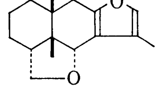
During the purification of the lactone (**1**), it was shown that the lactone (**1**) isomerizes easily into franoeremophilan-14α,6α-olide (**8**) on treatment with a base. The lactone (**1**) in benzene was kept contacting with basic alumina for 6 h and eluted with benzene. The eluent was examined by GLC and was shown to be a mixture of **1** and **8** in a ratio of 1 : 5. Prolonged contact with alumina resulted in a preferential isomerization into **8** accompanying concomitant hydrolysis of the lactones. Repetition of fractional recrystallization of the isomeric mixture of **1** and **8** gave pure furanoeremophilan-14α,6α-olide (**8**). The isomerized lactone (**8**) showed similar spectral features (Table 1) to those of **1**, and gave an ether (**10**) by the same treatment as in the case of **1**. Reduction of **8** with lithium aluminium hydride gave



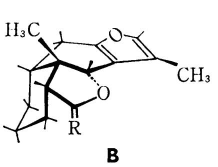
8



9



10



B

8 R = O
10 R = H₂

a diol (**9**; not identical with **2**), which, on dehydration with *p*-toluenesulfonyl chloride in pyridine, afforded the ether (**10**; not identical with **3**). From these observations, the isomerized lactone (**8**) was inferred to be a 4-epimer of **1**.

Proton magnetic double and triple resonance experiments gave the information on the stereochemistry of **8** and **10**. On triple irradiation at the resonance frequencies of 6-H and 12-H in **8**, the signals of 9α-H and 9β-H exhibited the AB part of an ABX spin system, which gave coupling constants, $^2J_{9\alpha,9\beta}=-17.1$, $^3J_{9\alpha,10}=1.7$, and $^3J_{9\beta,10}=6.3$ Hz. Irradiation on 12-H revealed the presence of the two homoallylic coupling constants, $^5J_{6,9\alpha}\leq 0.3$ and $^5J_{6,9\beta}=1.5$ Hz, between 6-H and the methylene protons on C-9. On triple irradiation at the resonance frequencies of 6-H and 11-methyl, the signal due to 12-H showed a quartet as the X part of an ABX spin system. This observation indicates the presence of a long-range coupling between 12-H and the methylene protons on C-9 ($^5J_{9\alpha,12}\leq 0.5$ and $^5J_{9\beta,12}=0.9$ Hz). On saturation of the signal due to the 5-methyl group by double irradiation, a triplet signal at δ 2.67 caused an increase in area (Table 2), indicating that the triplet could be assignable to 4β-H and, therefore, the lactone carbonyl grouping in **8** is oriented in the α-configuration.

The fact that the NMR spectrum of the ether (**10**) is similar to that of the epimerized lactone (**8**) indicates that there is no apparent conformational difference between **10** and **8**. In comparison of the NMR spectra of **1** and **3** with those of **8** and **10**, the following differences are seen: 1) the $^3J_{9\alpha,10}$ values of **8** and **10** (1.7 and 1.9, respectively) are small compared with those of **1** and **3** (11.3 and 11.5 Hz, respectively); 2) the $^3J_{4,14\beta}$ value of **3** (11.3) is larger than that of **10** (3.6 Hz); and 3) in the spectrum of **10**, the 6-H signal is shifted to a higher field by −0.46 ppm in $CDCl_3$ than that of **3**. The NOEs observed for **8** and **10** are quite similar to those observed for **1** and **3**, respectively, except for the data of 4-H (Table 2). From these observations, conformation **B** can be suggested to be the most popular in solution for furanoeremophilan-14α,6α-olide (**8**) and the ether (**10**).

Experimental

General Procedures. All melting points were measured on a hot block, unless otherwise stated, and reported uncorrected. IR spectra were taken on a Hitachi EPI-G2 spectrometer. UV absorption spectra were determined in a methanol solution on a Hitachi EPS-3 spectrometer. ORD curves were measured on a JASCO Model ORD/UV-5 spectrometer. Measurements of optical rotation were carried out using a JASCO-SL polarimeter. ^{1}H NMR spectra were taken on a JNM-3H-60, a JNM-4H-100 spectrometer (JEOL), or a Varian HA-100 spectrometer in the internal TMS-locked mode. Proton magnetic double and triple resonance experiments were performed using the Varian HA-100 spectrometer with two Hewlett-Packerd HP-200 ABR audio-oscillators and an HP-5212A electronic counter. NOEs were measured by % increases in integrated signal intensities with necessary caution.[10] Chemical shifts are expressed in δ (ppm downfield from internal TMS) and coupling constants in Hz. Accuracies are *ca.* ±0.02 ppm for δ and ±0.2 Hz for *J* values. Mass spectra were measured on a Hitachi RMU-6-Tokugata mass spectrometer at 70 eV with a direct inlet system, unless otherwise stated.

GLC analyses were carried out using a Shimadzu GC-4APF equipped with a hydrogen flame ionization detector (column: Diasolid H-523 (2 m), temp 230 °C). Column chromatography was carried out on silica gel (Wakogel C-200) or on activated alumina (Showa Chemicals). Kieselgel G (E. Merck) was used for analytical (in 0.25 mm thickness) and preparative (in 0.5 mm thickness) TLC.

Isolation. Dried roots (1.7 kg) of *Ligularia Hodgsoni* HOOK, f. were extracted with benzene (2.5 l) for 4 days. The extraction under the same conditions was repeated three times and the extracts were combined and concentrated to give a dark brown tar (54 g). The residue was dissolved in petroleum ether with warming and insoluble materials were removed by decantation. The organic layer, on evaporation, gave a residue (46 g), which was sublimed under reduced pressure. Recrystallization of the sublimate (11 g), which was obtained at 100—120 °C (bath temperature), from ethyl acetate afforded furanoeremophilan-14β,6α-olide (**1**; *ca.* 10 g) as white needles, mp 136—138 °C (in a sealed tube); $[\alpha]_D$ −45° (*c* 0.45, dioxane); UV λ_{max} 217 nm (ε 8500); IR (Nujol) 3140, 3090, 1767, 1634, 1564, and 1082 cm^{-1}; NMR (Table 1); MS *m/e* (%) 246 (M^+; 41), 202 (100), 187 (72), 173 (36), 159 (88), 145 (85), 131 (20), 115 (22), 95 (48), 91 (44), 79 (25), 77 (35), 67 (23), 65 (21), and 43 (15); ORD (*c* 0.45, dioxane) $[\alpha]^{20}$ (at λ nm) −38° (650), −58° (500), −67° (400), −15° (330), +45° (310), +336° (280), +1000° (260), +4980° (238), +5040° (234), and +4540° (228); Found: C, 73.10; H, 7.35 %. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37 %.

The materials sublimed below 100 °C and the mother liquor of the recrystallization were combined (total weight: 11 g) and chromatographed over silica gel (400 g). Elution with petroleum ether gave furanoeremophilane (*ca.* 50 mg).[3,4] Further elution with petroleum ether-benzene (100: 3) provided bakkenolide-A (690 mg),[5,6] additional furanoeremophilan-14β,6α-olide (**1**; 2.9 g), and eremophilenolide (10 mg, after purification by sublimation).[4,7]

Reduction of Furanoeremophilan-14β,6α-olide (1) with Lithium Aluminium Hydride. A mixture of **1** (500 mg) and lithium aluminium hydride (700 mg) in dry ether was heated under reflux for 2 h. Usual treatment and crystallization from ether gave a diol (**2**; 400 mg) as a white powder, mp 197—198 °C; UV λ_{max} 224 nm (ε 7500); IR (Nujol) 3200, 1638, and 1552 cm^{-1}; ^{1}H NMR [$(CD_3)_2CO$] δ 1.16 (3H, s; *t*-Me), 1.97 (3H, d; –C=C–Me), 4.3 and 4.5 (2H, m; –CH–C$\underline{H}_2$–OH), 4.68 (1H, br s; –C$\underline{H}$–OH), 5.55 and 5.72 (each 1H, s; –OH), and 7.11 (1H, t; –C=C–H); Found: C, 71.72; H, 8.64%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%. The mass spectrum was the same as that of the ether (**3**).

Dehydration of the Diol (2). A mixture of diol (**2**; 200 mg) and *p*-toluenesulfonyl chloride (350 mg) in pyridine (3 ml) was allowed to stand at room temperature overnight. The reaction product was extracted with ether and the extract was evaporated to afford a yellow residue (200 mg), which was chromatographed over silica gel (6 g). Elution with benzene gave an ether (**3**; 110 mg) as white needles, mp 114—115 °C (from petroleum ether); $[\alpha]_D^{21}$ −65° (*c* 0.40, dioxane); UV λ_{max} 218 nm (ε 7000); IR (Nujol) 3140, 3100, 1640, 1567, and 1084 cm^{-1}; NMR (Table 1); MS *m/e* (%) 232 (M^+; 97), 217 (30), 202 (35), 187 (72), 173 (36), 159 (88), 145 (100), 119 (59), 95 (58), 91 (88), 79 (56), 77 (64), 67 (60), 65 (41), and 55 (40); ORD (*c* 0.40, dioxane) $[\alpha]_D^{21.5}$ (at λ nm) −55° (650), −90° (500), −128° (400), −145° (350), −108° (300), +325° (260), +800° (250), +2190°

(240), and +1630° (230); Found: C, 77.64; H, 8.75%. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

Acetylation of the Diol (2). Acetic anhydride (0.2 ml) was added to a solution of diol (**2**; 77 mg) in pyridine (3 ml) and the reaction mixture was allowed to stand at room temperature overnight. Methanol (0.2 ml) was added to the mixture and the reaction product was extracted with ether. The ethereal extract was evaporated to afford a residue, which showed three spots on TLC. Only major product (38 mg) was isolated as a colorless oil by column chromatography on alumina (3 g). The structure was revealed to be a 14-acetoxy derivative of the diol (**2**) by the NMR spectrum. IR (neat) 3400, 1740, 1640, and 1560 cm^{-1}; NMR (C_6D_6) δ 0.85 (3H, s; *t*-Me), 2.07 (3H, d, J=1.2 Hz; -C=C-Me), 1.66 (3H, s; -CO-Me), 4.0 and 4.5 (dd, $J_{14\alpha,14\beta}=-11$, $J_{4,14\alpha}=7$, and $J_{4,14\beta}=4$ Hz; -CH-C$\underline{H}_2$-O-), 4.22 (1H, br s; -C$\underline{H}$-OH), and 7.05 (1H, br s; -C=C-H).

Hydrogenolysis of Furanoeremophilan-14β,6α-olide (1). A solution of furanoeremophilan-14β,6α-olide (**1**; 1.16 g) in ethanol (40 ml) was stirred under an atmospheric pressure of hydrogen in the presence of 10% palladium–charcoal (300 mg) at room temperature for 2 h. Usual work-up afforded a residue (1.2 g), which was sublimed under reduced pressure at 80—100 °C to give a crude carboxylic acid (**4**) as a white powder. The crude product was shown to contain unchanged starting material by TLC. Repetition of chromatography on silica gel furnished analytically pure carboxylic acid (**4**) as a colorless glass, UV λ_{max} 221 nm (ε 6800); IR (Nujol) 2900, 1710, 1650, and 1570 cm^{-1}; NMR (CDCl$_3$) δ 1.20 (3H, s; *t*-Me), 1.90 (3H, d, J=1.2 Hz; -C=C-Me), 7.08 (1H, br s; -C=C-H), and 7.37 (1H, s; -COOH); MS *m/e* (%) 248 (M$^+$; 38), 230 (3), 202 (3), 147 (36), 119 (9), 109 (24), 108 (100), 96 (13), 91 (14), 79 (17), 77 (15), 55 (22), and 43 (37); Found: C, 72.60; H, 7.90%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.

Methyl Ester of the Carboxylic Acid (4). Carboxylic acid (**4**; 115 mg) was treated with diazomethane in ether (2 ml). The ether solution was concentrated and subjected to separation by preparative TLC (developed with benzene–chloroform, 1: 1) to afford a methyl ester (60 mg) as a colorless oil, IR (neat) 1735, 1648, 1566, and 1150 cm^{-1}, no absorption band due to hydroxyl group was observed. NMR (CDCl$_3$) δ 1.02 (3H, s; *t*-Me), 1.92 (3H, d, J=1.2 Hz; -C=C-Me), 3.70 (3H, s; -COOMe), and 7.13 (1H, br s; -C=C-H); MS *m/e* (%) 262 (M$^+$; 26), 231 (3), 215 (4), 198 (6), 170 (12), 155 (25), 147 (37), 142 (35), 141 (100), 128 (19), 115 (25), 108 (70), 69 (20), 57 (40), 55 (34), and 43 (51).

Reduction of the Carboxylic Acid (4) with Lithium Aluminium Hydride. A mixture of carboxylic acid (**4**; 430 mg) and lithium aluminium hydride (600 mg) in ether (30 ml) was heated under reflux for 1 h. The reaction mixture was worked up in usual way and chromatographed on silica gel (15 g). Elution with benzene afforded an alcohol (**5**; 350 mg) as a colorless oil, UV λ_{max} 221 nm (ε 7600); IR (neat) 3350, 1642, and 1562 cm^{-1}; NMR (CDCl$_3$) δ 0.99 (3H, s; *t*-Me), 1.48 (1H, s; -OH), 1.92 (3H, d, J=1.1 Hz; -C=C-Me), 3.7 and 3.9 (dd, $J_{14\alpha,14\beta}=-11$, $J_{4,14\alpha}=5$, and $J_{4,14\beta}=8$ Hz; -CH-C$\underline{H}_2$-O-), and 7.07 (1H, q; -C=C-H); MS *m/e* (%) 234 (M$^+$; 20), 218 (6), 138 (5), 122 (8), 109 (25), 108 (98), 74 (40), 59 (65), 45 (60), and 31 (100).

Furanoeremophilane (7) from the Alcohol (5). A mixture of the alcohol (**5**; 250 mg) and *p*-toluenesulfonyl chloride (300 mg) in pyridine (4 ml) was allowed to stand at room temperature overnight. After usual work-up, an orange crude oil (300 mg) was dissolved in benzene and subjected to separation by preparative TLC (developed with chloroform–ether, 5: 1) to afford a tosylate (**6**; 130 mg) as a yellow oil, IR (neat) 1647, 1568, 1600, 1188, and 1176 cm^{-1}.

The tosylate (**6**), above obtained, was reduced with lithium aluminium hydride (500 mg) in ether for 2 h. The reaction mixture was treated as usual and chromatographed on silica gel (4 g). Elution with petroleum ether provided furanoeremophilane (**7**; 53 mg) as a colorless oil, $[\alpha]_D^{23}$ −11° (*c* 0.42, CHCl$_3$); UV λ_{max} 221 nm (ε 7000); IR (neat) 1649, 1568, and 1094 cm^{-1}; NMR (CDCl$_3$) δ 0.95 (3H, s; *t*-Me), 0.99 (3H, d, J=7.0 Hz; *s*-Me), 1.99 (3H, d, J=1.1 Hz; -C=C-Me), and 7.13 (1H, q; -C=C-H); MS *m/e* (%) 218 (M$^+$; 40), 203 (3), 190 (3), 133 (6), 123 (13), 122 (72), 109 (68), 108 (100), 105 (10), 91 (16), 79 (24), 77 (17), 67 (12), 55 (15), and 53 (13); ORD (*c* 0.42, CHCl$_3$) $[\alpha]^{23}$ (at λ nm) −10° (650), −12° (500), −16° (450), −23° (400), and −32° (350); Found: C, 82.56; H, 10.31%. Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.16%.

Isomerization of Furanoeremophilan-14β,6α-olide (1) into Furanoeremophilan-14α,6α-olide (8). Furanoeremophilan-14β,6α-olide (**1**; 900 mg) was dissolved in benzene and adsorbed on basic alumina (15 g) for 6 h. The fraction eluted with the same solvent was shown to be a mixture of furanoeremophilan-14β,6α-olide (**1**) and -14α,6α-olide (**8**) in a ratio of 1: 5 by GLC examination. Repetition of fractional crystallization from ether–petroleum ether afforded **8** (300 mg), mp 124—125 °C, $[\alpha]^{18}$ −147° (*c* 0.33, dioxane); UV λ_{max} 216 nm (ε 7900); IR (Nujol) 3140, 3090, 1759, 1640, 1566, and 1083 cm^{-1}; NMR (Table 1); MS *m/e* (%) 246 (M$^+$; 48), 202 (64), 187 (62), 173 (24), 159 (56), 145 (64), 124 (32), 115 (34), 95 (100), 77 (54), 67 (40), and 55 (34); ORD (*c* 0.33, dioxane) $[\alpha]^{18.5}$ (at λ nm) −120° (650), −209° (500), −345° (400), −495° (350), −690° (300), −810° (270), −675° (250), and −390° (242); Found: C, 73.08; H, 7.41%. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37%.

Reduction of Furanoeremophilan-14α,6α-olide (8) with Lithium Aluminium Hydride. A mixture of furanoeremophilan-14α,6α-olide (**8**; 240 mg) and lithium aluminium hydride (500 mg) in ether (30 ml) was refluxed for 1 h and the reaction mixture was worked up as usual. The residue (240 mg) was crystallized from petroleum ether to give a diol (**9**; 180 mg) as white wooly crystals, mp 123.5—125 °C; UV λ_{max} 219 nm (ε 9000); IR (Nujol) 3320, 1646, and 1571 cm^{-1}; NMR (DMSO) δ 0.94 (3H, s; *t*-Me), 1.92 (3H, d, J=1.2 Hz; -C=C-Me), 2.3 and 2.8 (dd, $J_{9\alpha,9\beta}$=*ca.* −17, $J_{9\alpha,10}$=*ca.* 1.5, and $J_{9\beta,10}$=*ca.* 5.5 Hz; -C=C-C$\underline{H}_2$-CH-), 3.78 (2H, m; -C$\underline{H}_2$-OH), 4.31 (1H, d, J=5.4 Hz; -C$\underline{H}$-OH), 4.66 (1H, d, J=5.4 Hz; -CH-O$\underline{H}$), 4.85 (1H, t, J=4.8 Hz; -CH$_2$-O$\underline{H}$), and 7.17 (1H, br. s; -C=C-H); MS *m/e* (%) (by a direct inlet) 250 (M$^+$; 6), 232 (4), 159 (3), 149 (5), 123 (100), 91 (4), 67 (7), and 57 (7); (by an indirect inlet) 232 (38), 202 (4), 187 (6), 159 (40), 145 (11), 124 (22), 109 (100), 91 (18), 81 (18), 79 (15), 77 (15), 67 (86), and 55 (32).

Dehydration of the Diol (9). A solution of the diol (**9**; 185 mg) and *p*-toluenesulfonyl chloride (350 mg) in pyridine (5 ml) was heated at 65—70 °C for 1.5 h. Benzene was added to the mixture and the solvents were evaporated under reduced pressure. The residue was dissolved in benzene and chromatographed on silica gel (10 g). 4-Epiether (**10**; 130 mg) was obtained by elution with benzene as a colorless oil, UV λ_{max} 218 nm (ε 6900); IR (neat) 3140, 3090, 1642, 1567, and 1082 cm^{-1}; NMR (Table 1); MS *m/e* (%) 232 (M$^+$; 100), 217 (7), 202 (5), 199 (16), 187 (7), 159 (40), 145 (8), 124 (13), 109 (40), 91 (6), 85 (19), 83 (29), 67 (16), and 57 (10).

References

1) A part of this work was reported in a preliminary form: Y. Ishizaki, Y. Tanahashi, T. Takahashi, and K. Tori, *Chem. Commun.*, **1969**, 551.

2) T. Takahashi, The 21st Symposium on the Chemistry of Perfumes, Terpenes, and Essential Oils, Tokushima, 1977, Abstract Papers, p. 305, and references cited therein.

3) L. Novotoný, V. Herout, and F. Šorm, *Tetrahedron Lett.*, **1961**, 697; J. Hochmannová, L. Novotoný, and V. Herout, *Collect. Czech. Chem. Commun.*, **27**, 1870 (1962).

4) Y. Ishizaki, Y. Tanahashi, Y. Moriyama, T. Takahashi, and H. Koyama, *Phytochemistry*, **13**, 674 (1974).

5) N. Abe, R. Onoda, K. Shirahata, T. Kato, M. C. Wood, and Y. Kitahara, *Tetrahedron Lett.*, **1968**, 369; K. Shirahata, T. Kato, K. Kitahara, and N. Abe, *Tetrahedron*, **25**, 3179 (1969).

6) K. Naya, I. Takagi, M. Hayashi, S. Nakamura, M. Kobayashi, and S. Katsumura, *Chem. Ind. (London)*, **1968**, 318.

7) L. Novotoný, J. Jizba, V. Herout, F. Šorm, L. H. Zalkow, S. Hu, and C. Djerassi, *Tetrahedron*, **19**, 1101 (1963); L. Novotoný, J. Jizba, V. Herout, and F. Šorm, *Collect. Czech. Chem. Commun.*, **31**, 371 (1966).

8) F. Patil, G. Ourisson, Y. Tanahashi, M. Wada, and T. Takahashi, *Bull. Soc. Chim. Fr.*, **1968**, 1047.

9) H. Ishii, T. Tozyo, and H. Minato, *J. Chem. Soc., C*, **1966**, 1545. The authors are grateful to Dr. H. Ishii of Shionogi Research Laboratory for the spectra of authentic furanoeremophilane.

10) J. H. Noggle and R. E. Schirmer, "The Nuclear Overhauser Effect. Chemical Applications," Academic Press, New York (1971).

11) J. T. Pinhey and S. Sternhell, *Tetrahedron Lett.*, **1963**, 275.