New Furanoeremophilane Derivatives from *Farfugium japonicum* Kitamura

Hajime NAGANO, Yoshiaki TANAHASHI, Yoshihiko MORIYAMA, and Takeyoshi TAKAHASHI

Department of Chemistry, Faculty of Science, The University of Tokyo, Bunkyo-ku, Tokyo 113

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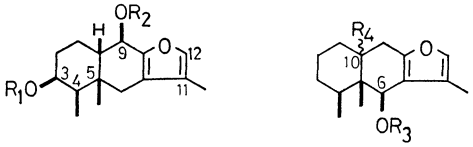
Five new furanoeremophilane derivatives, I, II, III, IV, and V, have been isolated from *Farfugium japonicum* Kitamura, and their structures have been determined. Conformations of some furanoeremophilane derivatives are discussed.

In addition to the previously reported farfugin A and B,[1] five new furanoeremophilane derivatives, I, II, III, IV, and V, have been isolated from *Farfugium japonicum* Kitamura (=*Ligularia tussilaginea* Makino). In this paper we wish to describe the structure determination of these compounds.



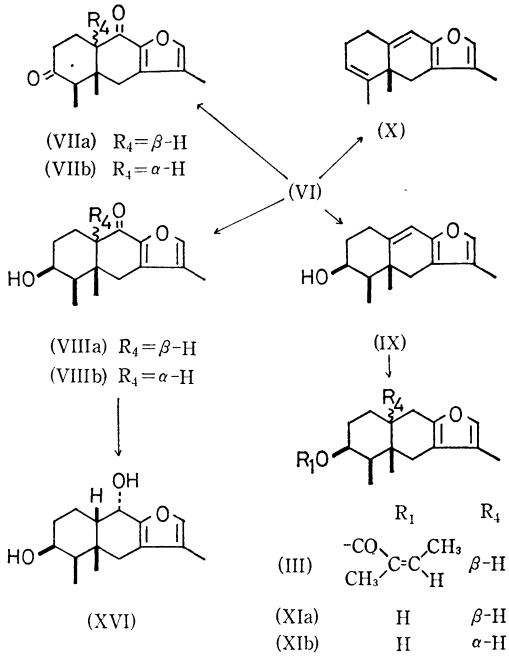
	R_1	R_2
(I)	$-CO-C(CH_3)=CH-CH_3$	$-CO-C(CH_3)=CH-CH_3$
(II)	$-CO-C(CH_3)=CH-CH_3$	H
(VI)	H	H
	R_3	R_4
(IV)	$-CO-C(CH_3)=CH-CH_3$	β-OH
(V)	$-CO-C(CH_3)=CH-CH_3$	β-H
(XIV)	H	β-OH
(XV)	H	β-H

Compound I, a viscous oil, M^+ at *m/e* 414 ($C_{25}H_{34}O_5$), $[\alpha]_D$ +17° (in MeOH), was positive to the Ehrlich test. IR, UV, PMR, and mass spectra (*cf.* Experimental and Table 1) suggest the presence of a β-methyl substituted furan ring, a secondary and a tertiary methyl and also that of partial structures: $(CH_3)_2C{=}CHCOO-$ and $CH_3CH{=}C(CH_3)COO-$. The latter moiety was determined as angeloyloxyl group by benzene induced solvent shift[2] ($\delta^{CCl_4}-\delta^{C_6D_6}=0.56$) of the olefinic proton found to be *trans* to the ester group.

Reduction of I with lithium aluminum hydride in ether gave a diol (VI), mp 187 °C (decomp.), M^+ at *m/e* 250 ($C_{15}H_{22}O_3$), $[\alpha]_D$ −24° (in EtOH), which on oxidation with active manganese dioxide[3] in benzene afforded a diketone (VIIa), mp 210 °C, M^+ at *m/e* 246 ($C_{15}H_{18}O_3$), $[\alpha]_D$ +26° (in $CHCl_3$), λ_{max} 282 nm (ε 15600), and a hydroxy-ketone (VIIIa), mp 176.5 °C, M^+ at *m/e* 248 ($C_{15}H_{20}O_3$), $[\alpha]_D$ −31° (in MeOH). Compound VIIa was found to be identical with known 3,9-dioxo-furanoeremophilane (VIIa) derived from kablicin, a furanoeremophilane derivative isolated from *Petasites kablikianus*.[4] Thus, the diol (VI) must be 3,9-dihydroxy-furanoeremophilane. Compound I would be either 3-angeloyloxy-9-senecioyloxy- or 3-senecioyloxy-9-angeloyloxy-furanoeremophilane.

Dehydration of VI with *p*-toluenesulfonyl chloride in pyridine at 110 °C gave two products, IX [M^+ at *m/e* 232 ($C_{15}H_{20}O_2$)] and X [M^+ at *m/e* 214 ($C_{15}H_{18}O$)]. The structures IX and X are compatible with their other spectral data, respectively (*cf.* Experimental).

Catalytic hydrogenation of IX over 10% palladium-charcoal in ethanol gave a pair of epimers at C-10: XIa, an oil, M^+ at *m/e* 234 ($C_{15}H_{22}O_2$), $[\alpha]_D$ −22° (in MeOH), and XIb, mp 79—80 °C, M^+ at *m/e* 234 ($C_{15}H_{22}O_2$), $[\alpha]_D$ +67° (in MeOH). The latter proved to be identical with furanoligularanol (XIb) (3β-hydroxy-10αH-furanoeremophilane),[5] derived from furanoligularenone.[5] Therefore, the stereochemistry including absolute configuration of 3-hydroxyl group of the diol (VI) should be β(*S*).



1) H. Nagano, Y. Moriyama, Y. Tanahashi, T. Takahashi, M. Fukuyama, and K. Sato, *Chemistry Lett.*, **1972**, 13.

2) J. Ronayne and D. E. Williams, *J. Chem. Soc., C*, **1967**, 2642.

3) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, **1952**, 1094.

4) L. Novotný, Z. Samek, V. Herout, and F. Šorm, *Tetrahedron Lett.*, **1968**, 1401.

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

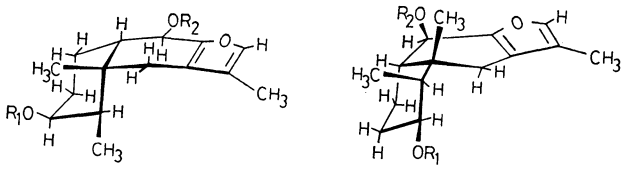
TABLE 1. PMR SPECTRAL DATA (δ values)[a)]

	I		II		III		IV		V
	CCl_4	C_6D_6	CCl_4	C_6D_6	CCl_4	C_6D_6	CCl_4	C_6D_6	CCl_4
$C_{(4)}$-CH_3	0.99d J=7	0.88d J=7	0.98d J=7	0.94d J=7	0.97d J=7	0.92d J=7	0.95m	0.82m	0.90m
$C_{(5)}$-CH_3	1.06s	1.12s	1.10s	1.07s	0.90s	0.73s	0.98s	1.14s	0.96s
$C_{(11)}$-CH_3	1.94d J=1.5	1.70d J=1.5	1.89	1.70d J=1	1.88	1.77d J=1	1.89	2.01	1.88
$C_{(3)}$-H	5.20m	5.27m	5.16m	5.32 quintet J=5	5.34m	5.50m			
$C_{(6)}$-H							6.07s	6.57s	6.22s
$C_{(9)}$-H	5.43s	5.82s	4.30s	4.23s			2.55 3.08 AB-type q J=19	2.87 3.07	
$C_{(12)}$-H	7.06q	6.97q	7.00m	6.98m	7.04m	7.13m	6.96m	7.09m	7.02m
CH_3>C=C<CO-CH_3 H	1.87	1.89m	1.89	1.89m	1.88	1.92q J=1	—	—	—
CH_3>C=C<CO-CH_3 H	1.95d J=7	1.96d J=7	1.96d J=7	2.03d J=7	1.99	2.03d J=8	—	—	—
CH_3>C=C<CO-H CH_3	1.87m	1.45d J=1.5	—	—	—	—	1.89m	1.47d J=1	1.88
CH_3>C=C<CO-H CH_3	2.16d J=1.5	2.10d J=1.5	—	—	—	—	2.17d J=1	2.14d J=1	2.17
CH_3>C=C<CO-CH_3 H	5.96q J=7	5.6m	5.93q J=7	5.70q J=7	6.01q J=8	5.81q J=8	—	—	—
CH_3>C=C<CO-H CH_3	5.54m	5.65m	—	—	—	—	5.58m	5.56m	5.67m

a) Coupling constants are expressed in Hz.
s: singlet, d: doublet, q: quartet, m: multiplet.

Compound II, an oil, M^+ at m/e 332 ($C_{20}H_{28}O_4$), $[\alpha]_D$ −11° (in MeOH), was related to I by partial hydrolysis of I with ethanolic potassium hydroxide at room temperature to give II. When I was absorped on silica gel and then eluted with solvent, II was formed.[6)] Reduction of II with lithium aluminum hydride gave VI. Spectral data of II show the presence of a secondary hydroxyl and the absence of a senecioyl group. Thus, II is a desenecioyl derivative of I. In the PMR spectrum of II (Table 1), an allylic proton on hydroxy-bearing carbon resonates at δ^{CCl_4} 4.30, while the corresponding allylic proton signal of I appears at δ^{CCl_4} 5.43. These observations show that the hydroxyl group of II and the senecioyloxyl group of I are located on C-9. Therefore, I must be 3β-angeloyloxy-9-senecioyloxy-furanoeremophilane, and II should be 3β-angeloyloxy-9-hydroxy-furanoeremophilane.

Furanoeremophilane derivatives would exist in two interchangeable conformations such as **A** (steroidal) and **B** (non-steroidal conformation).[7)] A number of furanoeremophilane derivatives have been isolated from the plants of Compositae. However, no description for the existence in non-steroidal conformation has yet been reported.



A **B**

In the PMR spectra of I, II, and VI, a broad signal (half-band width ~15 Hz) due to a proton at C-3α appears at δ^{CCl_4} 5.20, δ^{CCl_4} 5.16, and δ^{CDCl_3} 4.08, respectively, indicating an axial nature[8)] for this proton. In the spectrum of II in benzene-d_6, the 3α(axial)-proton signal is observed as a quintet due to a large diaxial ($J_{2\beta,3\alpha}$=10 Hz) and two smaller axial-equatorial ($J_{2\alpha,3\alpha}=J_{3\alpha,4\alpha}$=5 Hz) vicinal couplings. An allylic proton at C-9 of I, II, and VI resonates as a singlet (half-band width ~3 Hz), suggesting a vicinal coupling ($J_{9,10}$) is small. These data can only be interpreted on the basis of the non-steroidal conformation (**B**) with the substituent at C-9 in β-configuration, in which the dihedral angle between $C_{(9\alpha)}$-H and $C_{(10\beta)}$-H is about 70—80° on Dreiding model. This dihedral angle

6) This suggests that II might be an artifact derived from I during isolation procedures involving silica gel chromatography. In the crude extract of the plant the absence of II was detected on tlc. Therefore, II is considered to be an artifact.

7) Z. Samek, J. Harmatha, L. Novotný, and F. Šorm, *Coll. Czech. Chem. Comm.*, **34**, 2792 (1969).

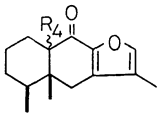
8) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco (1964), pp. 77, 165.

would increase more than 80° resulting in reduction of vicinal coupling ($J_{9\alpha,10\beta}$), when a 1,3-diaxial interaction between the methyl group at C-5β and the substituent at C-9β becomes more important.

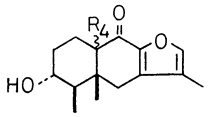
The structures including absolute configurations of I, II, and VI are thus determined as 3β-angeloyloxy-9β-senecioyloxyfuranoeremophilane (I), 3β-angeloyloxy-9β-hydroxyfuranoeremophilane (II) and 3β,9β-dihydroxy-furanoeremophilane (VI), respectively.

The hydroxy-ketone (VIIIa) exhibits an UV absorption at λ_{max} 281 nm (ε 17000), showing that the carbonyl group conjugated with furan ring is located on C-9.[9] The ORD data (*cf.* Experimental) of VIIIa is closely related to that of 9-oxo-furanoeremophilane (XIIa).[4] As VIIIa was formed by oxidation of VI, the hydroxyl group at C-3 of VIIIa must be β; this received support from the determination of absolute configuration at C-3 of VIIIa as *S* by the Horeau's method[10] (esterification 84%; optical yield (−) 25%). Therefore, the hydroxy-ketone (VIIIa) is (3*S*)-hydroxy-9-oxo-furanoeremophilane.

The same structure (VIIIa) has already been given by Rivett and Woolard for epieuryopsonol (mp 216—217 °C).[11] However, our hydroxy-ketone (VIIIa) (mp 176.5 °C) is different from epieuryopsonol. This discrepancy could be overcome when the structure of epieuryopsonol is revised from VIIIa to its 10αH-epimer, 3β-hydroxy-9-oxo-10αH-furanoeremophilane (VIIIb). This received support from an alkaline epimerization of the hydroxy-ketone (VIIIa) (mp 176.5 °C) to give its 10αH-epimer (VIIIb), mp 218—219 °C, whose PMR data are in accord with those[11] of epieuryopsonol. The structures of euryopsonol (XIIIa), dehydroeuryopsonol (VIIa), and of deoxydehydroeuryopsonol (XIIa)[11] are to be revised to XIIIb, VIIb, and XIIb, respectively. Expermiental data[11] of these euryopsonol derivatives can be best interpreted on the basis of 10αH-furanoeremophilane rather than furanoeremophilane skeleton, when compared with those of kablicin derivatives[4] (*cf.* Table 2). During isolation procedures of euryopsonol including treatment with alkali,[11] an epimerization at C-10 must have occurred to afford more stable 10αH-epimer (XIIIb).



(XIIa) $R_4=\beta$-H
(XIIb) $R_4=\alpha$-H



(XIIIa) $R_4=\beta$-H
(XIIIb) $R_4=\alpha$-H

Compound III, an oil, M^+ at *m/e* 316 ($C_{20}H_{28}O_3$), $[\alpha]_D$ −38° (in MeOH), was positive to the Ehrlich test. The PMR spectrum (Table 1) showed the presence of an angeloyl group. Reduction of III with lithium aluminum hydride in ether gave XIa, $[\alpha]_D$ −25° (in MeOH). Therefore, III is 3β-angeloyloxy-furanoeremophilane.[12]

Spectral data of compound IV, mp 82—84 °C, M^+ at *m/e* 332 ($C_{20}H_{28}O_4$), $[\alpha]_D$ −68° (in MeOH), suggest the presence of a hydroxyl and a senecioyl groups. On reduction with lithium aluminum hydride, IV yielded a diol, mp 126 °C (decomp.), $[\alpha]_D$ +50° (in MeOH), identical with 6β,10β-dihydroxy-furanoeremophilane (XIV) isolated from *Ligularia japonica* Less.[13] Thus, the structure of IV is represented by 6β-senecioyloxy-10β-hydroxy-furanoeremophilane (IV).

The presence of a senecioyl group is suggested for compound V, an oil, M^+ at *m/e* 316 ($C_{20}H_{28}O_3$), on the basis of spectral data. Reduction of V with lithium aluminum hydride gave known petasalbin (XV),[14] $[\alpha]_D$ −14° (in MeOH). Compound V must be 6β-senecioyloxy-furanoeremophilane (V).

In the PMR spectra of III and XIa, a broad multiplet (half-band width ~15 Hz) due to a proton at C-3α appears at δ^{CCl_4} 5.34 and 4.08 respectively. This shows an axial nature for this proton, suggesting that III and XIa are in a non-steroidal rather than a steroidal conformation.

The PMR spectrum of 3β,9α-dihydroxy-furanoeremophilane[15] (XVI), prepared from VIIIa by reduction with lithium aluminum hydride, shows a broad multiplet (half-band width ~15 Hz) at δ^{CDCl_3} 4.20 due to a proton at C-3α. A proton at C-9β resonates as a doublet ($J_{9\beta,10\beta}$=6 Hz) at δ^{CDCl_3} 4.80. These data are compatible with a non-steroidal conformation for XVI.

TABLE 2[a]

Furanoeremophilanes	3α-hydroxy-9-oxo-		3β-hydroxy-9-oxo-		3,9-dioxo-		9-oxo-	
Derivaitves of kablicin[4]	XIIIa (176 °C)	XIIIb (230 °C)			VIIa (210 °C)	VIIb (225 °C)	XIIa (112 °C)	XIIb (148—149 °C)
Derivatives of euryopsonol[11]		euryopsonol (230—231 °C)		epieuryopsonol (216—217 °C)		dehydro-euryopsonol (224—225 °C)		deoxydehydro-euryopsonol (145 °C)
This report			VIIIa (176.5 °C)	VIIIb (218—219 °C)	VIIa (210 °C)			

a) Mps are indicated in parentheses.

9) L. Novotný, Ch. Tabačíkova-Wlotzká, V. Herout, and F. Šorm, *Coll. Czech. Chem. Comm.*, **29**, 1922 (1964).
10) A. Horeau and H. B. Kagan, *Tetrahedron*, **20**, 2431 (1964).
11) D. E. A. Rivett and G. R. Woolard, *ibid*, **23**, 2431 (1967).
12) Recently, we have isolated the same compound (III) from *Farfugium hiberniflorum* Kitamura.
13) M. Tada, Y. Moriyama, Y. Tanahashi, T. Takahashi, M. Fukuyama, and K. Sato, *Tetrahedron Lett.*, **1971**, 4007.
14) L. Novotný, V. Herout, and F. Šorm, *Coll. Czech. Chem. Comm.*, **29**, 2189 (1964).
15) Oxidation of XVI with active manganese dioxide led to regeneration of VIIIa.

Compounds I, II, III, VI, XIa, and XVI were thus shown to be in the non-steroidal conformation[16] such as **B**. The 3β-acyloxyl or 3β-hydroxyl group of these compounds is in an equatorial conformation, which avoids the unfavorable 1,3-diaxial interaction between 3β-substituent and 5β-methyl group; this must be the driving force to bring these compounds in a non-steroidal conformation. A predominance of this driving force over the 1,3-diaxial interaction between 9β-substituent and 5β-methyl group was shown for I, II, and VI.

Experimental

IR, UV, and Mass spectra were measured using Hitachi EPI-G2, Hitachi EPS-3 and Hitachi RMU-6 spectrometers, respectively. PMR spectra were taken on JEOL JNM-PS-100 (100 MHz) and Hitachi R-20 (60 MHz) spectrometers. Chemical shifts are expressed in δ (TMS as an internal standard). Merck Kieselgel G and Kieselgel 60 PF_{254} were used for analytical and preparative tlc, respectively. For column chromatography Wakogel C 200 was used.

Isolation. The roots of *Farfugium japonicum* Kitamura (15 kg) were extracted with ether at room temperature. The extract was then filtered, dried over anhydrous sodium sulfate and evaporated to afford a viscous oil (80 g). The oil (30 g) was again dissolved in ether, washed with 5% aqueous sodium carbonate solution, dried with anhydrous sodium sulfate and evaporated. The residue (18 g) was immediately chromatographed on silica gel (400 g) with light petroleum–ether (10: 1) as eluent (each fraction 400 ml).

Fractions 1 and 2 gave a viscous oil (1.46 g), a half of which was repeatedly chromatographed on silica gel (eluent: light petroleum–ether (100: 1)) to give an oil (124 mg). The oil was further purified by preparative tlc to afford III (77 mg) and V (16 mg).

Fraction 3 afforded I, a viscous oil (4.92 g).

Fractions 4 and 5 afforded a pale yellow oil (2.96 g), containing IV, which was isolated by preparative tlc.

The extract residue (6 g) in light petroleum was absorped on silica gel. After one day, elution with light petroleum–ether (25: 1, 3 l) and then with light petroleum–ether (10: 1. 6 l) afforded an oil (917 mg). On repeated chromatography followed by preparative tlc of the oil, II (46 mg) was obtained.

3β-Angeloyloxy-9β-senecioyloxy-furanoeremophilane (I). Compound I was a viscous oil, $[\alpha]_D^{17}$ +17° (*c* 1.45, in MeOH). Its spot on tlc plate showed yellow green color to the Ehrlich test, and developed blue color when 2% ceric sulfate reagent was sprayed and then heated. Spectral data of I are as follows; UV: λ_{max}^{MeOH} 220 nm (ε 32000); IR: ν_{max}^{liquid} 1720, 1650, and 1560 cm^{-1}; PMR (Table 1); MS *m/e* 414 (relative intensity 1.5%, M^+ ($C_{25}H_{34}O_5$)), *m/e* 83 (54%, $[CH_3CH{=}C(CH_3)CO]^+$ and $[(CH_3)_2C{=}CHCO]^+$) and *m/e* 55 (100%, $[CH_3CH{=}CCH_3]^+$ and $[(CH_3)_2C{=}CH]^+$).

3β-Angeloyloxy-9β-hydroxy-furanoeremophilane (II). Compound II, an oil, $[\alpha]_D^{14}$ −11° (*c* 0.8, in MeOH), was positive to the Ehrlich test, and displayed blue coloring with 2% ceric sulfate reagent when heated on tlc plate. Characterization of II is as follows; UV λ_{max}^{EtOH} 219 nm(ε 14500); IR: ν_{max}^{liquid} 1700, 1640, and 1560 cm^{-1}; PMR (Table 1); MS: *m/e* 332 (4%, M^+ ($C_{20}H_{28}O_4$)), *m/e* 314 (5%, $[M-H_2O]^+$), *m/e* 124 (100%, *retro*-Diels-Alder fragment), *m/e* 83 (85%, $[CH_3CH{=}C(CH_3)CO]^+$), and *m/e* 55 (70%, $[CH_3CH{=}CCH_3]^+$).

Reduction of I with Lithium Aluminum Hydride. I (996 mg) in dry ether (50 ml) was refluxed with lithium aluminum hydride (200 mg) for 1.5 hr under nitrogen atmosphere. Then, the excess of lithium aluminum hydride was decomposed with water, and extracted with ether. The usual treatment gave a crystalline product, which was recrystallized from isopropyl ether to give VI (364 mg). The residue obtained from the mother liquid was chromatographed on silica gel (30 g) with light petroleum–ether (1:1) as eluent to give further VI (40 mg). 3β,9β-Dihydroxy-furanoeremophilane (VI), mp 187 °C (decomp.), $[\alpha]_D^{19}$ −24° (*c* 0.47, in EtOH); UV: λ_{max}^{EtOH} 222.5 nm (ε 7200); IR: ν_{max}^{Nujol} 3475, 3380, and 1565 cm^{-1}; PMR ($CDCl_3$): δ 1.00 (d, J=7 Hz, $C_{(4)}$–CH_3), 1.14 (s, $C_{(5)}$–CH_3), 1.90 (d, J=1.5 Hz, $C_{(11)}$–CH_3), 1.96 (d, J=(−) 17 Hz, $C_{(6)}$–H), 2.66 (d, J=(−) 17 Hz, $C_{(6)}$–H), 4.08 (m, $C_{(3)}$–H), 4.40 (s, $C_{(9)}$–H), and 7.12 (q, J=1.5 Hz, $C_{(12)}$–H); MS: *m/e* 250 (6%, M^+ ($C_{15}H_{22}O_3$)) and *m/e* 124 (100%, *retro*-Diels-Alder fragment). Found: C, 72.12; H, 8.70%. Calcd for $C_{15}H_{22}O_3$: C, 71.79; H, 8.86%.

Reduction of II with Lithium Aluminum Hydride. Treatment of II with lithium aluminum hydride by the same procedures described as above gave VI, mp 187 °C (decomp.), $[\alpha]_D^{15}$ −28° (*c* 1.0, in MeOH).

Hydrolysis of I. *A*: I (1.86 g) was chromatographed on silica gel (50 g) using light petroleum–ether (50: 1) as eluent. However, only 48 mg of I was recovered and from the fractions eluted with ether a yellowish oil (640 mg) was obtained. The oil was repeatedly chromatographed on silica gel (35 g) with light petroleum–ether (10: 1) to give II (96 mg).

B: A solution of potassium hydroxide (1 g) in ethanol (25 ml) was added to I (277 mg) and the mixture was allowed to stand overnight at room temperature, added water and extracted with ether. The extract was washed with water, dried with anhydrous sodium sulfate and evaporated under reduced pressure to give an oil (191 mg) containing II and VI. VI was not detected on tlc before the evaporation of the solvent. Therefore, this compound must be formed on heating during the above procedures.

C: The residue obtained by the procedures *A* and *B* were combined, dissolved in ethanolic potassium hydroxide and refluxed for 2.5 hr under nitrogen atmosphere. After usual treatment, the resulting residue was recrystallized from isopropyl ether to give VI. The aqueous layer was acidified with dil hydrochloric acid and extracted with ether. After the solvent was distilled off, the residue was allowed to stand for several days and tiglic acid (an isomerization product of angelic acid) was obtained as crystals.

Oxidation of VI with Active Manganese Dioxide. To a solution of VI (154 mg) in benzene (50 ml) was added active manganese dioxide[3] (1.5 g) and stirred for 22 hr under nitrogen atmosphere. After filtration, the solvent was removed to afford a residue, which was chromatographed on silica gel (7 g). Fractions eluted with light petroleum–ether (1: 1) gave VIIa (64 mg), and successive elution with ether gave VIIIa (70 mg).

3,9-Dioxo-furanoeremophilane (VIIa); mp 210 °C (recrystallized from ethanol), $[\alpha]_D^{19}$ +26° (*c* 0.71, in $CHCl_3$); UV: λ_{max}^{EtOH} 282 nm (ε 15600); IR: ν_{max}^{Nujol} 1715, 1657, and 1530 cm^{-1}; PMR ($CDCl_3$): δ 0.96 (d, J=7 Hz, $C_{(4)}$–CH_3), 1.11

16) The PMR spectra of furanopetasine[9] (2α-angeloyloxy-9α-hydroxy-furanoeremophilane; 2β-H at δ^{CDCl_3} 5.20, half-band width ~15 Hz) and furanopetasol[9] (2α,9α-dihydroxy-furanoeremophilane; 2β-H at δ^{CDCl_3} 4.06, half-band width~15 Hz), offered through courtesy of Dr. L. Novotný, showed that these compounds also existed in a non-steroidal conformation, in which the substituents at C-2α and C-9α were equatorial.

(s, $C_{(5)}$-CH_3), 2.01 (d, J=1.5 Hz, $C_{(11)}$-CH_3), and 7.42 (q, J=1.5 Hz, $C_{(12)}$-H); MS: *m/e* 246 (39%, M^+ ($C_{15}H_{18}O_3$)), *m/e* 175 (100%), and *m/e* 122 (5%). The PMR spectrum of VIIa in the presence of Eu(dpm)$_3$ (0.45 mol equivalent) as shift reagent revealed the presence of a partial structure –CO–CH(CH_3)–C–; namely, signals due to $C_{(4)}$-CH_3 and $C_{(4)}$-H appeared at δ^{CDCl_3} 3.39 (d, J=6.5 Hz) and at δ^{CDCl_3} 6.35 (q, J=6.5 Hz), respectively. Diketone (VIIa)[17] was found to be identical (mp 210 °C) with 3,9-dioxo-furanoeremophilane.

3β-Hydroxy-9-oxo-furanoeremophilane (VIIIa); mp 176.5 °C (recrystallized from isopropyl ether), $[\alpha]_D^{20}$ −31° (*c* 0.97, in MeOH); UV: λ_{max}^{EtOH} 281 nm (ε 17000); ORD (*c* 0.14, in MeOH): $[\phi]_{280}$ −6800°, $[\phi]_{260}^{trough}$ −14000°, $[\phi]_{230}^{peak}$ −10000°, $[\phi]_{208}^{trough}$ −27000° and $[\phi]_{200}$ −6800°; IR: ν_{max}^{Nujol} 3500, 1650, and 1525 cm^{-1}; PMR ($CDCl_3$): δ 0.99 (d, J=7 Hz, $C_{(4)}$-CH_3), 1.10 (s, $C_{(5)}$-CH_3), 1.98 (d, J=1.5 Hz, $C_{(11)}$-CH_3), 4.17 (m, $C_{(3)}$-H), and 7.41 (q, J=1.5 Hz, $C_{(12)}$-H); MS: *m/e* 248 (5%, M^+ ($C_{15}H_{20}O_3$)), *m/e* 91 (46%), *m/e* 77 (32%), and *m/e* 66 (100%). Found: C, 72.83; H, 7.82%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.

Application of the Horeau's Method[10] to VIIIa. VIIIa (18.6 mg, 0.075 mmol) in pyridine (3 ml) was allowed to stand with α-phenylbutyric anhydride (69.6 mg, 0.224 mmol) for 18 hr at room temperature. The reaction mixture was then heated with one drop of water. After benzene was added, the mixture was titrated with 0.1 M KOH in the presence of phenolphthalein. The aqueous layer was acidified with dil sulfuric acid and then extracted with benzene. After usual treatment of the extract, the solvent was evaporated to give α-phenylbutyric acid. The optical rotation value (α_D −0.025°) was observed for the benzene solution (5 ml) of the acid using a 0.5 dm cell.

Alkaline Epimerization of VIIIa. To a solution of VIIIa (45 mg) in ethanol (20 ml), 10% aqueous sodium hydroxide (5 ml) was added and the mixture was refluxed for 1 hr under nitrogen atmosphere. After the reaction mixture was treated as usual, the residue (41 mg) was chromatographed on silica gel (3 g) using light petroleum–ether (3: 1) as eluent to give the epimerized product VIIIb (12 mg). Successive elution with ether gave VIIIa (*ca.* 30 mg). Compound VIIIb; mp 218—219 °C (recrystallized from isopropyl ether); IR: ν_{max}^{Nujol} 3480 and 1650 cm^{-1}; PMR ($CDCl_3$): δ 1.02 (s, $C_{(5)}$-CH_3), 1.16 (d, J=7 Hz, $C_{(4)}$-CH_3), 1.97 (d, J=~1 Hz, $C_{(11)}$-CH_3), 3.88 (m, $C_{(3)}$-H), and 7.32 (q, J=~1 Hz, $C_{(12)}$-H).

Dehydration of VI with p-*Toluenesulfonyl Chloride in Pyridine.* To a solution of VI (398 mg) in pyridine (10 ml), *p*-toluenesulfonyl chloride (400 mg) was added and heated at 110 °C (oil bath temperature) for 20 min under nitrogen atmosphere. Evaporation of the solvent gave a reddish residue, which was immediately chromatographed on silica gel (30 g) using light petroleum–ether (20: 1) as eluent. (each fraction *ca.* 70 ml).

Fraction 2 gave a pale yellow oil, X (20 mg); UV: λ_{max}^{MeOH} 293 nm (ε ~10000); PMR (C_6D_6): δ 1.09 (s, $C_{(5)}$-CH_3), 1.60 (m, $C_{(4)}$-CH_3), 1.78 (d, J=1.5 Hz, $C_{(11)}$-CH_3), 5.35 (m, $C_{(3)}$-H), 6.13 (d, J=~1 Hz, $C_{(9)}$-H), and 6.93 (q, J=1.5 Hz, $C_{(12)}$-H); MS: *m/e* 214 (46%, M^+ ($C_{15}H_{18}O$)), and *m/e* 199 (100%, $[M-CH_3]^+$), which was sensitive to the air. This compound (X) on tlc plate developed a bright red color with 2% ceric sulfate reagent.

Fractions 7—16 gave a pale yellow oil, IX (140 mg); UV: λ_{max}^{MeOH} 292 nm (ε ~10000); IR: ν_{max}^{liquid} 3400 cm^{-1}; PMR (CCl_4): δ 1.05 (s, $C_{(5)}$-CH_3), 1.10 (d, J=6 Hz, $C_{(4)}$-CH_3), 1.90 (d, J=1.5 Hz, $C_{(11)}$-CH_3), 3.84 (m, $C_{(3)}$-H), 5.93 (d, J=2.5 Hz, $C_{(9)}$-H), and 6.86 (m, $C_{(12)}$-H); MS: *m/e* 232 (39%, M^+($C_{15}H_{20}O_2$)), *m/e* 199 (79%, $[M-CH_3-H_2O]^+$), *m/e* 159 (100%), and *m/e* 145 (44%), which was sensitive to the air. The compound (IX) on tlc plate developed a bright red color with 2% ceric sulfate reagent.

Hydrogenation of IX over Pd–C. Hydrogenation of IX (114 mg) in ethanol was effected over Pd–C (10%) (31 mg) with stirring for 3.5 hr. Filtration of the catalyst and evaporation of the solvent under reduced pressure gave an oil (95 mg). From the oil, XIa (20 mg) and XIb (40 mg) were separated by preparative tlc. Sublimation of the latter gave colorless crystals (XIb), mp 79—80 °C (recrystallized from light petroleum), $[\alpha]_D^{25}$ +67° (*c* 0.7, in MeOH); IR: ν_{max}^{Nujol} 3350, 1640, and 1560 cm^{-1}; PMR (CCl_4): δ 0.86 (s, $C_{(5)}$-CH_3), 1.10 (d, J=7 Hz, $C_{(4)}$-CH_3), 1.86 (d, J=~1 Hz, $C_{(11)}$-CH_3), 3.84 (m, $C_{(3)}$-H), and 7.00 (m, $C_{(12)}$-H); MS: *m/e* 234 (12%, M^+ ($C_{15}H_{22}O_2$)), and *m/e* 108 (100%, *retro*-Diels-Alder fragment), which was identical with furanoligularanol (XIb),[5] mp 79—80 °C, $[\alpha]_D^{24}$ +78° (*c* 0.8, in MeOH),[18] prepared from furanoligularenone.[5] Compound XIa was an oil, $[\alpha]_D^{24}$ −22° (*c* 1.0, in MeOH); IR: ν_{max}^{liquid} 3360, 1640, and 1560 cm^{-1}; PMR (CCl_4): δ 0.94 (d, J=7 Hz, $C_{(4)}$-CH_3), 0.94 (s, $C_{(5)}$-CH_3), 1.86 (d, J=1.5 Hz, $C_{(11)}$-CH_3), 4.12 (m, $C_{(3)}$-H), and 6.91 (m, $C_{(12)}$-H); MS: *m/e* 234 (10%, M^+ ($C_{15}H_{22}O_2$)), and *m/e* 108 (100%, *retro*-Diels-Alder fragment).

3β-Angeloyloxy-furanoeremophilane (III). Compound III, an oil, $[\alpha]_D^{14}$ −38° (*c* 1.3, in MeOH), was positive to the Ehrlich test (purple). Spectral data of III are as follows; IR: ν_{max}^{liquid} 1705, 1640, and 1560 cm^{-1}; PMR (Table 1); MS: *m/e* 316 (5%, M^+ ($C_{20}H_{28}O_3$)), 108 (100%, *retro*-Diels-Alder fragment), *m/e* 83 (40%, $[CH_3CH{=}C(CH_3)CO]^+$), and *m/e* 55 (30%, $[CH_3CH{=}CCH_3]^+$).

Reduction of III with Lithium Aluminum Hydride. To a suspension of lithium aluminum hydride (48 mg) in dry ether (2 ml), III (77 mg) in dry ether (4 ml) was added and stirred at room temperature under nitrogen atmosphere. After completion of the reaction, the mixture was treated as usual and the resulting residue was chromatographed on silica gel (4 g). Fractions eluted with light petroleum–ether (10: 1) gave a compound identical with XIa, M^+ at *m/e* 234 ($C_{15}H_{22}O_2$), $[\alpha]_D^{28}$ −25° (*c* 1.3, in MeOH). Identification was effected on $[\alpha]_D$, IR, PMR, MS, and tlc.

6β-Senecioyloxy-10β-hydroxy-furanoeremophilane (IV). Compound IV, mp 82—84 °C (recrystallized from light petroleum), $[\alpha]_D^{15}$ −68° (c, 0.84, in MeOH), was positive to the Ehrlich test (purple), and displayed intense blue coloring with 2% ceric sulfate reagent when heated on tlc plate. Characterization of IV is as follows; UV: λ_{max}^{EtOH} 218 nm (ε 21000); IR: $\nu_{max}^{CCl_4}$ 3513, 1715, and 1644 cm^{-1}; PMR (Table 1); MS: *m/e* 332 (1.4%, M^+($C_{20}H_{28}O_4$)), *m/e* 83 (100%, $[(CH_3)_2C{=}CHCO]^+$), and *m/e* 55 (23%, $[(CH_3)_2C{=}CH]^+$).

Reduction of IV with Lithium Aluminum Hydride. Reduction of IV (39 mg) with lithium aluminum hydride (39 mg) in ether (5 ml) gave a crystalline product (10 mg), mp 126° (decomp.), M^+ at *m/e* 250 ($C_{15}H_{22}O_3$), $[\alpha]_D^{20}$ +50° (*c* 0.17, in EtOH), which was identified with the authentic sample of 6β,10β-dihydroxyfuranoeremophilane (XIV)[13] by mp, $[\alpha]_D$, IR, PMR, MS, and tlc.

6β-Senecioyloxy-furanoeremophilane (V). Compound V,

17) In the PMR spectra of VIIa, a remarkable benzene-induced solvent shift ($\delta^{CDCl_3}-\delta^{C_6D_6}$=0.28) was observed for the signal due to a secondary methyl adjacent to carbonyl group. This shows an axial nature[8] for the 4β-methyl group suggesting that VIIa is in a non-steroidal conformation.

18) Pure furanoligularanol (XIb) has these physical constants. Mp 63°C and $[\alpha]_D$+53° (*c* 0.5, in $CHCl_3$) were given for the same compound in the literature.[5]

a viscous oil, was positive to the Ehrlich test. Characterization of V is as follows; IR: ν_{max}^{liquid} 1710, 1645, and 1563 cm^{-1}; PMR (Table 1); MS (indirect inlet system): *m/e* 316 (1%, $M^+(C_{20}H_{28}O_3)$), *m/e* 159 (77%), *m/e* 145 (29%), *m/e* 83 (100%, $[(CH_3)_2C{=}CHCO]^+$), and *m/e* 55 (23%, $[(CH_3)_2C{=}CH]^+$).

Reduction of V with Lithium Aluminum Hydride. Treatment of V with lithium aluminum hydride by the same procedures described above gave a compound, M^+ at *m/e* 234 ($C_{15}H_{22}O_2$), $[\alpha]_D^{18}$ −14° (*c* 0.7, in MeOH), identical with petasalbin (XV)[14] (IR, PMR, MS, and tlc).

Reduction of VIIIa with Lithium Aluminum Hydride. Reduction of VIIIa (33 mg) with lithium aluminum hydride (50 mg) in ether (30 ml) with stirring for 2 hr under nitrogen atmosphere, and then usual work-up gave XVI (29 mg), mp 81—83 °C (sublimation); IR: ν_{max}^{Nujol} 3330, 1660, and 1565 cm^{-1}; PMR ($CDCl_3$): δ 0.97 (s, $C_{(5)}$-CH_3), 1.00 (d, J=7 Hz, $C_{(4)}$-CH_3), 1.90 (d, J=1.5 Hz, $C_{(11)}$-CH_3), 4.20 (m, $C_{(3)}$-H), 4.80 (d, J=6 Hz, $C_{(9)}$-H), and 7.11 (q, J=1.5 Hz, $C_{(12)}$-H); MS: *m/e* 250 (6%, M^+ ($C_{15}H_{22}O_3$)) and *m/e* 124 (100%, *retro*-Diels-Alder fragment).

Oxidation of XVI with Active Manganese Dioxide. To a solution of XVI (20 mg) in benzene (4 ml) was added active manganese dioxide[3] (100 mg) and stirred for 4 hr under nitrogen atmosphere. After filtration, the solvent was removed to afford a crystalline product, which was recrystallized from isopropyl ether to give VIIIa (12 mg).

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