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1β,10β-EPOXYFURANOEREMOPHILAN-6β-OL, A NEW FURANOSESQUITERPENE FROM LIGULARIA FISCHERI TURCZ.

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A new sesquiterpene isolated from Ligularia Fischeri Turcz. (collected at Hakusan) has been shown to be 1β,10β-epoxyfuranoeremophilan-6β-ol(I).

Sesquiterpene components of Ligularia Fischeri Turcz. have been described by Ishii et al.$^{1)}$ In the course of chemical investigation on constituents of the genus Ligularia (Compositae), we have examined the diethyl ether extract of the roots of Ligularia Fischeri Turcz. collected at Hakusan$^{2)}$ and isolated a new furanosesquiterpene. We report here the evidence leading to the structure of 1β,10β-epoxyfuranoeremophilan-6β-ol(I) for this sesquiterpene.

The molecular formula of $C_{15}H_{20}O_3$ (M^+ at m/e 248) was given for I, an oil, which was positive to the Ehrlich test. The UV $\left(\lambda_{max}^{EtOH}\ 215.5\ nm,\ \varepsilon\ 7000\right)$, IR $\left(\nu_{max}^{Nujol}\ 1645\ and\ 1570\ cm^{-1}\right)$ and PMR spectra (in $CDCl_3$; an α-proton (δ 7.07 ppm, q, J = 1.5 Hz ; H_{12}) and a β-methyl (δ 2.09 ppm, d, J = 1.5 Hz ; H_{13}) on a furan ring) suggest the presence of a β-methyl substituted furan moiety. IR absorption at 3450 cm^{-1} is characteristic for a hydroxyl group ; one proton signal at δ 1.93 ppm disappears on addition of D_2O. The PMR spectrum also shows the presence of a secondary methyl (δ 1.11 ppm, d, J = 7 Hz ; H_{14}), a tertiary methyl (δ 1.14 ppm, s; H_{15}), one proton on oxygen-bearing carbon(δ 3.06 ppm, br. s ; H_1), an allylic methylene (an AB-type quartet ; δ_A 3.22 ppm, d, and δ_B 2.11 ppm, d, J = (-)16 Hz ; ■-CH_2-furan* ; $H_{9\alpha}$ and $H_{9\beta}$, respectively) and one allylic proton on hydroxyl-

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*The mark (■) indicates carbon with no proton.

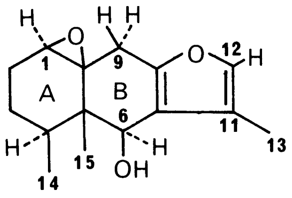
bearing carbon (δ 4.86 ppm, br. s ; ■-CH(OH)-furan ; H_6).

These spectral data are closely related to those of furanoeremophilane-6β,10β-diol(IIa)$^{3)}$ recently isolated from <u>L. japonica</u> Less. Indeed, reduction of I in THF with lithium aluminum hydride under reflux gave a diol, $C_{15}H_{22}O_3$, m.p. 123°, $[\alpha]_D$ +54°(EtOH), identical with IIa. Thus, the presence of furanoeremophilane skeleton(IIb) was shown for I ; the hydroxyl group of I should be located on C-6β. PMDR experiments afforded evidence for the presence of homoallylic coupling (J ~2 Hz) between the proton (H_6) at δ 4.86 ppm and one ($H_{9\alpha}$) of the allylic methylene protons. Therefore the former proton (H_6) must be in quasi-axial (α) conformation.

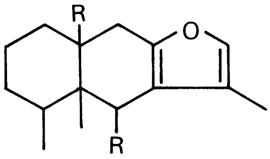
Of the three oxygen atoms for I, two are involved in the hydroxyl(at C-6) and furan ring, respectively. Since no carbonyl absorption is observed in the IR spectrum, the third oxygen is inferred to be present as an ether or an epoxide. The conversion of I into IIa, along with PMR spectral data of <u>one</u> proton at δ 3.06 ppm (br. s), leads to the location of an epoxy ring on C-1β and C-10β. Thus, the structure of I must be represented by 1β,10β-epoxyfuranoeremophilan-6β-ol(I).

PMR experiments using $Eu(dpm)_3$ as shift reagent$^{4)}$, coupled with PMDR technique, confirmed the above conclusion and revealed detailed stereochemical features of I (TABLE). The shift reagent associates more strongly with a hydroxyl than with an ether group$^{5)}$. A very large shift is observed for H_4 and H_{15}. Shift for H_{14} is small ; this shows that the epoxide ring is in β-configuration (the structure with 1α,10α-epoxide should cause a large shift of H_{14}). PMR spectral data shown in the TABLE are best interpreted on the basis of the stereostructure with ring A in half-chair and with ring B in half-boat conformation depicted as in I'$^{6)}$.

Another furanosesquiterpene was also obtained from the same plant. However, the substance has not yet been isolated in a pure state. This sesquiterpene is an ester ($\nu_{C=O}$ 1718 cm^{-1}) which on reduction with lithium aluminum hydride (in diethyl ether) gave I. Examination of the acidic moiety is now under way.

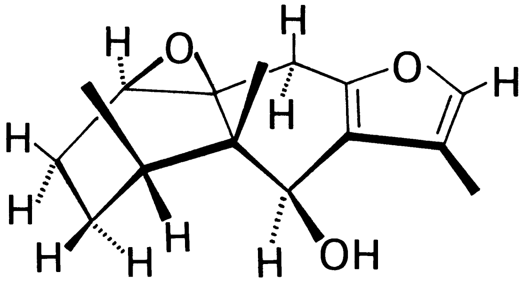


(I)



(IIa) R=OH

(IIb) R=H



(I′)

TABLE PMR Spectral Data

	δ_{CDCl_3} a)	$\delta_{Eu(dpm)_3}$ b)	$\Delta\delta$ c)	Coupling constants	
H_1	3.06(br. s)	11.45(ABX)	-8.4	$J_{1,2\alpha}$	~5
$H_{2\alpha}$		5.0(m)		$J_{1,2\beta}$	<1
$H_{2\beta}$		6.8(m)		$J_{2\alpha,2\beta}$	~(-)15
$H_{3\alpha}$		5.9(m)		$J_{2\alpha,3\alpha}$	~7
$H_{3\beta}$		2.6(m)		$J_{2\alpha,3\beta}$	~1.5
H_4	~1.5	16.3(m)	-14.8	$J_{2\beta,3\alpha}$	~15
H_6	4.86(br. s)	not measured		$J_{2\beta,3\beta}$	~5
$H_{9\alpha}$	3.22(d) d)	10.73(d)	-7.5	$J_{3\alpha,3\beta}$	~(-)15
$H_{9\beta}$	2.11(d)	9.08(d)	-7.0	$J_{3\alpha,4}$	~5
H_{12}	7.07(q)	10.17(br. s)	-3.1	$J_{3\beta,4}$	~1.5
H_{13}	2.09(d)	7.62(d)	-5.5	$J_{4,14}$	7
H_{14}	1.11(d)	5.55(d)	-4.4	$J_{9\alpha,9\beta}$	(-)16
H_{15}	1.14(s)	12.88(s)	-11.7	$J_{12,13}$	(-)1.5
				$J_{6\alpha,9\alpha}$	~2

a) Chemical shifts are expressed in δ ppm downfield from TMS and coupling constants in Hz.

b) 0.97 Mol equivalent of $Eu(dpm)_3$ was added to the 2%(w/w) solution of I.

c) $\Delta\delta = \delta_{CDCl_3} - \delta_{Eu(dpm)_3}$

d) With further splitting due to homoallylic coupling $J_{6,9\alpha}$.

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2) The presence of two kinds of Ligularia Fischeri Turcz. in Japan has been reported by Dr. H. Koyama (Acta Phytotax. Geobot., 22, 75(1966)). The VPC and TLC data for constituents of our plant were very similar to those of L. sibirica Cass., collected at Prague by one of the authors, but different from those of L. Fischeri Turcz., collected at Karuizawa(late-flowering species). Finally, our plant was recognized as "L. Fischeri Turcz.(collected at Hakusan)" from plant taxonomical point of view by Dr. H. Koyama, National Science Museum, Tokyo, to whom our thanks are due. We are also grateful to Drs. V. Herout, L. Novotný, and M. Toman for their kind aid in collection in Czechoslovakia.

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6) The structure(I) refers to that of relative configuration. Studies to determine the absolute configuration of IIa are under way.

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