Sesquiterpenoid Derivatives from *Ferula ferulioides*. II.[1)]

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A new farnesyl-benzofuranone type sesquiterpenoid derivative, 2,6-dihydroxy-2-[3,7,11-trimethyl-2(*E*),6(*E*),10-dodecatrien-1-yl]-3(2*H*)-benzofuranone was isolated from the roots of *Ferula ferulioides*. The structure was established by comprehensive spectral analysis.

Key words *Ferula ferulioides*; Umbelliferae; sesquiterpenoid; farnesyl-benzofuranone

Ferula ferulioides (STEUD.) KOROVIN (Umbelliferae) grows in Bulgan Somon of Hovd City, Mongolia, and has been used as a traditional medicine for the treatment of spasm. In a previous paper,[1)] we reported the isolation of four new compounds **1**—**4** together with four known compounds, myristicin, guaiol, nerolidol and dshamirone, from the plant. The present paper deals with the isolation and structural elucidation of an additional novel sesquiterpenoid derivative from *F. ferulioides*.

The dried and powdered roots were extracted with methanol. Removal of the solvent gave a waxy solid which was successively extracted with ethyl acetate and water. From the ethyl acetate extract, one novel compound (**5**) was isolated.

The molecular formula of compound **5** was determind to be $C_{23}H_{30}O_4$ ($[M]^+$ at *m/z* 370.2142) by high-resolution mass spectrometry (HR-MS). The ^{1}H- and ^{13}C-NMR spectra of **5** showed the existence of a 1,2,4-trisubstituted benzene ring (δ_H 6.43, 6.54, 7.50), four olefinic-methyl groups (δ_H 1.56, 1.58, 1.67, 1.67; δ_C 16.0, 16.4, 17.7, 25.7), three trisubstituted double bonds (δ_H 5.04, 5.07, 5.19), a carbonyl carbon (δ_C 196.8), an acetal carbon (δ_C 105.3), and five methylene groups. The NMR spectrum of **5** was similar to that of **1** except for the appearance of an acetal carbon in **5**. The information concerning the location of these units was obtained from a heteronuclear multiple bond correlation (HMBC) spectrum.

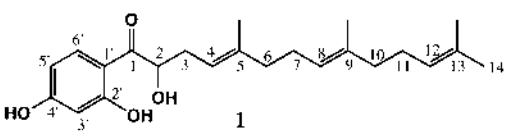
This information and the characteristic absorption in the IR spectrum (ν 1713, 1617 cm^{-1}) lead to a 3(2*H*)-benzofuranone structure[2)] for this compound, in which the chemical shift of C-7a shifted downfield by 7.3 ppm compared to C-2′ of **1** (δ_C 165.6) indicating that the 7a-oxgen is forming a ring.

The structure of the side chain was deduced from a nuclear Overhauser and exchange spectroscopy (NOESY) experiment, based on the cross-peaks observed from the following pairs: H-2′/H-4′, H-6′/H-8′ and H-10′/H-12′. These results indicated an *E* configuration for the C-2′–C-3′ and C-6′–C-7′ double bonds. The structure of compound **5** was thus elucidated as 2,6-dihydroxy-2-[3,7,11-trimethyl-2(*E*),6(*E*),10-dodecatrien-1-yl]-3(2*H*)-benzofuranone.

Compound **5** was a racemic compound, since it was optically inactive, as compounds **1**—**4** were.

To our knowledge, this is the first report on the isolation of a farnesyl-benzofuranone, whereas isolation of farnesyl-coumarins such as ferulenol (**6**), a prenylated 4-hydroxy-coumarin, has been reported previously.[3—6)]

In a previous paper[1)] we proposed a biosynthetic pathway leading to the sesquiterpenoid compounds **1**—**4** and dshamirone. Hydroxylation of dshamirone at the α position of the carbonyl leads to compound **1**. Further oxidation of **1** will give compound **5** by intramolecular acetal formation of the resulting 2-oxo-dshamirone.



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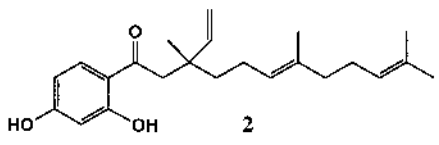

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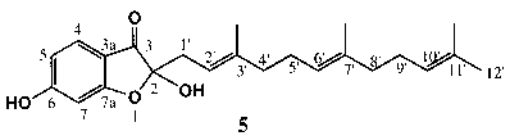

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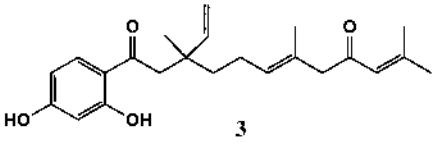

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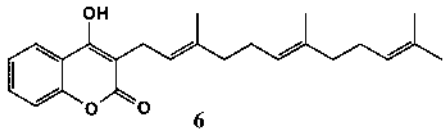

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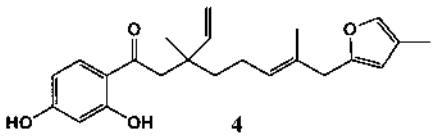

4

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Table 1. ^{1}H- and ^{13}C-NMR Spectral Data of Compound **5** in $CDCl_3$

	C	H
2	105.3	
3	196.8	
3a	112.1	
4	126.9	7.50 (1H, d, J=9 Hz)
5	112.0	6.54 (1H, dd, J=2, 9 Hz)
6	166.7[a)]	
7	98.9	6.43 (1H, d, J=2 Hz)
7a	172.9[a)]	
1′	34.7	2.53 (1H, dd, J=7, 14 Hz)
		2.75 (1H, dd, J=8.5, 14 Hz)
2′	114.4	5.19 (1H, t, J=7 Hz)
3′	143.4	
4′	39.9	2.03 (2H, m)
5′	26.7	2.05[b)]
6′	123.7	5.04 (1H, br t)
7′	135.7	
8′	39.7	1.94 (2H, m)
9′	26.4	2.05[b)]
10′	124.4	5.07 (1H, t, J=7 Hz)
11′	131.4	
12′	25.7	1.67 (3H, s)
3′Me	16.4	1.67 (3H, s)
7′Me	16.0	1.56 (3H, s)
11′Me	17.7	1.58 (3H, s)

a) These values may be interchanged. *b*) Overlapped with other signals.

Experimental

General Procedures NMR spectra were recorded on a JEOL JNM-A500 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. Electon impact mass spectra (EI-MS) were recorded on a JEOL JMS-DX300 spectrometer. Optical rotation was measured with a JASCO DIP-4 digital polarimeter. The IR spectrum was recorded on a Shimadzu FT-IR8100 spectrometer.

Plant Material The roots of *Ferula ferulioides* (STEUD.) KOROVIN were collected in July 1996 from Bulgan Somon of Hovd City, Mongolia. Voucher specimens have been deposited in the Botanical Department of Mongolian State University.

Extraction and Isolation The dried and pulverized roots of *Ferula ferulioides* (400 g) were extracted successively with methanol under reflux. After evaporation of this extract, a part of the methanol extract (20 g) was partitioned between ethyl acetate and water. The ethyl acetate layer was dried and evaporated under reduced pressure. The residue was chromatographed on silica gel with hexane–ethyl acetate (10 : 1—1 : 1) to afford two fractions. The polar fraction was subjected to RP-18 Lober (Merck) chromatography (55% CH_3CN) to give **5** (13 mg). Less polar fractions gave compounds **1**—**4**.

2,6-Dihydroxy-2-[3,7,11-trimethyl-2(*E*),6(*E*),10-dodecatrien-1-yl]-3(2*H*)-benzofuranone (**5**): Oil, $[\alpha]_D^{22}$ ±0° (c=1.3, MeOH), EI-MS m/z: 370 $[M]^+$, 219 $[C_{12}H_{11}O_4]^+$, 166 $[C_8H_6O_4]^+$, 137 $[C_7H_5O_3]^+$, HR-MS m/z: 370.2142 $[M]^+$ (Calcd for $C_{23}H_{30}O_4$: 370.2144), IR ν_{max} ($CHCl_3$): 1713, 1617 cm^{-1}, ^{1}H- and ^{13}C-NMR: Table 1.

References

1) Kojima K., Isaka K., Purev O., Jargalsaikhan G., Suran D., Mizukami H., Ogihara Y., *Chem. Pharm. Bull.*, **46**, 1781—1784 (1998).
2) Amick D. R., *J. Heterocycl. Chem.*, **12**, 1051—1052 (1975).
3) Lamnaouer D., Bodo B., Martin M.-T., Molho D., *Phytochemistry*, **26**, 1613—1615 (1987).
4) Appendino G., Tagliapietra S., Gariboldi P., Nano G. M., Picci V., *Phytochemistry*, 27, 3619—3624 (1988).
5) Valle M. G., Appendino G., Nano G. M., Picci V., *Phytochemistry*, **26**, 253—256 (1987).
6) Teresa J. de P., Villaseco M. A., Hernandez J. M., Moran J. R., Urones J. G., Grande M., *Planta Medica*, **1986**, 458—462.