Chem. Pharm. Bull. 27(12)3153—3155(1979)

UDC 547.913.02 : 581.192

Marmaricin, a New Sesquiterpenoid Coumarin from *Ferula marmarica* L.

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(Received May 17, 1979)

A new sesquiterpenoid coumarin, marmaricin, $C_{24}H_{30}O_4$, was isolated from the roots of *Ferula marmarica* L., grown in Egypt. The carbon skeleton of the sesquiterpenoid moiety was identified by selenium dehydrogenation, yielding 1,2,5,6-tetramethylnaphthalene. The coumarin moiety was determined by acid cleavage to give umbelliferone. The structure of marmaricin was assigned on the basis of spectral and chemical evidence.

Keywords——Umbelliferae; *Ferula*; marmaricin; umbelliferone; 1,2,5,6-tetramethylnaphthalene

The coumarin constituents of *Ferula* species have received a great deal of attention and several reports have appeared recently on this subject.[2–4] Phytochemical studies on the root of *Ferula marmarica* L., an Egyptian desert plant, were undertaken by Shalaby *et al.*[2] They isolated a compound from the benzene extract and named it marmarin, $C_{21}H_{30}O_3$, mp 83°. No chemical study was performed on the previously isolated material. Reinvestigation of the root of the same plant by us resulted in the isolation from the coumarin fraction, a sesquiterpenoid coumarin, designated here as marmaricin. Its structure is reported here.

The isolated material, marmaricin, has the composition $C_{24}H_{30}O_4$ on the basis of elemental analysis and mass spectrometry (M^+, *m/e* 382). It showed bands characteristic of alcohol (3400 cm^{-1}) and exocyclic methylene (890 cm^{-1}) groups in its IR spectrum. The main maxima of the IR and UV spectra confirmed that marmaricin belongs to the coumarin series.[5] Dehydrogenation of marmaricin with selenium resulted in the formation of 1,2,5,6-tetramethylnaphthalene, indicating the presence of a *gem*-dimethyl group at C-4 and a hydroxyl group at C-3, as in farnesiferol.[6] Mild acetylation of marmaricin yielded a monoacetate derivative, $C_{26}H_{32}O_5$, mp 189—192°, which exhibited no hydroxylic absorption in the IR region, indicating the presence of only one hydroxyl group. Acid cleavage of marmaricin resulted in the formation of umbelliferone.[7] The carbon resonance of the isolated sesquiterpenoid coumarin was measured; Its chemical shifts (δ_C in ppm) are given in Table I and are assigned tentatively. The signal at δ_C 78.4 is assigned to C-3, carrying the hydroxylic group, which is probably equatorial (an axial hydroxylic function at C-3 is displaced by *ca* 2.8 ppm upfield[8]). The chemical shifts of the coumarin moiety are in agreement with

1) Location: *a) Mansoura, Dakahliah, Egypt; b) El-Tahrir st., Dokki, Cairo, Egypt; c) No. 58-62, Hittorfstr., 4400-Münster/Westf, BRD.*
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Table I. ^{13}C Chemical Shifts of Marmaricin (in $CDCl_3$, $\delta_C^{TMS}=0$)

Carbon No.	ppm	Carbon No.	ppm
C- 1	38.8	C-13	15.5
C- 2	27.6	C-14	28.4
C- 3	78.4	C-15	15.3
C- 4	39.2	C- 2	162.9
C- 5	54.5	C- 3	107.9
C- 6	23.4	C- 4	146.0
C- 7	28.0	C- 5	132.4
C- 8	90.4	C- 6	124.0
C- 9	54.2	C- 7	165.7
C-10	37.4	C- 8	133.2
C-11	66.5	C- 9	153.4
C-12	115.8	C-10	116.7

Table II. ^1H-NMR Spectrum of Marmaricin

	Signals due to protons of C-11	Exocyclic methylene	C–Me
Farnesiferol A	Appears as AB of an ABX system (δ_A4.27, δ_B4, J=10 Hz) $J_{AX}=J_{BX}$= 5.5 Hz	Two distinct triplets (J=1.5 Hz) at δ 4.7 and 4.79	1.04 0.98 0.80
Coladonin	Doublet at δ 4.17 J=5.5 Hz	Two broad singlets at δ 4.52 and 4.88	1.01 0.83 0.80
Marmaricin	Doublet at δ 4.26 J=6 Hz	Two broad singlets at δ 4.51 and 4.90	1.04 0.87 0.82

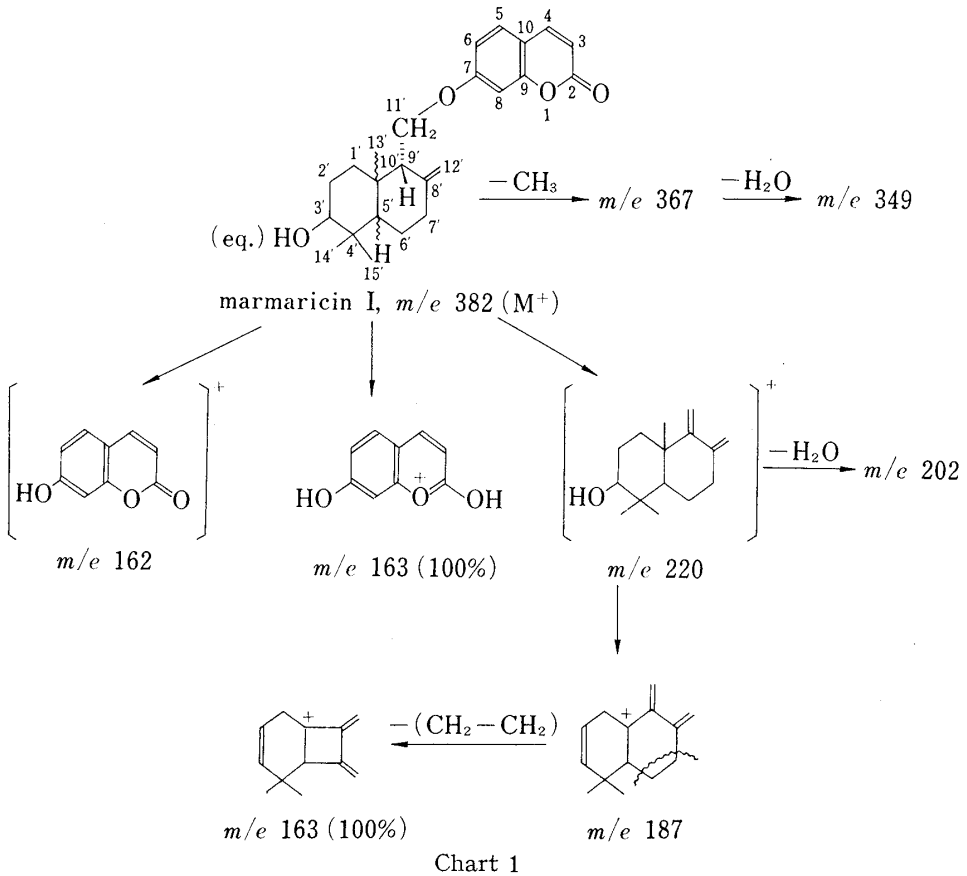

Chart 1

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those determined by Bergenthal *et al.*[9] for 7-methoxy coumarin. Structure I was assigned to marmaricin based on the above results and ^{1}H–NMR data. Pinar and his collaborators[4] examined the ^{1}H–NMR spectrum of coladonin and compared it with that of farnesiferol A, a sesquiterpenoid coumarin having the same structural features, and differing only in the stereochemistry at C-9. The only difference in their spectra appear in the signals due to the protons on C-11, exocyclic methylene (C-12) and the C–Me groups. Table II shows the signals corresponding to these particular protons of the two coumarins together with those of marmaricin; marmaricin probably has the same configuration at C-9 as coladonin (equatorial $-CH_2-O-R$). The isolated coumarin is not identical with badrakemin[3] or coladonin.[4] Badrakemin has a C-3 axial hydroxyl group and axial $-CH_2-O-R$ at C-9, while coladonin possesses an equatorial C-3 OH and also an axial $-CH_2-O-R$ at C-9. Both badrakemin and coladonin have α-CH_3 at C-10 and β-H at C-5. In the case of marmaricin, the stereochemistry of the methyl group and the hydrogen attached to C-10 and C-5, respectively, has not yet been assigned. The fragmentation pattern of marmaricin is illustrated in Chart 1 and supports the proposed structure. Work is in progress to elucidate the stereochemistry of marmaricin and to study the other minor constituents of *Ferula marmarica* L.

Experimental[10]

Isolation of Marmaricin——The dried, powdered roots of *Ferula marmarica* L. (1200 g) were exhaustively extracted with ethanol (95%). The extract was concentrated to one l and processed as usual[11] to give the coumarin fraction. It constituted 1.2% (on a dry wt basis) of the root. It was fractionated on an alumina column to give marmaricin (830 mg), eluted with benzene–pet. ether (1: 1).

Marmaricin (I)——This compound was isolated as colorless needles from ethanol, mp 184—186°, $[\alpha]_D$ 39°. IR ν_{max}^{KBr} cm^{-1}: 3400, 2910, 2820, 1680, 1620, 1605, 1555, 1490, 1450, 890. NMR, δ: 7.80, 7.34 (4H), 5.67 (1H), 4.51, 4.90 (1H), 4.26 (2H, J=6 Hz), 3.31 (1H), 1.04 (3H, s), 0.87 (3H, s) and 0.82 (3H, s). MS, *m/e*: 382 (M^+), 367, 349, 219, 202, 187, 162, 163 (100%), 135, 107, 93, 78. UV, λ_{max} nm: 227, 265, 304, 314 (sh.). *Anal.* Calcd. for $C_{24}H_{30}O_4$: C, 75.36; H, 7.71%. Found.: C, 75.24; H, 7.88%.

Acetylation of Marmaricin——A soln. of marmaricin (100 mg) in pyridine (5 ml) was treated with Ac_2O (5 ml) and the mixture was heated on a water-bath for 2 hr. Water was added and the precipitated derivative was filtered and crystallized from ethanol to give colorless needles, mp 189—192°. IR ν_{max}^{KBr} cm^{-1}: 2490, 1720, 1620, 1600, 1560, 1450, 1490, 890, 820. MS, *m/e*: 424 (M^+, $C_{26}H_{32}G_5$).

Acid Hydrolysis of Marmericin——A soln. of marmaricin (5 mg) in AcOH was treated with one drop of conc. H_2SO_4. After standing for 15 min at room temperature, the mixture was chromatographed on thin layers of silica gel, developing with benzene–ethyl acetate (9: 1), gave a spot corresponding to that of authentic umbelliferone (*Rf* 0.09). Both showed the same color under UV light and after spraying with iodine reagent.[7]

Dehydrogenation of Marmaricin——Marmaricin (10 mg) was mixed with selenium (10 mg) and heated at 290° for 0.5 hr. The reaction mixture was extracted, after cooling, with light pet. ether (40—60°). The extracted material was purified on a silica gel column and eluted with pet. ether. Crystallization from aqueous ethanol gave colorless needles of 1,2,5,6-tetramethylnaphthalene, mp 114—116°, reported[6] mp 113—115°.

Acknowledgement We are indebted to Alexander von Humboldt-Stiftung, Bonn, BRD, for the Fellowship awarded to A.M. Dawidar. Thanks are due to Prof. M. Zahran for collection and identification of the plant material, to Dr. D. Bergenthal for the carbon resonance measurements.

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10) Melting points were determined using a Kofler hot-stage instrument and are uncorrected. IR spectra were recorded using a Perkin-Elmer 457 spectrophotometer. NMR spectra were recorded at 100 MHz with a Varian T-100 instrument, in $CDCl_3$, using tetramethylsilane as an internal standard. Mass spectral data were obtained with a Hitachi Perkin-Elmer RMU-6D spectrophotometer. Optical rotation was measured using a Perkin-Elmer 241 polarimeter.
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