

FURTHER NEW SESQUITERPENES FROM *FERULA JAESCHKEANA*¹

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In continuation of our work on *Ferula jaeschkeana* Vatke (Umbelliferae) (1-3) rhizomes, we describe here the structural determination of two new sesquiterpenes with a carotane skeleton. In addition, a known sesquiterpene is also reported for the first time from this plant.

Column and preparative layer chromatography of the defatted MeOH extract of *F. jaeschkeana* rhizomes afforded three more sesquiterpenes **1**, **4**, and **5**.

The most polar compound, mp 104-105, was assigned the structure of the 5 α -vanillate of 2,3-epoxy-jaeschkeanadiol [**1**]. It analyzed for C₂₃H₃₂O₆, but

droxyl function at C-7 (3). Its ir spectrum contained absorption for hydroxyl (3410 cm⁻¹) and ester carbonyl (1690 cm⁻¹) groups. The ¹H-nmr spectrum of **1** displayed a proton geminal to an oxygen (epoxide), isopropyl methyls, an angular methyl, a methyl attached to a carbon with an oxygen function, and aromatic protons (Table 1).

Compound **1** formed a monoacetate and, on alkaline hydrolysis, yielded an acid, identified as 4-hydroxy-3-methoxybenzoic acid (ms, ir, and ¹H nmr) and an alcohol **3**. This alcohol also did not show the molecular ion, but a fragment at *m/z* 211 [M - C₃H₇]⁺ was observed. It was

TABLE 1. ¹H-nmr Data of Compounds **1**, **2**, and **4**.^a

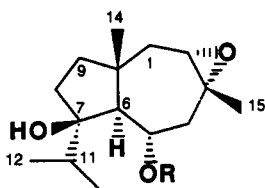
Proton Assignments	Compound		
	1 (400 MHz)	2 (80 MHz)	4 (400 MHz)
H-1	—	—	—
H-2	2.90 t (8)	2.85 t (8)	3.70 br d (12)
H-4	—	—	3.06 d (6)
H-5	5.40 td (10, 10, 3)	5.40 td (10, 10, 3)	3.82 dd (10, 6)
H-6	1.90 d (10)	—	1.70 d (10)
H-11	1.99 sep (7)	—	2.19 sep (7)
H-12	0.85 d (7)	0.85 d (7)	0.85 d (7)
H-13	0.92 d (7)	0.95 d (7)	0.98 d (7)
H-14	1.24 s	1.25 s	1.20 s
H-15	1.51 s	1.45 s	1.40 s
H-1'	7.55 s	7.20 s	—
H-5'	7.60 d (8)	7.60 d (8)	—
H-6'	6.95 d (8)	7.05 d (8)	—
-OMe	3.95 s	3.85 s	—
-AcMe	—	2.30 s	—

^as = singlet, d = doublet, t = triplet, br = broad, sep = septet; Hz in parentheses.

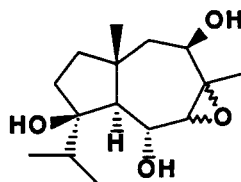
in its mass spectrum the molecular ion was not observed; instead a fragment was produced by the loss of C₃H₇ from the molecular ion. This is a typical loss in carotane-type sesquiterpenes with a hy-

droxyl function at C-7 (3). Its ir spectrum contained absorption for hydroxyl (3410 cm⁻¹) and ester carbonyl (1690 cm⁻¹) groups. The ¹H-nmr spectrum of **1** displayed a proton geminal to an oxygen (epoxide), isopropyl methyls, an angular methyl, a methyl attached to a carbon with an oxygen function, and aromatic protons (Table 1).

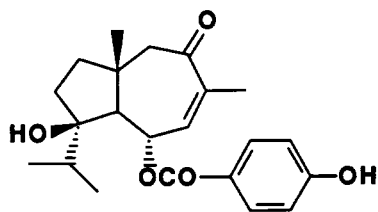
Compound **1** formed a monoacetate and, on alkaline hydrolysis, yielded an acid, identified as 4-hydroxy-3-methoxybenzoic acid (ms, ir, and ¹H nmr) and an alcohol **3**. This alcohol also did not show the molecular ion, but a fragment at *m/z* 211 [M - C₃H₇]⁺ was observed. It was



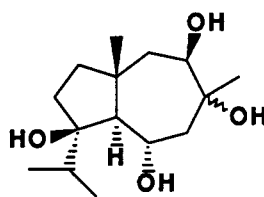
- 1 R=COC₆H₃ (OH) (OMe)
 2 R=COC₆H₃ (OAc) (OMe)
 3 R=H



4



5



6

epoxy-jaeschkeanadiol esters have been reported from *Ferula linkii* (5).

The second, less polar compound, **4**, analyzed for C₁₅H₂₆O₄ and showed an ion at *m/z* 227 [M - C₃H₇]⁺ but no molecular ion. Its ¹³C-nmr spectrum displayed 15 signals assigned for five oxygen-bearing (three methine, two quaternary), four methyl, three methylene, two methine, and one quaternary carbons (Table 2). The absence of a double bond suggested **4** was tricyclic with one ring an epoxide. Its ir spectrum showed a hydroxyl (3350 cm⁻¹) absorption band. The remaining ¹³C- and ¹H-nmr data of **4** were comparable with the data of known similar bicyclic carotane derivatives (1,4).

The ¹H-nmr spectrum (Table 1) of **4** displayed the presence of two secondary hydroxyls, one epoxide and a methyl geminal to oxygen. Positions of one secondary hydroxyl group and the epoxide ring were determined on the basis of chemical shifts of **4** (4) and a series of ¹H-nmr homo-decouplings at C-5 and between C-3 and C-4, respectively. The hydroxyl was placed at C-2 because of the following considerations. Compound **4** did not form the acetonide when reacted with Me₂CO and anhydrous CuSO₄, and it also failed to react

TABLE 2. ¹³C-nmr Data of Compounds **1** and **4**.

Carbon	Compound	
	1	4
C-1	41.87 t	41.70 t
C-2	60.92 d ^a	70.71 d
C-3	56.09 s	55.54 s
C-4	40.59 t	69.42 d
C-5	70.20 d	71.66 d
C-6	60.92 d ^a	53.38 d
C-7	86.03 s	86.21 s
C-8	40.59 t	42.23 t
C-9	31.82 t	32.44 t
C-10	44.36 s	47.15 s
C-11	36.79 d	37.50 d
C-12	17.28 q	16.08 q
C-13	18.42 q	17.16 q
C-14	19.35 q	18.37 q
C-15	23.23 q	19.41 q
C-1'	122.26 s	
C-2'	111.96 d	
C-3'	146.44 s	
C-4'	150.53 s	
C-5'	114.97 d	
C-6'	124.26 d	
C-7'	166.02 s	

^aInterchangeable.

with sodium periodate, eliminating a C-8 hydroxy. The C-9 position was also discarded on the basis that the oxy-methine appeared at δ 3.70 as compared

to a C-9 oxymethine at δ 3.30 (6). Compound **4** on LiAlH_4 reduction yielded **6** which consumed sodium periodate confirming the position of hydroxy group at C-2.

Looking at the Drieding model and the coupling constants, the relative stereochemistry of oxygenated functions at C-2 and C-5 was confirmed as β and α , respectively (3). The stereochemistry of the oxirane ring remains undetermined. Compound **5** was characterized as the 5α -[4-hydroxybenzoate] of lancerotol (4).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were measured in capillaries on a Toshniwal Apparatus and are uncorrected. Optical rotations were determined with a Jasco Dip-181 Polarimeter. Ir spectra were recorded with a 399B Perkin Elmer, and uv spectra with a SPB-100 Pye Unicam Spectrometer. ^1H -nmr spectra were obtained in Bruker 400 and Varian FT-80A (CDCl_3 , TMS as internal standard) instruments. The mass spectra were measured with a Finnigan MAT.

EXTRACTION AND ISOLATION PROCEDURES.—A chromatographic eluate [SiO_2 column, CHCl_3 -MeOH (9:1) 8.5 g] from the MeOH extract of *F. jaeschkeana* rhizomes was obtained in accordance with the experimental data reported by Garg *et al.* (2) and was further chromatographed on a SiO_2 column using petroleum ether (40–60°)/ Me_2CO (1–15%) mixtures. The petroleum ether (40–60°)/ Me_2CO (6%) eluate on preparative tlc separation with SiO_2 yielded three compounds, the 5α -vanillate of 2,3-epoxy-jaeschkeanadiol (R_f 0.52) [**1**], the 5α -[4-hydroxybenzoate] of lancerotol (R_f 0.44) [**5**], and 2 β -hydroxy-3,4-epoxy-jaeschkeanadiol (R_f 0.35) [**4**], when developed in CHCl_3 -MeOH (85:15). These tlc plates, when sprayed with a 1% solution of vanillin/ H_2SO_4 , produced red, blue, and orange colors for compounds **1**, **4**, and **5**, respectively, on heating at 110° for 10 min. Only the red spot changed into blue on keeping the tlc plate at room temperature.

5α -Vanillate of 2,3-epoxy-jaeschkeanadiol [1**].**—This compound (100 mg) crystallized as colorless needles (MeOH), mp 104–105°, $\text{C}_{23}\text{H}_{32}\text{O}_6$, uv λ max (MeOH) 262, 292 nm (log ϵ 4.6, 4.23), $[\alpha]^{20}_{\text{D}} + 11.2$ ($c = 3.0$, CHCl_3), ir (KBr) ν max 3410, 3150, 2960, 2920, 1690, 1600, 1530, 1470, 1380, 1290, 1230, 1190, 1130, 1040, 960, 880, 770 cm^{-1} ; ^1H nmr see Table 1; ^{13}C nmr see Table 2; ms m/z (rel. int.) $[\text{M} - \text{C}_3\text{H}_7]^+$ 361 (5), $[\text{M} - \text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COO}]^+$ 237

(7), $[\text{M} - \text{H}_2\text{O} - \text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COO}]^+$ 219 (4), $[\text{M} - \text{C}_3\text{H}_7 - \text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COOH}]^+$ 193 (13), $[\text{M} - \text{H}_2\text{O} - \text{C}_3\text{H}_7 - \text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COOH}]^+$ 175 (8), $[\text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COOMe}]^+$ 168 (40), 151 (100), 133 (8), 123 (13), 109 (5), 93 (4), 83 (18). Found C 68.10, H 8.0; $\text{C}_{23}\text{H}_{32}\text{O}_6$ requires C 68.31, H 7.91.

MONOACETATE 2.—Acetylation of **1** (20 mg) in pyridine (0.5 ml) and Ac_2O (0.5 ml) at room temperature followed by usual work-up and cc on SiO_2 using petroleum ether (40–60°)/ Me_2CO (2%) as eluent yielded **2** as colorless amorphous powder $[\alpha]^{20}_{\text{D}} + 18$ ($c = 2.0$, CHCl_3); uv λ max (MeOH) 242, 290 nm; ir (KBr) ν max 3500, 2930, 2920, 1740, 1695, 1595, 1500, 1450, 1400, 1370, 1360, 1260, 1230, 1180, 1160, 1020, 950, 870, 750 cm^{-1} ; ^1H nmr see Table 1; ms m/z (rel. int.) $[\text{M} - \text{C}_3\text{H}_7]^+$ 403 (5), $[\text{M} - \text{C}_3\text{H}_7 - \text{COCH}_3]^+$ 361 (3), 279 (2), 251 (1), $[\text{M} - \text{C}_3\text{H}_7 - \text{COCH}_2 - \text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COOH}]^+$ 193 (45), $[\text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COOH}]^+$ 168 (65), $[\text{C}_6\text{H}_3(\text{OH})(\text{OMe})\text{COOH} - \text{OH}]^+$ 151 (100).

HYDROLYSIS OF 1.—Compound **1** (30 mg) in MeOH (2 ml) was refluxed with 5% aqueous methanolic KOH for two h. Its usual work-up for acidic and alcoholic compounds afforded vanillic acid and 2,3-epoxy-jaeschkeanadiol [**3**], respectively (identical mp, ir, ^1H nmr, and mass).

2 β -Hydroxy-3,4-epoxy-jaeschkeanadiol [4**].**—Colorless viscous mass (20 mg), $\text{C}_{15}\text{H}_{26}\text{O}_4$, $[\alpha]^{20}_{\text{D}} + 47$ ($c = 1.5$, CHCl_3); ir (KBr) ν max 3350, 2930, 1450, 1370, 1260, 1160, 1040, 1000, 920, 910, 870, 800, 760 cm^{-1} ; ^1H nmr see Table 1, ^{13}C nmr see Table 2; ms m/z (rel. int.) $[\text{M} - \text{C}_3\text{H}_7]^+$ 227 (72), $[\text{M} - \text{C}_3\text{H}_7 - \text{H}_2\text{O}]^+$ 209 (16), $[\text{M} - \text{C}_3\text{H}_7 - 2\text{H}_2\text{O}]^+$ 191 (54), 163 (82), 149 (100), 135 (38), 121 (88), 71 (90). Found C 66.90, H 9.50; $\text{C}_{15}\text{H}_{26}\text{O}_4$ requires C 66.67, H 9.63.

5α -[4-hydroxybenzoate] of lancerotol [5**].**—Compound **5**, crystallized as colorless needles (30 mg), mp 160°, $\text{C}_{22}\text{H}_{28}\text{O}_5$ $[\text{M}]^+$ 372, was found identical to 5α -[4-hydroxybenzoate] of lancerotol.

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