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Sesquiterpenes from *Ferula hermonis* Boiss

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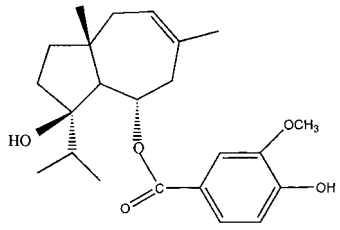
The roots of *Ferula hermonis* Boiss yielded the new 8,9-epoxy derivative of the carotane sesquiterpene jaeschkeanadiol (**2**), together with two other known sesquiterpenes: the less frequently occurring (+)-α-bisabolol and jaeschkeanadiol vanillate (**1**). The identities of the isolated compounds were established from their spectral data and by comparison with published reports.

The genus *Ferula* has been extensively studied, *Ferula hermonis* Boiss was not yet among the investigated species. This note presents the first report on the isolation of epoxyjaeschkeanadiol benzoate (**2**) from nature, besides isolation of the known compounds; jaeschkeanadiol vanillate (**1**) and the less widespread enantiomer (+)-α-bisabolol from *Ferula hermonis* Boiss for the first time.



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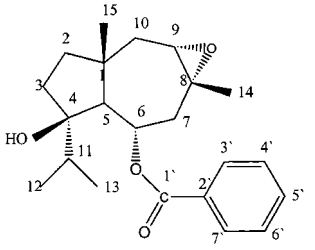

2

The known compound **1** has been reported before in *Ferula eloeochytris* [1], *Ferula jaeschkeana* [2], and in *Ferula rigidula* [3]. (+)-α-Bisabolol was previously isolated from *Atalantia monophylla* Correa [4].

The *n*-hexane extract of the root of *Ferula hermonis* Boiss was fractionated between n-hexane and MeCN. The MeCN fraction was chromatographed on a series of Si gel columns to afford three compounds. The ^{1}H and ^{13}C NMR spectra of **2** (see Experimental section) showed close similarity to the spectra of the previously reported compound jaeschkeanadiol benzoate (the parent compound) [1, 2] except for the presence of two oxygenated carbon signal at δ 56.1 (C-8) and δ 60.8 (C-9), which are typical epoxide carbon signals, instead of the olefinic carbon signals belonging to the parent compound. The occurrence in the ^{13}C NMR of downfield methyl signal at δ 23.3 (Me-14) versus signal at δ 20.2 (Me-14) in the parent compound was a further evidence for the existence of epoxide group between C-8 and 9 in **2**. Inspection of the ^{1}H NMR revealed a signal at δ 1.51 (3 H, s, Me-14) supporting the presence of a methyl group attached to C-8

that became incorporated in an oxirane ring, versus a methyl signal at δ 1.88 (Me-14) attached to the C-8 olefinic carbon in jaeschkeanadiol benzoate The ^{1}H NMR also exhibited a proton signal at δ 2.89 (1 H, t, j = 7.1 Hz, H-9) in place of an olefinic proton at δ 5.61 (1H, brt, H-9) in the parent compound, that is a further indication of the existence of the epoxide group.

The CIMS of the new carotane sesquiterpine **2** showed a molecular ion at m/z 359 $(M + 1)^+$ for $C_{22}H_{30}O_4$ molecular formula, and a base peak at m/z 219 (loss of a hydroxyl group and benzoic acid), another important fragment is m/z 237 (8) (loss of benzoyl moiety), which confirmed structure **2**. The stereochemistry of the oxirane ring was assigned based on biogenetic considerations, chemical transformation and comparison with related compounds [3, 5–6] .

Compound **1** was identified as jaeschkeanadiol vanillate, on the bases of comparing its spectral data with those previously reported [1]. (+)-α-bisabolol (the less frequently occurring enantiomer) was identified by comparing its spectral data with the data pertaining to the hitherto isolated compound [7, 8]. Its relative stereochemistry at C-6 and C-7 was tentatively assigned by comparison with published data [7, 8].

Experimental

1. Apparatus

IR spectra were obtained as thin film on a Perkin-Elmer 5808 spectrophotometer. Optical rotations were recorded in $CHCl_3$ at ambient temperature using a Perkin-Elmer 241 MC polarimeter. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ employing a Varian XL-300 instrument operating at 300 MHz and 75.6 MHz respectively. MS were recorded on a Finnigan MAT 300 mass spectrophotometer, using methane as ionizing gas. TLC was performed on precoated Silica gel 60 F 254 (Merck) using *n*-hexane-EtOAc mixtures as solvent systems. Visualization was accomplished by spraying with *p*-anisaldehyde reagent followed by heating using a hot-air gun [9].

2. Plant material

The dried roots of *Ferula hermonis* Boiss were purchased from herbal stores in Syria and identified by Dr. Sultan-ul-Abdeen, a voucher specimen is deposited at the herbarium of the College of Pharmacy, King Saud University, Ryiadh 11451, Saudi Arabia.

3. Extraction, isolation and purification of the compounds

The dried and ground root cuts of *Ferula hermonis* Boiss (25 g) were extracted with *n*-hexane in a soxhlet apparatus. The *n*-hexane extract (4.7 g) was partitioned between MeCN and *n*-hexane. The MeCN fraction was chromatographed on a series of Si gel columns using *n*-hexane with increasing amounts of EtOAc. The pure fractions were pooled and concentrated to afford compound **1** and compound **2**. The impure fractions were pooled and concentrated to provide an oil. A portion of this oil (80 mg) was further purified by employing reverse-phase CC on RPC18 silica gel (25–40 μ, 6.8 × 3.3 cm), using MeOH–MeCN–H_2O, 4.5:4.5:1.0) for elution. This column yielded (+)-α-bisabolol. Epoxyjaeschkeanadiol benzoate (**2**) (24 mg, oil). R_f 0.27 (10% EtOAc in n-hexane). $[\alpha]_D$ + 41.4 (c 0.074; CH_2Cl_2). IR (film) ν_{max} cm^{-1}:3495 (OH), 1701 (aromatic ester). ^{1}H NMR ($CDCl_3$): δ 0.84 (3 H, d, j = 6.8 Hz, H-13), 0.96 (3 H, d, j = 6.8Hz, H-12), 1.28 (3H, s, H-15), 1.51 (3H, s, H-14). 1.35 (1 H, d, j = 7.4 Hz, H-10b). 2.27 (1 H, d, j = 13.9 Hz, H-10a), 2.29 (1 H, d, j = 13.7 Hz, H-5), 2.89 (1 H, t, j = 7.1 Hz, H-9), 5.47 (1 H, d, t, j = 9.8, 1.7 Hz, H-6), 7.47 (2H, t, j = 7.3 Hz, H-4′, H-6′), 7.56 (1 H, t, j = 7.4 Hz, H-5′), 8.01 (2 H, dd, j = 8.7, 1.8 Hz, H-3′, H-7′). ^{13}C NMR ($CHCl_3$) : δ 44.3 s (C-1), 31.9 t (C-2), 41.3 t (C-3), 86.0 s (C-4), 60.8 d (C-5), 70.4 d (C-6), 44.4 t (C-7), 56.1 s (C-8), 61.0 d (C-9), 41.5 t (C-10), 37.2 d (C-11), 18.5 q (C-12), 17.3 q (C-13), 23.3 q (C-14), 19.4 q (C-15), 166.4 s (C-1′), 130.1 s (C-2′), 128.6 d (C-3′), 129.6 d (C-4′), 133.3 d (C-5′), 129.6 d (C-6′), 128.6 d (C-7′). CIMS (methane) m/z 359 $(m + 1)^+$ (<1), 219 (base peak, loss of hydroxyl group and benzoic acid) (100), 237 (loss of benzoyl moiety) (8). Preparation of **2**: To a strirred solution of jaeschkeanadiol benzoate [10] (13 mg) in $CHCl_3$ (1 ml) was added a solution of m-chloroperbenzoic acid (13 mg) in $CHCl_3$ (1 ml). Stirring was continued for 90 min at room temperature. The reaction was then quenched by addition of saturated aqueous solution of $NaHCO_3$ (1 ml). Usual work up and purification gave **2** (12 mg, white solid) (co chromatography and NMR). (+)-α-Bisabolol : Oil (27 mg). R_f 0.51 (15% EtOAc in *n*-hexane). $[\alpha]_D$ + 13.1 (c 0.064; CH_2Cl_2). IR (film) ν_{max} cm^{-1}:3440 (OH). ^{1}H NMR ($CDCl_3$) : δ 1.12 (3 H, s, H-14), 1.63 (3 H, s, H-13), 1.66 (3 H, s, H-15), 1.69 (3 H, s, H-12), 5.14 (1 H, brt, H-10), 5.38 (1 H, br s, H-2). ^{13}C NMR ($CHCl_3$): δ 27.0 t (C-1), 120.6 d (C-2), 134.2 s (C-3), 31.0 t (C-4), 23.3 t (C-5), 42.9 d (C-6), 74.4 s (C-7), 40.1 t (C-8), 22.1 t (C-9), 124.6 d (C-10), 131.8 s (C-11), 23.4 q (C-12), 17.7 q (C-13), 25.8 q (C-14), 23.2 q (C-15). CIMS (methane) m/z 223 $(M + 1)^+$ (<1), 205 (base peak, loss of hydroxyl group) (100), 207 (loss of methyl group) (5.7).

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