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NEW DITERPENOIDS FROM *SALVIA DIVARICATA*

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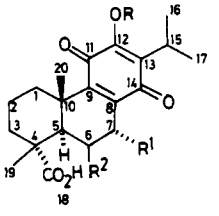
ABSTRACT.—Three new diterpenoids, 6-oxoroyleanone-18-oic acid [**1**], 6-oxo-12-methylroyleanone-18-oic acid [**2**], and horminone-18-oic acid [**3**], and a new linear sesquiterpene, salvinine [**4**], together with a group of known aromatic acids, were isolated from the aerial parts of *Salvia divaricata*.

In our continuing chemical investigations of Turkish *Salvia* species, we now report on the aerial parts of *Salvia divaricata* Montbret et Aucher ex. Bentham (Labiatae). We have isolated three new abietane diterpenoids, 6-oxoroyleanone-18-oic acid [**1**], 6-oxo-12-methylroyleanone-18-oic acid [**2**], and horminone-18-oic acid [**3**], and a new linear sesquiterpne, salvinine [**4**], in addition to the known aromatic acids salicylic, 3-methoxysalicyclic, *p*-hydroxybenzoic, and *cis*- and *trans-p*-coumaric acids as well as ursolic and oleanolic acids and β-sitosterol. All structures were established by spectral data.

The hrms of 6-oxoroyleanone-18-oic acid [**1**] indicated molecular formula $C_{20}H_{24}O_6$ (*m/z* 360.1566, calcd 360.1572). The uv spectrum of **1** exhibited maxima at 405 and 343 nm, indicating a quinoid ring system. In the ir spectrum signals were observed at 1680, 1660 cm^{-1} (*p*-quinoid system), 1700 cm^{-1} (carboxyl), 1720 cm^{-1} (carbonyl) and 3460 cm^{-1} (hydroxyl). The ^{1}H-nmr spectrum showed resonances for an acid proton at 12.88 (1H, br s), an isopropyl group at δ 1.32 (6H, d, J=7 Hz, H-16 and H-17), 3.54 (1H, septet, J=7 Hz, H-15), and two methyl signals at δ 1.27 (3H, s, H-19) and 1.37 (3H, s, H-20). The chemical shift of the latter signal indicated the presence of a carbonyl group at C-6 (1,2); this conclusion was supported by signals for isolated protons at C-7, δ 3.01 (1H, d, J=14.5 Hz, H-7β) and 2.81 (1H, d, J=14.5 Hz, J-7α), as well as by a signal at δ 2.79 (1H, s, H-5). The protons of the three sequential methylene groups at C-1, C-2, and C-3 we observed at δ 2.35 (1H, ddd, J=15, 5, and 1 Hz, H-1β), 1.60 (1H, ddd, J=15, 13 and 5 Hz, H-1α), 2.12 (1H, m, H-2β), 1.72 (1H, ddd, J=13, 12.7, 5, and 4.2 Hz, H-2α), 1.56 (1H, ddd, J=14, 12.7 and 3.9 Hz, H-3β), and 1.22 (1H, m, H-3α) and assigned by spin-



1 R=R^1=H, R^2=O
2 R=Me, R^1=H, R^2=O
3 R=R^2=H, R^1=OH

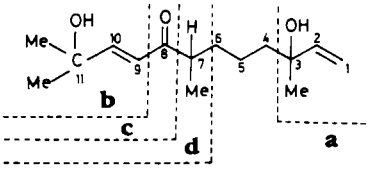


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FIGURE 1. Mass fragmentation analysis of **4**.

decoupling experiments. Signals for the isoproyl group and for two other methyl groups, as well as biogenetic considerations, were reminiscent of an abietane skeleton for compound **1** (3,4). ^{13}C-nmr, SFORD, and APT experiments showed four methyl, four methylene, two methine, and ten quaternary carbon atoms for **1**. The presence of a six-membered ring ketone at 200.9 ppm, two quinoid carbonyl signals at 186.7 and 182.3 ppm, and the carboxyl signal at 177.9 ppm (Table 1) were also in agreement with the suggested structure. The acid group could be either at C-4 or at C-10. In cases where there is a substituent at C-10 the two methyl groups at C-4 appear at ca. 33.0 ppm (Me-18) and 22.0 ppm (Me-19); the absence of a 33.0 ppm signal in the ^{13}C-nmr spectrum indicated that the carboxyl group should be at C-4 (5). Since Me-18 would not be expected to be at higher field (ca. 12–17 ppm), compound **1** should have the given structure.

TABLE 1. ^{13}C-nmr Data for Compounds **1**, **2**, and **3**.

Carbon	Compound		
	1	**2**	**3**
C-1	35.40	35.79	35.90
C-2	19.85	20.01	20.40
C-3	41.85	40.91	39.72
C-4	36.77	36.80	36.70
C-5	47.94	48.25	45.62
C-6	200.90	201.70	41.20
C-7	29.60	29.60	65.40
C-8	142.80	142.75	143.40
C-9	148.40	149.10	148.00
C-10	38.66	39.01	39.80
C-11	182.30	183.60	184.20
C-12	150.20	150.80	151.40
C-13	124.20	123.90	124.40
C-14	186.70	187.00	184.50
C-15	28.85	29.02	27.75
C-16	21.50	21.45	21.80
C-17	21.50	21.55	21.80
C-18	177.90	178.20	181.70
C-19	16.28	15.30	16.10
C-20	23.18	23.30	26.20
OMe	—	57.73	—

The hrms of compound **2** showed a molecular formula $C_{21}H_{26}O_6$ (*m/z* 374.1735, calcd 374.1729). The uv (406, 346 nm) and the ir (1722, 1700, 1680, 1650 cm^{-1}) spectra were similar to those of compound **1**. The ^{1}H-nmr spectrum of **2**, with the signals at δ 12.85 (1H, s, COO*H*), 1.32 (6H, d, J=7 Hz, H-16 and H-17), 3.53 (1H, septet, J=5 Hz, H-15), 1.26 (3H, s, H-19), 1.37 (3H, s, H-20), and the isolated protons at C-7, δ 2.99 (1H, d, J=14 Hz, H-7β) and 2.75 (1H, d, J=14 Hz, H-7α), and the signal for H-5 at δ 2.78 (1H, s), was quite similar to that of **1**, with the exception of the signal at δ3.96 (3H, s, OMe) which could only be at C-12. Thus the spectral data indicate that compound **2** is the 12-methyl derivative of **1**. ^{13}C-nmr, SFORD, and APT experiments indicated five methyl, four methylene, two methine, and ten quaternary carbon atoms for **2** (Table 1) in agreement with the given structure.

Compound **3** had a molecular formula $C_{20}H_{26}O_6$ as indicated by hrms (*m/z* 362.1722, calcd 362.1729). The ir spectrum of **3** indicated the presence of hydroxyl (3450 cm^{-1}), acid (1700 cm^{-1}) and *p*-quinoid (1675, 1650 cm^{-1}) absorbancies. The ^{1}H-nmr spectrum was similar to that of horminone (6) with the resonances at δ 1.22 (6H, d, J=7 Hz, H-16 and H-17), 3.18 (1H, septet, J=7 Hz, H-15), 1.21 (3H, s, H-20), 1.14 (3H, s, H-19), 4.76 (1H, m, H-7), 7.25 (1H, br s, 12-OH) (D_2O exchange). The stereochemistry of the hydroxyl group at C-7 was decided as α by measuring the J values of the signal at δ4.74 (1H, dd, J=2.2 Hz and 4.1 Hz, H-7β) after the addition of D_2O in the ^{1}H-nmr spectrum and by studying a Dreiding model. The absence of one methyl signal and the presence of an acid proton signal at δ 12.88 clearly indicate that compound **3** is horminone-18-oic acid. The position of the acid group at C-18 was decided using the same reasoning given for **1**. The ^{13}C-nmr data is in agreement with **1**.

The ir spectrum of the last com-

pound, salvinin [**4**], showed resonances for hydroxyl (3450 cm^{-1}), carbonyl (1725 cm^{-1}), and unsaturation (1630 cm^{-1}). The hrms of **4** indicated molecular formula $C_{15}H_{26}O_3$ (*m/z* 254.1888, calcd 254.1877). The ^{1}H-nmr spectrum indicated a terminal ethylene group, signals at δ 5.85 (1H, dd, *J*=10 Hz and 17 Hz), 5.17 (1H, dd, *J*=1.5 Hz and 17 Hz), and 4.99 (1H, dd, *J*=1.5 Hz and 10 Hz). Signals at δ 6.4 (1H, d, *J*=16 Hz, H-9) and 6.9 (1H, d, *J*=16 Hz, H-10) indicated the presence of a trans ethylene group. Methyl signals were present at δ 1.37 (6H, s, 2×Me, C-11), 1.28 (3H, s, 3-Me), 1.17 (3H, d, *J*=7 Hz, 7-Me), and additional signals were at δ 4.1 (1H, m, H-7), 3.03 (2H, t, *J*=7 Hz, H-4), and 1.6 (4H, m, H-5 and H-6). The latter two signals indicated three adjacent methylene groups. Mass degradation of **4** (Figure 1) fully supported its assigned structure. The base peak at *m/z* 71.0779 (fragment **a**) (C_4H_7O) showed that the ethylene group was attached to a carbon atom carrying a methyl and a hydroxyl group, and the fragments at *m/z* 85.064 (fragment **b**) (C_5H_9O), *m/z* 113.0063 (fragment **c**) ($C_6H_9O_2$), *m/z* 141.0090 (fragment **d**) ($C_8H_{13}O_2$) were consistent with the tail part of the molecule.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Spectra were recorded with the following instruments: ^{1}H nmr and ^{13}C nmr on a Bruker AC 200 L; ir on a Perkin-Elmer 983; uv Varian Techtron 635; ms Kratos MS 30.

PLANT MATERIAL.—Aerial parts of *S. divaricata* were collected from eastern Turkey (Erzincan) in July 1987 and identified by one of us (E. Tuzlaci). A voucher specimen (MARE 858) is deposited in the Herbarium of the Faculty of Pharmacy, University of Marmara, Istanbul.

ISOLATION OF THE COMPOUNDS.—Air-dried and powdered plant (1.1 kg) was extracted with petroleum ether and Me_2CO; 28 and 40 g residues were obtained, respectively. The Me_2CO extract was chromatographed on a Si gel column (5×70 cm). The compounds were eluted with petroleum ether, and a gradient of Me_2CO was aded up to 100%, followed by MeOH up to 100%. Compounds were obtained in the following order: salvinin (8 mg), 6-oxo-12-methylroyleanone-18-oic acid (15 mg), 6-oxoroyleanone-18-oic acid (12 mg), horminone-18-oic acid (10 mg), 3-methoxysalicylic acid (5 mg), β-sitosterol (200 mg), *cis-p*-coumaric acid (6 mg), *trans-p*-coumaric acid (12 mg), salicylic acid (8 mg), *p*-hydroxybenzoic acid (10 mg). Oleanolic and ursolic acids precipitated during the evaporation of the Me_2CO extract (the crude mixture was 10 g). Previously known compounds were identified by comparison with known standards.

6-Oxoroyleanone-18-oic acid [**1**].—Light yellow amorphous compound: uv λ max (MeOH) 405 (log ε 2.9), 343 (log ε 3.5), 273 (log ε 4.3) nm; ir ν max ($CHCl_3$) 3460, 2980, 2860, 1720, 1700, 1680, 1660, 1450, 1360 cm^{-1}; ^{1}H nmr ($CDCl_3$) see text; ^{13}C nmr ($CDCl_3$) see Table 1; hrms *m/z* (rel. int. %) [M]$^+$ 360.1566 (25) ($C_{20}H_{24}O_6$), [M−Me]$^+$ 345 (27), 314 (35), 299 (17), 245 (6), 203 (10), 187 (10).

6-Oxo-12-methylroyleanone-18-oic acid [**2**].—Light yellow amorphous compound: uv λ max (MeOH) 406 (log ε 2.88), 346 (log ε 3.6), 272 (log ε 4.3) nm; ir ν max ($CHCl_3$) 3450, 2980, 2850, 1722, 1700, 1680, 1650, 1450, 1380 cm^{-1}); ^{1}H nmr ($CDCl_3$) see text; ^{13}C nmr ($CDCl_3$) see Table 1; hrms *m/z* (rel. int. %) [M]$^+$ 374.1735 (55) ($C_{21}H_{26}O_6$), [M-Me]$^+$ 359 (27), 314 (35), 299 (17), 245 (6), 203 (10), 187 (10).

Horminone-18-oic acid [**3**].—Light yellow amorphous compound: uv λ max (MeOH) 408 (log ε 2.9), 346 (log ε 3.6), 273 (log ε 4.0) nm; ir ν max ($CHCl_3$) 3450, 2980, 2870, 1700, 1675, 1650, 1630, 1600, 1460, 1395, 1150, 1100, 960 cm^{-1}; ^{1}H nmr ($CDCl_3$) see text; ^{13}C nmr see Table 1; hrms *m/z* (rel. int. %) [M]$^+$ 362.1722 (40), [M-Me]$^+$ 347 (70), [M-COOH]$^+$ 317 (20), 277 (20), 252 (10), 187 (10).

Salvinin [**4**].—Colorless amorphous compound: $[\alpha]^{20}D \pm 0°$ (MeOH, *c*=0.1); uv λ max (MeOH) 226 (log ε 4.5) nm; ir ν ($CHCl_3$) 3450, 2960, 2840, 1725, 1630, 1480, 1350, 1200, 1130, 1020, 980 cm^{-1}; ^{1}H nmr ($CDCl_3$) see text; hrms *m/z* (rel. int. %) [M]$^+$ 254.1888 (1.5) ($C_{15}H_{26}O_3$). 71 (fragment **a**, 100). 85 (fragment **b**, 28), 113 (fragment **c**, 31), 141 (fragment **d**, 7).

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