Phytochemistry, Vol. 21, No. 7, pp. 1812–1813, 1982.
Printed in Great Britain.

0031-9422/82/071812-02$03.00/0

SESTERTERPENES FROM *SALVIA HYPOLEUCA**

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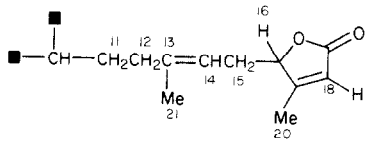
(*Received* 6 *October* 1981)

Key Word Index—*Salvia hypoleuca*; Labiatae; sesterterpenes.

Abstract—The aerial parts of *Salvia hypoleuca* afforded two sesterterpenes with a previously unknown carbon skeleton.

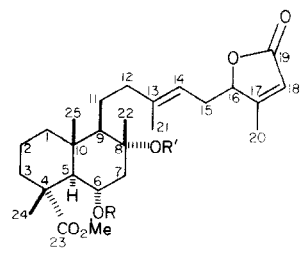
The aerial parts of *Salvia hypoleuca* Benth. afforded two crystalline compounds, molecular formula $C_{26}H_{40}O_6$ and $C_{25}H_{36}O_5$. Acetylation of the former gave a mono- and a diacetate, while the IR spectrum showed the presence of an ester group (1740 cm^{-1}) and of a γ-lactone (1765 cm^{-1}). Thus the nature of all oxygen functions of the first compound was established. The second compound was also an alcohol as shown by the IR spectrum, which further displayed bands for two γ-lactones (1790, 1775 cm^{-1}).

The ^1H NMR data (Table 1) of the two lactones were in part very similar. However, a three-fold doublet at δ 3.61 was shifted to 4.29 in the dilactone, indicating that the second compound was most likely the lactone of a hydroxy acid which corresponded to the ester. The nature of the second lactone ring, present in both compounds, was evident from the downfield signals at δ 4.90 and 5.89. The latter signal was due to an olefinic proton which coupled with an olefinic methyl group. Spin decoupling of the spectrum of the ester showed that the olefinic proton was coupled with the proton which resonates at δ 4.90. The latter was further coupled with a pair of three-fold doublets which were themselves coupled with an olefinic proton (δ 5.04). Irradiation of these signals sharpened a further olefinic methyl signal at 1.67 and a broadened triplet at 2.09, which was coupled with two protons which gave rise to complex signals at 1.34 and 1.50. As these signals were altered on irradiation of a double doublet at 1.13 sequence **A** was established.

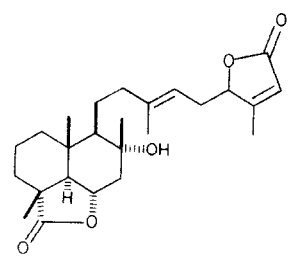


A (carbon numbering as in the final structure)

The remaining signals in the spectra of both compounds were similar to those of labdanes with a carboxyl group at C-4. The position of the hydroxyl groups were established by the ^1H NMR data of the ester, the dilactone and the acetates (Table 1). The introduction of the tertiary acetoxy group caused a downfield shift of one methyl singlet and of the double doublet of H-9 indicating the presence of a tertiary hydroxyl at C-8. As two further double doublets, which were coupled with the proton under the second hydroxyl group were shifted downfield in the spectra of the acetates, a 1, 3-position of the hydroxyls was most likely. Irradiation of a doublet at δ 2.09 collapsed the signal at 3.61 to a double doublet indicating that the former signal most likely was that of H-5. Similar results were obtained by spin decoupling of the dilactone. In this case addition of $Eu(fod)_3$ and spin decoupling allowed the assignment of the remaining signals of H-1–H-3 clearly establishing the presence of a labdane with an additional isoprene unit at C-15. Irradiation of the signals of H-12 and H-5 further showed *W*-couplings with the corresponding methyl groups. All the data and the observed $Eu(fod)_3$-induced shifts agreed with the structures **1** and **4** for the new sesterterpenes. The stereochemistry at C-5 and C-6 followed from the couplings observed, while that at C-8 was proposed following the chemical shifts of H-6β, H-7β and H-9 which favoured an equatorial hydroxyl at C-8. Also the $Eu(fod)_3$-induced shifts supported this assignment.



1 R = R′ = H
2 R = Ac, R′ = H
3 R = R′ = Ac



4

*Part 403 in the series "Naturally Occurring Terpene Derivatives". For Part 402 see Sarg, T. H., Omar, A. A., Khafagy, S. M., Grenz, M. and Bohlmann, F. (1982) *Phytochemistry* **21**, 1163.

Table 1. ^{1}H NMR and ^{13}C NMR spectral data of compounds **1–4**

	^{1}H NMR*					^{13}C NMR	
	1	**2**	**3**	**4**	+ Eu(fod)$_3$	**1**	$CDCl_3$
H-1α	1.05*ddd*	1.08*ddd*	1.12*ddd*	0.98*ddd*	1.73*ddd*	C-1	38.2*t*
H-1β	1.60*m*	1.60*m*	1.60*m*	1.75*m*	2.38*dbr*	C-2	17.4*t*
H-2α				1.63*m*	2.20*m*	C-3	39.2*t*
H-2β	1.55*m*	1.55*m*	1.55*m*		2.09*dbr*	C-4	44.4*s*
H-3α				1.67*m*	2.48*ddd*	C-5	60.3*d*
H-3β				1.87*ddd*	2.70*dbr*	C-6	67.1*d*
H-5	2.09*d*	2.30*d*	2.36*d*	1.50*d*	2.83*d*	C-7	53.9*t*
H-6	3.61*ddd*	4.84*ddd*	4.92*ddd*	4.29*ddd*	5.25*ddd*	C-8	73.5*s*
H-7α	1.55*m*	1.58*m*	1.90*m*	1.68*m*	3.12*dd*	C-9	56.0*d*
H-7β	2.20*dd*	2.18*dd*	2.88*dd*	2.46*dd*	3.59*dd*	C-10	38.2*s*
H-9	1.13*dd*	1.16*dd*	1.68*dd*	1.21*dd*	2.73*m*	C-11	23.2*t*
H-11	1.34*ddt*	1.36*ddt*	1.39*ddt*	1.47*m*	2.85*m*	C-12	42.7*t*
H-11′	1.55*m*	1.55*m*	1.58*ddt*	1.65*m*		C-13	141.0*s*
H-12	2.09*tbr*	2.09*tbr*	2.09*tbr*	2.15*tbr*	3.34*m*	C-14	117.5*d*
H-12′					3.00*m*	C-15	30.3*t*
H-14	5.04*ddbr*	5.05*dd*	5.08*dd*	5.03*ddbr*	6.10*tbr*	C-16	84.4*d*
H-15	2.73*ddd*	2.71*ddd*	2.68*ddd*	2.73*ddd*	3.50*ddd*	C-17	168.4*s*
H-15′	2.30*ddd*	2.28*ddd*	2.32*ddd*	2.30*ddd*	3.18*ddd*	C-18	116.2*d*
H-16	4.90*ddbr*	4.91*ddbr*	4.90*ddbr*	4.91*ddbr*	6.26*tbr*	C-19	181.4*s*
H-18	5.89*dq*	5.88*dq*	5.86*dq*	5.82*dq*	7.32*sbr*	C-20	16.4*q*
H-20	2.07*dd*	2.07*dd*	2.07*dd*	2.07*dd*	2.55*sbr*	C-21	16.4*q*
H-21	1.67*sbr*	1.66*sbr*	1.66*sbr*	1.66*sbr*	2.20*s*	C-22	25.0*q*
H-22	1.27*s*	1.22*s*	1.53*s*	1.21*s*		C-23	173.3*s*
H-24	1.16*s*	1.10*s*	1.10*s*	1.20*s*	2.06*s*	C-24	13.9*q*
H-25	0.87*s*	0.91*s*	0.93*s*	0.92*s*	1.59*s*	C-25	16.4*q*
OMe	3.64*s*	3.69*s*	3.69*s*	—	—	OMe	52.0*q*
OAc	—	1.94*s*	1.95*s*	—	—		
	—	—	1.92*s*	—	—		

J(Hz): 1α, 1β = 1α, 2β = 13; 1α, 2α = 4.5; 5α, 6β = 6β, 7α = 11; 6β, 7β = 4; 9α, 11 = 5; 9α, 11′ = 4; 11, 11′ = 14; 11, 12 = 11′, 12′ = 7; 14, 15 = 7.5; 14, 15′ = 7; 15, 15′ = 15; 15, 16 = 4.5; 15′, 16 = 6.5; 16, 18 = 1.5; 16, 20 = 1; 18, 20 = 1.5 (compound **4**: 2α, 2β = 15; 2β, 3α = 3α, 3β = 13; 2β, 3α = 4; 6β, 7α = 7α, 7β = 12; 6β, 7α = 4).

*400 MHz, $CDCl_3$, TMS as int. standard.

Furthermore, the ^{13}C NMR spectrum of **1** was in good agreement with the proposed stereochemistry. However, the configuration at C-16 and the absolute one were not determined. We have named the free acid which corresponds to **1** and **4** salvileucolide.

EXPERIMENTAL

The air-dried plant material (300 g) collected north of Teheran was extracted with Et_2O. The extract was treated with MeOH to remove saturated hydrocarbons followed by CC (Si gel) and TLC (Si gel) affording 80 mg **1** and 50 mg **4** (C_6H_6–CH_2Cl_2–Et_2O, 1:1:1).

Salvileucolide methyl ester (**1**). Colourless crystals, mp 165°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1765 (γ-lactone), 1740 (CO_2R), 1655 (C=C); CIMS (*iso*-butane) *m/z* (rel. int.): 449 $[M+1]^+$ (18) ($C_{26}H_{40}O_6+1$), 431 $[449-H_2O]^+$ (17), 413 $[431-H_2O]^+$ (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+22.5 \quad +24 \quad +25 \quad +40} \quad (CHCl_3;\ c\ 0.2).$$

Compound **1**. (10 mg) in 1 ml Ac_2O was heated for 2 hr at 70°. TLC afforded 4 mg **2** and 3 mg **3**.

Compound **2**. Colourless gum, MS *m/z* (rel. int.): 490 $[M]^+$ (1), 430.271 $[M-AcOH]^+$ (7) ($C_{26}H_{38}O_5$), 412 $[430-H_2O]^+$ (7), 397 $[412-Me]^+$ (9), 234 [412 – side-chain]$^+$ (65), 202 $[234-MeOH]^+$ (38), 81 $[C_5H_5O]^+$ (100).

Compound **3**. Colourless gum, MS *m/z* (rel. int.): 532 $[M]^+$ (0.1), 472 $[M-AcOH]^+$ (0.6), 412.260 $[472-AcOH]^+$ (5) ($C_{26}H_{36}O_4$), 397 $[412-Me]^+$ (17), 234 [412 – side-chain]$^+$ (100), 202 $[234-MeOH]^+$ (41), 81 $[C_5H_5O]^+$ (97).

Salvileucolide-6,23-lactone (**4**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1790, 1775 (γ-lactone); CIMS (*iso*-butane) *m/z* (rel. int.): 417 $[M+1]^+$ (100) ($C_{25}H_{36}O_5+1$); 399 $[417-H_2O]^+$ (75), 355 $[399-CO_2]^+$ (38).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+143 \quad +145 \quad +147 \quad +165} \quad (CHCl_3;\ c\ 0.34).$$

Acknowledgement—A.R. thanks Dr. Termeh for identification of the plant material.