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SALVILEUCOLIDE METHYLESTER, A SESTERTERPENE FROM *SALVIA SAHENDICA*

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Abstract—The sesterterpenoid salvileucolide methylester has been isolated from the aerial parts of *Salvia sahendica* as the major constituent. A full assignment of its ^{13}C NMR spectral data is presented. Additionally, salvigenin (5-hydroxy-6,7,4′-trimethoxyflavone) and sclareol (14-labdene-8α,13*S*-diol) have been isolated from the title plant.

INTRODUCTION

Salvia sahendica BOISS & BUHSE is an endemic plant of Iran which is widely distributed in the northern hilly areas of Azerbayjan, preferentially in the surroundings of Mountain 'Sahand' after which the species is named [1].

The recently reported presence of interesting sesterterpenoid compounds in Iranian *Salvia* species [2] prompted us to undertake a systematic phytochemical investigation of these species. In this note we report our study of *Salvia sahendica* which has not been investigated previously.

RESULTS AND DISCUSSION

Extraction of the aerial parts of *Salvia sahendica* followed by column chromatography, yielded from the polar fractions, a crystalline main constituent (0.072%), molecular formula $C_{26}H_{40}O_6$. The spectral data, in particular extensive homo-(COSYDQF, TOCSY, NOESY) and hetero-(HMQC, long range ^{13}C–^1H COSY) 2D NMR experiments led to the assignment of the sesterterpenoid constitution **1** for this compound. The relative configuration at C-16 and the absolute one were not determined.

A similar substance (**1**), named 'salvileucolide methylester' was isolated several years ago from *Salvia hypoleuca* in Iran, as a main constituent (0.027%) together with its corresponding 6,23-lactone (0.017%) [3]. The comparison of the physical data of **1** showed the identity of the numerical values reported in ref. [3] and confirmed the proposed formula. However, due to the use of more sophisticated NMR techniques which enabled the unambiguous allocation of all the protons and carbons of **1**, several assignments have to be revised. Concerning the

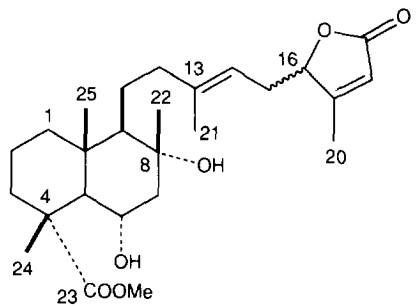

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Table 1. ^{13}C NMR spectral data of **1**

	$CDCl_3$	Pyridine-d_5		$CDCl_3$	Pyridine-d_5
C-1	39.0	37.1	C-14	116.1	114.4
C-2	17.3	15.5	C-15	30.2	28.3
C-3	37.9	35.8	C-16	84.2	82.1
C-4	44.3	42.3	C-17	168.2	166.9
C-5	55.8	54.6	C-18	117.3	114.9
C-6	67.0	63.5	C-19	173.3	170.8
C-7	53.7	52.6	C-20	13.9	11.2
C-8	73.3	70.5	C-21	16.3	14.2
C-9	60.1	59.0	C-22	24.9	23.4
C-10	38.1	36.0	C-23	181.2	178.0
C-11	23.1	21.8	C-24	16.2	14.6
C-12	42.6	41.2	C-25	16.3	14.3
C-13	140.9	138.6	OMe	51.9	49.2

^1H NMR, only those of H-1α (δ2.20, *dd*, $J = 11$, 4 Hz, axial H) and H-1β (1.55, *m*) as well as those of H-22 (1.13, $^1J_{H,C}$-correlation with the Me-signal at 24.9) and H-24 (1.24, $^1J_{H,C}$-correlation with the Me-signal at 16.4) must be interchanged. The more significant revision of the ^{13}C NMR spectrum is reported in Table 1. In order to

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verify the assignments, selected 2D NMR experiments were performed in pyridine-d_5. According to these pyridine-induced solvent shifts [4], the assignment of all the carbons could be confirmed via their correlation of the relevant paramagnetically shifted ^{1}H signals (see Experimental).

The medium polar fraction afforded salvigenin (5-hydroxy-6,7,4′-trimethoxy-flavone, 0.009%) [5–7] and sclareol (14-labdene-8α, 13*S*-diol, 0.05%) [8, 9]. Both compounds were compared with authentic samples and proven to be identical in every respect (see Experimental).

This is the second report on the occurrence of salvileucolide methylester (**1**). It seems that Iranian *Salvia* species contain such sesterterpenoids as main constituents, a fact that might be of chemotaxonomical importance.

EXPERIMENTAL

General. 2D NMR experiments were performed on BRUKER AMX-600 ($CDCl_3$) and ARX-300 (pyridine-d_5) instruments.

Plant material. Aerial parts of *Salvia sahendica* BOISS & BUHSE were collected near Bostanabad, *ca* 40 km east of Tabriz, Iran in September 1991 and identified by Eng. G.R. Amin (Faculty of Pharmacy, Tehran University). A voucher specimen is deposited at the Herbarium of the Faculty of Pharmacy, Tehran University.

Extraction and isolation. Air-dried aerial parts (1.7 kg) of *S. sahendica* were pulverized and extracted with petrol–$CHCl_3$ (1:1) at room temp. for 24 hr, the extract evapd to dryness and the residue treated with MeOH to remove waxy components. CC (silica gel, increasing polarity of petrol–EtOAc) of the MeOH soluble part followed by CC (silica gel, hexane–toulene–Me_2CO, 2:3:1) yielded salvigenin (160 mg) and sclareol (840 mg), and the polar fr. (hexane–toluene–Me_2CO, 1:2:2) afforded crude **1** which was recrystallized from hexane–CH_2Cl_2 to give pure **1** (1.22 g, 0.072%).

Salvileucolide–methylester (**1**). Leaflets, *mp* 175.5°; $[\alpha]_D$ + 21.5 ($CHCl_3$, *c* 1.03); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3690, 3490 (OH), 1760sh, 1745, 1718sh (γ-lactone and CO^2Me), 1645 (C = C): ^{1}H NMR (pyridine-d_5): δ0.89 (*s*, 3H, H-25), 1.12 (*dt*, 1H, *J* = 3.5, 12.8, 7.8 Hz, H-1α), 1.35 (*s*, 3H, H-22), 1.50 (*dd*, 1H, *J* = 4, 5 Hz, H-9α), 1.51 (*s*, 3H, H-24), 1.69 (*s*, 3H, H-21), 1.87 (*d*, 3H, *J* = 1.3 Hz, H-20), 2.43 (*d*, 1H, *J* = 11 Hz, H-5), 2.54 (*dd*, ^{1}H, *J* = 3.8, 11.9 Hz, H-7α), 3.67 (*s*, 3H, OMe), 3.96 (*dt*, 1H, *J* = 3.8, 11 Hz, H-6), 4.92 (*t*, 1H, *J* = 5 Hz, H-16), 5.27 (*t*, 1H, *J* = 7 Hz, H-14), 5.90 (*q*, 1H, *J* = 1.3 Hz, H-18); ^{13}C NMR see Table 1; EIMS *m/z* (rel. int.): 448 $[M]^+$ (10) ($C_{26}H_{40}O_6$), 430 $[M - H_2O]^+$ (26), 416 $[M - MeOH]^+$ (3), 398 $[M - H_2O - MeOH]^+$ (11), 363 (3), 362 (11), 334 (19), 330 (12), 302 (15), 273 (6), 255 (10), 234 (26), 195 (19), 175 (29), 159 (19), 147 (21), 121 (36), 109 (100), 69 (16), 51 (21); ^{1}H NMR in $CDCl_3$, and EIMS as in ref. [3].

Salvigenin (*5-hydroxy-6,7,4′-trimethoxyflavone*). Yellow crystals, mp 190–191.5° (188–189° [5]). R_f, UV/VIS, IR, ^{1}H, ^{13}C NMR, and EIMS were compared with an authentic sample and all data are in full agreement with reported values [5–7].

Sclareol (*14-labdene-8α, 13S-diol*). Needles, mp 104–105° (104.5–105.0° [9]). R_f, $[\alpha]_D$, IR, ^{1}H, ^{13}C NMR and EIMS were compared with an authentic sample and all data are in full agreement with reported values [8, 9].

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