Pergamon

Phytochemistry, Vol. 46, No. 3, pp. 587–589, 1997

Printed in Great Britain
0031–9422/97 $17.00+0.00

PII: S0031–9422(97)00306–3

A NEO-CLERODANE DITERPENOID FROM *SCUTELLARIA ORIENTALIS* SUBSP. *PINNATIFIDA*

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(*Received* 4 *February* 1997)

Key Word Index—*Scutellaira orientalis* subsp. *pinnatifida*; Labiatae; neo-clerodane derivatives; scutorientalin E.

Abstract—An acetone extract of the aerial parts of *Scutellaria orientalis* subsp. *pinnatifida* provide a new neo-clerodane, scutorientalin E, whose structure, 7β,19-diacetoxy-6α(*E*)-cinnamoyloxy-4α,18-epoxy-8β-hydroxy-neo-clerod-13-en-15,16-olide, was established by spectroscopic means and by comparison with related compounds. © 1997 Elsevier Science Ltd

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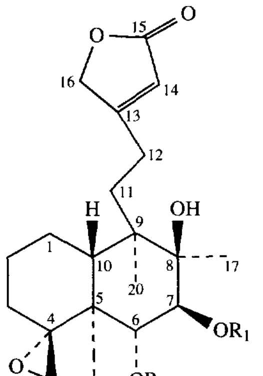
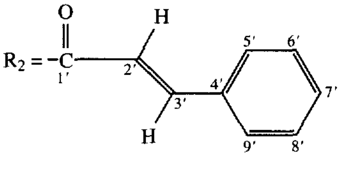
INTRODUCTION

The neo-clerodane diterpenes isolated from *Scutellaria* species [1] are of interest on account of their biological activity as insect anti-feedants [2, 3]. In continuation of our studies on this class of compounds [4–9], we have now reinvestigated aerial parts of *Scutellaria orientalis* subsp. *pinnatifida* and isolated a new neo-clerodane (scutorientalin E, **1**) besides scutorientalin B and D previously found in this plant [8, 9].



1 $R_1 = Ac$

2 $R_1 = R_2 = Bz$



RESULTS AND DISCUSSION

Scutorientalin E (**1**) was assigned the molecular formula $C_{33}H_{40}O_{10}$. Its IR spectrum showed bands for hydroxyl, α,β-unsaturated γ-lactone and ester groups. The ^1H NMR and ^{13}C NMR spectra of **1** (Table 1) were almost identical with those of scutalpin L(**2**) [10]. In fact, the observed differences were consistent with the existence in the former of an (*E*)cinnamoyloxy group (δ_H 6.32*d*, H-2′; 7.58 *d*, $J = 16$ Hz, H-3′; 7.51 *m*, 2H-5′,9′; 7.38 *m*, 3H-6′,7′,8′; δ_C 165.5 *s* C-1′; 117.5 *d*, C-2′; 146.0 *d*, C-3′; 134.3 *s*, C-4′; 128.3 *d*, C-5′ and C-9′, 128.9 *d*, C-6′ and C-8′ and 130.4 *d*, C-7′) and an acetoxyl group instead of the two benzoate groups

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Table 1. ^1H NMR (250 MHz) and ^{13}C NMR (62.9 MHz) spectral data of compound **1** (in $CDCl_3$), δ values relative to residual $CHCl_3$ (δ 7.25) and (δ 77.0)*

H		*J* (Hz)		C†	
1α	~1.43 *m*‡	6β,7β	10	1	21.3 *t*
1β	~2.25 *m*‡	10β,1α	11.8	2	24.8 *t*
2α	~1.60 *m*‡	10β,1β	2.1	3	32.3 *t*
2β	~1.48 *m*‡	12A,12B	13.6	4	65.1 *s*
3α	~2.03 *m*‡	12A,11A	3.6	5	45.9 *s*
3β	~1.12 *m*‡	12A,11B	3.6	6	70.5 *d*
6β	5.30 *d*	18A,18B	3.8	7	74.9 *d*
7α	5.49 *d*	18B,3α	2.0	8	78.6 *s*
10β	2.28 *dd*	2′,3′	16	9	42.5 *s*
11A	~1.54 *m*			10	42.8 *d*
11B	~1.68 *m*‡			11	34.9 *t*
12A	~2.05 *m*‡			12	25.1 *t*
12B	3.12 *ddd*			13	171.3 *s*
14	5.83 *br s*			14	114.5 *d*
16(2H)	4.75 *br s*			15	174.1 *s*
Me-17	1.17 *s*			16	73.2 *t*
18A§	2.32 *d*			17	21.6 *q*
18B¶	3.28 *dd*			18	49.8 *t*
19(2H)	4.71 *br s*			19	62.2 *t*
Me-20	1.01 *s*			20	20.5 *q*
2′	6.32 *d*			1′	165.5 *s*
3′	7.58 *d*			2′	117.5 *d*
5′,9′	7.51 *m*			3′	146.0 *d*
6′,7′,8′	7.38 *m*			4′	134.3 *s*
OAc	1.99 *s*			5′,9′	128.3 *d*
OAc	2.08 *s*			6′,8′	128.9 *d*
				7′	130.4 *d*
				OAc	170.8 *s*
					20.6 *q*
					169.9 *s*
					21.2 *q*

* Spectral parameters were obtained by first-order approximation. All assignments were confirmed by double resonance experiments and were in agreement with ^1H-^{13}C COSY spectra.

† Multiplicities were established by DEPT pulse sequence. All these assignments were in agreement with the HMBC spectrum.

‡ Overlapped signals.

§ *Exo* hydrogen with respect to ring B.

¶ *Endo* hydrogen with respect to ring B.

present in the latter [10]. The ^1H NMR and ^{13}C NMR spectra of **1** showed also signals for two acetoxyl groups (δ 1.99 *s* and 2.08 *s*; δ_C 169.9 *s* and 170.8 *s*) and for an AB system corresponding to the C-6β and C-7α axial protons ($\delta_{H\text{-}6\beta}$ 5.30 *d*; $\delta_{H\text{-}7\alpha}$ 5.49 *d*, $J_{6\beta,7\alpha} = 10.0$ Hz) [4].

The location of the (*E*) cinnamoyloxy group in scutorientalin E (**1**) was established from the heteronuclear multiple bond connectivity (HMBC) spectrum, which showed correlations between the carbonyl carbon of the cinnamoyl moiety (δ 165.5) and the H-6β (δ 5.30) proton, whereas the carbonyl carbons of the two acetoxyl groups (δ 169.9 *s* and 170.8 *s*) were connected with the 7Hα (δ 5.49) and 2H-19 (δ 4.71) protons, thus establishing the positions of the (*E*) cinnamoyloxy (C-6) and the two acetoxy (C-7 and C-19) groups.

Likewise, the presence of a cinnamoyloxy moiety was confirmed by the presence of significant base peak at m/z 131 in the mass spectrum of **1** [11]. The tertiary hydroxyl group of **1** must be at the C-8β position, because the Me-17 protons were paramagnetically shifted at δ_H 1.15 *s* and δ_C 21.3 *q* (C-17) [5, 10]. The relative configuration of **1** was deduced from a NOESY experiment. The axial 6β proton showed NOE's with H-10β, $H_{B\text{-}18}$ and the acetoxyl group at C-7β. Moreover, the Me-20 protons showed NOE's with the H-7α, Me-17 and 2H-19, consequently scutorientalin E(**1**) possessed the same stereochemistry as scutalpin L(**2**) [10]. From all the above data, it was evident that scutorintalin E had the structure depicted in **1**. This neo-clerodane diterpene is the first to be isolated from a *Scutellaria* species with a cinnamoyloxy group. The absolute configuration of **1** was not ascertained. However, on biogenetic grounds, it may be supposed that **1** belongs to the neo-clerodane series, like the other diterpenoids isolated from *Scutellaria* species [1–10].

EXPERIMENTAL

General. Mps: uncorr. Plant materials of *Scutellaria orientalis* subsp. *pinnatifida* were collected in June, 1995 near Sliven, Bulgaria. Voucher specimens are deposited in the herbarium of the Higher Institute of Agriculture of Plovdiv, Bulgaria.

Extraction and isolation of the diterpenoids. Dried and powdered aerial parts of *S. orientalis* subsp. *pinnatifida* (580 g) were extracted as described previously [8].

The $CHCl_3$ extract (3.5 g) was chromatographed on a silica gel column (Merck No 7734, deactivated with 15% H_2O, 130 g). Elution with petrol–EtOAc (4:1) gave scutorientalins B (33 mg) and D (58 mg) [8, 9] and elution with petrol–EtOAc (7:3) gave scutorientalin E (**1**) 103 mg.

Scutorientalin E (**1**). Amorphous solid, mp 116–118°, $[\alpha]_D^{20}$ $-9.56°$ ($CHCl_3$, *c*, 0.283). IR ν_{max}^{KBr} cm^{-1}: 3458 (OH), 2950, 1780, 1746, 1637, 1578, 1500, 1497, 1415, 1376, 1310, 1274, 1240, 1204, 1173, 1129, 1087, 1035, 986, 909, 891, 769, 709, 592. ^1H NMR and ^{13}C NMR (Table 1). EIMS (70 eV, direct inlet) *m/z* (rel. int.): $[M]^+$-absent, 465 ($M-C_9H_7O$) (1.3), 333 (1.7), 315 (3), 285 (1), 201 (1), 189 (1), 187 (2), 173 (1), 149 (2), 147 (3), 133 (2), 131 (100), 113 (3), 111 (3), 103 (16), 98 (5), 97 (4), 95 (4), 91 (4), 87 (6), 85 (28), 83 (43), 81 (5), 69 (6), 57 (7), 55 (9), 43 (40). Found: C 66.18; H 6.87, $C_{33}H_{40}O_{10}$, requires: C 66.43; H 6.76%.

Acknowledgement—This work was supported by the Bulgarian Ministry of Education, Science and Technology (Funds for Scientific Research).

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