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A CLERODANE DITERPENE FROM *SCUTELLARIA ALTISSIMA*

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Key Word Index—*Scutellaria altissima*; Labiatae; neo-clerodane diterpene; scutaltisin; (15*R*,15*S*)-15-hydroxyscutecolumnin C.

Abstract—A mixture of the C-15 epimers of the 15-hydroxy derivative of scutecolumnin C has been isolated from the aerial parts of *Scutellaria altissima*. The structures of the epimers were established by chemical and spectroscopic means.

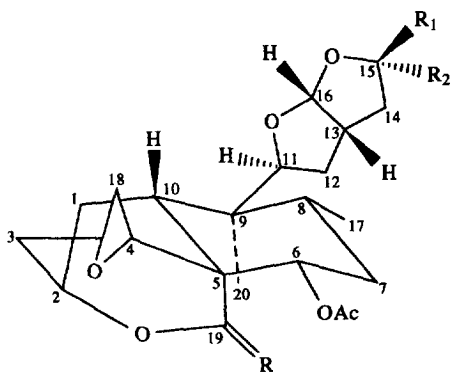
INTRODUCTION

In a continuation of our systematic studies of neo-clerodane diterpenoids within the Labiatae [1–6], we investigated the aerial parts of *Scutellaria altissima*. We report on the isolation and structure determination of a new clerodane derivative, which we have named scutaltisin.

RESULTS AND DISCUSSION

The acetone extract of the aerial parts of *S. altissima*, after column chromatography, provided substance (**1**, $C_{22}H_{32}O_8$) homogenous on TLC. Its ^{1}H NMR spectrum (Table 1) showed essentially the same signals as those present in the spectum of scutecolumnin C (**2**), a neo-clerodane diterpene recently isolated from *S. columnae* [7].

The observed differences between the ^{1}H NMR spectra of compounds **1** (Table 1) and **2** [7] were in agreement with the existence of the former as a 1:1 mixture of the C-15 epimers of the scutaltisin (**1**). Thus, the ^{1}H NMR spectrum of **1** showed a series of double signals i.e. (H-15, H-16, H-11 and H-13) appearing as pairs of doublets [8–10]. Pairs of double doublets and multiplets at δ5.53 *d* (0.5 H, J = 5.5 Hz) and 5.63 *br d* (0.5 H, J = 3.7 Hz); δ5.79 *d* and 5.77 *d* (0.5 H each, both J = 5.3 Hz); δ3.95 *dd* (0.5 H, J_1 = 4.8 Hz; J_2 = 11.4 Hz) and 4.50 *dd* (0.5 H, J_1 = 4.5 Hz; J_2 = 10.3 Hz) and 2.78 and 2.90 *m* (0.5 H each), respectively, were also observed. The only differences between the ^{1}H NMR spectra of the 15*R* and the 15*S* epimers of scutaltisin (**1**) were in the chemical shifts of H-11 ($\Delta\delta$ − 0.55 ppm); H-13 ($\Delta\delta$ + 0.12 ppm) and H-15 ($\Delta\delta$ − 0.10 ppm) (Table 1).



	R	R_1	R_2
1	αH,βOH	OH(*R*)	OH(*S*)
2	αH,βOH	H	H
3	O	O	O

These data clearly established the stereochemistry of the hexahydrofuro-furan side-chain in **1** [8–10]. It is notable that these differences in the chemical shifts of the hexahydrofurofuran side-chain in the C-15 epimers are observed when ring A of the *trans* decalin system is in a boat-twist or chair conformation [11] (the chemical shifts of H-11 (4.34 *dd* and 3.98 *dd*) and H-13 (2.77 *m* and 2.95 *m*) for clerodinin A and B may be reversed [11]). However, these differences were small in compounds with a deformed chair conformation of ring A and only for H-15, H-16, H_3-17 and H_3-20 protons [8–10].

Treatment of scutaltisin (**1**) with acetic anhydride–pyridine at room temperature for 48 hr gave a less polar substance. The ^{1}H NMR spectrum of this substance revealed that the C-19, 2α-hemiacetal grouping had been opened to form the C-19 aldehyde (δ10.17 and 10.16, whereas the doublets at δ5.53 and 5.63 were

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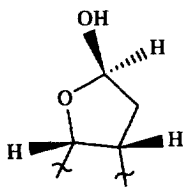
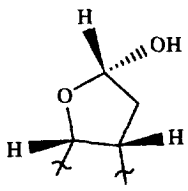
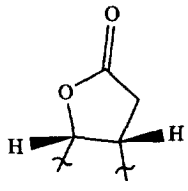
Table 1. ^{1}H NMR spectral data of compounds **1** and **3** (250 MHz, $CDCl_3$, TMS as internal standard)*

	1			3	
					
	15*R*	15*S*	Δ ppm		*J* (Hz)
2β	4.16 *m*	4.16 *m*	—	4.72 *m*	2β, 3α = 4.1
3α (eq)	2.52 *dt*	2.52 *dt*	—	—	6β, 7α = 12.1
6β	4.68 *m*	4.68 *m*	—	4.70 *dd*	6β, 7β = 4.8
11α	3.95 *dd*	4.50 *dd*	− 0.55	4.05 *dd*	11α, 12A = 5.3
13β	2.90 *m*	2.78 *m*	+ 0.12	3.18 *m*	11α, 12B = 11.3
14A	—	—	—	2.22 *dd*	18A, 18B = 4.0
14B	—	—	—	2.88 *dd*	14A, 14B = 18.6
15	5.53 *d*	5.63 *d*	− 0.10	—	16,13 = 5.5
16β	5.79 *d*	5.77 *d*	+ 0.02	6.04 *d*	17, 8β = 6.7
Me-17	0.90 *d*	0.92 *d*	− 0.02	0.90 *d*	
18A	2.43 *d*	2.43 *d*	—	2.45 *d*	
18B	2.95 *m*	2.95 *m*	—	3.20 *d*	
19α	5.72 *s*	5.73 *s*	− 0.01	—	
Me-20	1.08 *s*	1.10 *s*	− 0.02	1.05 *s*	
OAc	2.06 *s*	2.06 *s*	—	2.06 *s*	

*Spectral parameters were obtained by first-order approximation. All these assignments were confirmed by double resonance experiments.

Table 2. ^{13}C NMR spectral data of compound **3** (62.9 MHz, $CDCl_3$ TMS as internal standard)*

C	3	C	3
1	29.1 *t*	12	32.3 *t*†
2	67.1 *d*	13	41.4 *d*
3	36.3 *t*	14	35.1 *t*
4	61.6 *s*	15	174.9 *s*
5	46.9 *s*	16	106.9 *d*
6	72.4 *d*	17	16.4 *q*
7	32.9 *t*†	18	50.1 *t*
8	36.1 *d*	19	170.0 *s*†
9	41.6 *s*	20	12.0 *q*
10	37.5 *d*	$CH_3\underline{C}$=O	170.9 *s*†
11	84.9 *d*	$\underline{C}H_3C$=O	21.3 *q*

*Multiplicities were determined by the DEPT pulse sequence.

†These assignments may be reversed.

paramagnetically shifted at δ6.35 and 6.37 by acetylation).

Oxidation of **1** with chromium trioxide in pyridine yielded the derivative **3** ($C_{22}H_{28}O_8$). Its infrared spectrum revealed the presence of a γ-lactone moiety (ν_{CO} 1783 cm^{-1}), a δ-lactone (ν_{CO} 1747 cm^{-1}) and an ester group (ν_{CO} 1727, 1260 cm^{-1}). There was a downfield resonance of the H-16 proton (δ6.04 *d*) and the C-14 methylene protons as the AB part of an ABX system (Table 1) [8–10]. In agreement with all the above data, the new diterpenoid isolated from *S. altissima* is a C-15 epimeric mixture of 15-hydroxyscutecolumnin C (**2**), in which the location of the acetate group at the C-6 position and the 19,2α-hemiacetal function were supported by the identical shifts of the H-2β, H-3α (eq), H-6β, H-19 and acetate protons in **1** (Table 1) and scutecolumnin C [2: δ H-2β 4.17 m, δ H-3α (eq) 2.58 *dt*, δH-6 4.68 *dd*, δH-19α 5.27 *s* and δ acetyl 2.05 *s* [7]. The ^{13}C NMR spectrum of the derivate **3** (Table 2) also supported this point.

The absolute stereochemistry of the new diterpenoid (**1**) was not ascertained. However, on biogenetic grounds it is reasonable to assume that it possesses a neoclerodane absolute configuration like other clerodane derivatives isolated from *Scutellaria* species [7, 12, 13].

EXPERIMENTAL

Mps: uncorr. Plant materials were collected in July 1993 near Plovdiv, Bulgaria and voucher specimens are deposited in the Herbarium of the Higher Institute of Agriculture at Plovdiv, Bulgaria.

Extraction and isolation of scutealtisin (**1**). Dried and powdered aerial parts of *Scutellaria altissima* (1 kg) were extracted with Me_2CO (3 × 6 l) at room temp. for 6 days. The combined extracts were evapd under vacuum almost to dryness, MeOH (600 ml) was added and the mixture extracted with petrol (5 × 150 ml). The MeOH phase was

concd (20 g) and subjected to CC (silica gel Merck No. 7734, deactivated with 15% H_2O). Elution with petrol–EtOAc (1:2) gave crude **1** (120 mg), which was rechromatographed (CC, silica gel, deactivated with 15% H_2O, 30 g, petrol–EtOAc (2:3) as eluent, yielding pure **1** (92 mg): mp 133–138° (EtOAc–hexane) $[\alpha]_D^{20}$ −6.76° (MeOH, *c*, 0.325). IR ν_{max}^{KBr} cm^{-1}: 3543 (OH), 3464, 3338 (OH), 1736, 1225 (ester group), 2961, 2950, 1465, 1441, 1374, 1296, 1200, 1182, 1162, 1114, 1090, 1071, 1059, 1019, 980, 965, 943, 902, 887; ^1H NMR: Table 1; EIMS (70 eV, direct inlet) *m/z* (rel. int.): $[M]^+$ absent, 406 $[M - H_2O]^+$ (0.8), 365 (0.4), 301 (0.2), 269 (0.1), 190 (23), 175 (15), 172 (20), 159 (12), 157 (10), 131 (10), 129 (12), 119 (11), 117 (12), 111 (50), 105 (20), 95 (8), 93 (10), 91 (21), 83 (22), 82 (8), 81 (9), 79 (11), 69 (12), 57 (15), 43 (100), $C_{22}H_{32}O_8$, M_r 424.

Oxidation of **1** *to* **3**. Treatment of **1** (30 mg) in dry pyridine (2 ml) with CrO_3 (120 mg) in the usual manner yielded crude crystals (22 mg), which on recrystallization from EtOAc–petrol yielded **3** (19 mg): mp 126–130°, $[\alpha]_D^{20}$ −11.7° (MeOH, *c*, 0.128). IR ν_{max}^{KBr} cm^{-1}: 1783 (γ-lactone), 1747 (δ-lactone), 1727, 1260, (ester group) 2972, 1454, 1375, 1323, 1195, 1123, 1106, 1092, 1026, 993, 970, 928, 885; ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS (70 eV, direct inlet) *m/z* (rel. int.): 420 $[M]^+$ (0.7), 360 (11), 348 (0.2), 218 (5), 190 (10), 172 (8), 127 (15), 111 (4), 85 (17), 71 (38), 55 (12), 43 (100). Found: C, 62.37; H, 6.82; $C_{22}H_{28}O_8$, requires: C, 62.84; H, 6.69%.

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