Phytochemistry Letters 15 (2016) 103–107

Contents lists available at ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Short communication

Minor diterpenoids from *Scutellaria galericulata*

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ARTICLE INFO

Article history:
Received 11 September 2015
Received in revised form 3 December 2015
Accepted 11 December 2015
Available online xxx

Keywords:
Scutellaria galericulata
Labiatae
Neo-clerodane diterpenoids
Scutegalerins C–E

ABSTRACT

Three new neo-clerodane diterpenoids, one C-16 epimeric pair, scutegalerins C and D, and scutegalerin E, together with the known scutaltisin B, were isolated from the acetone extract of the aerial parts of *Scutellaria galericulata*. The chemical structures of the new compounds were elucidated by spectroscopic techniques and a comparison with data of similar compounds as (13*S*,16*R*,19*S*)-6α-acetoxy-2α,19;4α,18;15,16-triepoxy-16,19-dimethoxy-neo-clerodane (scutegalerin C), (13*S*,16*S*,19*S*)-6α-acetoxy-2α,19;4α,18;15,16-triepoxy-16,19-dimethoxy-neo-clerodane (scutegalerin D) and (11*S*,13*R*,16*S*,19*S*)-6α-acetoxy-2α,19;4α,18;11,16;15,16-tetraepoxy-19-methoxy-neo-clerodan-3β-ol (scutegalerin E). Detailed NMR spectra of scutaltisin B were included to rationalize the new assignments in the ^{1}H NMR spectrum and the correction of some of the previously reported carbon signals in the ^{13}C NMR spectrum for the isolated mixture of the two C-11 epimers scutaltisin B and scutaltisin C.

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1. Introduction

In previous papers (Bozov et al., 2014a,b) we communicated the isolation from *Scutellaria galericulata* (Labiatae) of two new compounds: scutegalerins A and B, along with six known neo-clerodane diterpenoids: 14,15-dihydrojodrellin T, scutegalin A, scutegalin D, scutalbin A, scutecolumnin C and neoajugapyrin A. In continuation of our studies on this species we report here on the isolation and structure elucidation of three new compounds: scutegalerins C (**2**), D (**3**) and E (**4**). Also was isolated the known 11*R* scutaltisin B (**1**) which had been obtained previously as an inseparable mixture with the 11*S* epimer, scutaltisin C from *Scutellaria altissima* (Bozov and Coll, 2015). In that work some of the ^{1}H and ^{13}C NMR signals could not be unequivocally assigned to either epimer since both were close to 1:1 ratio. In the present work **1** was isolated as a pure compound and a full assignment of all signals in the NMR spectra was made with the help of DEPT, HSQC, COSY and HMBC.

2. Results and discussion

The bitter fraction obtained from the acetone extract of the aerial parts of *S. galericulata* was subjected to column chromatography yielding five fractions (I–V, Section 3). The compounds reported in this paper (**1–4**) were received from fractions II and IV. Fraction II yielded two subfractions (IIa and IIb), each giving a TLC-homogeneous spot. Compound **1** was isolated from IIa subfraction, the epimeric mixture of **2** and **3** from IIb and **4** from IV.

The interpretation of all measured 1D and 2D NMR spectra of **1** pointed out that it was one of the components of the epimeric mixture scutaltisin B/scutaltisin C reported earlier (Bozov and Coll, 2015). Now, with all ^{1}H- and ^{13}C NMR signals (Table 1) unambiguously assigned to scutaltisin B, it is shown that in **1**, signals at δ_C 33.45 and 33.30 are due to C-7 and C-12, respectively, and point out a wrong conclusion in our previous assignment of both δ_C 33.38/33.55 to C-7. Also the corrected assignment for C-9 is at δ_C 41.3 (42.47/41.67 reported previously).

HR-EIMS spectrum for the second TLC-homogeneous substance showed a molecular formula $C_{24}H_{38}O_7$ which corresponded to the $[M-1]^+$ ion with mass at *m/z* 437.2493. The peaks at *m/z* 407, 378 and 347 were due to the fragments $[M-CH_3O]^+$, $[M-CH_3COOH]^+$ and $[M-CH_3COOH-CH_3O]^+$, respectively. The ^{1}H NMR spectrum revealed the presence of two structurally very similar clerodane diterpenes in a close to 1:2 ratio (in the following discussion the area under a proton signal is given in parenthesis so that it sums 1.0 for both) named as scutegalerin C and scutegalerin D (**2**,**3**). Characteristic signals for two 4α,18-epoxy-neo-clerodane skeletons were easily distinguished (Table 1) at δ_H 0.79s/0.80s (Me-20), 0.787d/0.791d (Me-17), 2.33d (1H, C-18a) and 2.92d (0.33H, C-18b)/2.90d (0.67H, C-18b). Whereas only one acetate signal is

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http://dx.doi.org/10.1016/j.phytol.2015.12.003
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Table 1
NMR spectroscopic data for compounds **1**–**4**.[a]

Position	**1**		**2**		**3**		**4**		Neoajugapyrin A	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1a	28.7	1.53dd (14.2, 11.7)	26.9[e]	1.47[d]	26.9[e]	1.47[d]	22.9	1.83dd (14.0, 11.6)	22.6	1.90ddd, 14.6, 11.5, 0.9
1b		2.29dt[b]d (14.2, 4.8, 3.0)		1.75dm (13.2)		1.75dm (13.2)		2.25dddd (14.1, 5.0, 3.3, 2.0)		2.30dddd, 14.7, 4.9, 4.0, 2.1
2	66.7	4.07dt[b]d (5.1, 2.4, 0.7)	66.6	4.116dt[b] (4.4, 2.2)	66.5	4.109dt[b] (4.4, 2.2)	70.7	3.89brdd (4.7, 2.9)	71.0	3.98ddd, 4.9, 3.1, 0.8
3a	36.8	1.63dd (14.0, 2.7)	36.81	1.61[d]	36.77	1.61[d]	70.1	4.39brs ($w^1/_2$ = 5.9)	70.1	4.40ddd, 5.1, 2.9, 1.9
3b		2.50dt[b] (14.1, 2.7)		2.503dt[b] (14.0, 2.6)		2.507dt[b] (14.2, 2.6)				
4	60.7		60.7[e]		60.7[e]		66.1		65.9	
5	42.6		42.5[e]		42.5[e]		43.5		42.5	
6	68.2	4.59dd (11.5, 4.4)	68.4	4.58dd (12.2, 4.9)	68.3	4.56dd (11.5, 4.6)	68.0[f]	4.61dd (11.7, 4.3)	68.2	4.63dd, 11.9, 4.7
7a	33.5	1.37dd (9.9, 4.5)	33.0	1.44[d]	32.9	1.44[d]	33.7[e]	1.41dd (9.8, 4.6)	33.3	1.39ddd, 13.1, 4.6, 3.0
7b		1.62[d]		1.54[d]		1.54[d]		1.57[d]		1.65[c]
8	35.1	1.62[d]	34.45	1.58[d]	34.54	1.58[d]	35.5	1.56[d]	35.4	1.53dqd 12.8, 6.6, 3.1
9	41.3		38.84		38.77		41.2		41.2	
10	40.8	1.93[d]dd (11.4, 4.4)	41.0	1.70dd (11.2, 4.1)	41.1	1.65dd (11.3, 4.2)	40.8	1.89dd (11.7, 3.1)	40.7	1.98dd, 11.6, 3.9
11	86.1	4.05dd (11.0, 5.7)	36.2	1.21[d] (2H)	35.6	1.21[d] (2H)	86.5	4.08dd (11.0, 5.6)	86.4	4.09dd, 11.0, 5.7
12a	33.3	1.61[d]	21.8	1.10[d]	25.9	0.975t[b]dd (12.6, 8.2, 4.5)	32.6[e]	1.61ddd (12.6, 5.5. 1.3)	33.3	1.65[c]
12b		1.93[d]		1.41[d]		1.35[d]		1.90ddd (12.6, 11.1, 9.3)		1.92[c]
13	41.8	2.82t[b]ddd (9.2, 5.0, 3.7, 1.6)	44.5	1.85m	45.9	1.92[d]	41.80	2.83t[b]ddd (9.3, 5.1, 4.6, 1.4)	41.8	2.84br t[b]ddd, 9.2, 5.1, 3.0, 1.2
14a	32.6	1.68ddt[b] (12.6, 6.0, 4.3)	29.4	1.57[d]	30.6	1.40[d]	33.2[e]	1.68ddt[b] (12.6, 6.2, 4.2)	32.6	1.72[c]
14b		2.13ddt[b] (12.8, 9.1, 8.4)		1.93[d]		2.07dt[b]d (16.3, 7.5, 4.0)		2.14ddt[b] (12.7, 9.2, 8.2)		2.15ddt[b], 12.7, 9.2, 8.3
15a	68.2	ca 3.850ddd (8.2, 7.8, 4.5)	66.5[e]	3.79dt[b] (10.2, 8.2)	66.5[e]	3.81d (8.2, 7.4)	68.3[f]	3.857ddd (8.6, 8.0, 4.5)	68.3	3.8765ddd, 8.8, 8.7, 6.6
15b		ca 3.856ddd (8.9, 7.8, 6.2)		3.92ddd (9.3, 8.2, 3.0)		3.88t[b]d (8.2, 4.1)		3.866ddd (8.6, 8.5, 6.3)		3.8617ddd, 8.7, 8.1, 4.5
16	108.2	5.61d (5.1)	104.6	4.73d (4.5)	109.8	4.59d (1.7)	108.1	5.62d (5.1)	108.1	5.63d, 5.1
17	16.7	0.88d (6.1)	15.1	0.787d (6.5)	15.3	0.791d (6.5)	16.5	0.88d (6.0)	16.4	0.89d, 6.1
18a	49.8	2.34d (4.4)	49.8	2.33d (4.4)	49.7	2.33d (4.4)	43.9	2.82d (4.6)	44.1	2.88d, 4.3
18b		2.92d (4.4)		2.915d (4.4)		2.897d (4.4)		3.01d (4.6)		3.09d, 4.3
19	100.2	5.08s	100.3	5.05s	100.2	5.04s	99.8	5.05s	91.0	6.76s
20	14.0	1.07s	16.81	0.787s	16.75	0.799s	14.3	1.11s	14.3	1.19s
$CH_3\underline{C}O$	170.4		170.3[e]		170.3[e]		170.4		170.0	
$\underline{CH_3}CO$	21.2	1.99s	21.1[e]	1.97s	21.1[e]	1.97s	21.2	2.00s	21.0	1.79s
$O\underline{CH_3}$-16*R*			54.5	3.33s						
$O\underline{CH_3}$-16*S*					54.7	3.35s				
$O\underline{CH_3}$-19	55.2	3.47s	55.2[e]	3.45s	55.2[e]	3.45s	55.3	3.47s		
1′ (**C**O)									166.0	
2′ (**C**=)									128.7	
3′ (**HC**=)									138.7	7.06qq, 7.1, 1.4
4′ ($\underline{CH_3}$)									14.5	1.80dq, 7.1, 1.2
5′($\underline{CH_3}$)									11.9	1.87 quint[b], 1.3

[a] H NMR (^{1}H 600.13 MHz) and ^{13}C NMR (^{13}C 150.9 MHz), recorded in $CDCl_3$ (solvent reference: ^{1}H δ_{ref} 7.26, ^{13}C δ_{ref} 77.0 ppm); chemical shift values δ are in ppm, mult. *J* in Hz, all assignments in agreement with COSY and HSQC spectra.
[b] Apparent multiplicity (*t* = dd and quint. = dq with two close coupling constants).
[c] Weak correlation.
[d] Overlapped signal (data from HSQC or COSY).
[e] Interchangeable assignments within the same column or same value for **2** and **3**.
[f] Interchangeable assignments within the same column or same value for **2** and **3**.

present at δ_H 1.97, two methoxy groups display singlet signals at δ_H 3.451/3.450 (3.1H), 3.33 (1.08H) and 3.35(2.07H). The signals at δ_H 3.45 were assigned to the methoxy groups at C-19 based on HMBC correlations. As C-16 is closer to the epimeric center, the two C-16 methoxyls display a larger chemical shift difference. The above discussion together with some other duplicate signals [δ 4.73/4.59 (d, H-16); 5.05/5.04 (s, H-19α)], pointed out an identical decalin core with scupolins H and I for the mixture of **2** and **3** [H-2β (δ 4.12dt/4.11dt vs. 4.10m/4.08m), H-3α (δ 2.50dt/2.51dt, vs. 2.53dt/2.54dt), H-6β (δ 4.58dd/4.56dd vs. 4.62dd /4.62dd), Me-17 (δ 0.787d/0.791d vs. 0.89d/0.90d), H_2-18 (δ 2.33d and 2.92d/2.90d vs. 2.37d/2.35d and 2.97d/2.95d), H-19α (δ 5.05s/5.04s vs. 5.11s/5.11s)] (de la Torre et al., 1997). The signals for H-19α at δ 5.05/5.04 have overlapping ^{1}H–^{13}C HMBC cross peaks with δ_C 68.4/68.3 (C-6), 66.6/66.5 (C-2), 60.7 (C-4), 55.2 (C-19-O$\underline{CH_3}$), 49.8/49.7 (C-18, weak, ^4J), 36.81/36.77 (C-3, very weak, ^4J). The H-2β at δ_H 4.12/4.11 shows HMBC cross peaks with δ_C 100.3/100.2 (C-19), 60.7 (C-4) and 41.0/41.1 (C-10) and COSY correlations with δ_H 2.50/2.51 (H-3α) and 1.61 (H-3β). The six side-chain atoms C-11–C-16 display a lactol ring across C-15–C-16 as reported for scuterepenosides A_1–A_4 (Kizu et al., 1998). Weak HMBC correlations were observed in compound **2** of H-13 (δ_H 1.85/1.92) with the carbon atoms C-16 (δ_C 104.6), C-14 (δ_C 29.4), C-12 (δ_C 21.8) and C-11 (δ_C 36.2) and in diterpene **3** with C-16 (δ_C 109.8), C-15 (δ_C 66.5), C-14 (δ_C 30.6), C-12 (δ_C 25.9) and C-11 (δ_C 35.6). Chemical shifts for methylene protons 12a/12b in **2** appeared at δ_H 1.10/1.41, while in **3** they were upfield shifted at δ_H 0.98/1.35, whereas the signal of H_2-11 isochronous protons appeared at δ_H 1.21 in both based on COSY and HSQC. These assignments were supported by the HMBC correlations of H_2-11 with C-9 (δ_C 38.84/38.77), and the ^{1}H–^{1}H

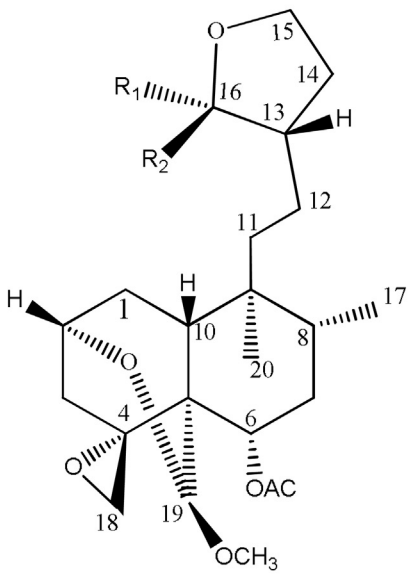
COSY cross peaks with H_2-12 at δ_H 0.98/1.35 for **3**. In the HMBC spectrum correlations were observed from H-12a (δ_H 0.98) to C-16 (δ_C 104.6/109.8), C-13 (δ_C 44.5/45.9), C-11 (δ_C 36.2/35.6) and C-14 (δ_C 29.4/30.6). The ^1H–^1H COSY spectrum displays correlations of H-12a (δ_H 1.10/0.98) with H-13 (δ_H 1.85/1.92) and H_2-11 (δ_H 1.21). It was remarkable the big deviation of 4.12 ppm in the value of the signal for C-12 in the two epimers but such deviation was in agreement with the values reported for scuterepenosides A_1–A_4 (Kizu et al., 1998). H-13β in both epimers showed ^1H–^1H COSY correlation with H-14a and H-16β (Fig. 1).

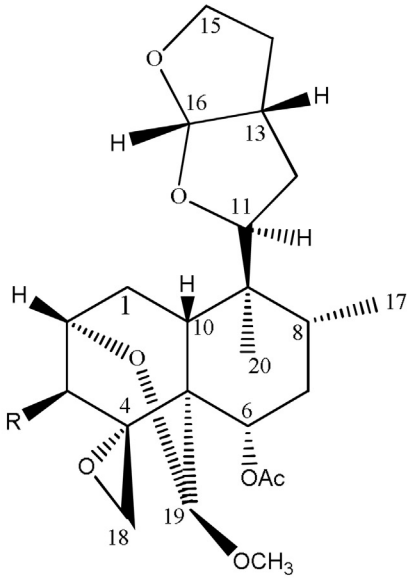
The two diterpenoids **2** and **3** are distinguished from one another by the configuration of C-16 asymmetric carbon. In the 16*R* epimer (**2**) this carbon appeared at δ_C 104.6 and in the 16*S* epimer (**3**) at δ_C 109.8 giving a chemical shift deviation of 5.2 ppm. That deviation is very similar to those displayed in scuterepenosides A_3/A_1 ($\delta_{C\text{-}16}$ 104.9/110.2) and scuterepenosides A_4/A_2 ($\delta_{C\text{-}16}$ 105.0/110.3). H-16β from clerodane **2** resonated at δ_H 4.73 ($^3J_{H\text{-}16\beta,\ H\text{-}13\beta}$ = 4.5 Hz) and the signal for H-16β from **3** is upfield shifted at 4.59 ($^3J_{H\text{-}16\beta,\ H\text{-}13\beta}$ = 1.7 Hz). In accordance with the Karplus equation (Karplus, 1963) the higher value of ^3J —coupling constant in **2** is conditioned by the dihedral torsion angle between H-16β–C-16–C-13–H-13β of about 0°. The smaller value of the ^3J—constant in **3** (1.7 Hz) is in agreement with an angle close to 120°. The constants measured for scuterepenosides A_1–A_4 (4.0 Hz for 16*R** and average 1.5 Hz for 16*S**) were close to ours. In both epimers H-16 displayed HMBC correlations to carbons C-15, C-14, C-13 and CH_3–O–C-16 and ^1H–^1H COSY correlation with H-13β. Based on all spectral data for the constituents of the epimeric mixture, structures **2** and **3** were assigned.

The measured NOESY spectrum of the epimeric mixture supports the proposed stereochemistry. In the NOESY spectrum both epimers show a cross peak between signals of OCH_3-16 and H-16 thus confirming the position of this methoxy group. Also, for both epimers there are NOESY correlations between H-16 and H_2-11 due to the free rotation along C-11–C-12 and C-12–C-13 bonds. Whereas the rotation along C-12–C-13 can bring near proton H-16α to both H-12 atoms (as it is in **3**) but not H-16β–H-12 atoms (in **2**). Actually, there are two NOESY correlations δ_H 4.59–δ_H 1.35 and δ_H 4.59–δ_H 0.98 (for compound **3**) and there are no NOESY correlations δ_H 4.73–δ_H 1.41 and δ_H 4.73–δ_H 1.10 (for compound **2**). There are several more NOESY correlations in the decaline moiety which are the same as those previously reported for scutecyprin (Penchev et al., 2014).

Repeated preparative TLC of fraction IV yielded compound **4** with a molecular formula $C_{23}H_{34}O_8$ after the $[M\text{-}OCH_3]^+$ peak at *m/z* 407.2102. The ^1H and ^{13}C NMR spectra of **4** (Table 1) showed characteristic signals for a neo-clerodane structure (Me-17 at δ_H 0.88d, *J* = 6.0 Hz; Me-20 at δ_H 1.11s) possessing one 4α,18-oxirane (H-18a at δ_H 2.82d and H-18b at δ_H 3.01d with a coupling of J_{gem} = 4.6 Hz), one 2α,19-acetal moiety ($\delta_{H\text{-}19\alpha}$ 5.05s; $\delta_{H\text{-}2}$ β 3.89brdd; $\delta_{C\text{-}19}$ 99.8) and a C-11–C-16 hexahydrofurofuran side-chain [$\delta_{H\text{-}11}$ 4.08dd, *J* = 11.0, 5.6; $\delta_{H\text{-}13}$ 2.83; $\delta_{H2\text{-}15}$ ca. 3.857/3.866ddd; $\delta_{H\text{-}16}$ 5.62d, *J* = 5.1; $\delta_{C\text{-}16}$ 108.1]. In addition, the NMR spectra revealed the presence of one acetate (δ_H 2.0s, 3H; δ_C 170.4 and 21.2), one methoxy group (δ_H 3.47s, 3H; δ_C 55.2) and one hydroxyl at C-3 (δ_C 70.1). The chemical shifts of H-19α at δ_H 5.05s and C-19 at δ_C 99.8 are in agreement with structures **2** and **3** (δ_H 5.04 and 5.05; δ_C 100.3 and 100.2). These signals are similar to the reported values for 19-*O*-methyl ether derivatives such as scupolins H and I, both 5.11/100.3 (de la Torre et al., 1997). The attachment of the hydroxyl group at the 3β position was in agreement with the chemical shifts of H-18a (δ_H 2.82) as in

Formulae





	R_1	R_2
scutegalerin C **(2)**	OMe	H
scutegalerin D **(3)**H	OMe	

	R
scutaltisin B (**1**)	H
scutegalerin E **(4)**	OH

Fig. 1. Structures of isolated neo-clerodanes.

Table 2
C-1/C-3 substitution effects in neo-clerodanes with 2α,19 and 4α,18 epoxy rings.

Compound	Substitution		δ_H	δ_H	δ_C	δ_C
	C-1	C-3	H-1α	H-3α	C(4)/C(18)	C-10
Scutegalerin E, **4**	H_2	H,OH	2.25dddd	4.39m	66.1/43.9	40.8
Neoajugapyrin A	H_2	H,OH	2.30dddd	4.40ddd	65.9/44.1	40.7
Scutecyprin[a]	H_2	H_2	2.36dtd	2.55brd	60.6/50.2	40.8
14,15-Dihydrojodrellin T[b]	H,OTig	H_2	5.51m	2.48brd	59.6/50.2	48.3

[a] Data from Penchev et al. (2014).
[b] Data from Cole et al. (1990).

neoajugapyrin A (Bozov et al., 2014b), scupolin G (de la Torre et al., 1997) and in scupolins J and K (Bruno et al., 2000), all at δ_H 2.88. The H-18a resonated at δ_H 2.44 in scutecyprin which is devoid of substituents at C-1 and C-3. In diterpenes with C-1 substitution, the signal for H-18a appeared in the region close to that of scutecyprin as δ_H 2.46 in 14,15-dihydrojodrellin T and δ_H 2.51 in scutegalerin A. The signal of the 3α-proton, which appeared in scutecyprin at δ_H 2.55dt, is downfield shifted in **4** to δ_H 4.39brs. In the ^{13}C NMR of **4** the signal for carbon C-4 was downfield shifted with 5.5 ppm (see Table 2), as compared to that in scutecyprin, while the signal for C-18 (that is at γ position to hydroxyl) was upfield shifted with 6.3 ppm. The same changes were observed for the C-3 substituted derivatives of scutecyprin as scupolins G (de la Torre et al., 1997), J and K (Bruno et al., 2000) and neoajugapyrin A (Table 2). Derivatives with C-1 substitution, as in 14,15-dihydrojodrellin T, showed significant downfield shifting (as compared to scutecyprin) for carbon C-10 by about 7.5 ppm (Table 2). Finally, the ^1H and ^{13}C NMR spectra of scutegalerin E were almost identical with those of neoajugapyrin A (Table 1). The remarkable differences between the spectra of both compounds were the presence of signals for methoxy group at δ_H 3.47 and δ_C 55.3 instead those of tiglate, as well as the H-19 chemical shift at δ_H 5.05s vs. 6.76s ($\Delta\delta$ − 1.71) and the downfield shifted signal of C-19 acetalic carbon at δ_C 99.8 vs. 91.0 ($\Delta\delta$ + 8.8).

3. Experimental

3.1. Structural data

The ^1H and ^{13}CNMR spectra were recorded in $CDCl_3$ on a Bruker Avance at 600.130 MHz and 150.903 MHz. The chemical shift values for both ^1H and ^{13}C are reported as parts per million (ppm), and coupling constants ($J_{H,H}$) are in Hertz (in parentheses). The IR spectra were registered in KBr pellet for solids and as a capillary film between KBr plates for oily substances on a PerkinElmer 1750 FT-IR spectrometer from 4000 cm^{-1} to 450 cm^{-1} at resolution 4 cm^{-1} with 9 scans. The mass spectra were measured on Hewlett Packard 6890 GC System Plus/5973 MSD. Silica gel 60 H (Merck N. 7734) was used for column chromatography (CC), silica gel 60 F_{254} aluminum sheets (Merck N. 5554) were used for TLC monitoring ($CHCl_3$/MeOH 98:2; and EtOAc) and 2 mm plates PSC-Fertigplatten Kieselgel 60 (Merck N. 5745) for preparative TLC.

3.2. Plant material

The plant material of *S. galericulata* L. was collected in July 2014 near Pleven, Bulgaria and voucher specimens (N. 11927) were deposited in the Herbarium of the Higher Institute of Agriculture at Plovdiv, Bulgaria.

3.3. Extraction and isolation

The dried and finely powdered stems (5.2 kg) were extracted with Me_2CO (2 × 15 L) at room temperature for a week. The acetone extract was concentrated under reduced pressure and low temperature (40 °C). After removal of the solvent, the residue (225 g) was dissolved in 1 L aq. Me_2CO (40% H_2O, v/v) and the solution was cooled to 4 °C for 24 h and filtered. The filtrate was extracted with $CHCl_3$ (3 × 300 mL). The combined extracts were dried (Na_2SO_4) and solvent was evaporated under reduced pressure and 40 °C yielding a residue (17.9 g, bitter fraction) which was separated into five fractions, I (150 mg), II (450 mg), III (140 mg), IV (83 mg) and V (250 mg), on a silica gel column (350 g; deactivated with 10% H_2O, w/w) eluting with CH_2Cl_2-MeOH mixtures from 10:0 to 9.9:0.1. After a rechromatography of fraction II eluted with CH_2Cl_2 36 mg of scutaltisin B (**1**) and 15.3 mg from a 1:2 inseparable (by TLC using different solvents and mixtures of solvents or by crystallization) mixture of the C-16 epimers, scutegalerin C (**2**) and scutegalerin D (**3**) were isolated. Preparative TLC of fraction IV (EtOAc as eluent, ×2) yielded 8 mg of the third new diterpene scutegalerin E (**4**). Recrystallization from acetone supplied 6 mg of pure **4**.

Scutaltisin B (**1**). White powder from $(CH_3)_2CO$, mp 140–144 °C. TLC: R_f 0.75 (EtOAc). IR ν_{max} (KBr) cm^{-1}: 2981, 2958, 2941, 2875, 1730, 1489, 1370, 1329, 1250, 1188, 1102, 1087, 983, 973, 949, 826, 624. ^1H and ^{13}C NMR: see Table 1/1S. EIMS (70 eV, direct inlet) *m/z* (rel. int.): 421 $[M-1]^+$ (2), 407 $[M-CH_3]^+$ (4), 391 $[M-OCH_3]^+$ (6), 363 $[M-OOCCH_3]^+$ (3), 232 (5), 218 (9), 190 (27), 172 (20), 166 (8), 159 (7), 113 (100), 69 (29). HR-EIMS *m/z* 421.3152 $[M-1]^+$ (calcd for $C_{23}H_{33}O_7$, 421.2217).

Scutegalerins C + D (**2 + 3**). Colorless resin. TLC: R_f 0.70 (EtOAc). IR ν_{max} (KBr) cm^{-1}: 2828, 1732, 1655, 1610, 1491, 1468, 1451, 1372, 1250, 1189, 1164, 1102, 1070, 1052, 1024, 978, 929, 906, 829. ^1H and ^{13}C NMR: see Table 1/2S. HR-EIMS (70 eV, direct inlet) *m/z* (rel. int.): 437 $[M-1]^+$ (5), 407 $[M-OCH_3]^+$ (75), 378 $[M - HOOCCH_3]^+$ (8), 347 $[M-HOOCCH_3-OCH_3]^+$ (13), 303 (12), 286 (99), 274 (43), 256 (19), 245 (13), 217 (28), 187 (91), 173 (75), 159 (46), 134 (31), 99 (16), 69 (6); HR-EIMS *m/z* 437.2493 $[M-1]^+$ (calcd for $C_{24}H_{37}O_7$, 437.2529).

Scutegalerin E (**4**). White powder from $(CH_3)_2CO$, mp 174–177 °C; IR ν_{max} (KBr) cm^{-1}: 3520, 3454, 2966, 2932, 1747, 1715, 1452, 1374, 1277, 1251, 1229, 1189, 1163, 1086, 1058, 1028, 1007, 964, 935, 919, 833, 788, 738, 629, 531. ^1H and ^{13}C NMR: see Table 1/3S. EIMS (70 eV, direct inlet) *m/z* (rel. int.): 407 $[M-OCH_3]^+$ (11), 379 $[M-OOCCH_3]^+$ (8), 279 (6), 234 (10), 206 (12), 188 (42), 167 (12), 159 (13), 149 (14), 113 (100), 69 (16); HR-EIMS *m/z* 407.2102 $[M-OCH_3]^+$ (calcd for $C_{22}H_{31}O_7$, 407.2061).

Acknowledgments

This work has been supported by the Bulgarian National Science Fund, Contract DDWU02/37.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.phytol.2015.12.003.

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