Bioorganic & Medicinal Chemistry Letters 26 (2016) 1750–1753

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

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

New cytotoxic *neo*-clerodane diterpenoids from *Scutellaria strigillosa*

Sheng-Jun Dai *, Lei Zhang, Kai Xiao, Qing-Tong Han

School of Pharmaceutical Science, Yantai University, Yantai 264005, PR China

ARTICLE INFO

Article history:
Received 3 November 2015
Revised 2 February 2016
Accepted 17 February 2016
Available online 17 February 2016

Keywords:
Scutellaria strigillosa
neo-Clerodane diterpenoid
Scutestrigillosins A–C
Cytotoxic activity

ABSTRACT

Three new *neo*-clerodane diterpenoids, named scutestrigillosins A–C (**1**–**3**), were isolated from the whole plant of *Scutellaria strigillosa*. Their chemical structures including absolute configurations were established on the basis of detailed physical data analyses. In vitro, the isolated three new compounds exhibited significant cytotoxic activities against four tumor cell lines (HONE-1, P-388, MCF7 and HT29), and gave IC_{50} values in the range 3.5–7.7 μM.

Scutellaria is a unique cosmopolitan genus of the subfamily Scutellarioideae belonging to Lamiaceae (Labiatae) family. About 360 species are found to spread throughout the world and in different climatic areas. Plants of this genus have been widely used in local medicine of many countries of the world for thousands of years, and modern pharmacology research has confirmed that their extracts or monomeric compounds possess antitumor effects.[1,2] On the basis of cDNA microarray analysis, the mechanism underlying the antitumor activity appears to involve DNA damage, cell cycle control, nucleic acid binding, protein phosphorylation and dephosphorylation, and dendritic cell functions. There is evidence that these actions are triggered by *neo*-clerodane diterpenoids.[3–6]

In the course of ongoing search for more new *neo*-clerodane diterpenoids, we investigated the whole plants of *Scutellaria strigillosa*, which is a perennial herb and mainly distributed in Hebei, Shandong, Zhejiang and Jilin provinces in China. In traditional Chinese medicine, the whole plants have been used to clear away heat-evil, expel superficial evils, eliminate stasis and reduce edema.[7] This phytochemical investigation led to the isolation of three new *neo*-clerodane diterpenoids, named scutestrigillosins A–C (Fig. 1, **1**–**3**), the structures of which were elucidated by means of extensive spectroscopic analyses. Furthermore, three new compounds were screened for cytotoxicity against selected cancer cell lines, including HONE-1, P-388, MCF7 and HT29. Herein, we report on the structural elucidation and cytotoxicity of three new *neo*-clerodane diterpenoids.

The air-dried whole plant of *Scutellaria strigillosa* (45.0 kg) was extracted with refluxing EtOH and then partitioned with $CHCl_3$. The $CHCl_3$ fraction (199.3 g) was chromatographed over various columns and preparative HPTLC to obtain compounds **1** (206 mg), **2** (114 mg), and **3** (116 mg) (see detailed experimental procedures in the Supporting information).

Scutestrigillosin A (**1**)[8] was obtained as white needles with optical rotation $[\alpha]_D^{29}$ −24.7° (*c* 0.79, MeOH), and exhibited a positive response to Dragendoff reagent. In the HR-ESI mass spectrum, **1** gave a positive quasi-molecular ion peak at *m*/*z* 681.2799 $[M+H]^+$, corresponding to a molecular formula $C_{39}H_{40}N_2O_9$. The IR spectrum showed absorption bands at 1753, 1638, 1599, 1560, 1489, 1423, 1390, 1285, 1221 and 1105 cm^{-1}, which were in agreement with carbonyl, conjugated carbonyl, aromatic and γ-lactone groups. In the ^1H NMR spectrum, the following signals were observed: four tertiary methyl groups [δ_H 1.43 (3H, s, H-17); 1.60 (3H, s, H-18); 1.50 (3H, s, H-19); 1.28 (3H, s, H-20)], two nicotinic acid ester moieties [δ_H 9.29 (1H, br s, H-3′), 8.89 (1H, br s, H-5′), 7.55 (1H, dd, *J* = 4.8, 7.8 Hz, H-6′), 8.37 (1H, br d, *J* = 8.0 Hz, H-7′); 8.99 (1H, br s, H-3″), 8.71 (1H, br s, H-5″), 7.31 (1H, overlap, H-6″), 8.06 (1H, br d, *J* = 8.0 Hz, H-7″)], a benzoyloxy moiety [δ_H 7.77 (2H, d, *J* = 7.3 Hz, H-3‴ and H-7‴), 7.30 (2H, overlap, H-4‴ and H-6‴), 7.47 (t, *J* = 7.5 Hz, H-5‴)], a tri-substituted double bond unit (δ_H 5.36, 1H, br s, H-3) and an oxygenated methylene group [δ_H 4.35 (1H, d, *J* = 9.5 Hz, Ha-16), 4.50 (1H, d, *J* = 9.5 Hz, Hb-16)]. The ^{13}C NMR displayed 39 carbon resonances and the DEPT spectrum was consistent with the presence of four methyls, five methylenes (sp^3 hybridized), eighteen methines (fourteen sp^2 hybridized and four sp^3 hybridized), and twelve quaternary carbons (eight sp^2 hybridized and four sp^3 hybridized). Detailed analysis of above 39 carbon signals displayed that 20 carbons were due to one *neo*-clerodane diterpenoid skeleton with a 13-spiro-15,16-γ-lactone moiety,[1,9,10] 12 carbons to two nicotinoyloxy moieties,

* Corresponding author. Tel.: +86 535 6706025; fax: +86 535 6706036.
E-mail address: daishengjun_9@hotmail.com (S.-J. Dai).

http://dx.doi.org/10.1016/j.bmcl.2016.02.045
0960-894X/

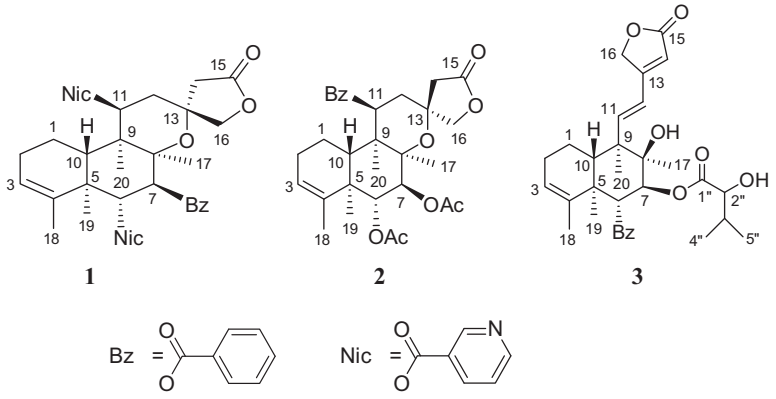

Figure 1. The structures of new *neo*-clerodane diterpenoids from *Scutellaria strigillosa*.

and 7 carbons to a benzoyloxy moiety, respectively. The cross peaks in the HMBC spectrum of H-6/C-1″, H-7/C-1‴ and H-11/C-1′ confirmed the benzoyloxy group was attached to C-7 and two nicotinoyloxy moieties were attached to C-6 and C-11 (Fig. 2), respectively. The relative configuration of **1** was elucidated by the ^{1}H–^{1}H coupling constant and ROESY spectrum. The large coupling constant (10.2 Hz) of H-6 with H-7 indicated two protons must be in the *trans*-diaxially oriented. In the ROESY spectrum (Fig. 3), cross peaks from H_3-20 to H-7, H-11, H_3-17 and H_3-19, from H-6 to H-10, from H_3-17 to H-7, H-11, H_a-14, H_b-14 and H_3-20, as well as from H-11 to H_a-14, H_b-14, H_3-17 and H_3-20 indicated that H_3-17, H_3-19, H_3-20, H-7, H-11 and H_2-14 were co-facial and α-oriented, while H-6 and H-10 were on the opposite side of the molecular plane and thus β-oriented. Furthermore, the absolute configuration of **1** was determined by the ECD exciton chirality method. The ECD spectrum of **1** showed the negative first Cotton effect at 240 nm ($\Delta\varepsilon$ −5.0) and positive second Cotton effect at 223 nm ($\Delta\varepsilon$ +5.6), which were consistent with the absolute configuration 5*R*,6*R*,7*S*,8*R*,9*R*,10*R*,11*S*,13*R*, as was determined for barbatine B.[11]

Scutestrigillosin B (**2**)[12] was isolated as white needles with optical rotation $[\alpha]_D^{29}$ −68.3° (*c* 0.14, MeOH), and the molecular formula was established as $C_{31}H_{38}O_9$ by HR-ESI mass spectrum, which showed a positive quasi-molecular ion at *m*/*z* 555.2589 $[M+H]^+$. The IR spectrum exhibited absorption bands at 1770, 1731, 1642, 1595, 1466, 1385, 1229 and 1020 cm^{-1}, which were indicative of carbonyl, conjugated carbonyl, aromatic and γ-lactone groups. In the ^{1}H and ^{13}C NMR spectra (Table 1), it showed the signals of four tertiary methyl groups and characteristic of one *neo*-clerodane diterpenoid skeleton as in **1**. In addition, a benzoyloxy moiety

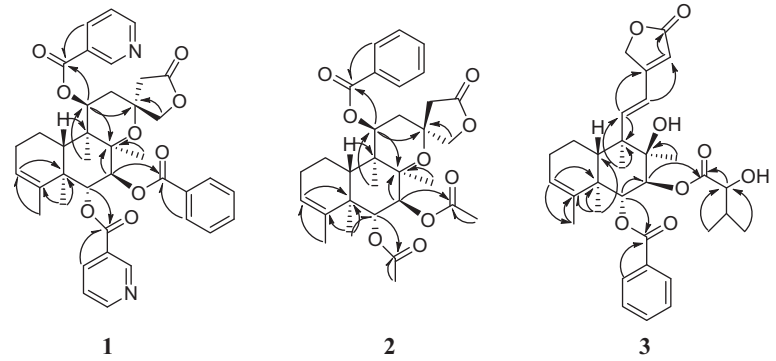

Figure 2. Key HMBC correlations for compounds **1**–**3**.

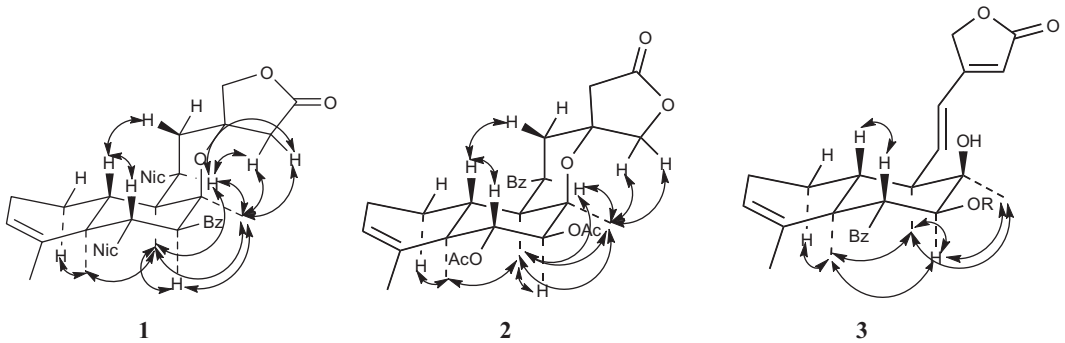

Figure 3. Selected NOE correlations for compounds **1**–**3**.

Table 1
^{1}H (500 MHz) and ^{13}C (125 MHz) NMR data for compounds **1**–**3** (in $CDCl_3$)[a,b]

No.	**1**		**2**		**3**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	1.89 (m, H_a-1)	18.2 CH_2	1.58 (m, H_a-1)	28.5 CH_2	1.36 (m, H_a-1)	19.3 CH_2
	2.58 (m, H_b-1)		2.07 (overlap, H_b-1)		1.66 (m, H_b-1)	
2	2.21 (m, 2H)	26.1 CH_2	2.19 (m, H_a-2)	33.1 CH_2	2.06 (m, 2H)	26.2 CH_2
			2.69 (m, H_b-2)			
3	5.36 (br s)	123.6 CH	5.31 (br s)	120.2 CH	5.25 (br s)	123.3 CH
4		140.6 C		143.2 C		140.8 C
5		43.3 C		44.3 C		43.5 C
6	5.76 (d, 10.2)	75.7 CH	5.41 (d, 10.3)	73.2 CH	5.75 (d, 10.0)	75.5 CH
7	5.65 (d, 10.2)	74.7 CH	5.26 (d, 10.3)	74.1 CH	5.56 (d, 10.0)	76.7 CH
8		83.6 C		80.9 C		77.0 C
9		43.7 C		38.7 C		48.4 C
10	2.63 (br d, 11.0)	40.3 CH	2.71 (br d, 11.9)	43.2 CH	2.36 (br d, 10.5)	42.7 CH
11	5.72 (dd, 4.0, 12.9)	75.0 CH	5.78 (m)	70.9 CH	6.41 (d, 16.8)	146.7 CH
12	2.16 (overlap, H_a-12)	35.1 CH_2	1.71 (m, H_a-12)	29.4 CH_2	6.46 (d, 16.8)	122.0 CH
	2.28 (overlap, H_b-12)		2.10 (overlap, H_b-12)			
13		77.6 C		76.5 C		162.1 C
14	2.84 (d, 17.0, H_a-14)	42.8 CH_2	2.58 (d, 17.4, H_a-14)	44.3 CH_2	5.96 (br s)	115.0 CH
	2.86 (d, 17.0, H_b-14)		3.12 (d, 17.4, H_b-14)			
15		172.9 C		173.7 C		174.1 C
16	4.35 (d, 9.5, H_a-16)	79.1 CH_2	4.12 (d, 8.7, H_a-16)	77.3 CH_2	5.02 (br d, 16.4, H_a-16)	70.6 CH_2
	4.50 (d, 9.5, H_b-16)		4.18 (d, 8.7, H_b-16)		5.04 (br d, 16.4, H_b-16)	
17	1.43 (s, 3H)	19.7 CH_3	1.13 (s, 3H)	19.6 CH_3	1.05 (s, 3H)	22.5 CH_3
18	1.60 (s, 3H)	20.5 CH_3	1.68 (s, 3H)	20.0 CH_3	1.58 (s, 3H)	20.2 CH_3
19	1.50 (s, 3H)	17.3 CH_3	1.37 (s, 3H)	16.7 CH_3	1.45 (s, 3H)	17.5 CH_3
20	1.28 (s, 3H)	16.9 CH_3	1.09 (s, 3H)	21.1 CH_3	1.25 (s, 3H)	15.4 CH_3
1′		164.8 C		165.6 C		166.5 C
2′		125.3 C		130.1 C		129.9 C
3′	9.29 (br s)	150.3 CH	7.95 (d, 8.2)	129.5 CH	8.03 (dd, 1.2, 9.0)	129.7 CH
4′			7.47 (t, 8.0)	128.7 CH	7.47 (br t, 9.0)	128.6 CH
5′	8.89 (br s)	152.2 CH	7.59 (t, 7.5)	133.4 CH	7.60 (br t, 9.0)	133.5 CH
6′	7.55 (dd, 4.8, 7.8)	123.9 CH	7.47 (t, 8.0)	128.7 CH	7.47 (br t, 9.0)	128.6 CH
7′	8.37 (br d, 8.0)	138.0 CH	7.95 (d, 8.2)	129.5 CH	8.03 (dd, 1.2, 9.0)	129.7 CH
1″		163.8 C		169.8 C		173.6
2″		125.7 C	2.01 (s, 3H)	21.5 CH_3	3.78 (d, 5.1)	75.7
3″	8.99 (br s)	149.6 CH			1.93 (m)	31.7
4″					0.71 (3H, d, 6.0)	16.0
5″	8.71 (br s)	153.5 CH			0.81 (3H, d, 6.0)	19.0
6″	7.31 (overlap)	123.7 CH				
7″	8.06 (br d, 8.0)	138.1 CH				
1‴		166.3 C		170.9 C		
2‴		128.6 C	2.09 (s, 3H)	20.8 CH_3		
3‴	7.77 (d, 7.3)	129.8 CH				
4‴	7.30 (overlap)	128.4 CH				
5‴	7.47 (t, 7.5)	133.5 CH				
6‴	7.30 (overlap)	128.4 CH				
7‴	7.77 (d, 7.3)	129.8 CH				

[a] Chemical shift values were in ppm and *J* values (in Hz) were presented in parentheses.
[b] The assignments were based on HSQC, HMBC and ^{1}H–^{1}H COSY experiments.

[δ_H 7.95 (2H, d, *J* = 8.2 Hz, H-3′ and H-7′), 7.47 (2H, t, *J* = 8.0 Hz, H-4′ and H-6′), 7.59 (1H, t, *J* = 7.5 Hz, H-5′); δ_C 165.6, C-1′; 130.1, C-2′; 129.5, C-3′ and C-7′; 128.7, C-4′ and C-6′; 133.4, C-5′] and two acetyloxy groups [δ_H 2.01 (3H, s), 2.09 (3H, s); δ_C 169.8, 21.5; 170.9, 20.8] were observed. The long-range correlations in the HMBC experiment of H-11/C-1′, H-6/C-1″ and H-7 to C-1‴ proved that the benzoyloxy group was linked to C-11, and two acetyloxy moieties were connected to C-6 and C-7, respectively. However, the proton signals arising from CH_2-14 and CH_2-16 [δ_H 2.58 (1H, d, *J* = 17.4 Hz, H_a-14), 3.12 (1H, d, *J* = 17.4 Hz, H_b-14); 4.12 (1H, d, *J* = 8.7 Hz, H_a-16), 4.18 (1H, d, *J* = 8.7 Hz, H_b-16)] were significantly different from those of **1** [δ_H 2.84 (1H, d, *J* = 17.0 Hz, H_a-14), 2.86 (1H, d, *J* = 17.0 Hz, H_b-14); 4.35 (1H, d, *J* = 9.5 Hz, H_a-16), 4.50 (1H, d, *J* = 9.5 Hz, H_b-16)]. The marked differences in their NMR data could be interpreted by their configurations in Figure 3. In the case of the configuration of **1**, in which C-16 was in an equatorial disposition, the chemical shifts of two protons of C-16 were significantly different, whereas for **2** (C-16 was in an axial) the chemical shifts of corresponding protons were not remarkably different. Moreover, in the ROESY experiment, NOE enhancements from H_3-20 to H-7, H-11, H_3-17 and H_3-19, from H-6 to H-10, from H_3-17 to H-7, H_a-16, H_b-16 and H_3-20, as well as from H-11 to H_3-19 and H_3-20 established that H_3-17, H_3-19, H_3-20, H-7, H-11 and H_2-16 were on the same face and α-oriented whilst H-6 and H-10 were on the opposite face and thus β-configuration. Thus, the configuration of the C-13 chiral center of **2** was inverted in comparison with that of **1** and determined to be *S*. Additionally, the ECD spectrum of **2** showed a positive Cotton effect at 224 ($\Delta\varepsilon$ +3.7) nm and two negative effects at 247 ($\Delta\varepsilon$ −7.3) and 205 ($\Delta\varepsilon$ −7.6) nm. Taken together, the absolute configuration of **2** was assigned as 5*R*,6*R*,7*S*,8*R*,9*R*,10*R*,11*S*,13*S*.[11]

Scutestrigillosin C (**3**)[13] was isolated and purified as white needles with optical rotation $[\alpha]_D^{29}$ −96.7° (*c* 0.13, MeOH). The molecular formula was established as $C_{32}H_{40}O_8$ by HR-ESI mass spectrum, which displayed a positive quasi-molecular ion at *m*/*z* 553.2785 $[M+H]^+$. The IR spectrum showed absorption bands at 3480, 1741, 1644, 1453, 1376, 1270, 1110 and 1033 cm^{-1}, indicating the presence of hydroxy, conjugated carbonyl, aromatic and α,

Table 2
Cytotoxicity[a] of compounds **1**–**3** against cultured four tumor cell lines

Compound	Growth inhibition constant (IC_{50})[a] (μM)			
	P-388	HONE-1	HT-29	MCF7
Etoposide[b]	1.3 ± 0.9	1.2 ± 0.7	2.0 ± 0.8	2.2 ± 1.0
Cisplatin[b]	1.4 ± 1.0	1.2 ± 1.1	2.3 ± 0.9	2.1 ± 1.1
1	5.8 ± 1.3	3.5 ± 1.9	4.7 ± 2.0	5.7 ± 1.8
2	5.2 ± 1.2	4.2 ± 1.5	4.1 ± 1.7	6.0 ± 1.5
3	7.1 ± 1.6	3.9 ± 1.1	6.4 ± 1.2	7.7 ± 2.1

[a] IC_{50} is means ± standard deviation of three independent replicates.
[b] Positive control substance.

β-unsaturated γ-lactone groups. The ^{1}H NMR spectrum of **3** revealed the presence of the following fragments: four tertiary methyl groups at δ_H 1.05 (3H, s, H-17), 1.58 (3H, s, H-18), 1.45 (3H, s, H-19) and 1.25 (3H, s, H-20); an α,β-unsaturated γ-lactone moiety at δ_H 5.96 (1H, br s, H-14), 5.02 (1H, br d, J = 16.4 Hz, H_a-16) and 5.04 (1H, br d, J = 16.4, H_b-16); a double bond with *E* configuration at δ_H 6.41 (1H, d, J = 16.8 Hz, H-11) and 6.46 (1H, d, J = 16.8 Hz, H-12); a tri-substituted double bond unit at δ_H 5.25 (1H, br s, H-3); a benzoyloxy moiety at δ_H 8.03 (2H, dd, J = 1.2, 9.0 Hz, H-3′ and H-7′), 7.47 (2H, br t, J = 9.0 Hz, H-4′ and H-6′), 7.60 (1H, br t, J = 9.0 Hz, H-5′); and a 2-hydroxy-3-methylbutanoyloxy function at δ_H 3.78 (1H, d, J = 5.1 Hz, H-2″), 1.93 (1H, m, H-3″), 0.71 (3H, d, J = 6.0 Hz, H-4″) and 0.81 (3H, d, J = 6.0 Hz, H-5″). The ^{13}C NMR and DEPT spectra gave 32 carbon resonances, including six methyls, three methylenes (sp^3 hybridized), fourteen methines (nine sp^2 hybridized and five sp^3 hybridized), and nine quaternary carbons (six sp^2 hybridized and three sp^3 hybridized). Careful analysis of above 32 carbon signals revealed that 20 carbons were attributable to a *neo*-clerodane diterpenoid skeleton,[1,9,10] 5 carbons to a 2-hydroxy-3-methylbutanoyloxy group, and 7 carbons to a benzoyloxy moiety, respectively. The cross peaks in the HMBC spectrum of H-7/C-1′ and H-6/C-1″ proved the benzoyloxy and 2-hydroxy-3-methylbutanoyloxy moieties were attached to C-6 and C-7, respectively. The relative stereochemical assignments of the stereogenic centers in **3** were accomplished by analyses of the ^{1}H–^{1}H coupling constants and ROESY spectrum. The coupling constants between H-10 and H_2-1, as well as H-6 and H-7 were observed to be 10.5 Hz and 10.0 Hz, respectively, this confirmed H-10, H-6 and H-7 must be in the axial position. The NOE correlations from H-6 to H-10, H_3-20 to H-7, H_3-17 and H_3-19, as well as from H-7 to H_3-17, H_3-19 and H_3-20 indicated that H_3-17, H_3-19, H_3-20 and H-7 were on the same side of the octalin ring and α-oriented whilst H-6 and H-10 were on the opposite side of the octalin ring and thus β-oriented. Furthermore, the ECD spectrum of **3** exhibited Cotton effects at 263 (Δε −2.9), 223 (Δε −5.9) and 210 (Δε −5.2) nm similar to those of *neo*-clerodane diterpenoids with the same skeletons, which were reported in literature.[14] Accordingly, the absolute configuration of **3** was assigned as 5*R*,6*R*,7*S*,8*R*,9*R*,10*S*.

Compounds **1**–**3** were evaluated for their cytotoxic activities against HONE-1, P-388, MCF7 and HT29 tumor cell lines by using MTT assay performed as previously reported[15] and anti-cancer drugs, etoposide and cisplatin,[16,17] as positive controls. The IC_{50} values resulting from 50% inhibition of cell growth were shown in Table 2. Based on the results, it is found three new *neo*-clerodane diterpenoids exhibited significant cytotoxicity.

Acknowledgements

This study was financially supported by the Natural Science Foundation of China (21372189) and Natural Science Foundation of Shandong Province (ZR2013HM023). The authors are grateful to Mr. Zhen-Duo Shen and Ms. Xiu-Li Yin (School of Pharmaceutical Science, Yantai University) for the measurements of ESIMS, HR-ESIMS, UV, IR and NMR spectra, respectively. The authors also gratefully acknowledge Mr. Yun-Xue Zhao (School of Pharmaceutical Science, Shandong University) for the bioactivity screenings.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bmcl.2016.02.045.

References and notes

1. Bruno, M.; Piozzi, F.; Rosselli, S. *Nat. Prod. Rep.* **2002**, *19*, 357.
2. Shang, X.-F.; He, X.-R.; He, X.-Y.; Li, M.-X.; Zhang, R.-X.; Fan, P.-C.; Zhang, Q.-L.; Jia, Z.-P. *J. Ethnopharmacol.* **2010**, *128*, 279.
3. Rugo, H.; Shtivelman, E.; Perez, A.; Vogel, C.; Franco, S.; Melisko, M.; Tagliaferri, M.; Cohen, I.; Shoemaker, M.; Tran, Z.; Tripathy, D. *Breast Cancer Res. Treat.* **2007**, *105*, 17.
4. Suh, S. J.; Yoon, J. W.; Lee, T. K.; Jin, U. H.; Kim, S. L.; Kim, M. S.; Kwon, D. Y.; Lee, Y. C.; Kim, C. H. *Phytother. Res.* **2007**, *21*, 135.
5. Wong, B. Y.; Lau, B. H.; Yamasaki, T.; Teel, R. W. *Cancer Lett.* **1993**, *68*, 75.
6. Yin, X.; Zhou, J.; Jie, C.; Xing, D.; Zhang, Y. *Life Sci.* **2004**, *75*, 2233.
7. He, C.-N.; Peng, Y.; Xiao, W.; Xiao, P.-G. *Mod. Chin. Med.* **2012**, *14*, 16.
8. *Scutestrigillosin A* (**1**): White needles; mp 153–154 °C; $[\alpha]_D^{29}$ −24.7° (*c* 0.79, MeOH); UV ($CHCl_3$) λ_{max} 222, 263 nm; ECD (MeOH) λ_{max} (Δε) 223 (+5.6), 240 (−5.0) nm; IR (KBr) ν_{max} 2930, 1753, 1638, 1599, 1560, 1489, 1423, 1390, 1285, 1221 and 1105 cm^{-1}; ESIMS *m*/*z* 681.3 $[M+H]^+$; HR-ESIMS *m*/*z* 681.2799 $[M+H]^+$ (calcd for $C_{39}H_{41}N_2O_9$, 681.2810); ^{1}H and ^{13}C NMR data, see Table 1.
9. Malakov, P. Y.; Papanov, G. Y. *Phytochemistry* **1996**, *43*, 173.
10. Malakov, P. Y.; Papanov, G. Y.; Spassov, S. L. *Phytochemistry* **1997**, *44*, 121.
11. Nguyen, V. H.; Pham, V. C.; Ha Nguyen, T. H.; Tran, V. H.; Doan, T. M. H. *Eur. J. Org. Chem.* **2009**, *33*, 5810.
12. *Scutestrigillosin B* (**2**): White needles; mp 157–158 °C; $[\alpha]_D^{29}$ −68.3° (*c* 0.14, MeOH); UV ($CHCl_3$) λ_{max} 222, 257 nm; ECD (MeOH) λ_{max} (Δε) 205 (−7.6), 224 (+3.7), 247 (−7.3) nm; IR (KBr) ν_{max} 1770, 1731, 1642, 1595, 1466, 1385, 1229 and 1020 cm^{-1}; ESIMS *m*/*z* 555.4 $[M+H]^+$, HR-ESIMS *m*/*z* 555.2589 $[M+H]^+$ (calcd for $C_{31}H_{39}O_9$, 555.2592); ^{1}H and ^{13}C NMR data, see Table 1.
13. *Scutestrigillosin C* (**3**): White needles; mp 156–157 °C; $[\alpha]_D^{29}$ −96.7° (*c* 0.13, MeOH); UV ($CHCl_3$) λ_{max} 258 nm; ECD (MeOH) λ_{max} (Δε) 210 (−5.2), 223 (−5.9), 263 (−2.9) nm; IR (KBr) ν_{max} 3480, 2970, 1741, 1644, 1453, 1376, 1270, 1110, 1033 and 712 cm^{-1}; ESIMS *m*/*z* 553.2 $[M+H]^+$; HR-ESIMS *m*/*z* 553.2785 $[M+H]^+$ (calcd for $C_{32}H_{41}O_8$, 553.2801); ^{1}H and ^{13}C NMR data, see Table 1.
14. Wu, T.; Wang, Q.; Jiang, C.; Morris-Natschke, S. L.; Cui, H.; Wang, Y.; Yan, Y.; Xu, J.; Lee, K. H.; Gu, Q. *J. Nat. Prod.* **2015**, *78*, 500.
15. Wang, H.-B.; Li, H.-Y.; Zuo, M.-X.; Zhang, Y.; Liu, H.; Fang, W.-S.; Chen, X.-G. *Cancer Lett.* **2008**, *268*, 89.
16. Chang, J. Y.; Liu, J. F.; Juang, S. H.; Liu, T. W.; Chen, L. T. *Cancer Res.* **2002**, *62*, 3716.
17. Chang, C. I.; Kuo, C. C.; Chang, J. Y.; Kuo, Y. H. *J. Nat. Prod.* **2004**, *67*, 91.